

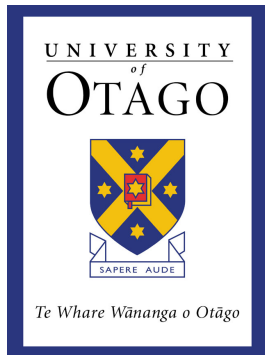
Influenza Globally

Lance Jennings

APACI Influenza Workshop,

Kuala Lumpur, Malaysia,

24 October 2016

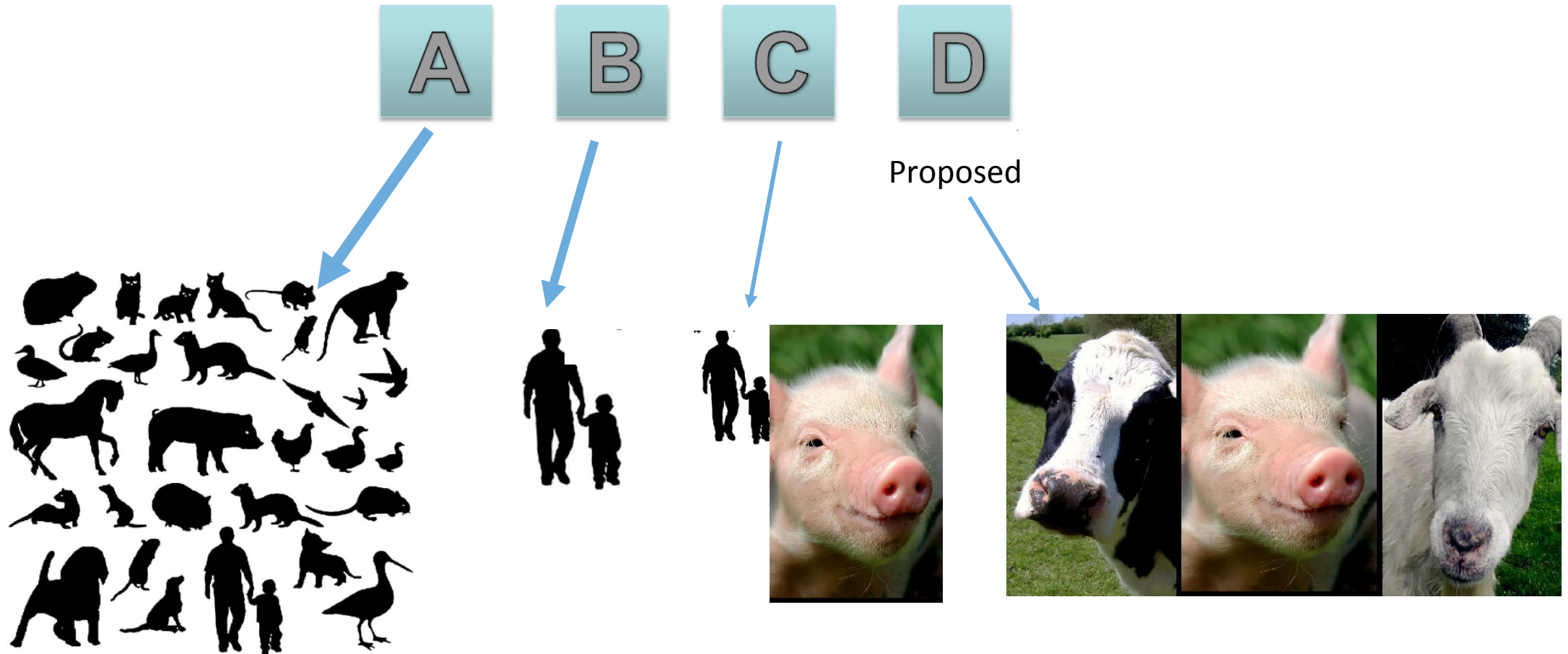


Outline

SESSION 1: Impact of Influenza

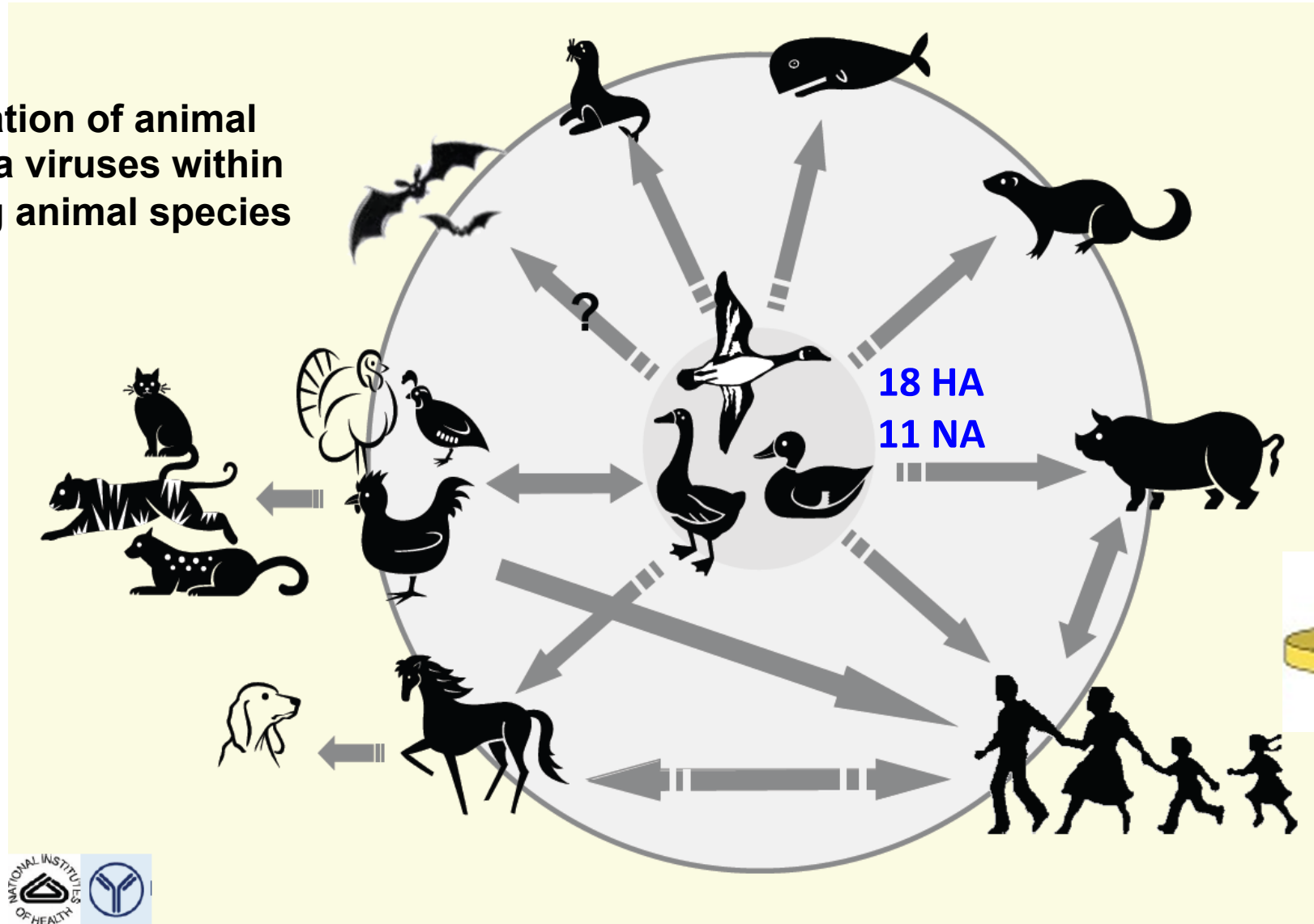
- Influenza
- Understanding the disease
- Measuring the impact
 - Global surveillance
 - Regional surveillance
 - Hospitalisation
 - Mortality
- Importance of understanding burden for policy development

