Outline

- Timeline of the pandemic
- Pandemic expectations
- Evolution of the pandemic virus
- What we experienced
- What should we expect next?

Timeline of Pandemic Influenza A (H1N1) 2009

- April 12: an outbreak of influenza-like illness in Veracruz, Mexico reported to WHO
- April 15-17: two cases of the new A(H1N1) virus infection identified in Southern California, U.S.A.
- April 23: Novel influenza A (H1N1) virus infection confirmed in several patients in Mexico.
- April 24: WHO HQ SHOC activated (first TC with Mexico)
- April 26: IHR Emergency Committee convened and WHO declares a “Public Health Emergency of International Concern”
- April 27: WHO increases pandemic alert phase from 3 to 4 and concludes geographic containment not feasible
- April 29: WHO raises pandemic alert phase from 4 to 5
- June 11: WHO declares pandemic phase 6 (spread to 2 WHO regions)
- In 9 weeks, all WHO 6 regions reporting cases of pandemic A(H1N1) 2009

NZ Influenza Pandemic Action Plan

Plan for it
- Engage with all relevant agencies

Keep it out
- Border management

Stamp it out
- Cluster control operations

Manage it
- Public health measures,
  - Public gatherings, antivirals

Recover from it
- Return to normal service delivery

1918 Pandemic:
Life expectancy shortened to <40 yrs

American Society for Microbiology News

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Dr. Lance Jennings, University of Otago, New Zealand
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Age Distribution of Deaths in UK 1918-1919: Females
- 1st Quarter 1918
- 2nd Quarter 1918
- 3rd Quarter 1918
- 4th Quarter 1918
- 1st Quarter 1919

Proportion per 1000 deaths
0
50
100
150
200
Age groups (years)
0-5
5-10
10-15
15-20
20-25
25-30
30-35
35-40
40-45
45-50
50-55
55-60
60-65
65-70
70-75
75-80
80-85
>85

Pandemic Expectations
• Expecting a novel influenza subtype
  – Novel quadruple reassortant of influenza A(H1N1) subtype
• Expecting the pandemic to start somewhere in Asia
  – Started in Mexico
• Expecting increased morbidity and mortality
  – Mortality due to death from lab confirmed infection less than mortality modelled due to seasonal influenza

Influenza Pandemics in 20th century
1918: “Spanish Flu”
1957: “Asian Flu”
1968: “Hong Kong Flu”

~50 million deaths
1-4 million deaths
~1 million deaths

2009: “Swine Flu”
13,554 deaths

Influenza Virus
Haemagglutinin
N
Neuraminidase
8 ss RNA segments
High mutation rate
Genetic reassortment

Ecology of Influenza A Viruses

16 HA
9 NA

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NZ Sunday Star Times, May 3 2009
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Pandemics of Influenza
Recorded human pandemic influenza (early sub-types inferred)

1889 Russian influenza H2N2
1900 Old Hong Kong influenza H3N2
1918 Spanish influenza H1N1
1957 Asian influenza H2N2
1968 Hong Kong influenza H3N2
2005 Novel influenza A/H1N1

Recorded new avian influenza
H7
H5


Reassortant Events Among Swine Influenza Viruses in North America

Source: Dr. Amy Vincent, NADC, USDA.

Origin of the 2009 Pandemic H1N1 Virus

Source: Dr. Amy Vincent, NADC, USDA.

Phylogenetic tree of the HA gene of H1N1 influenza viruses

Common swine ancestor
Homogeneous so far, few differences (nt or aa) in H1N1 2009 viruses
Distinct from previous swine & human swine viruses
Distinct from seasonal H1N1 viruses
Reference and vaccine virus is A/California/7/2009

NZ Epidemic curve of Pandemic A (H1N1) 2009 cases

25 April: importation of the pandemic cases
30 April: a notifiable disease
May: 21 June: containment phase
22 June: present: management phase
3283 cases
1014 hospitalisations
40 Deaths

