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Original Article

Epidemiologic and virologic assessment of the 2009 influenza A (H1N1) pandemic on selected temperate countries in the Southern Hemisphere: Argentina, Australia, Chile, New Zealand and South Africa

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Introduction and Setting Our analysis compares the most comprehensive epidemiologic and virologic surveillance data compiled to date for laboratory-confirmed H1N1pdm patients between 1 April 2009 - 31 January 2010 from five temperate countries in the Southern Hemisphere–Argentina, Australia, Chile, New Zealand, and South Africa.

Objective We evaluate transmission dynamics, indicators of severity, and describe the co-circulation of H1N1pdm with seasonal influenza viruses.

Results In the five countries, H1N1pdm became the predominant influenza strain within weeks of initial detection. South Africa was unique, first experiencing a seasonal H3N2 wave, followed by a distinct H1N1pdm wave. Compared with the 2007 and 2008 influenza seasons, the peak of influenza-like illness (ILI) activity in four of the five countries was 3-6 times higher with peak ILI consultation rates ranging from 35/1,000 consultations/week in Australia to 275/100,000 population/week in New Zealand. Transmission was similar in all countries with the reproductive rate ranging from 1.2–1.6. The median age of patients in all countries increased with increasing severity of disease, 4–14% of all hospitalized cases required critical care, and 26–68% of fatal patients were reported to have ≥1 chronic medical condition. Compared with seasonal influenza, there was a notable downward shift in age among severe cases with the highest population-based hospitalization rates among children <5 years old. National population-based mortality rates ranged from 0.8–1.5/100,000.

Conclusions The difficulty experienced in tracking the progress of the pandemic globally, estimating its severity early on, and comparing information across countries argues for improved routine surveillance and standardization of investigative approaches and data reporting methods.

Keywords H1N1, influenza circulation, pandemic, severity, Southern Hemisphere, transmission.

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Introduction

The detection of the 2009 influenza A H1N1 (H1N1pdm) virus in the USA and Mexico in April 2009, followed by widespread infection throughout North America, prompted the World Health Organization (WHO) to declare the first public health emergency of international concern under the 2005 International Health Regulations.[1–3] Within weeks, the virus had spread rapidly around the world, and on 11 June 2009, WHO raised the pandemic alert to phase 6, formally indicating that the world was at the start of the first influenza pandemic of the twenty-first century.[4] By August 2009, the H1N1pdm virus was the predominant influenza A virus subtype reported throughout the world.[5]

The H1N1pdm virus appears to have emerged early in 2009 in the Northern Hemisphere near the end of the typical annual influenza season, and subsequent transmission continued during summer when influenza virus transmission is usually, at most, sporadic. However, the introduction of the virus into the Southern Hemisphere's temperate countries was nearly coincident with, although a few weeks earlier than, the beginning of their usual influenza season, which typically occurs sometime during May through October. As a result, the assessment of the pandemic in these countries provides a picture of transmission similar to seasonal spread later seen in other temperate areas of the world. This report describes the pandemic in five temperate countries of the Southern Hemisphere – Argentina, Australia, Chile, New Zealand and South Africa – and focuses on three key facets of the pandemic: transmission dynamics, indicators of severity and co-circulation of H1N1pdm virus with seasonal influenza viruses.

None of the five countries experienced widespread out-of-season transmission before their first wave, as occurred in North America and parts of Europe, and therefore, they provide an opportunity to observe in-season transmission in unexposed populations with levels of prior immunity, which were unknown at the time. The experience of the pandemic in these areas has served as a useful benchmark against which to observe changes in the behaviour of the H1N1pdm virus in the future seasons in temperate countries.

Surveillance systems

All five countries had country-wide sentinel-based outpatient (community) surveillance systems in place prior to the arrival of the H1N1pdm virus that collected virologic and epidemiologic data.[a] The number of sentinel sites varied by country and included general practitioners (GP) or primary health care centres (all five countries), hospital virologic surveillance (Chile), or occupational health clinics and paediatric outpatient departments (South Africa). All of these systems reported cases of ILI and obtained specimens for testing by real-time reverse transcriptase polymerase chain reaction (rRT-PCR) and viral culture. Sentinel ILI case definitions varied by country and used slightly different inclusion criteria including symptoms such as fever, cough, chills, myalgia and sore throat. South Africa did not have historical ILI data available from the sentinel outpatient surveillance programme. Instead, South Africa was able to provide data collected retrospectively on inpatient and outpatient consultations clinically judged as influenza [as recorded using the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes] from a second network of private hospitals in four provinces (Respiratory Consultations Surveillance System). This system has monitored key diagnoses associated with influenza in outpatient consultations since 2005.[6]

In addition to having sentinel surveillance for ILI, all five countries implemented nationwide reporting of laboratory-confirmed cases of H1N1pdm. Initially, widespread testing of suspect cases was carried out in all five countries. However, as the level of respiratory disease in each country increased, each switched to a strategy of prioritized testing of severe cases around mid-June 2009 (New Zealand, Australia, Argentina, Chile) or mid-July 2009 (South Africa) albeit for different rationales.[7] Australia and New Zealand increased surveillance throughout the season, including monitoring hospital admissions, intensive care unit (ICU) admissions, deaths and clinical outcomes. Australia also monitored ILI presentations to emergency departments in some jurisdictions and community-entered ILI data on a national online system.

