Pandemic Influenza H1N1 – The Southern Hemisphere Experience

Dr. Lance Jennings, University of Otago, New Zealand

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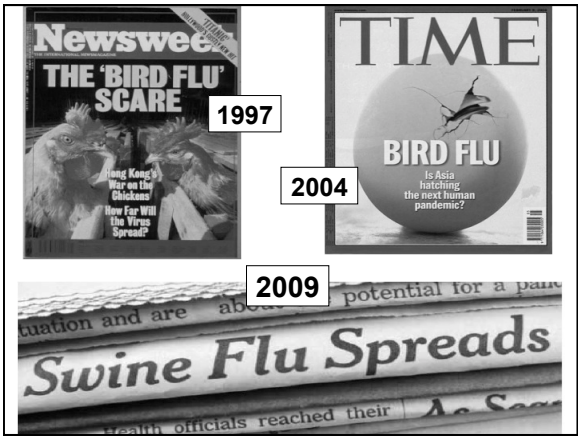
Canterbury Health Laboratories



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.
- NZ 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

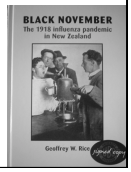
Keep it out
- Border management

Stamp it out
- Cluster control operations

Enhanced Surveillance

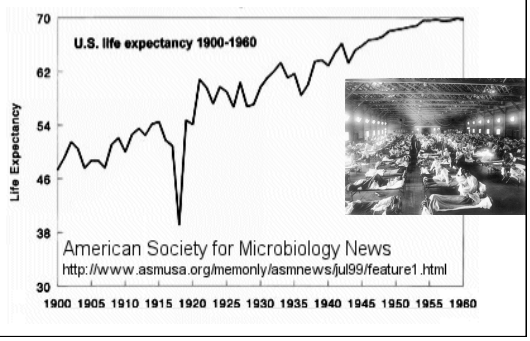
Manage it
- Public health measures,
- Public gatherings, antivirals

Recover from it
- Return to normal service delivery



1918 Pandemic:

Life expectancy shortened to <40 yrs



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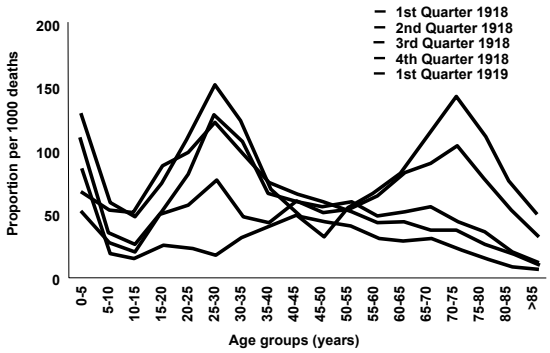
Age Distribution of Deaths in UK 1918-1919: Females



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"

~50 million deaths

A(H1N1)

1957: "Asian Flu"

1-4 million deaths

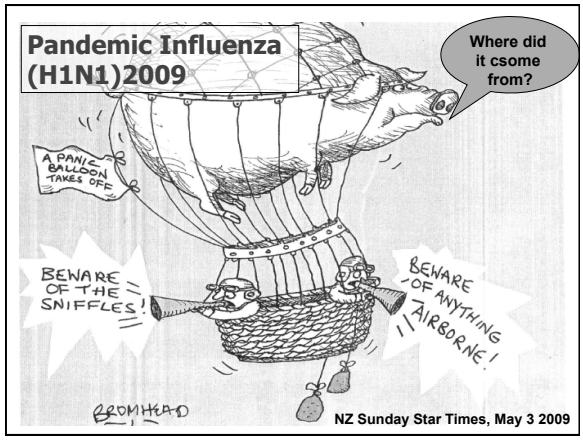
A(H2N2)

1968: "Hong Kong Flu"

~1 million deaths

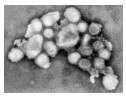
A(H3N2)