Influenza Types

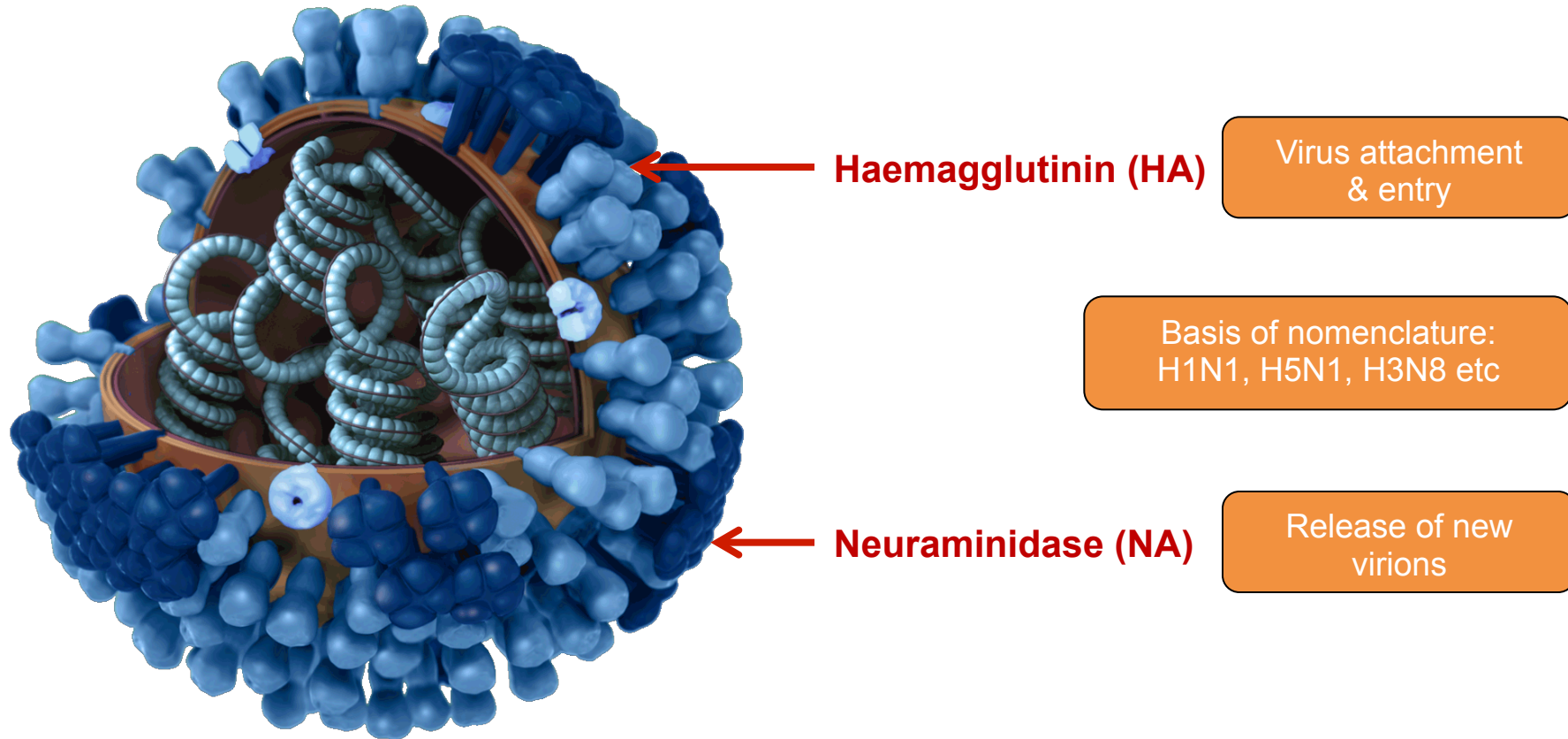


Animal-human interface of influenza A virus

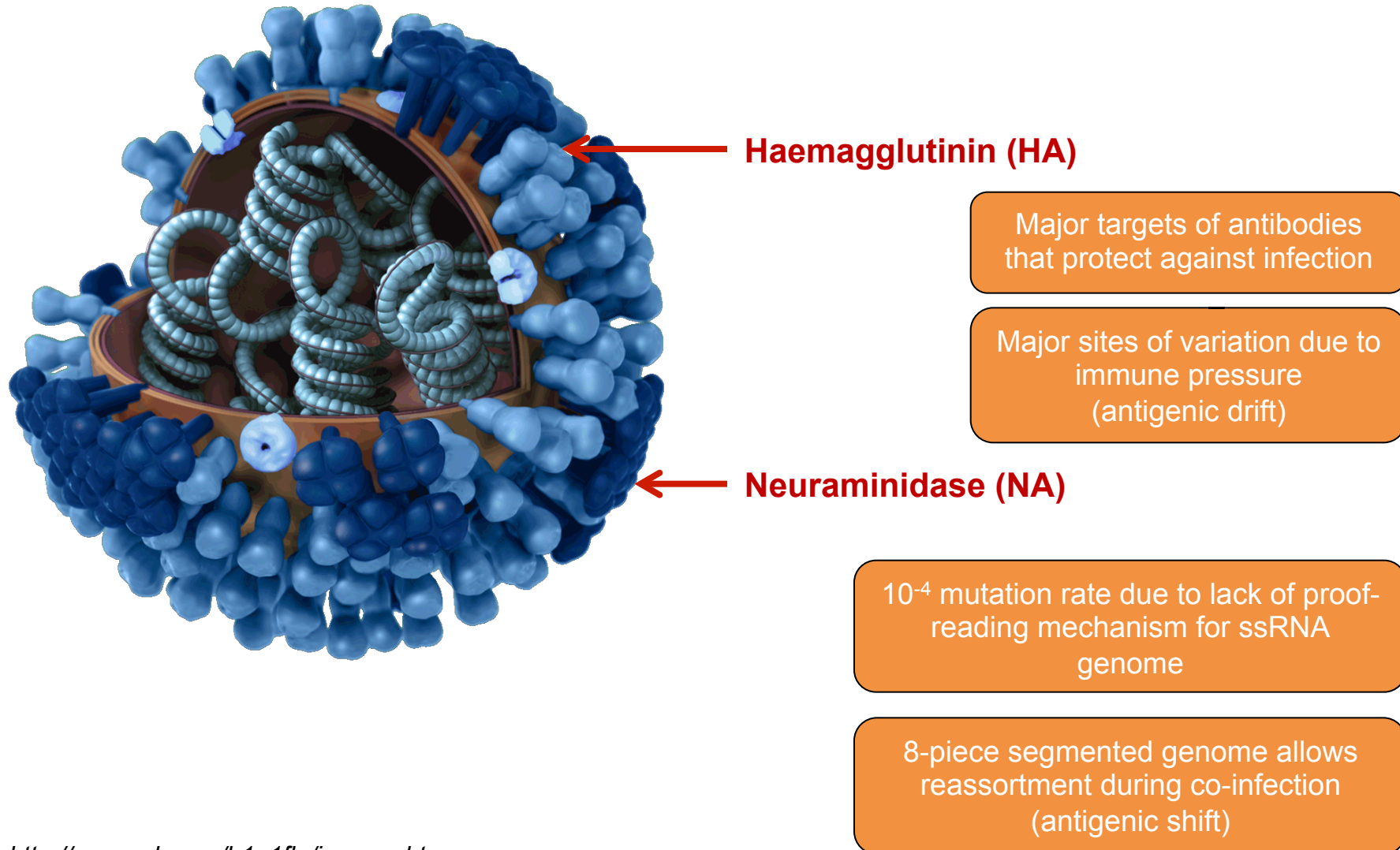
Circulation of animal influenza viruses within & among animal species