[a]Note that New Zealand had in place two different GP-based sentinel surveillance systems for influenza-like illness (ILI). Only one (ESR surveillance) is used in the analysis here.

Both Australia and New Zealand also tracked ILI-related phone calls requesting free advice through the National Health Call Centre Network and Healthline during the pandemic.[8] In addition to their pre-existing surveillance systems, Chile and Argentina established intensive population-based surveillance in one or more sites to establish the relative proportions of deaths, hospitalizations, clinic visits and non-medically attended outcomes and to better define the entire spectrum of H1N1pdm disease severity.

Control measures

Early in the outbreak, border controls were implemented to varying degrees. Argentina cancelled all flights from Mexico until 14 May 2009, and Chile recommended against non-essential travel to Mexico and the USA in early May 2009. Also early in the outbreak, thermal scanners were used at international airports in Australia, Chile and South Africa to screen incoming passengers. Australia and New Zealand provided information about H1N1 to incoming passengers and recorded additional passenger details (e.g. Health Declaration Cards in Australia and Passenger Locator Forms in New Zealand) to assist with case finding and contact tracing. Ill passengers were assessed, and actions taken, including voluntary isolation, use of antivirals and contact tracing for suspect cases, were based on the particulars of the case. Australia, Chile and South Africa also asked airline passengers from ''countries of concern'' to self-report specific symptoms. Passengers arriving in New Zealand with an ILI symptom were assessed, treated and cared for in isolation. Contact tracing and post-exposure antiviral prophylaxis were used in all countries for people travelling on flights with confirmed cases until countries made the decision to change from the ''containment'' to ''mitigation'' phase.[9]

Policies for the use of antiviral medication varied across the five countries. During the early ''containment'' stages, most countries used antivirals for cases and contacts, as well as isolation and quarantine measures. South Africa did not use antivirals for post-exposure prophylaxis for contacts, but did recommend antiviral treatment for patients with significant comorbidities or immunodeficiencies presenting with ILI. As the epidemic progressed, treatment for persons with moderate and severe disease became the priority. Countries also began to prioritize antiviral use for the treatment of cases, and, in particular, for those most at risk of severe outcomes, and stopped the routine prophylactic use of antivirals for all contacts.

Community-based mitigation measures included (complete or partial) school closures, plans to reduce mass gatherings and educating the public on measures to protect themselves and reduce transmission. Schools were closed in four countries as follows: in Argentina schools closed nationally early in the pandemic from July until 3 August early in the pandemic, 2 weeks ahead of the winter break; some affected schools in Australia closed or partially closed for varying periods of time from late May to mid-June, and, at one point, Australian health authorities recommended that children returning from areas of higher incidence not attend school for 7 days; in New Zealand, a small number of schools (<20) or early childcare centres (<5) either partially or fully closed. In Chile, only the first affected schools were closed for only 7 days, but the school year then proceeded normally. Previously scheduled winter school recess occurred during July in New Zealand and Australia and between 13 and 24 July in Chile. In the Buenos Aires Province of Argentina, which makes up approximately 25% of the country's population, sporadic theatre closures and social distancing measures were recommended during the second and third weeks of July. In South Africa, a previously scheduled winter school recess occurred from 27 June to 19 July. Additionally, all countries disseminated guidance on personal hygiene, social distancing and seeking medical advice. For instance, Australia provided a dedicated health emergency website, as well as TV and radio campaigns on personal hygiene and social distancing for the general community and for vulnerable groups. New Zealand emphasized personal hygiene and home isolation of milder cases in public health messages and used a radio and television campaign, regular media updates and various other media such as posters, billboards and websites for messages.

None of the five countries had H1N1pdm vaccine available before spring 2009, when Australia started its vaccination campaign.

Methods

This review compares data primarily obtained from surveillance programmes of the Ministries of Health of the selected countries prior to their pandemic period (1 April 2009) through 31 January 2010. Additional sources of information include official government publications, peer-reviewed publications and informal reporting from public health authorities in each country. Ministries of Health or affiliated institutions in each of the countries provided surveillance data, including ILI consultations and virologic data in a standardized format that allowed for direct comparisons. As the data used in this review was from surveillance programmes in the five countries, the data were analysed anonymously and no ethics approval was required.

To illustrate circulation of viruses by strain over time, we display data that were available from both sentinel and non-sentinel systems (Figure 1). However, given that not all isolate data were available for all countries, we have also used other sources to determine first-identified