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3283 Cases
H1N1 09

Weekly ILI Consultation Rates in 1992-2009

Source: ESR PEH & NZBID

Hospitalisation & Ethnicity

Rate

- Māori: 48.6
- Pacific: 101.2
- Other: 26.4
- European: 14.0

Overall Case Rate: 81.5/100,000
n = 1014 cases: Rate: 25.2/100,000

Source: ESR PEH & NZBID

ANZ ICU Admissions

Viral pneumonia cases

ANZICS Research Centre

ANZ ICU Admissions

Incidence & daily prevalence
1 June-31 Aug

Bed occupancy

Risk factors:
- Incidence highest in infants & adults aged 25-64
- 1/3 had severe comorbidity
- 1/3 had risk factors without severe co-morbidity (pregnancy, obesity, asthma)
- 1/3 were previously fit and well

ANZICS Research Centre

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ANZ ICU Admission Summary

- 28.7 ICU admissions per million (856 admissions)
- 64.6% received mechanical ventilation
  - mean 8 days
  - 11.6% of ventilated patients treated with ECMO
- Median duration of stay 7.4 days
- Risk factors:
  - Incidence highest in infants & adults aged 25-64
  - 1/3 had severe comorbidity
  - 1/3 had risk factors without severe co-morbidity (pregnancy, obesity, asthma)
  - 1/3 were previously fit and well
- Survival 84.2% (16.2% died)

Deaths

- Mortality rates: n=38
  - Overall all cases: 1.2%
  - Hospitalised cases: 2.5%
  - Community cases: 0.6%
- CFR
  - Accepted 1918-19 ~2%
  - Expected pandemic >0.1%
  - NZ ~0.005%
  - Aus ~0.009%
  - UK ~0.026%

Goals of Public Health Intervention

- Delay outbreak peak
- Delay spread and shift an epidemic curve to the right side
  - to reduce peak burden on health care facilities (e.g. hospitals)
  - to “buy time” for other measures (e.g. vaccination)
- Reduce morbidity and mortality through reducing the total number of cases

Containment ‘Keep It Out’ Phase

Effectiveness?
- WHO has placed little emphasis on border closure except for ‘isolated communities’ Positive practice of all incoming aircraft and ships (ie, 100% health status reported from all aircraft).
- New Zealand’s response
  - Positive practice (100% health status on all aircraft)
  - Completed passenger locator card to allow contact tracing.
  - Public health staff at airports to carry out clinical assessments.
  - All suspect cases and contacts managed with treatment and quarantine

Containment Phase, April-May 2009

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**NZ & Australia 1918-19 Pandemic**

Maritime quarantine appeared to protect South Pacific Islands from the 1918-19 influenza pandemic.

**Pacific Island Nations 1918-19 Pandemic**

Maritime quarantine appeared to protect South Pacific Islands from the 1918-19 influenza pandemic.

**Comparison of Available Influenza Diagnostic Tests**

<table>
<thead>
<tr>
<th>Influenza Diagnostic Tests</th>
<th>Method</th>
<th>Availability</th>
<th>Typical Processing Time</th>
<th>Sensitivity for influenza H1N1 2009</th>
<th>Distinguishes 2009 H1N1 influenza from other influenza A viruses?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid influenza diagnostic tests (RIDT)</td>
<td>Antigen detection</td>
<td>Wide</td>
<td>≤ 0.5 hour</td>
<td>10 – 70%</td>
<td>No</td>
</tr>
<tr>
<td>Direct and indirect immunofluorescence assays (IFA and IFI)</td>
<td>Antigen detection</td>
<td>Wide</td>
<td>2 – 4 hours</td>
<td>47 – 93%</td>
<td>No</td>
</tr>
<tr>
<td>Virus isolation in tissue culture</td>
<td>Virus isolation</td>
<td>Limited</td>
<td>2 - 10 days</td>
<td>-</td>
<td>Yes</td>
</tr>
<tr>
<td>Nucleic acid amplification tests (RT-PCR)</td>
<td>Nucleic acid detection</td>
<td>Limited</td>
<td>48 – 96 hours (6-8 hours to perform test)</td>
<td>66 – 100%</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**6th June: A(H1N1)2009 Cases**

Available & Confirmed Cases of Influenza (H1N1) by Public Health Service (PHS) Region

**Laboratory: Pandemic Planning**

Keep-it-out Cluster Control Manage-it

Response Phases

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Laboratory: Pandemic Reality

Containment Management

PCR Automation:
Abbott m2000sp Diagnostic Platform
FluTime PCR System

Containment:
Cases & Risk Factors April-June

Community spread

The spread of swine flu in one person has infected or affected more than 600 people.