Influenza A viruses

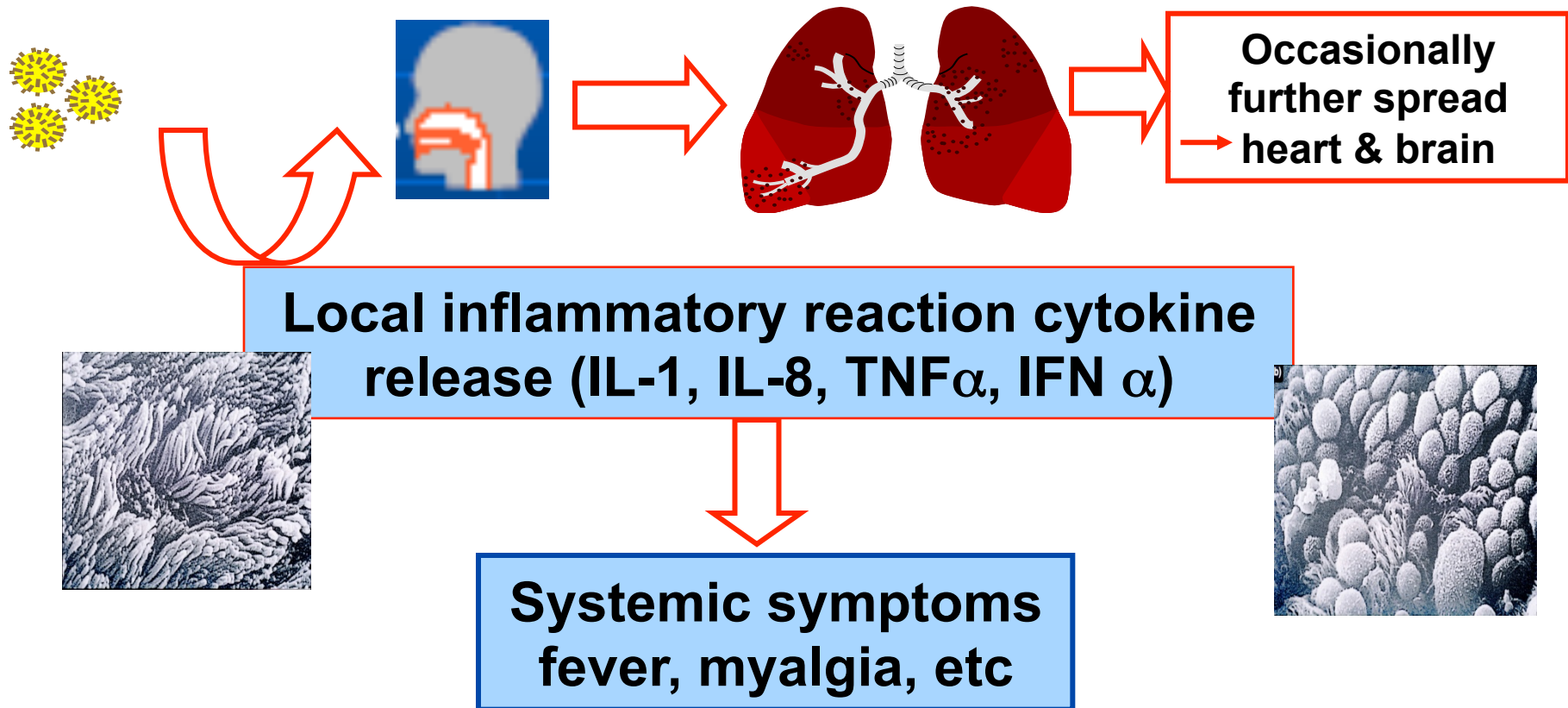


Influenza A viruses



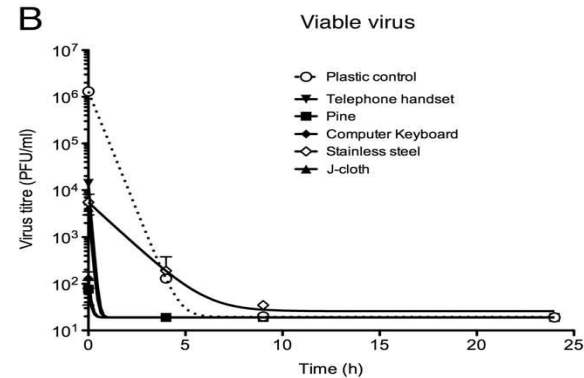
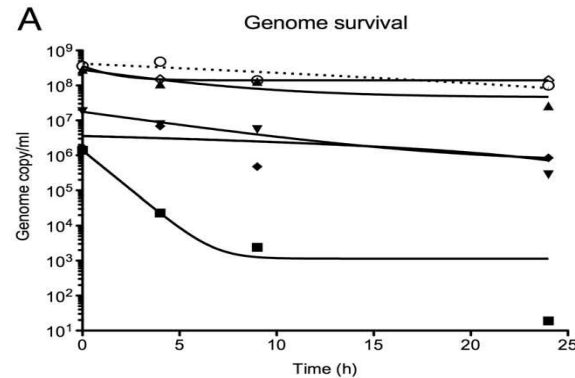
Influenza: pathology of infection

Infection of upper respiratory tract (possibly eyes)
Sometimes direct infection of/or spread to lung

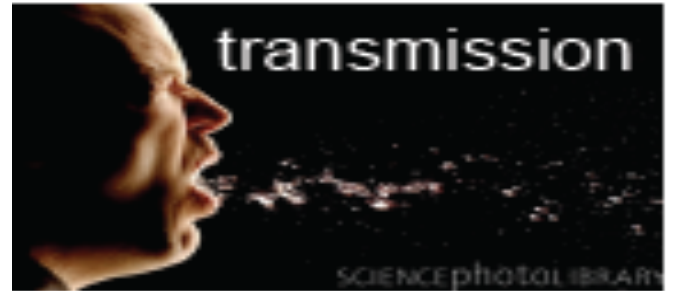


Transmission

- Aerosols and droplets, Direct contact, fomites
 - ? Relative importance

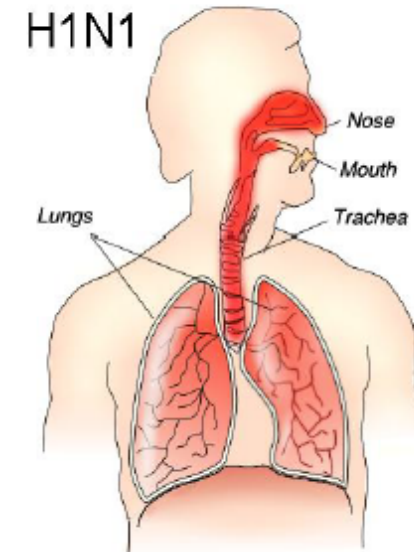
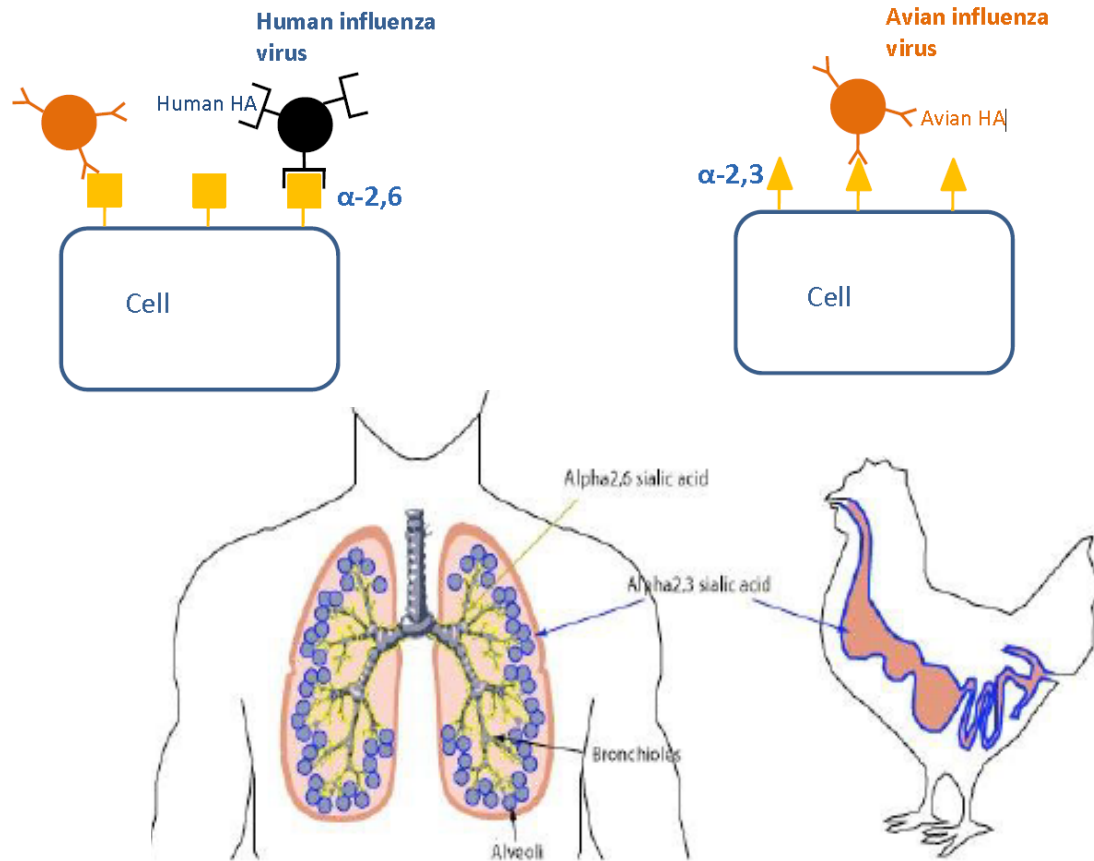


Household surfaces
Greator *et al.* PLoSOne2011

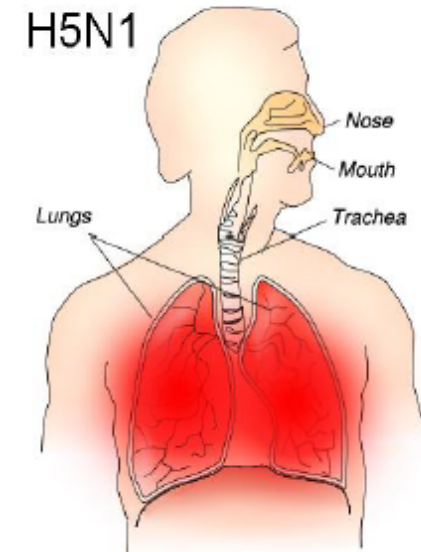


- Through the air
 - Large droplets >5mm travel short distances
 - Small droplets <5mm and aerosols 1mm travel more than 2 metres
(Implications for guidelines on bed spacing in wards)

Receptor binding specificity and the balance between pathogenicity and transmission