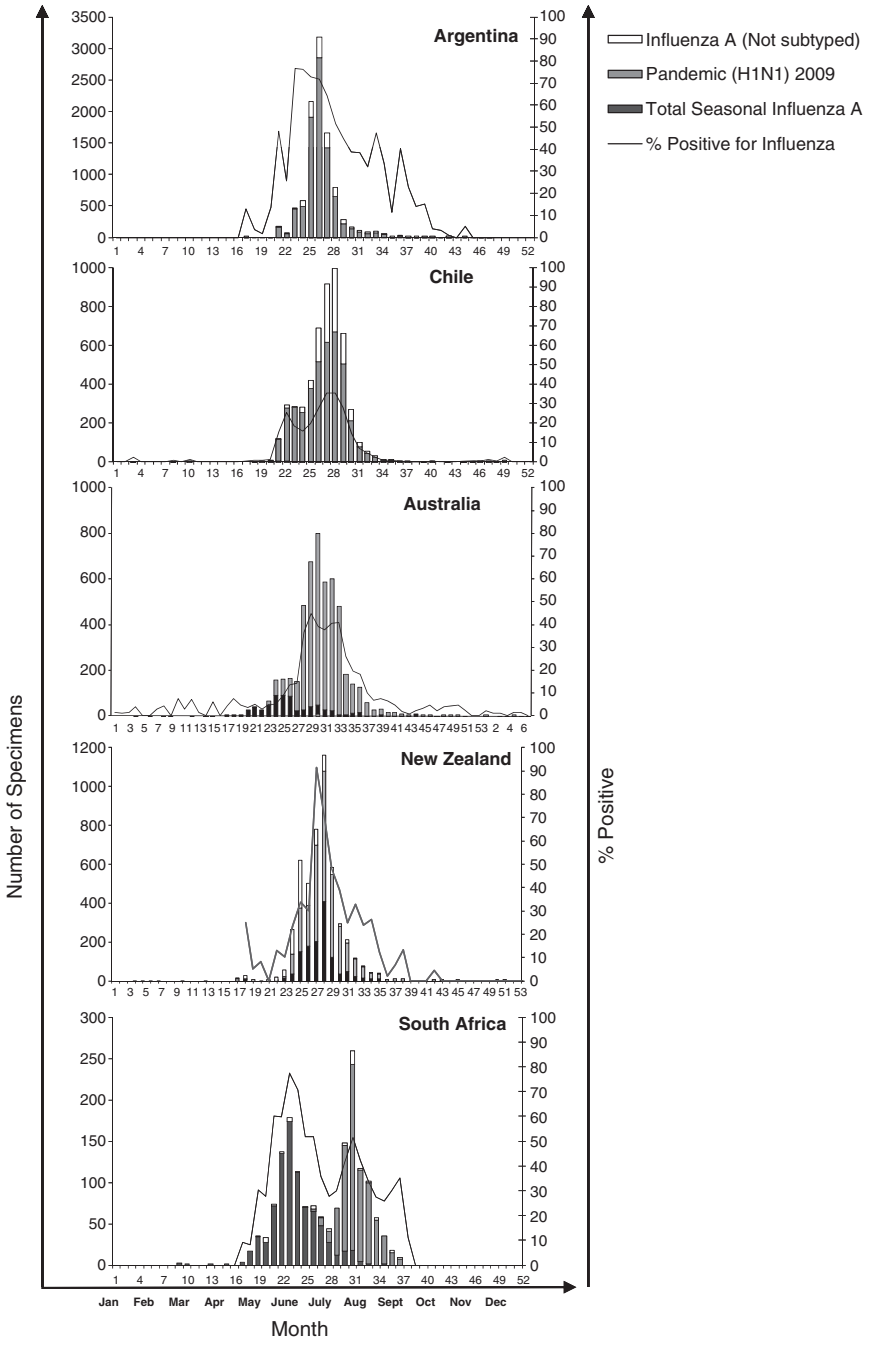

Figure 1. The figures illustrate virus circulation by strain [pandemic H1N1, influenza A (not subtyped), and total seasonal influenza A] and the percent of all specimens tested that are positive for influenza over time by country. **Data sources include available virus isolate data from sentinel and non-sentinel systems; graphs include all national isolate data (NZ, SA, Chile, Argentina), or a subset of all available data (Australia).

cases, the predominance of H1N1pdm and disappearance of seasonal strains, and the duration and peak of the pandemic.

Hospitalization, ICU admissions and mortality rates were calculated for each country using the total number of confirmed cases in each category divided by population estimates from 2008.[10] Age-specific mortality rates (<5, 5–14, 15–64 and ≥65 years old) were calculated for New Zealand using 2010 population estimates from the United Nations[10] and for Australia using the 2008 mid-point estimates from the Australian Bureau of Statistics.

In addition to data from 2009, countries provided baseline comparison data from the 2007–2008 influenza seasons, where available. Data describing transmission characteristics including the basic reproductive rates of infection (R_0), clinical attack rates, estimates of population infection rates, generation time and incubation time were obtained from published literature.

Results

Transmission dynamics

General and country-specific time course of the pandemic

Pandemic influenza largely occurred during each country's usual period of seasonal influenza transmission. With the exception of South Africa, the countries included in this report detected their first cases of H1N1pdm in late April or early May [Epidemiologic week (EW) 17–20]. South Africa reported its first case of H1N1pdm in the first week of June (EW 23). Rapid nationwide spread occurred in all countries within weeks of the first detections. In New Zealand and Australia, cases were detected 11 and 12 weeks, respectively, prior to the peak. Following a containment effort, very few cases were detected for the next several weeks until sustained community transmission became apparent. Using virologic data, time from first detection of the virus to the peak of laboratory-confirmed cases ranged from 6 (South Africa) to 12 weeks (Australia). However, the rise and fall of cases as reflected in all five countries was very similar and resembled the pattern observed in a typical winter influenza season (although with a higher peak). Australia experienced a comparatively shorter season (18 weeks) than that of the five prior influenza seasons, which ranged from 21 to 29 weeks.