4th June 2009
Christchurch Pacific Island Cluster

The Press, 12th June 2009

Analysis of Epi Data for Pandemic Decision Support

The number of cases and exposed non cases available for analysis:

<table>
<thead>
<tr>
<th>Location</th>
<th>Cases</th>
<th>Exposed non cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christchurch</td>
<td>35</td>
<td>387</td>
</tr>
<tr>
<td>Wellington</td>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>Auckland</td>
<td>7</td>
<td>57</td>
</tr>
</tbody>
</table>

Used to calculate:
Serial interval
Reproductive ratio (Ro)
Attack rate

Source: G MacKereth, C Hope, S Sharpe, S Grey

Cluster Control Data up to 15th June
Source: MacKereth et al

<table>
<thead>
<tr>
<th>Possible risk factor</th>
<th>Risk group</th>
<th>Average effective reproductive ratio ($R_o$)</th>
<th>Serial interval or average onset to onset interval in day ($n$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>0.85 (94)</td>
<td>2.9 (12)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>0.81 (84)</td>
<td>2.4 (35)</td>
</tr>
<tr>
<td>Age group</td>
<td>0-5 years</td>
<td>1.05 (25)</td>
<td>2.3 (26)</td>
</tr>
<tr>
<td></td>
<td>5-14 years</td>
<td>0.73 (15)</td>
<td>2.42 (12)</td>
</tr>
<tr>
<td></td>
<td>15-24 years</td>
<td>0.76 (15)</td>
<td>2.22 (5)</td>
</tr>
<tr>
<td></td>
<td>25-39 years</td>
<td>1.08 (28)</td>
<td>3.39 (27)</td>
</tr>
<tr>
<td></td>
<td>40-64 years</td>
<td>0.14 (7)</td>
<td>2.43 (7)</td>
</tr>
<tr>
<td></td>
<td>65+ years</td>
<td>4.00 (1)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Samoan (Chch)</td>
<td>0.83 (54)</td>
<td>2.4 (48)</td>
</tr>
<tr>
<td></td>
<td>European</td>
<td>0.92 (31)</td>
<td>3.3 (19)</td>
</tr>
<tr>
<td></td>
<td>Maori</td>
<td>1.10 (1)</td>
<td>2.3 (8)</td>
</tr>
<tr>
<td></td>
<td>Pacific</td>
<td>1.05 (20)</td>
<td>2.2 (30)</td>
</tr>
</tbody>
</table>

Source: G MacKereth, C Hope, S Sharpe, S Grey

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Cluster Control Data: Attack Rates

<table>
<thead>
<tr>
<th>Ethnicity of exposed</th>
<th>Count of exposed non cases</th>
<th>Count of exposed that became cases</th>
<th>Attack rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td>42</td>
<td>7</td>
<td>17%</td>
</tr>
<tr>
<td>Samoan</td>
<td>83</td>
<td>35</td>
<td>42%</td>
</tr>
<tr>
<td>Age group of exposed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-5</td>
<td>98</td>
<td>29</td>
<td>29%</td>
</tr>
<tr>
<td>6-12</td>
<td>78</td>
<td>15</td>
<td>19%</td>
</tr>
<tr>
<td>13-19</td>
<td>115</td>
<td>10</td>
<td>9%</td>
</tr>
<tr>
<td>20-29</td>
<td>59</td>
<td>38</td>
<td>64%</td>
</tr>
<tr>
<td>30-39</td>
<td>39</td>
<td>7</td>
<td>18%</td>
</tr>
<tr>
<td>40+</td>
<td>8</td>
<td>1</td>
<td>12%</td>
</tr>
<tr>
<td>Tamiflu Prophylaxis</td>
<td>388</td>
<td>1</td>
<td>0.26%</td>
</tr>
<tr>
<td>No Tamiflu Proph</td>
<td>56</td>
<td>97</td>
<td>18%</td>
</tr>
</tbody>
</table>

Did Containment work?