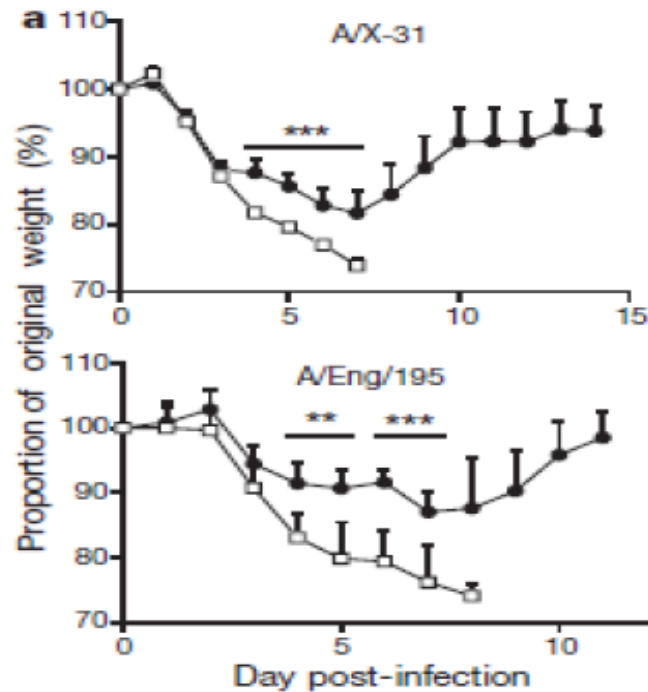


Easily spread
Rarely fatal

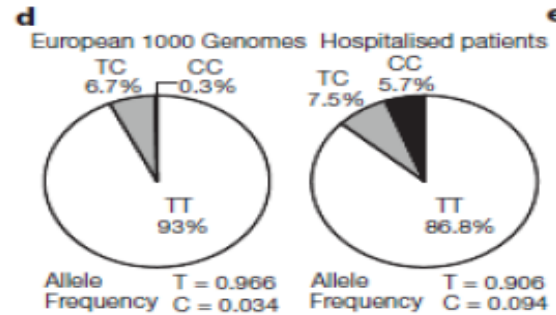


Spreads slowly
Often fatal

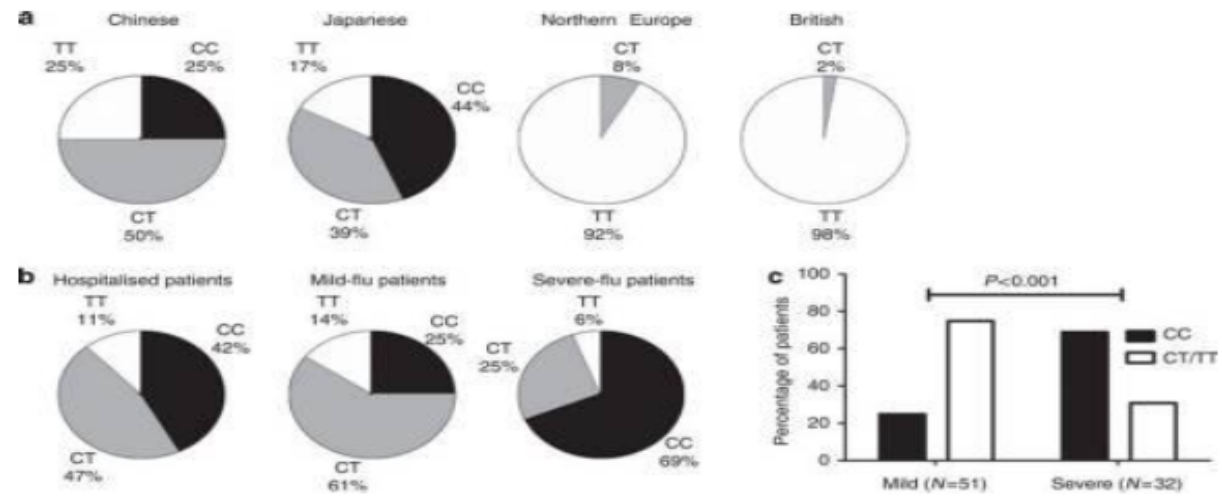
Genetic determinants of influenza susceptibility: Mice & people lacking IFITM3 prone to severe influenza



Everitt et al. Nature 2011;



Interferon-induced transmembrane proteins inhibit infection



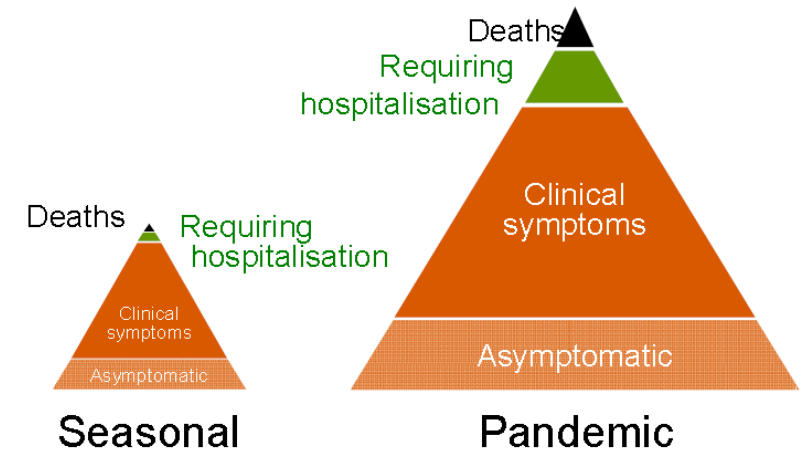
Dong et al. Nature Med 2013;

Why is influenza important?

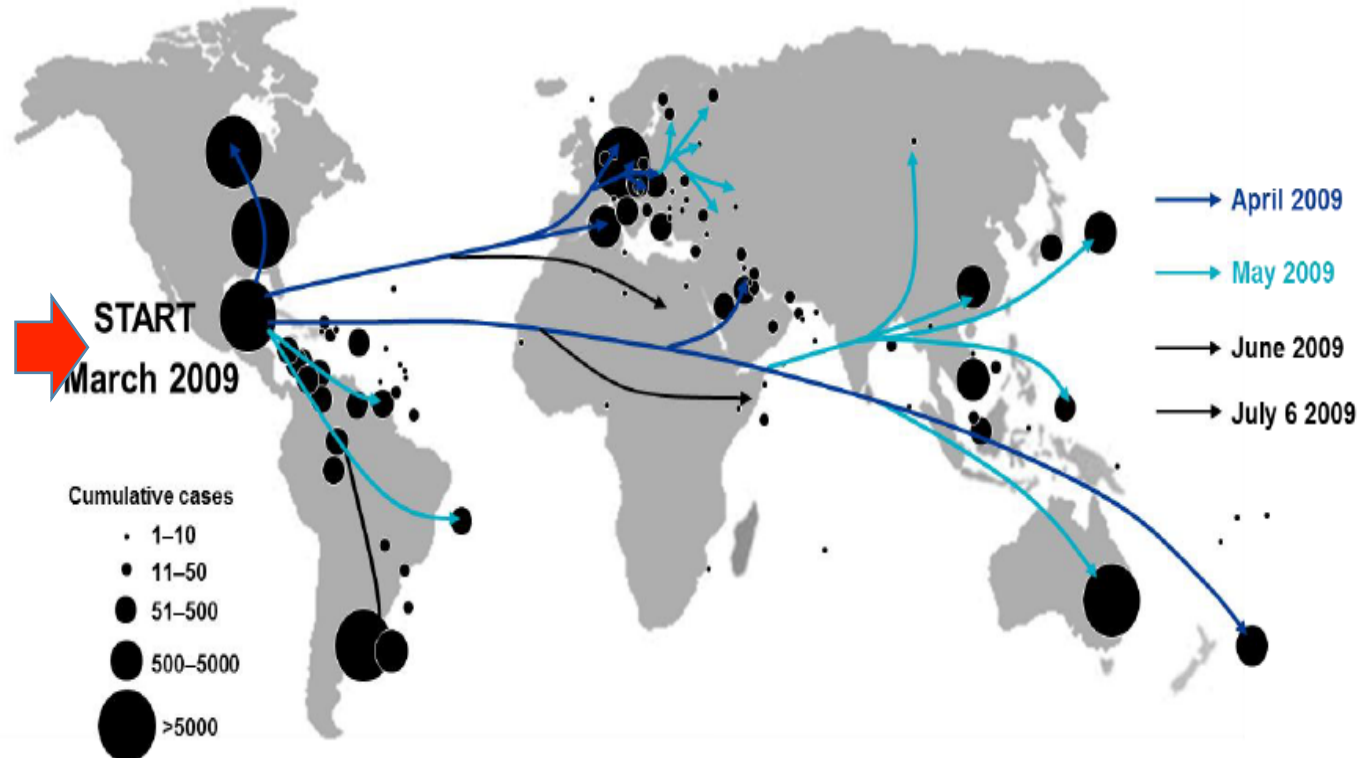
- Influenza viruses cause infections and diseases in all age groups during epidemics.
- Severe disease particularly in the extremes of age.
- Influenza virus infections have a high incidence: varies as high as 20-30% in children and 10-20% in adults in epidemics.
- Most infections associated with mild disease, some fraction of infections are asymptomatic.

Pandemic influenza

- Influenza A virus that is novel in humans
- Majority of global population susceptible (no pre-existing antibodies)
- Able to spread easily from human-to-human
- Causes clinical illness (symptomatic infection)
- Not necessarily more severe than seasonal influenza, but potential to be so not excluded.