In all countries, confirmed cases of pandemic influenza declined rapidly within 2–3 weeks of the peak and more than 90% of all cases occurred within a 12–14 week period of time in each country. Local outbreaks were much shorter, generally lasting 6–8 weeks. Sporadic cases continued to be reported into early 2010 in all countries, during the summer season, but with no evidence of sustained community transmission once the major wave was over. Rates of ILI above the seasonal influenza baseline continued on average for 10–17 weeks. Although elevated ILI rates were observed in New Zealand for an extended period from June through mid-September (EW 23–39) (Figure 2), this was not accompanied by high rates of H1N1pdm laboratory confirmation after week 12 of the pandemic (Figure 1), which in part is likely to be due to the fact that testing practices had changed (after a change in the response phase, routine laboratory testing for all patients with ILI was no longer required). In most countries, active case finding and levels of confirmatory testing had declined significantly by week 12 of the pandemic.

South Africa was unique among the five countries in that influenza A (H3N2) was the predominant circulating subtype beginning in late February 2009 (EW 9) (Figure 1). H1N1pdm appeared in June as circulation of the H3N2 virus was declining, and this resulted in a second peak of influenza transmission in early August (EW 32). This second peak followed a pattern similar to that seen in the other four countries, with H1N1pdm activity lasting approximately 11 weeks (Figure 1).

Attack rates and R_0

Based on a variety of epidemiologic data – including individual case patient data, trend data for ILI and physician visits over time, and results of outbreak investigations in schools and other settings – estimates of the basic reproductive rate (R_0) and effective reproductive rate (R), infection and ILI clinical attack rates, the incubation period and the generation time for the H1N1pdm virus have been estimated.[11] Estimates to date of R_0 are relatively consistent and range from 1·2 in Chile to 1·96 in New Zealand.[12–16] Higher values of R_0 (e.g. in New Zealand and Australia) were estimated from data collected early in the pandemic, but have subsequently been revised downwards.[12,17] For example, in the state of Victoria, Australia, early data from the pandemic suggested an R_0 of 2·4 that reduced to 1·6 after accounting for undetected community transmission.[12] Higher values of R_0 (i.e. >1·5) may reflect that in some countries, younger age groups comprise a larger portion of the overall population, and transmission of the pandemic virus was especially efficient among children in school settings.[13] Regional differences in R_0 and attack rates have been noted in New Zealand and Australia.[13,18]

Data from the five countries as well as other countries indicate that the incubation period (mean 2·5–3, range up to 7 days) and generation time (mean 1·5–2 days) estimates for H1N1pdm influenza are comparable with seasonal influenza.[9,11,13,19] Without serologic data, it is difficult to accurately determine the infection attack rates during the first wave; however, infection attack rates have been estimated to range from 10% to 40%, with higher estimates among populations with larger proportions of children.[13] Seroprevalence data for New South Wales, Australia, suggest that 16% of residents were infected by H1N1pdm during 2009, with the highest infection rates (27%) among adolescents and young adults. Higher infection rates were also found among residents of the major metropolitan area versus other areas (19·3% and 9·6%, respectively).[18] Western Australia estimated the serologic infection rate to be 25% in the 1- to 4-year-olds and 40% in 5- to 19-year-olds, indicating high levels of mild or asymptomatic infection in children.[20] Estimates of serologic infection rates were 10% among 18- to 65-years-olds in Melbourne, Australia.[21] ILI clinical attack rates of 7·5% and 95% CI 3·4–11·2 have been estimated for New Zealand,[8] which is consistent with data from other countries in Europe and North America at 7–15%.[11]

Severity

The overall severity of the pandemic as reflected in the proportion of infected individuals who developed severe