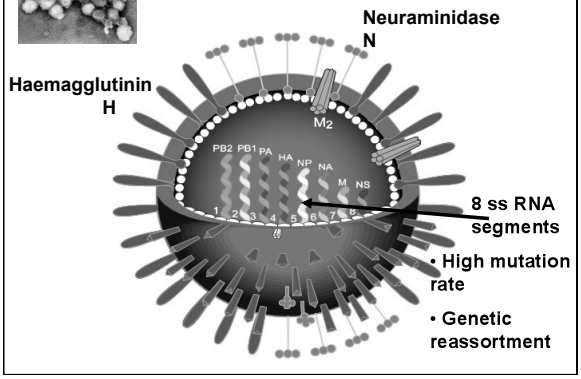
2009: "Swine Flu"
13,554 deaths

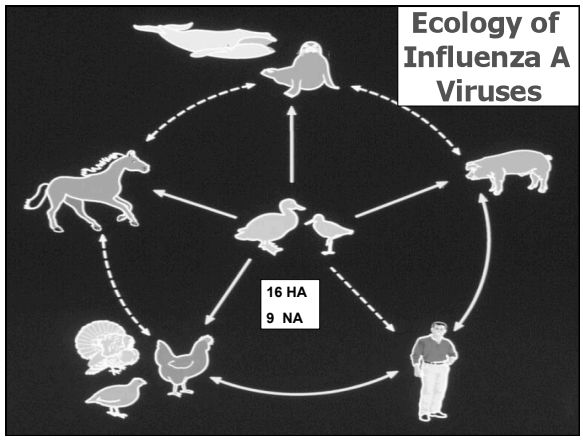


NZ Sunday Star Times, May 3 2009

Influenza Virus







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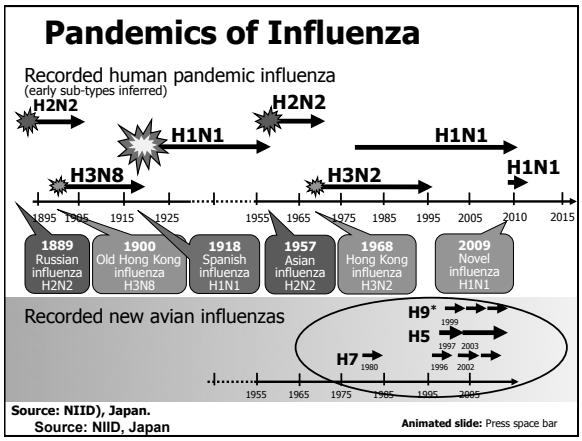