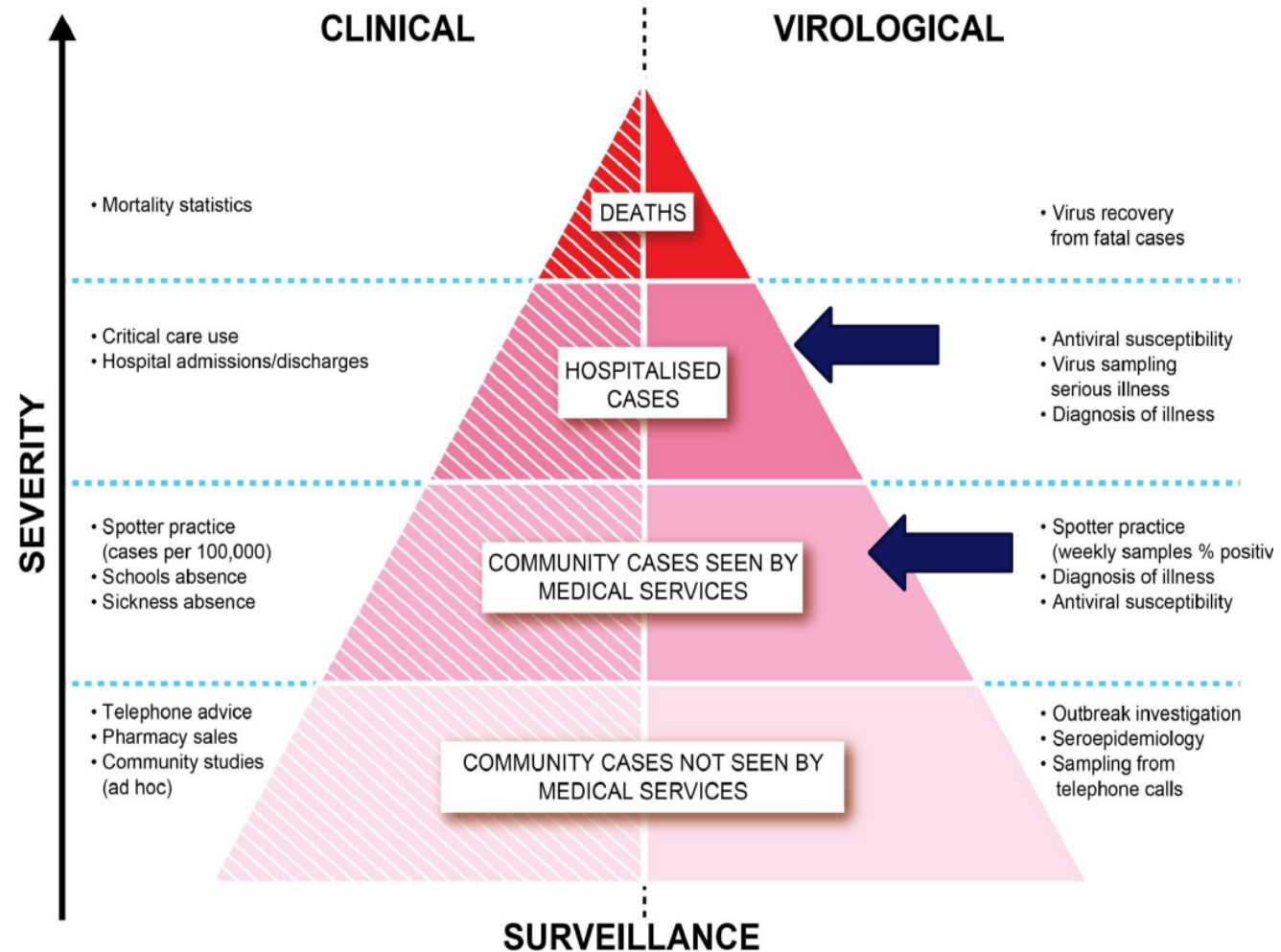


H1N1pdm09 Pandemic



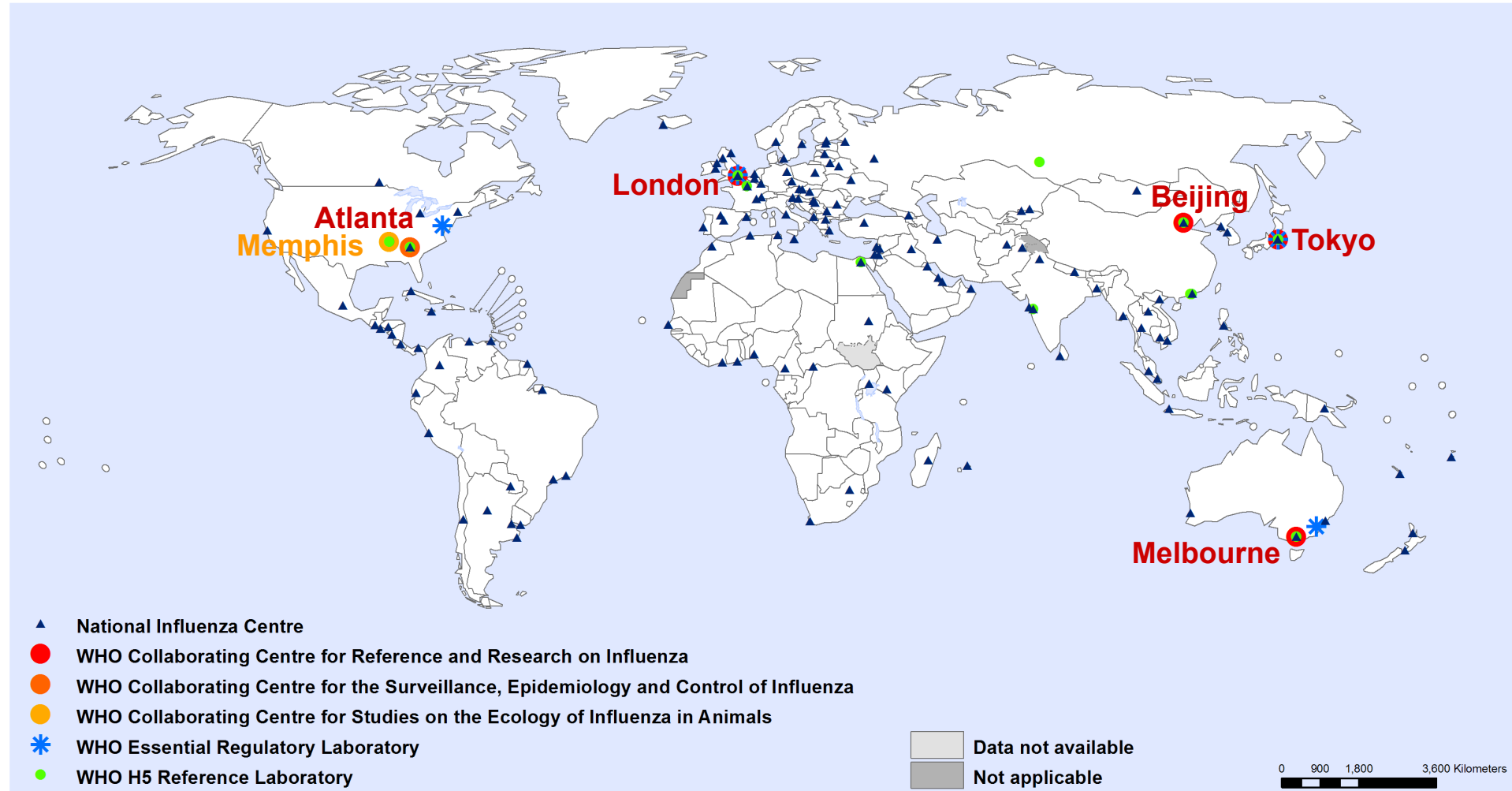
Pandemic	Est No. Deaths
1918 H1N1	20-40x10 ⁶
1957 H2N2	1 x 10 ⁶
1968 H3N2	7 x 10 ⁵
2009 H1N1p09	2 x 10 ⁴ - 3 x 10 ⁵

Understanding the impact of seasonal influenza



WHO Global Influenza Surveillance and Response System (GISRS)

25 September 2012



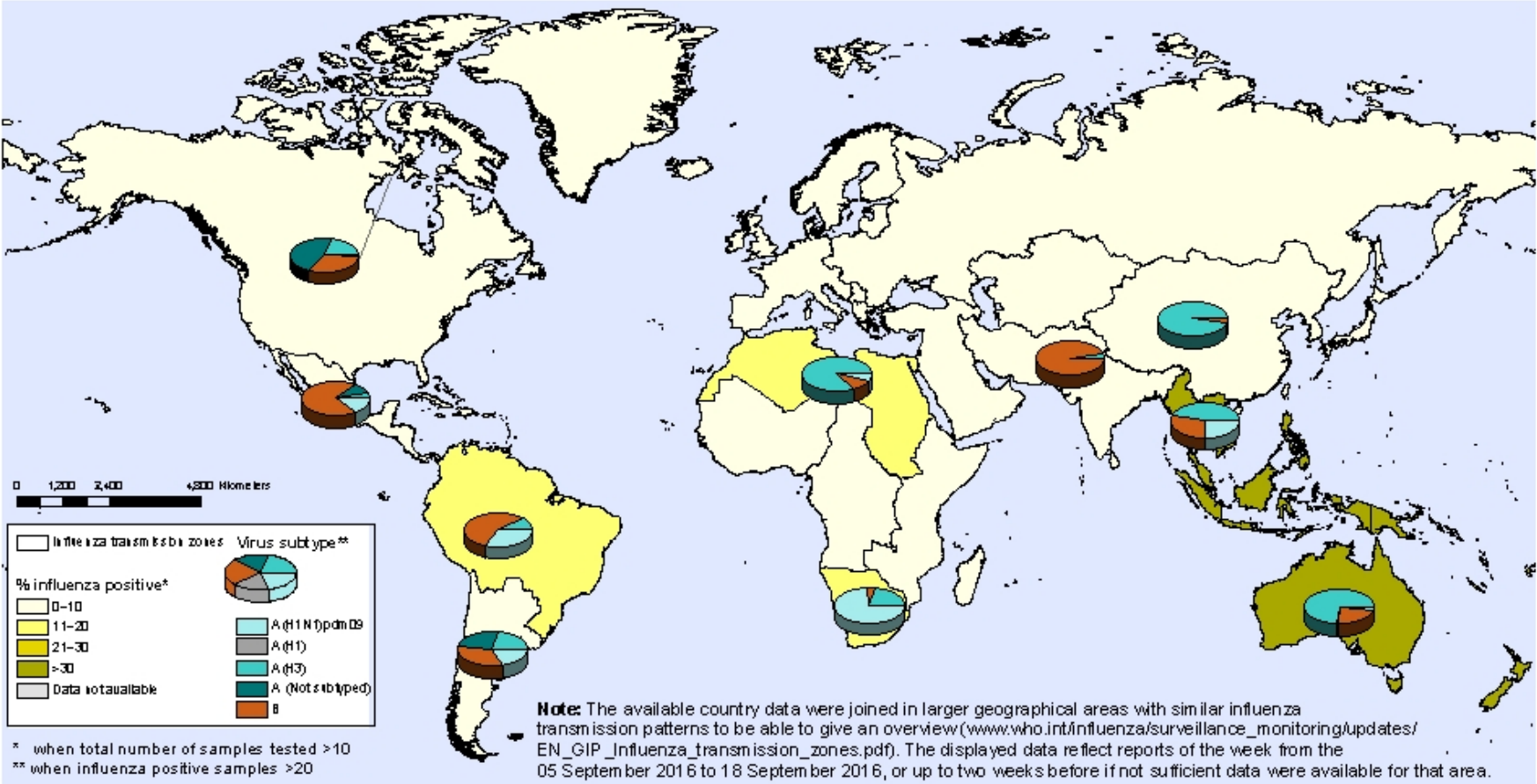
141 WHO National Influenza Centres in 111 countries (>92% population)
5 WHO Collaborating Centres for Influenza (human), one for animal
13 H5 Reference Laboratories
4 Essential Regulatory Laboratories (FDA, TGA, NIBSC, NIID)