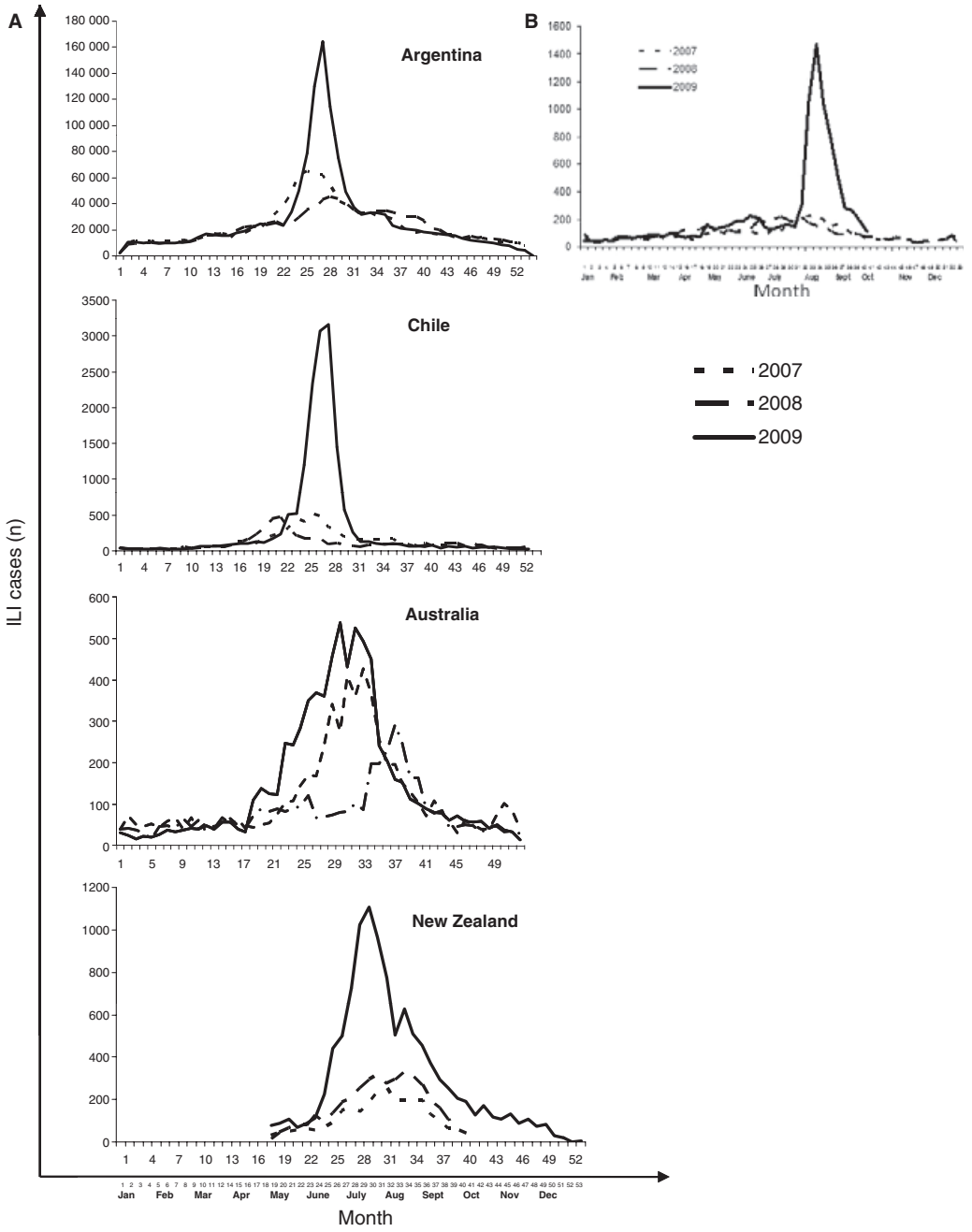

Figure 2. (A) Weekly Number of influenza-like illness Consultations 2007–2009 by country. Data sources vary by country and include: primary health care centres/national sentinel surveillance system (Argentina/Chile); national general practitioner (GP) sentinel surveillance system (New Zealand); and national GP sentinel surveillance system (Australia) N.B. differences in scale in the *Y* axis. (B) Inpatient and outpatient hospital consultations for influenza (ICD 10) 2007–2009 in South Africa. Data source includes sentinel surveillance from private hospitals in four provinces (South Africa).

illness or died was difficult to estimate. Over time, however, a clearer picture has emerged based on population estimates of hospitalization, ICU admission rates, mortality rates, the impact of the H1N1pdm pandemic on the health care infrastructure and the clinical syndrome caused by infection.

Hospitalizations, critical care and fatalities

The cumulative number of H1N1pdm patients who were hospitalized, admitted to an ICU or died are reported by country in Table 1. The median age of patients with laboratory-confirmed H1N1pdm varied by country (15·5 years in South Africa,[22] 21 years in Australia, 26 years in Argen-

tina and New Zealand, and 32 years in Chile). The median age of patients who were hospitalized, required care in an ICU or died ranged from 26·7 to 32 years (data from Argentina, Australia, Chile, New Zealand), 33 to 45 years (data from Australia, Chile, New Zealand) and 33 to 59 years (data from all five countries), respectively.

Countries reported overall population-based hospitalization rates ranging from approximately 10/100 000 persons in Chile to 34/100 000 in Argentina. Children and young adults comprised the majority of hospitalized cases, and the highest population-based rates of hospitalization were consistently observed among children under 5 years, varying from 54·1 cases/100 000 population for women and 67·9 for men in Australia[23] to 75·6 cases/100 000 in Argentina[24] and 76·1/100 000 among <1-year-old in Chile[25] to 274·3/100 000 among <1-year-olds in New Zealand.[8] Australia noted that during the 2009 pandemic season, the rate of hospital admission for children under 5 years of age was higher than during previous influenza seasons.[26]

The proportion of hospitalized patients requiring admission to an ICU ranged from 4% in Chile to 11–14% in Australia, Argentina and New Zealand (Table 1). In Victoria, Australia, the proportion was 21% (92/433).[27] Data on hospitalizations and ICU admission were not available for South Africa. In Australia, the median age of ICU patients was higher than for all other patients with confirmed H1N1pdm infection (median age 44 versus 21 years, respectively).[28] The highest absolute number of ICU admissions was among patients with H1N1pdm who were between 25 and 49 years, whereas the number of ICU admissions among children <5 years was low. However, population-based ICU admission rates in Australia were highest among infants aged <5 years and in New Zealand were highest among children <1 year.[23]

Population-based mortality rates of confirmed patients with H1N1pdm were available for all countries except South Africa and ranged from 0·8/100 000 in Chile to 1·5/100 000 in Argentina. As noted previously, the relatively small number of severe cases in older age groups resulted in a lower overall mortality rate compared with recent seasonal influenza epidemics. Age-specific mortality rates were available for Australia and New Zealand. In Australia, the lowest population-based mortality rates were in children aged <5 years and 5–14 years (0·29/100 000) and highest in adults aged ≥65 years (1·48/100 000); adults aged 15–64 years had a population-based rate of 0·9/100 000. In New Zealand, the mortality rates were lowest in 5- to 14-year-old children (0·17/100 000) and highest in 15- to 64-year-old adults (1·1/100 000); young children <5 years and older adults ≥65 years had population-based rates of 0·34/100 000 and 0·36/100 000, respectively. The deaths-to-hospitalizations ratio was similar in four of the five countries (data on hospitalizations from South Africa were not available), ranging from 0·035 in New Zealand to 0·082 in Chile (Table 1).