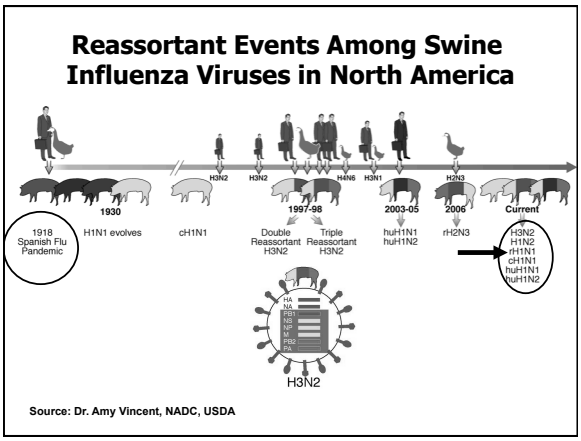

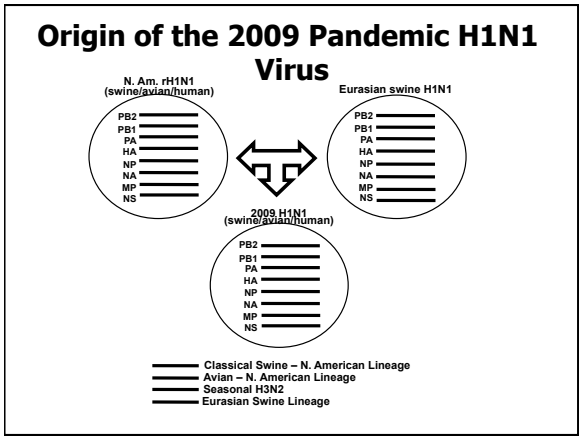

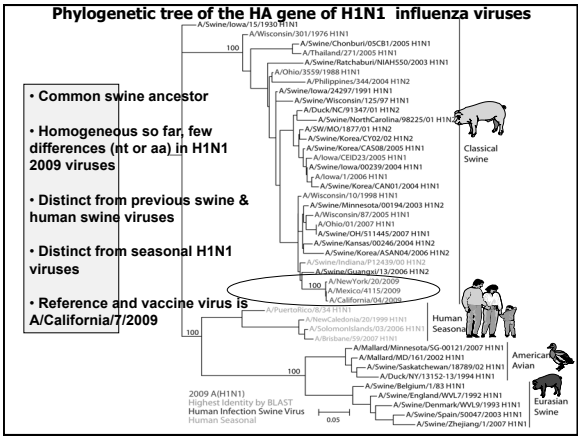

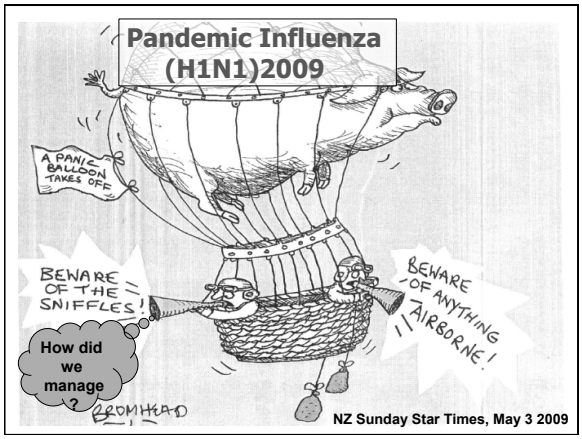

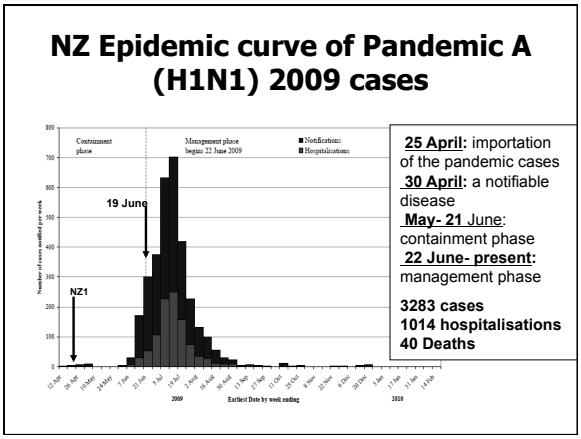

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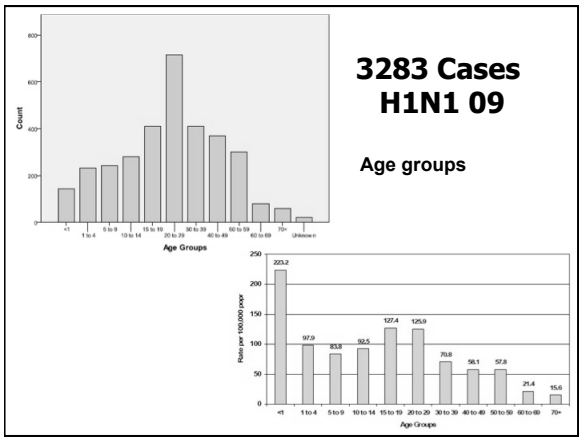