- Containment/cluster control phase in NZ successful (or just good luck?)
  - Contained spread for ~6.5 weeks
  - Extended containment phase allowed the planning & communication of key messages to public.
    - Stay at home message
    - If concerned phone GP or 0800 Health line

- No Crystal Ball
  - Can only learn from past pandemics
  - We must not become complacent

Has the H1N1 09 Virus Changed in Pathogenicity?

- D222G mutation in HA found in Norway & Ukraine
- ? Cause higher pathogenicity or are they selected in more serious cases (lung involvement)
- Viruses not antigenically distinct

H1N1 2009 Antigenic Mapping

<table>
<thead>
<tr>
<th>(CDC, 54 antigens; 16 sera)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/Auckland/1/2009</td>
</tr>
<tr>
<td>A/Mexico/10/2009</td>
</tr>
<tr>
<td>A/Texas/5/2009</td>
</tr>
<tr>
<td>A/Texas/15/2009</td>
</tr>
<tr>
<td>A/Mexico/10/2009</td>
</tr>
</tbody>
</table>

Pandemic Vaccines

- Seasonal vaccines provided little/no protection against pandemic influenza
  - VE = 8% (-42 to 38) in Victoria
  - VE = -10% (-43 to 15) in 8 US States

- Pandemic vaccines safe & immunogenic
  - But no VE estimates and trials did not enrol at-risk groups
  - Aus government committed to 20 million doses CSL vaccine, 725% distributed.
  - NZ government rolling out 100,000 doses Baxter vaccine to health care workers (1 February 2010)
WHO Seasonal Vaccine Composition Recommendations 2010

- Southern Hemisphere 2010
  - A/California/7/2009 (H1N1)-like virus
  - A/Perth/16/2009 (H3N2)-like virus (A/Wisconsin/15/
  - B/Brisbane/60/2008-like virus (B Victoria lineage)
- Decision made in September 2009
- supply March 1, but likely to be late)

Serum Antibodies to (H1N1) 09

- Pre-existing antibody titres 1:32 or more ranged from
  - 1.8% in children aged 0–4 years
  - 31.3% in adults aged 80 years or older.
- Post-pandemic:
  - 21.3% children <5 yrs
  - 42% children 5-14
  - 20.6% 15-20 year olds
  - Older = no change

Antivirals: BMJ Article- Cochrane Review Seasonal Influenza

<table>
<thead>
<tr>
<th>Measure</th>
<th>Oseltamivir</th>
<th>Zanamivir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic laboratory confirmed influenza</td>
<td>78% (69-85)</td>
<td>63% (85-85)</td>
</tr>
<tr>
<td>Not exposure prophylaxis</td>
<td>56% (48-64)</td>
<td>51% (44-59)</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td>11% (9-13)</td>
<td>93% (91-95)</td>
</tr>
<tr>
<td>Seroconversion</td>
<td>1.23 (1.12-1.34)</td>
<td>1.34 (1.13-1.56)</td>
</tr>
<tr>
<td>Reduction of influenza-related deaths</td>
<td>Not effective (0.22-1.32)</td>
<td>n/a</td>
</tr>
<tr>
<td>Side effects</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Antiviral Conclusions

- "The data suggest that NI’s are effective at reducing the symptoms of influenza. The evidence is of modest benefit – reduction of illness by about 1 day.”
- "Because of the moderate effectiveness of NI's we believe that they should not be used for the routine control of seasonal influenza."
- Independent randomised trials to resolve the uncertainties surrounding effectiveness are needed.”

Mortality Distributions and Timing of Waves of Previous Influenza Pandemics

Google trends mapping world influenza

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**SUMMARY 2009-10**

- Pandemic H1N1 dominated 2009 and still dominates in early 2010 – little change (most A/Cal/7/2009-like)
- Influenza activity generally low in Nth Hemisphere normally at peak – remains generally mild disease
- In China, increasing B activity in recent months – no seasonal H1, little H3
- 2010 SH seasonal vaccine trivalent; contains H1N1 09; H3N2; B components
- 2010 SH Influenza season ????
- Will we see a ripple or a wave?
- High level of exposure in 2009 (30% of children)
- Other adults (>53 years) refractory to pandemic H1N1 (pre 1957)
- Lower level of exposure in young adults 20-40 years (10-15%)
- ? ICU admissions & deaths lower in 2010