Clinical pattern of illness and risk factors for severe disease

The majority of patients with confirmed infections in all five countries experienced mild, uncomplicated illness. Risk factors for severe illness were similar to those observed in seasonal outbreaks of influenza and included chronic respiratory disease [23% (806/3492) of hospitalized patients in Australia; 11% (6/56)[29]–21·2% of hospitalized patients in Chile; 9·5% (19/199) of hospitalized patients in Argentina[30]]; asthma (31% of hospitalized cases in Melbourne, Australia,[31] 20·6% in Chile), diabetes (12·5% in Chile;[25] 10% (359/3492) in Australia), heart disease (10·6% of severe cases in Chile; 8% (292/3492) in Australia), and pregnancy (6% of hospitalized cases in Australia). Among H1N1pdm patients who progressed to severe disease and death in Australia, New Zealand, Chile and South Africa, 26–68% had at least one chronic medical illness.[23,25,32,33] Conversely, therefore, a large proportion of severe cases did not have previously recognized underlying chronic conditions. In Australia, for example, 54% of hospitalized cases, 33% of ICU admissions and 38% of fatalities had no known underlying comorbidities.[33]

Certain populations appeared to be at higher risk of severe H1N1pdm disease including people of Pacific and Maori ethnicity in New Zealand and the Aboriginal and Torres Strait Islander population of Australia.[8,33,34] It remains unclear whether this is a result of higher rates of infection, reduced access to health care, increased comorbidities or other factors. Data from South Africa suggested that co-infection with influenza and HIV or tuberculosis (TB) may be associated with an increased risk of death;[22] however, this finding has not been reported by the other four countries, where the prevalence of these conditions is much lower, and it is not clear whether patients with HIV or TB might have had other underlying conditions.[35]

While one of the presentations of severe illness was an exacerbation of underlying medical conditions such as chronic obstructive pulmonary disease, the most common cause of death was severe pneumonia and acute respiratory distress syndrome. In Australia, rates of viral pneumonitis (2/100 000 population) were significantly higher among adults hospitalized with H1N1pdm compared with those hospitalized with seasonal influenza infection between 2005 and 2009.[26] Secondary bacterial infections were also observed in H1N1pdm patients in Australia, New Zealand and Chile.[23,32,36–38]

Impact on health care systems

Outpatient care facilities' clinical care capacity was strained in most areas. Four of the five countries saw peak consultations for ILI above those seen in previous influenza seasons (Figure 2). Compared with the 2007 and 2008

Table 1. H1N1pdm hospitalization, ICU admission and mortality rates by country

Country	Hospitalizations			ICU		Deaths		
	Number (Rate/ 100 000)	Median age (range)	% Hosp requiring ICU	Number (Rate/ 100 000)	Median age (range)	Number (Rate/ 100 000)	Median age (range)	Deaths-to-hosp ratio
Argentina[24]	13 819* (34·1)	28	11·4	1578 (3·9)	NA	621 (1·5)	50–59†	0·045
Australia[33]	4992 (28)	31	13·6	681 (3·2)	44	191 (0·9)	53	0·038
Chile[5,32]	1875 (9·3–10·8)	32 (7 days–94)	4·0	75 (0·4)	45 (16–77)	153 (0·78)	44 (4 month–89)	0·082
New Zealand	1122 (26·1)	26·7 (19 days–91)	10·6	119 (2·8)	33 (1 month–68)	35 (0·81)	40 (1–79)	0·035
South Africa[22]	NA	NA	NA	NA	NA	93 (NA)‡	33 (<1–70)	NA

*SARI cases requiring hospitalizations.
†Age group most affected (mean age of deaths not available).
‡Population-based mortality rates from South Africa could not be calculated because there was no population denominator.
NA, data not available.
Table adapted and updated from reference 51.

influenza seasons, the peak of ILI consultations in 2009 was 5–6 times higher in Chile, three times higher in Argentina and 3–4 times higher in New Zealand (Figure 2a). Peak rates ranged from 34 per 1000 primary care consultations per week in Australia[33] (which were comparable with the observed rates in 2007 and 2008 but were lower than the peak of the 2007 influenza season) to 275 per 100 000 population per week in New Zealand, the latter being three times the peak in an average influenza season. ILI consultations in New Zealand were above seasonal baseline levels for about 15 weeks, longer than what was experienced in the other four countries. This was also despite advice in New Zealand for people with mild symptoms to remain at home, and consequently a smaller proportion of people with ILI in that country may have visited a GP in 2009. In New South Wales, Australia, emergency department (ED) consultations for ILI peaked at 38/1000 consultations.[26] EDs in Victoria, Australia, experienced a 30% increase in demand for services during their ''containment'' phase.[28] This declined to seasonal baseline rates within a few weeks with the help of community diversion influenza clinics, even as hospital and ICU admissions increased.[27] While GP consultation rates did not exceed previous years in Australia, visits to ED due to ILI slightly exceeded the 2007 influenza season in Western Australia.[34]

Although all countries reported short-term, yet significant, impacts on their inpatient health care systems, demand did not exceed capacity even during the peak of the outbreak.[8] Compared with the 2007 and 2008 influenza seasons, hospital outpatient consultations and admissions for influenza during the 2009 season were 2–3 times higher in South Africa (Figure 2b). During the peak of influenza activity, the ministries of health in Argentina and Chile hired more health care workers and purchased additional equipment and antivirals (C. Gonzalez and L. Carlino, personal communication). In Chile and Argentina, non-critical gynaecologic, orthopaedic and elective general surgeries were cancelled. In Chile, acute care and intensive care capacities were increased 25–35% in some parts of the country by converting surgical and gynaecological acute care beds into critical respiratory care beds.[32] Argentina deployed 28 mobile hospitals during the peak of the epidemic to help cover health care needs in Buenos Aires. Australia and New Zealand deferred many instances of elective surgery, where post-operative intensive care was anticipated.