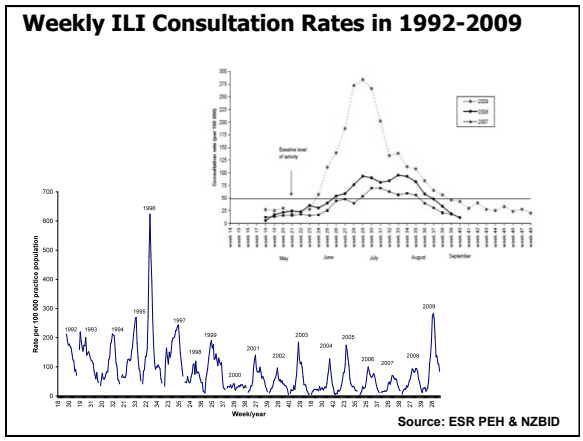

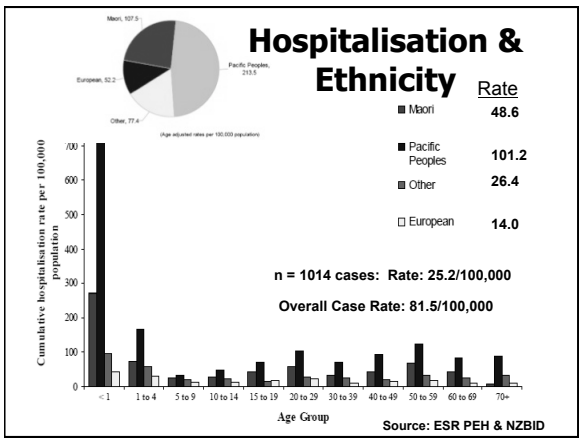

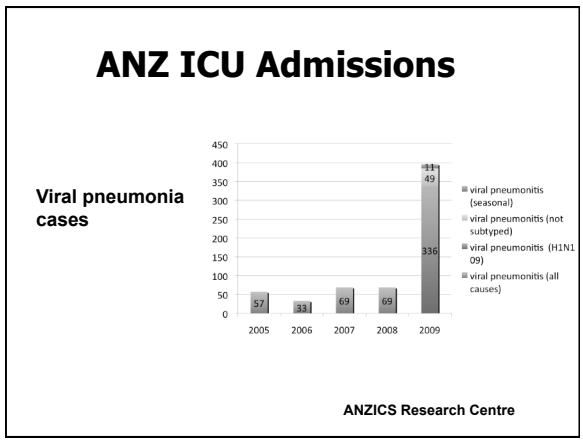

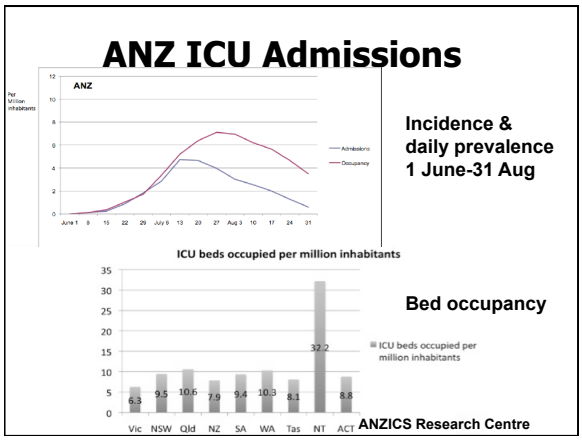

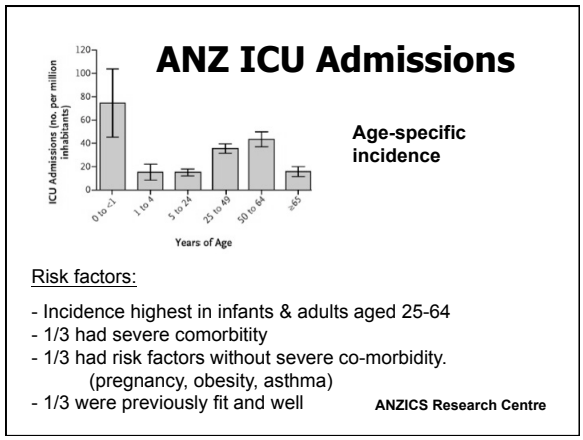

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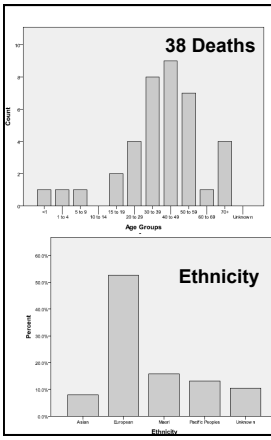
ANZ ICU Admission Summary

- 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 7.4days
- Risk factors:
  - Incidence highest in infants & adults aged 25-64
  - 1/3 had severe comorbitity
  - 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)



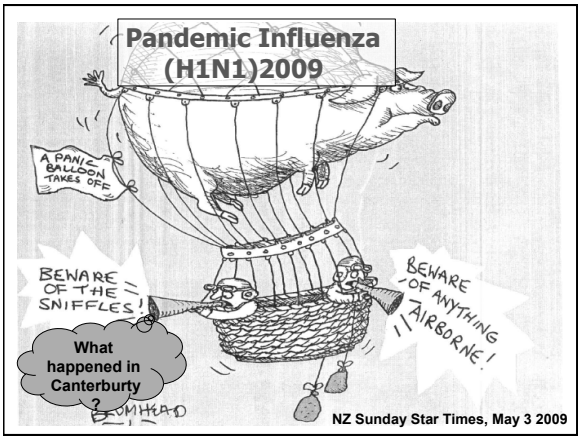
Deaths

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%

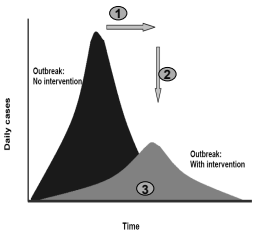


NZ Sunday Star Times, May 3 2009