Coordinated by WHO
Global Influenza Program
in Geneva

Global picture to September 2016

Percentage of respiratory specimens that tested positive for influenza
By influenza transmission zone

Status as of 30 September 2016



Viruses (September)
73 countries

Total 44,178/2763 pos

Influenza A: 81.8%

Influenza B: 18.2%

A(H1N1)pdm09: 12%

A(H3N2): 88%

B-Yam: 24.6%

B-Vic: 75.4%

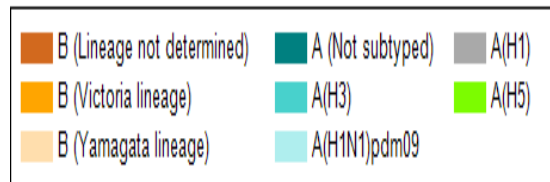
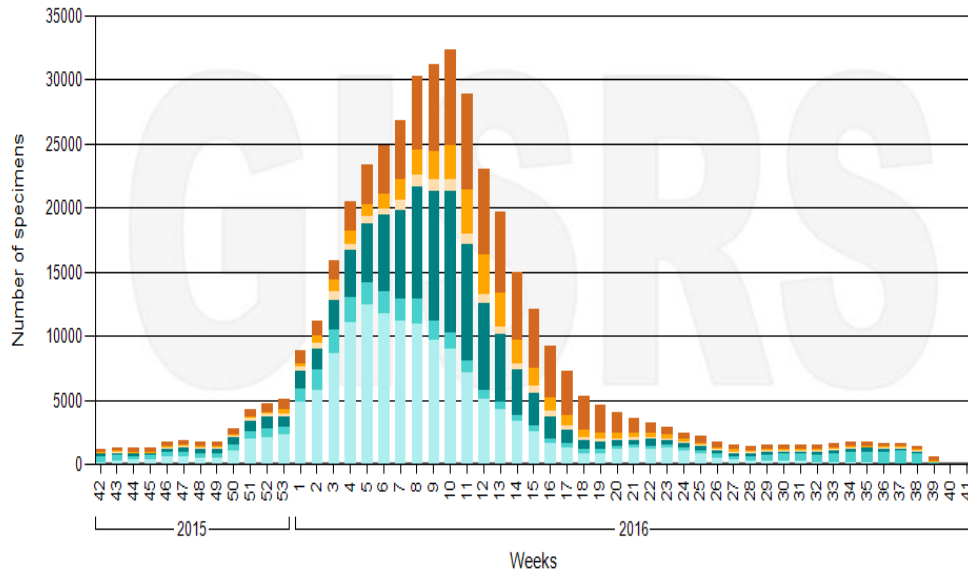
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Influenza Surveillance and Response System (GISRS), FluNet (www.who.int/flu-net).

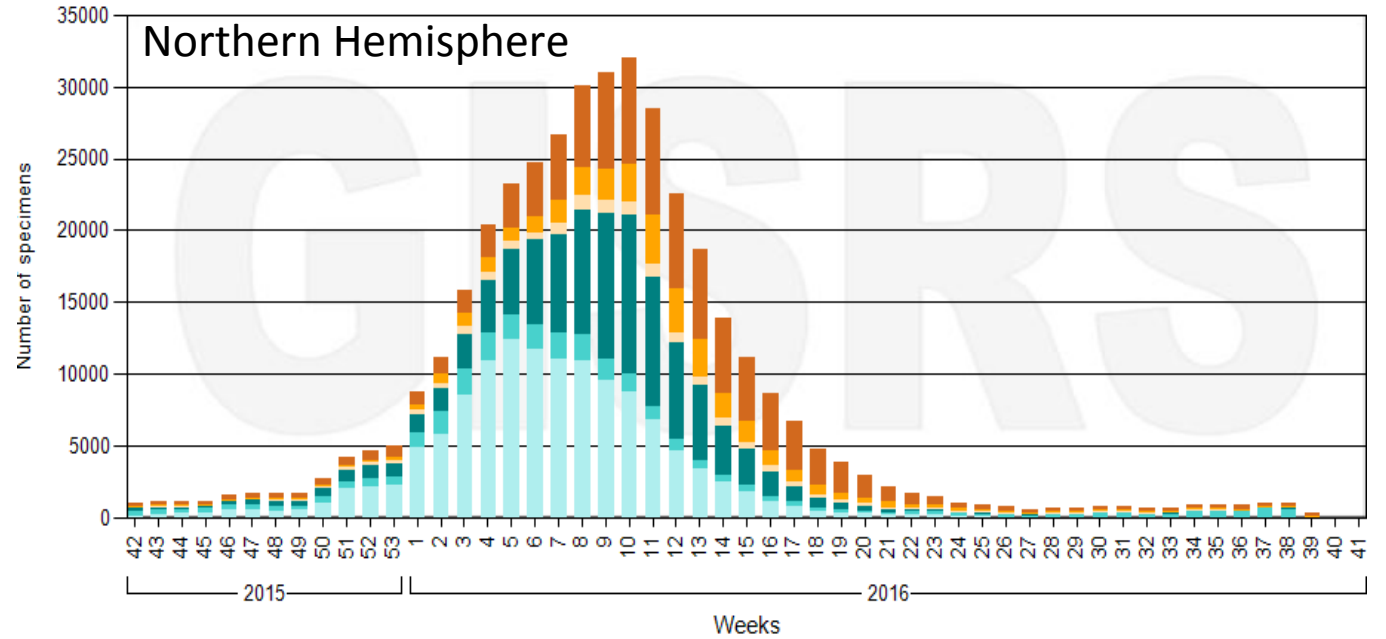
Global, Northern & Southern Hemisphere activity

Global 2015-2016

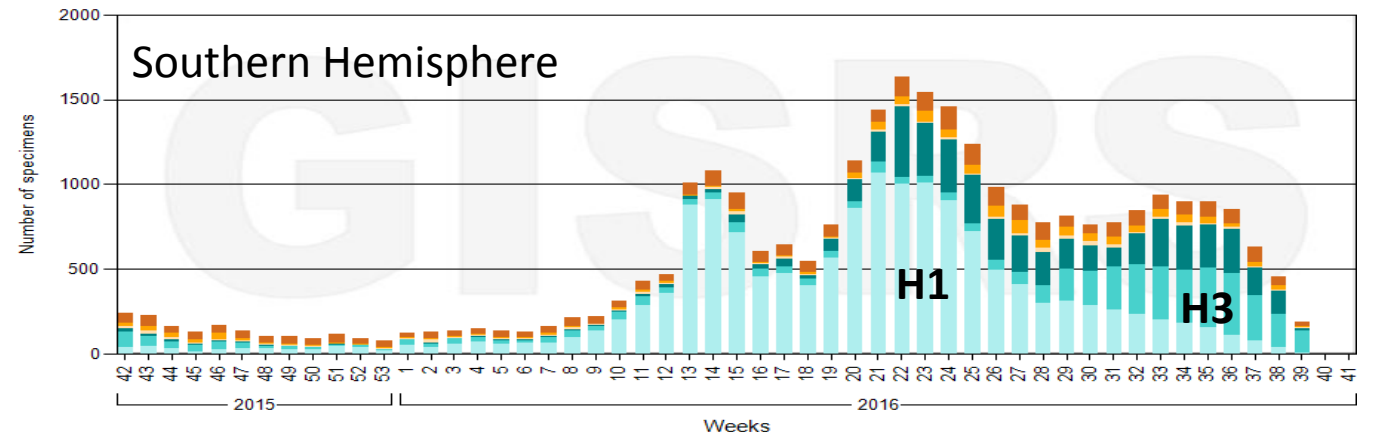
Number of specimens positive for influenza by subtype



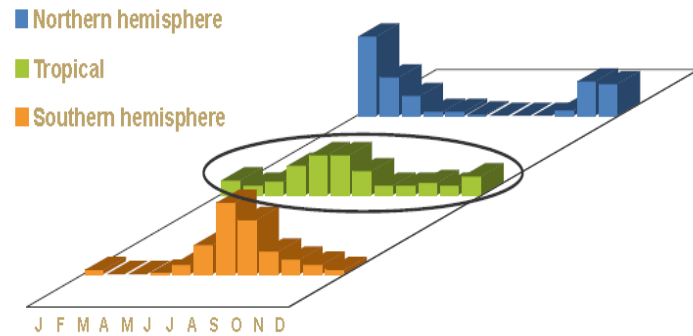
Number of specimens positive for influenza by subtype



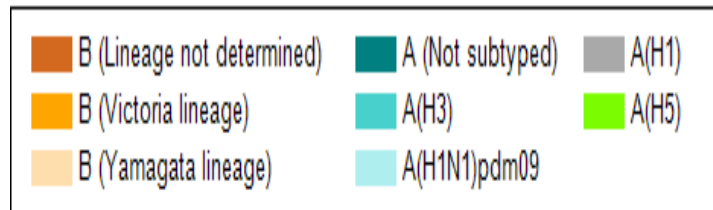
Number of specimens positive for influenza by subtype