All countries reported that the care of H1N1pdm patients in ICUs had a substantial impact on the health care system; some of these patients required aggressive and/or lengthy critical care.[8,23,27,38] In Australia, the median length of stay for confirmed hospitalized cases and patients in ICU was 3 and 11 days, respectively. Overall, approximately one-fifth of confirmed hospitalized cases stayed in hospital for >7 days.[39] While health systems were not overwhelmed in New Zealand, at the height of the pandemic, demand for ICU services for H1N1pdm peaked at 25% of the national ICU occupancy.[8] This was in part because of an above-average number of patients requiring mechanical ventilation and other interventions, including extracorporeal membrane oxygenation (ECMO), as well as the prolonged stays required by many H1N1pdm-infected patients. In Chile, 75% of 75 patients admitted to an ICU required mechanical ventilation and 6% required ECMO.[32] In New Zealand and Australia, 2·87 cases/100 000 population (95% CI 26·5–30·8) were admitted to an ICU, and 64·6% required mechanical ventilation.[23] In Australia and

New Zealand, it was estimated that approximately 2·1 patients/1 000 000[23] and 1·9 patients/million, respectively, required ECMO. By the end of August 2009, 71% of ECMO patients in Australia and New Zealand had survived to ICU discharge and 21% had died.[40] In Victoria, Australia, 72% of ICU admissions received mechanical ventilation and 7% required ECMO.[27]

Absenteeism among health care workers contributed to the strain on the health care infrastructure. In some regions of Argentina, as many as 40% of health care workers stayed away from work during the peak of the pandemic.[41] Twenty per cent of health care staff were absent because of respiratory illness during Chile's peak period of demand for health care.[32] Absenteeism was in part because of a national furlough of government employees who were at higher risk for infection or severe disease (e.g. pregnant women, parents with young children and persons with underlying conditions). In Australia, rates of work absenteeism during the 2009 H1N1 pandemic peaked at 1·3% and were similar to those observed during the 2007 and 2008 seasonal influenza seasons.[33,42,43] New Zealand reported regional variations, with additional strain due to health care worker absenteeism in some parts of the country, such as Wellington; however, overall absenteeism was not a significant issue relative to previous years.

Virology

Countries provided data on the number of cases that tested positive by rRT-PCR for H1N1pdm, influenza A (not subtyped) and seasonal influenza A and B strains (A/H1N1, A/H3N2, B) for 2009 and previous years. Countries did not collect and could not provide data on the total number of samples or cases tested. Virus identification was performed primarily by the national reference laboratories; however, other laboratories were also employed during later stages of the epidemic. Early H1N1pdm virology data are likely to be biased towards greater identification and reporting of H1N1pdm, as much of the initial testing supported case finding, outbreak investigations and contact tracing of suspect cases. This included virus sampling from a range of sources across health systems, in addition to the sentinel and non-sentinel surveillance that was in place. Sentinel surveillance testing continued throughout the season in all five affected countries. In the four countries where seasonal influenza viruses and H1N1pdm circulated simultaneously, the H1N1pdm virus very rapidly became the predominant influenza virus (Figure 1). Some seasonal viruses continued to be occasionally detected through the first half of the season or longer, but accounted for <5% of all samples positive for influenza. As noted previously, in South Africa, H1N1pdm appeared after the peak of seasonal influenza circulation. The country had pronounced circulation of seasonal influenza A (H3N2) from May to August (EW 18–30) and sporadic cases to September (EW 35, Figure 1) closely followed by a peak of H1N1pdm virus in August. Seasonal influenza A (H3N2) was the most common seasonal virus detected in all countries except New Zealand, where seasonal H1N1 predominated over H3N2. Of note, respiratory syncitial virus (RSV) actively co-circulated with influenza viruses in New Zealand, Chile and Argentina, adding significantly to the burden of respiratory disease seen in young children during the course of the pandemic (data not shown).[24,25] Very little influenza type B was detected in any of the five countries during the season (data not shown).

Discussion

The experience of the temperate countries of the Southern Hemisphere provides a model for the spread of the disease after the introduction of a novel virus into a largely naïve population during the normal influenza season. The data gathered during the course of the pandemic in these five countries provide useful reference points to observe for possible changes in the epidemiology of pandemic influenza-related illness in coming seasons. Our review indicates that the virus spread rapidly nationwide, penetrating much of the population, albeit with regional differences within countries, and exhibited a seasonal pattern of transmission similar to seasonal influenza viruses with a distinct season of 10–12 weeks in duration on a national level but only 6–8 weeks in any given region. This is markedly different from the experience of North America and parts of Western Europe where the first introductions occurred during the 2009 spring and summer season. It is notable that only South Africa, where introduction of the H1N1pdm virus occurred after the influenza season was well underway, had significant levels of circulation of seasonal influenza viruses. Although all five countries identified isolates of seasonal influenza A H3N2 and H1N1 either before or after the appearance of H1N1pdm, seasonal viruses appeared to be quickly outcompeted in countries where the H1N1pdm virus appeared early.