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

Figure 1: Objectives of implementing public health measures



Containment 'Keep It Out' Phase

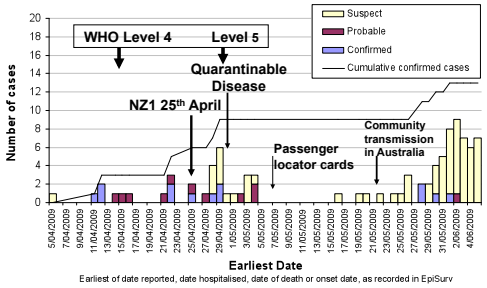
Border Closure vs Border Management

Effectiveness?

- WHO has placed little emphasis on border closure except for 'isolated communities' Positive pratique of all incoming aircraft and ships (ie, 100% health status reported from all aircraft).

- New Zealand's response
  - Positive pratique (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

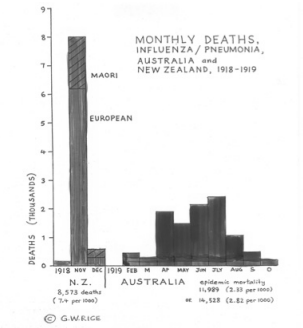
Containment Phase, April-May 2009

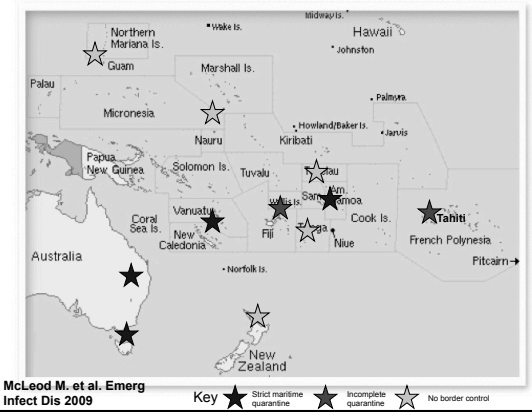


Earliest of date reported, date hospitalised, date of death or onset date, as recorded in EpiSurv