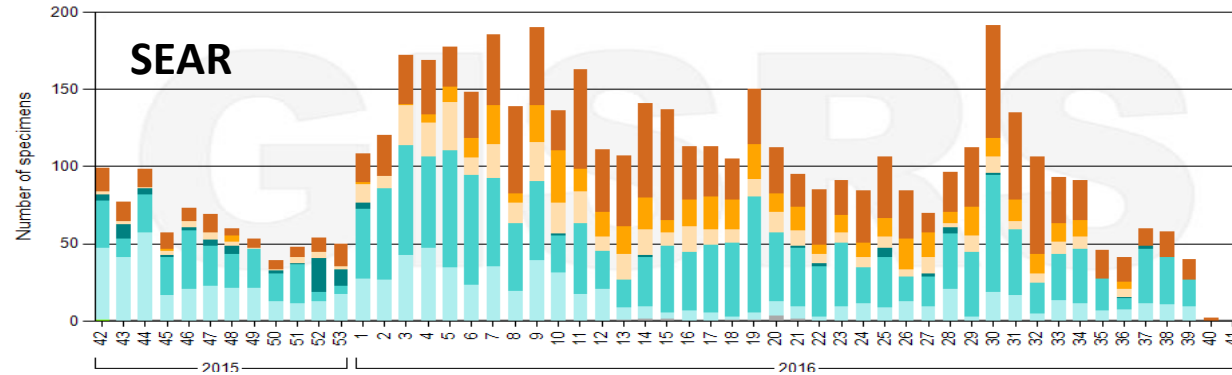
South East Asian & Western Pacific WHO Regions



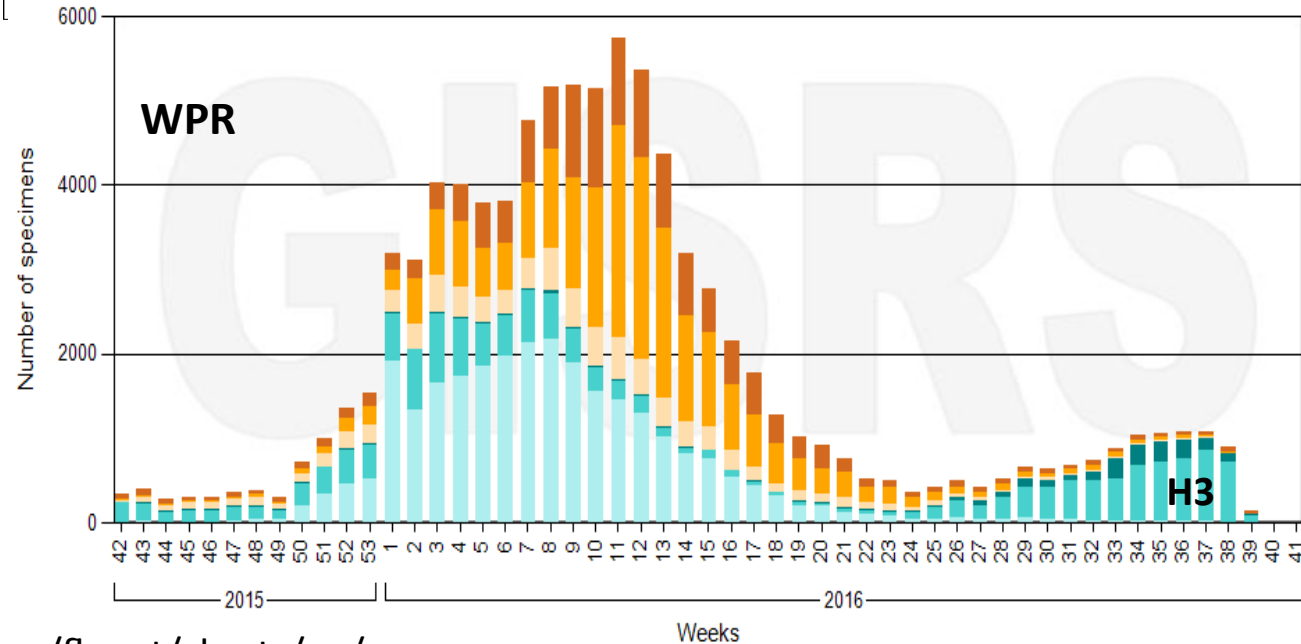
Reichelderfer PS *et al* Influenza surveillance in the Pacific basin in: Current topics in medical virology 1998;41:2-38



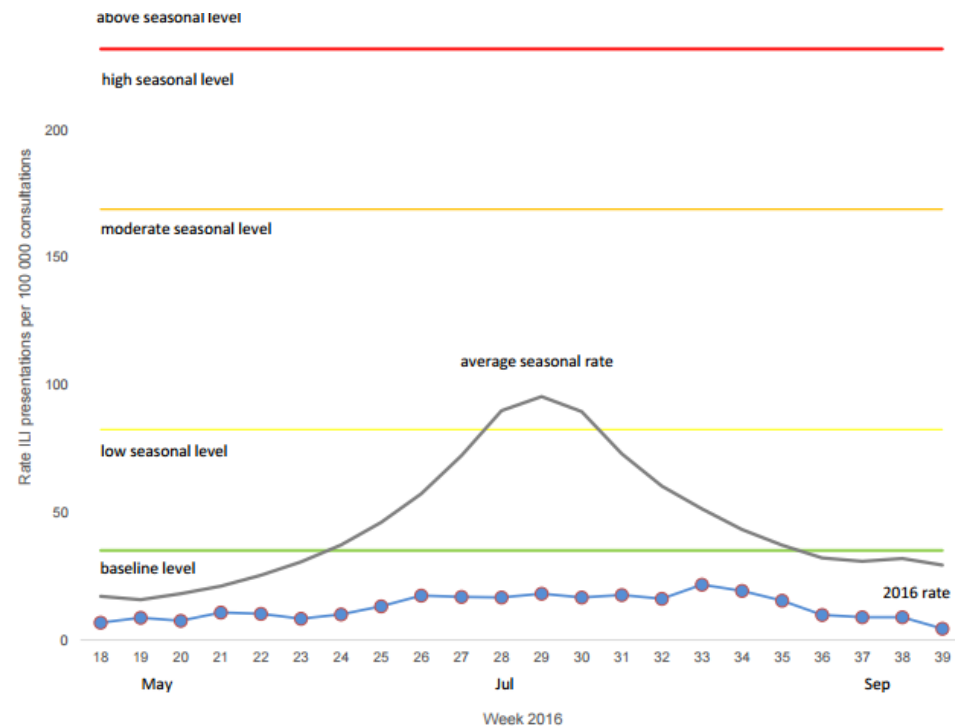
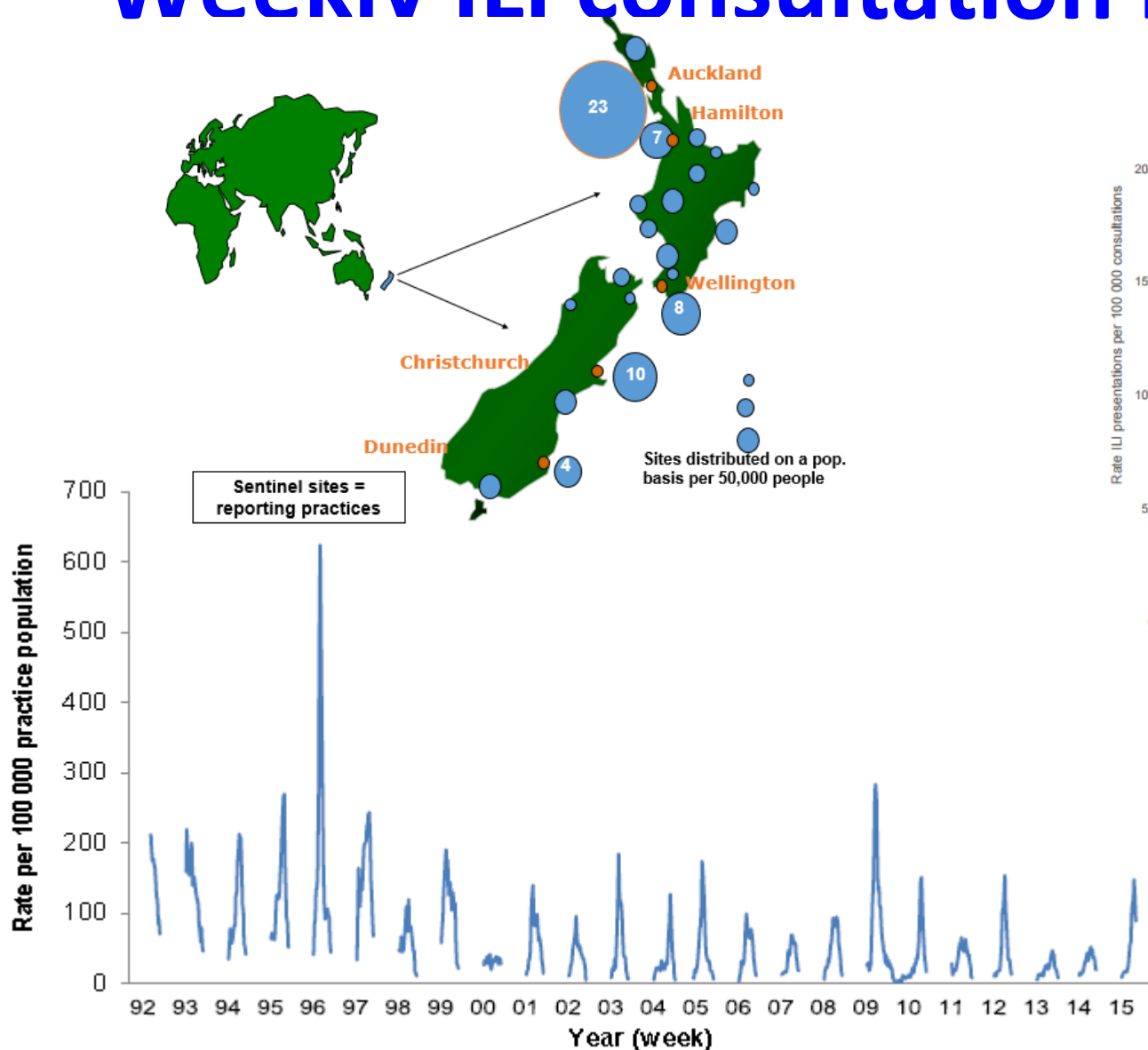
Number of specimens positive for influenza by subtype