It is important to note that transmission of influenza in all five countries declined after the 2009 winter in the Southern Hemisphere, and H1N1pdm virus activity during the Southern Hemisphere summer resulted only in sporadic cases, without sustained community transmission. This contrasts with the experience in Northern Hemisphere temperate countries where the initial spread of H1N1pdm virus occurred in their 2009 spring and summer (April–October) period. This may suggest that transmission was much more intense and penetrated further into the community during the Southern Hemisphere winter, likely resulting in levels of population immunity sufficient to prevent out-of-season transmission. However, seroepidemiology studies, with early results suggesting that approximately 10–35% of the

population, significantly varied by age and ethnicity of the population, may have been infected during their first wave,[21,44,45] are needed to determine the actual rates of infection and resulting levels of population immunity.

There were a few notable differences in the experience of the five countries included in our analysis, some of which are not fully explained. The population-based mortality rates varied by country by approximately twofold from lowest to highest and were unavailable for South Africa, illustrating the problems in measuring mortality, a key parameter of severity. Countries had varying testing practices, and health care utilization patterns, which complicates comparison of raw data between countries. We have attempted to adjust for biases to some extent by use of proportions of different outcomes. For instance, Argentina appears to have had the highest rate of laboratory-confirmed deaths; however, the ratio of deaths to hospitalizations in Argentina is lower than that in Chile. The deaths-to-hospitalizations ratio was similar in four of the five countries where data were available, and by this measure, severity appeared to be similar in all countries. Procedures for investigating and classification of fatal cases varied by country and may explain some of the variation. Argentina had an aggressive programme to proactively investigate every fatal case and in doing so often discovered additional fatal cases that had not been reported initially by the health care provider; also, every person who died after a positive test was reported as a fatal case of pandemic influenza, which likely resulted in misclassification of some deaths. In New Zealand, each suspect fatal case was assessed during the 2009 season as to whether it was associated with H1N1pdm. New Zealand convened a pandemic morbidity and mortality review panel to review deaths, so the final mortality count for 2009 is likely to be higher. In Chile, of 153 PCR test-positive patients who died and were reported as fatal cases, influenza was judged to be the primary cause of death in only 44.

While the reported numbers of fatal cases almost certainly represents a significant undercount of the actual number of deaths associated with this pandemic, they do provide a useful reference point for comparison with future seasonal epidemics caused by the H1N1pdm virus. Determination of the true mortality associated with the pandemic will require retrospective analysis of vital statistics data to account for unrecognized and untested cases. Furthermore, as the reporting of a confirmed case required laboratory testing, countries with more limited access to laboratory testing or with large populations that have limited access to care, such as South Africa, may have artificially low population rates of mortality. It is also worth noting the high numbers of patients requiring mechanical ventilation and ECMO, treatment modalities that were much less available during previous pandemics. The numbers of these cases were more than three times the numbers of fatal cases in three of the four countries for which data were available.

Compared to recent influenza seasons in these five countries, the overall rates of severe disease and death during the pandemic wave in the Southern temperate countries appear to have been low. This is partially because of underreporting, but is also related to the lower attack rates in older adults,[46] who constitute more than 90% of influenza-related deaths in seasonal influenza epidemics.[47,48] The USA recently estimated that the overall number of fatal H1N1pdm cases was approximately one-third that estimated to have occurred during 1990–1999 influenza seasons when A/H3N2 viruses largely predominated.[49] However, the H1N1pdm-associated mortality rate was markedly increased compared with seasonal rates for younger age groups. It is important to note that the global fatal case count reported by WHO also underrepresents low-resourced countries that are less likely to have sufficient capacity to detect and test fatal cases.

Conclusions

The difficulties experienced in tracking the progress of this event globally, estimating its severity early on, communicating and comparing information across countries, argue for improved routine surveillance and standardization of investigative approaches and data reporting methods. Routine, representative, standardized and timely sentinel surveillance has the greatest potential for providing unbiased data to describe risk factors, rates of severe illness, and historical data with which to compare new events. Countries are encouraged to develop sustainable respiratory disease surveillance that is consistent with global standards.[50]

Conflict of interests

LCJ has received research funding from Hoffmann La-Roche and honoraria or travel assistance from Hoffmann La-Roche, GlaxoSmithKline, Sanofi Pasteur, Abbott, Novartis, Wyeth, Pfizer, CSL and Kimberly-Clark for participation in advisory groups and scientific meetings. LB has received honoraria from GSK for educational talks to medical professionals on malaria and infectious diseases, but not including influenza. Sanofi Pasteur sponsors an annual influenza symposium held at the National Institute for Communicable Diseases through an unrestricted educational grant.

Authors contributions

LQ, EB, LOC, VS, OU, RO, FG, BP, AF, RF, GT, WA, PB, JM, CG, AO, VS, MNDF, AB, DH, QSH, LCJ, MM, LDL,

CM, CC, BA, LB, AC, CM, JM, VM, DN, AP, BS, JT, MV all collected and contributed data from their countries to the analysis. MVK, SM and AWM analysed the data and drafted the manuscript. JM drafted sections of the manuscript. All authors reviewed and edited drafts of the manuscript, and all authors read and approved the final manuscript.

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