NHCC data 2009

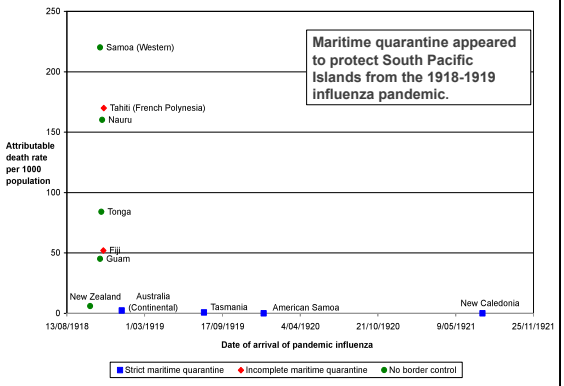
NZ & Australia 1918-19 Pandemic





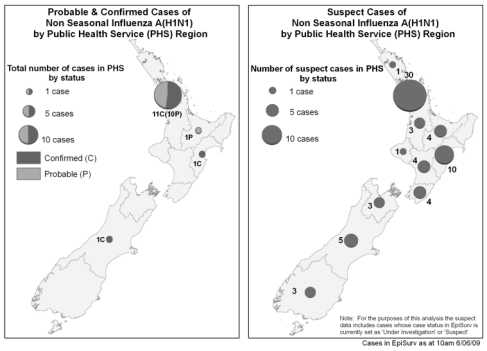
McLeod M. et al. Emerg Infect Dis 2009

Pacific Island Nations 1918-19 Pandemic



McLeod M. et al. Emerg Infect Dis 2009

6th June: A(H1N1)2009 Cases

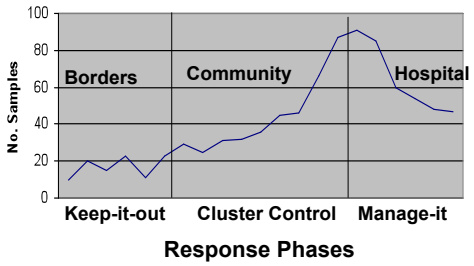


Comparison of Available Influenza Diagnostic Tests

Influenza Diagnostic Tests	Method	Availability	Typical Processing Time	Sensitivity for influenza H1N1 2009	Distinguishes 2009 H1N1 influenza from other influenza A viruses?
Rapid influenza diagnostic tests (RIDT)	Antigen detection	Wide	0.5 hour	10 – 70%	**No**
Direct and indirect immunofluorescence assays (DFA and IFA)	Antigen detection	Wide	2 – 4 hours	47–93%	**No**
Viral isolation in tissue cell culture	Virus isolation	Limited	2 -10 days	-	**Yes**
Nucleic acid amplification tests (rRT-PCR)	RNA detection	Limited	48 – 96 hours [6-8 hours to perform test]	86 – 100%	**Yes**

Canterbury Health Laboratories

Laboratory: Pandemic Planning



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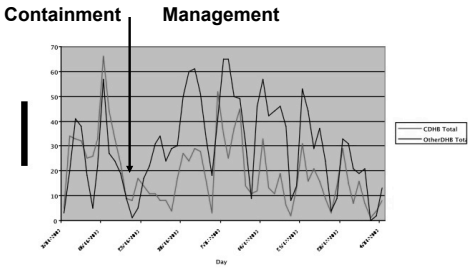
Laboratory: Pandemic Reality



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PCR Automation:

