#### Investigating severe and fatal influenza



#### Colin McArthur

Clinical Director Department of Critical Care Medicine Auckland City Hospital

Vice-Chair Clinical Trials Group Australia and New Zealand Intensive Care Society







# **ANZ Intensive Care Influenza Registry**

- Established in 5 weeks (May 2009)
- Prospective; broad but not deep
- All 187 ANZ ICUs June 1 August 31
- >95% case ascertainment
- 901 ICU admissions due to influenza A (11% not subtyped, 4% seasonal)

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766 admissions with H1N1 2009 diagnosed by PCR (or specific serology)
 722 with full data available at analysis; 119 admissions to NZ ICUs

Additional data collected retrospectively on

- 64 admissions during pregnancy or 28d post-partum
- 68 cases receiving ECMO (confirmed and suspected H1N1 09)







# ICU Admissions per week by region









# ANZ: Duration of ICU stay

ANZICS Clinical Trials Group

- Median ICU LOS = 7.4 days
- Median hospital
  LOS = 12.3 days







## NZ ICU admissions and occupancy



# Incidence of ICU admission by age









### NZ ICU admissions by ethnicity









# Co-morbidity / risk factors

	ANZ	NZ
	incidence	incidence
BMI > 35 kg/m <sup>2</sup>	29%	33%
Pregnancy	9%	7%
(including 28d postpartum)	(64 cases)	(7 cases)
Severe co-morbidity	28%	23%
(immune suppressed, cancer, severe CVS/RS disease, liver or renal failure)		
Chronic lung disease	33%	29%
(CORD, asthma, restrictive, infective)		
No pre-existing disease	32%	45%







## ANZ: Pregnancy and post-partum risk

Gestation at symptom onset	ICU admit	Absolute	Relative risk
Non-pregnant women 15 – 44 yrs	145	1 : 35,300	1
<20 weeks	10	1 : 14,600	<b>2.4x</b> (95% CI 1.3 – 4.6)
≥20 weeks	49	1 : 2700	(95% CI 9.6 – 18.3)
Post-partum 0 – 28d	5	1 : 5500	<b>6.4x</b>
			BMJ 2010; 340:c1279







## **Clinical Syndromes**



Viral pneumonitis / ARDS (50%)

- Diffuse bilateral infiltrates; bacterial culture negative
- Respiratory failure: difficult oxygenation > difficult ventilation
- Multiple organ failure infrequent



#### Secondary bacterial pneumonia (20%)

- S. pneumoniae, S. aureus, (MSSA/MRSA), S. pyogenes most common
- Multiple organ failure common



#### **Airflow limitation**

- Bronchiolitis & croup in infants / children
- Exacerbation of asthma or chronic obstructive pulmonary disease







# Hospital outcome



Censoring of data was a limitation of early publication

Factors associated with mortality:

- Age (> 65 years OR = 6.9, compared to <4 years)</li>
- Any severe co-morbidity (OR = 2.6)
- Mechanical ventilation at ICU admission (OR = 5.5)

6 November: 94% discharged from hospital, mortality 16% NZ final mortality for ICU cases = 21/119 (17.6%)







# **ANZ Pregnancy outcomes**

- 29% delivered prior to ICU admission
- 22% delivered during ICU (93% by Cesarean section, indications maternal not fetal)

#### Baby outcomes

- 49% preterm
- 71% neonatal ICU admssion
- 4 fetal deaths, 3 neonatal deaths
- 2/20 tested were H1N1 positive

#### Maternal outcomes

- 69% ventilated (similar syndromes to non-pregnant)
- 14% ECMO
- 11% mortality







#### Hospitalisation trends 2010 vs 2009

Weekly Influenza Hospitalisations



## Regional trends 2010 vs 2009

Lab-confirmed Pandemic H1N1 Hospitalisation Rates (per 100,000 by DHB of domicle) 2009 vs 2010 (to 14 October 2010)



## ANZ intensive care 2010 vs 2009



# ANZ intensive care 2010 vs 2009

- Australia 7.2 vs 35.2 per million
- NZ 17.9 vs 28.3 per million
  - higher rate of community infection rather than severity of illness
- Maximum daily ICU occupancy
  - 2.0 vs 7.4 per million
- 17% of ICU admissions had been vaccinated









#### Pandemic Influenza Mortality and Morbidity Review Group

- Ministerial committee "To review mortality & morbidity related to pandemic influenza A(H1N1)"
- Definition: The death of a person with confirmed influenza A(H1N1) 2009 infection from a clinically compatible illness or complications attributable to that infection, with no period of complete recovery between illness and death, and no alternate cause of death
- Identification (49 cases in 2009, 26 in 2010)
  - EpiSurv (notifiable disease database) n=42
  - NHI matched EpiSurv +ve tests & death registry n= 5
  - Child & Youth Mortality Review Committee (CYMRC) database n=1
  - Hospital discharge coding (National Minimum Dataset) n=1
- Clinical Data sources hospital & GP records, autopsy (43%)

#### Influenza mortality rates











# Mortality by age group









# Mortality by ethnicity









# NZ socioeconomic deprivation scores (NZDep)









<b>Co-morbidities/</b> associated conditions	Total deaths (N=49)			
• 	n	N	%	
Immunocompromised	4	45	9	
Malignancy	4	46	9	
Cardiac disease	6	48	13	
Haemoglobinopathy	1	46	2	
Metabolic disease	2	46	4	
Respiratory disease	22	45	(49)	
Asthma	9	45	20	
Other respiratory disease	13	45	29	
Diabetes	6	45	13	
Neurological disease (respiratory impairment)	2	45	4	
Morbid obesity: ≥35	18	32	56	
Obesity: ≥30	23	32	74	
Pregnant or postpartum (to 42 days)	4	49	8	
Substance abuse	8	42	19	
Alcohol abuse	5	40	13	
Recreational drug use or methadone	3	41	7	
No co-morbidity/associated condition noted	7	49	(14)	







# Deaths: syndromes at presentation

Influenza syndromes	Total d (n=4		
	n	%	
Classical influenza-like illnesses (ILI)* with no other symptoms	4	8	41%
ILI plus other symptoms	16	33	
Fever, no ILI, other symptoms**	7	14	
No fever or ILI , other symptoms only**	18	37	
Insufficient information to categorise	4	8	

\*Influenza-like illness (ILI) is defined as (i) history of fever, chills, and sweating and/or clinically documented fever ≥38 °C, plus (ii) cough or sore throat" (MOH 2009) \*\* 43% presented with shortness of breath; 10% confusion/drowsiness







# Deaths at home

- 16 cases died unexpectedly at home:
  - 5 had prior contact with health professional
  - 7 cases not been seen by any health services
  - 4 not known

## Autopsy (43%)

- 17 had pneumonia
- 2 pulmonary thromboembolism
- 2 pulmonary oedema









#### RESEARCH

#### The NEW ENGLAND JOURNAL of MEDICINE

Critical illness due to 2009 A/H1N1 influenza in pregnant and postpartum women: population based cohort study

The ANZIC Influenza Investigators and Australasian Maternity Outcomes Surveillance System

BMJ 2010; 340:c1279

Critical Care Services and 2009 H1N1 Influenza in Australia and New Zealand

The ANZIC Influenza Investigators\*

NEJM 2009; 361 Oct 8



Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome

Online article and related content current as of October 12, 2009.

The Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators

JAMA 2009; 302(17) Oct 12