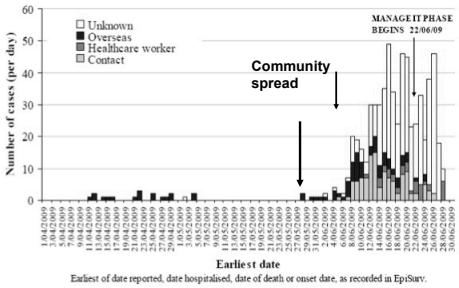
Abbott m2000sp Diagnostic Platform

RealTime PCR System

Canterbury Health Laboratories

Containment:

Cases & Risk Factors April-June



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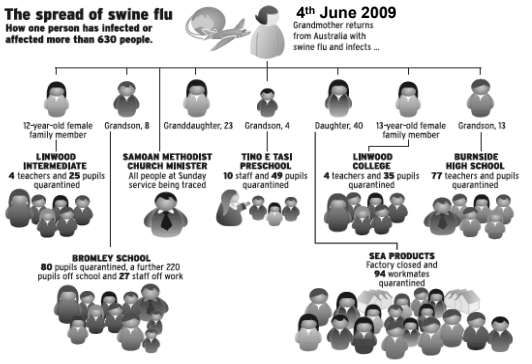
Christchurch Pacific Island Cluster



The Press, 12th June 2009

Analysis of Epi Data for Pandemic Decision Support

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

Location	Cases	Exposed non cases
Christchurch	35	367
Wellington	45	0
Auckland	7	57

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

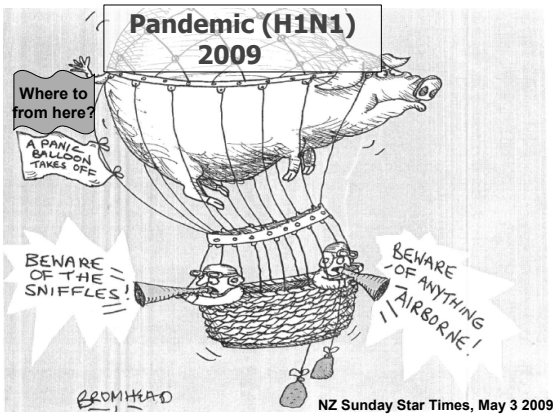
Possible risk factor	Risk group	Average effective reproductive ratio (n)	Serial interval or average onset to onset interval in day (n)
Sex	F	0.86 (44)	2.6 (35)
	M	0.81 (54)	3.4 (39)
Age group	0-5 years	1.62 (29)	2.88 (24)
	6-12 years	0.23 (13)	2.42 (12)
	13-19 years	0.20 (10)	2.22 (9)
	20-39 years	0.66 (38)	3.30 (27)
	40-59 years	0.14 (7)	2.43 (7)
	60+ years	4.00 (1)	
Ethnicity	Samoan (Chch)	0.83 (54)	2.4 (46)
Ethnicity (taken from a subset of the data)	Asian	0.33 (3)	3 (2)
	European	0.52 (21)	3.9 (18)
	Maori	1.29 (7)	2.8 (4)
	Pacific	0.92 (60)	2.4 (50)
Onset to Tamiflu interval	0-2 day	0.77 (58)	3.1 (53)
	> 2 days	1.25 (30)	2.3 (15)
Grand Total		0.84 (98)	2.84 (79)

Cluster Control Data: Attack Rates

Ethnicity of exposed	Count of exposed non cases	Count of exposed that became cases	Attack rate
European	42	7	14%
Samoan	83	35	30%
Age group of exposed			
0-5	90	29	24%
6-12	78	13	14%
13-19	115	10	8%
20-39	59	38	39%
40-59	39	7	15%
60 +	9	1	10%
Tamiflu Prophylaxis	388	1	0.26%
No Tamiflu Proph	36	97	85.84%

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



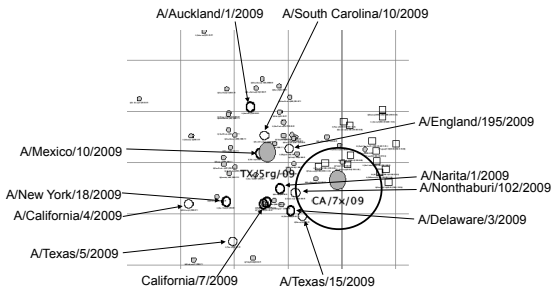
NZ Sunday Star Times, May 3 2009

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

(CDC, 54 antigens; 16 sera)



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, ?25% 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

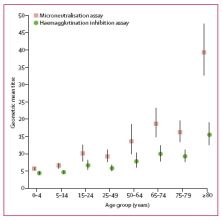


Figure 1: Geometric mean titre by age group as measured by the haemagglutination inhibition and microneutralisation assays in baseline serum samples obtained in 2008
Error bars represent 95% CIs

Miller et al The Lancet 2010

Antivirals: BMJ Article- Cochrane Review Seasonal Influenza

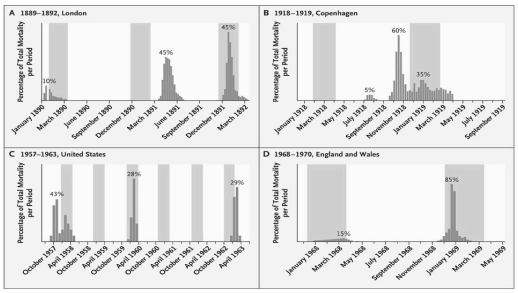

BMJ RESEARCH
Neuraminidase inhibitors for preventing and treating influenza in healthy adults: systematic review and meta-analysis

Measure	Oseltamivir	Zanamivir
Symptomatic laboratory confirmed influenza	75mg 61% (0.18-0.85) 150mg 73% (0.11-0.67)	10mg 62% (0.17-0.85)
Post exposure prophylaxis	58% (15-79%) Households: 84% (49-95%)	Households: 79%[1]
Alleviation of ILI	1.20 (1.06-1.35)	1.24 (1.13-1.36)
Reduction of influenza-related LRTIs	Not effective (0.22-1.35)	n/a
Side effects	Nausea (1.10-2.93)	n/a

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

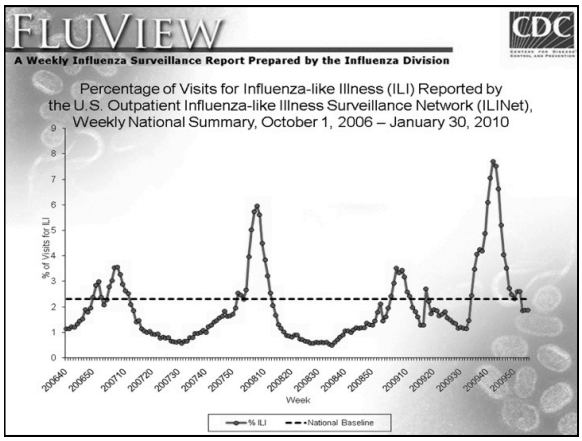


Miller M et al. N Engl J Med 2009;10.1056/NEJMp0903906

Google trends mapping world influenza

www.google.org/flutrends

WHO Collaborating Centre for Reference and Research on Influenza Melbourne



UK ILI Consultation Rates

Figure 2: RCGP weekly consultation rate for influenza-like illness 2009/10 and recent years

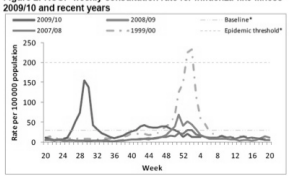
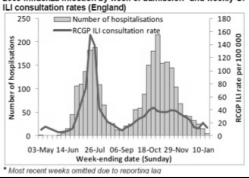


Figure 8: Hospitalised cases with confirmed pandemic (H1N1) 2009 influenza infection by week of admission* and weekly GP ILI consultation rates (England)



* Most recent weeks omitted due to reporting lag

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