Number of specimens positive for influenza by subtype



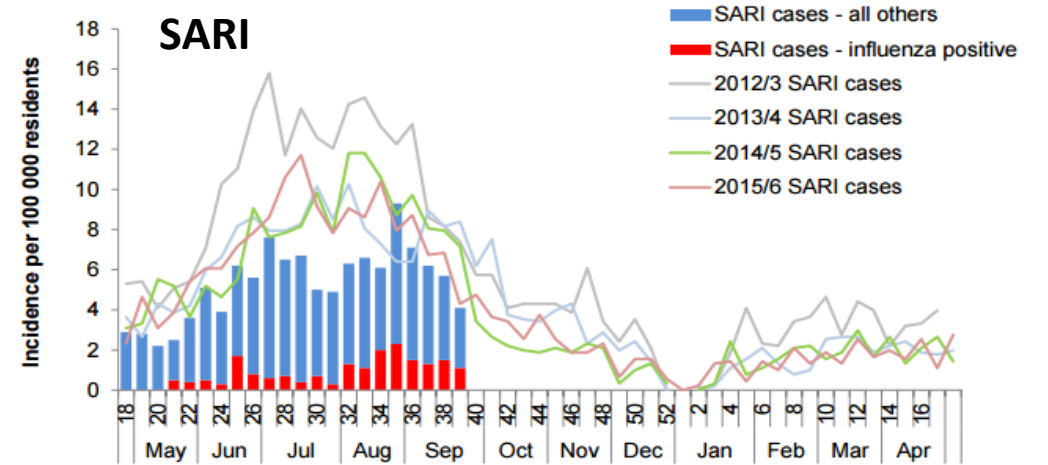
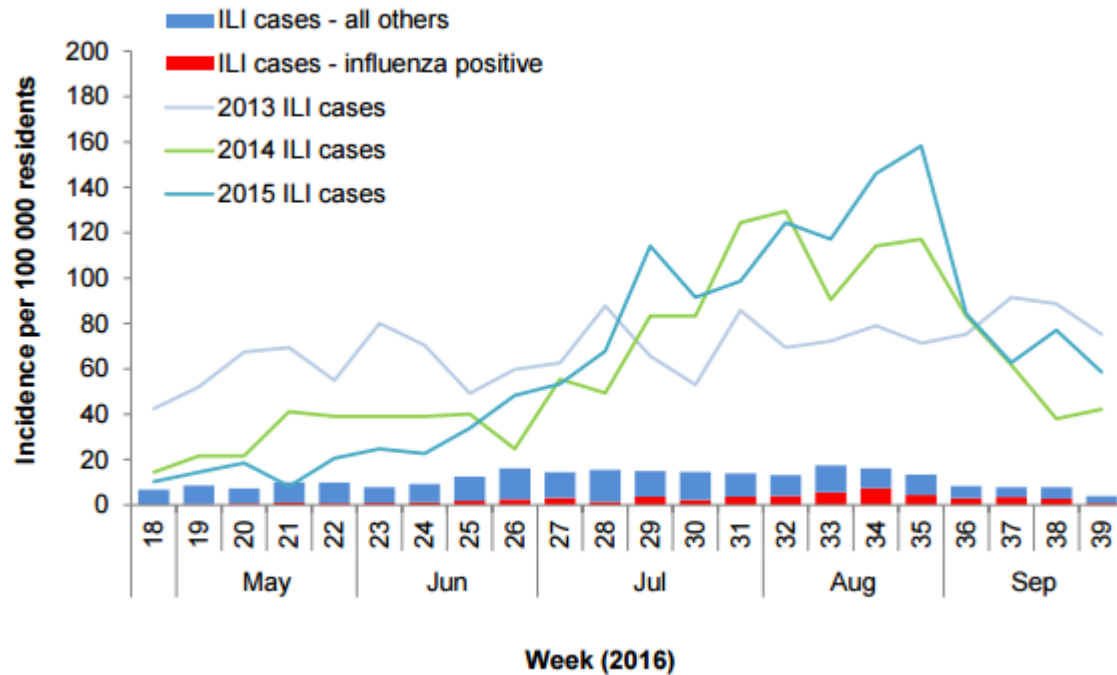
Weekly ILI consultation rates 1992-2016



Below seasonal level (baseline, per 100,000)	Seasonal level (per 100,000)			Above seasonal level (per 100,000)
	low	moderate	high	
<35.1	35.1-82.5	82.5-168.9	168.9-231.8	>231.8

Influenza surveillance

ILI and influenza incidence



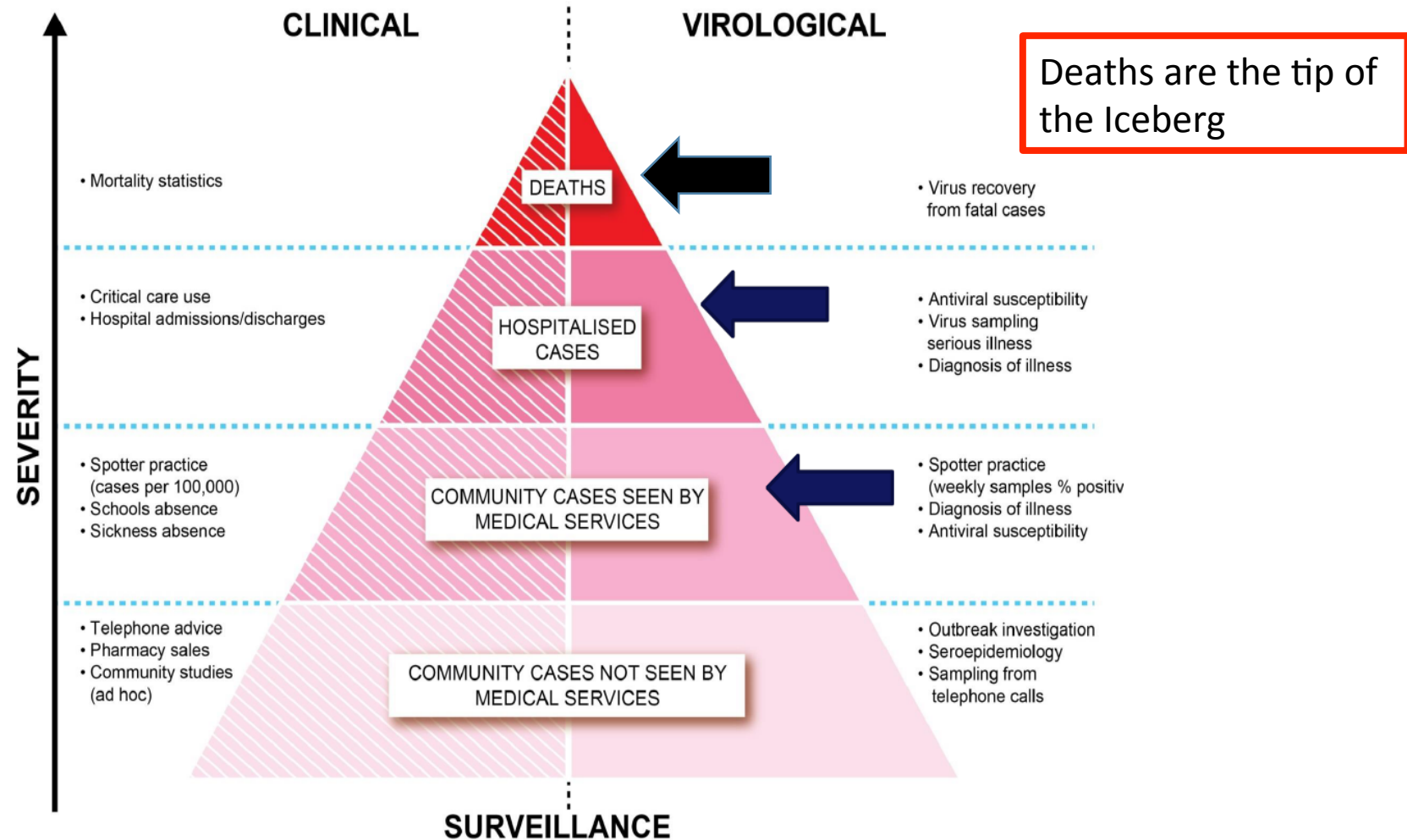
Week (2016/2017) SARI case demographics

Characteristics	Admissions	Assessed	SARI & influenza cases among all hospital patients			SARI & influenza cases among ADHB & CMDHB residents			
			SARI Cases (%)	Cases per 1000 hospitalisations	Influenza positive ¹ (%)	SARI cases	SARI incidence (per 100 000)	Influenza Cases	Influenza incidence (per 100 000)
Overall	60546	3586	1439 (40.1)	23.8	147 (15.7)	1058	116.8	134	14.8
Age group (years)									
<1	2509		302	120.4	13 (5.6)	270	1999.1	10	74.0
1-4	4140		247	59.7	24 (14.4)	209	395.2	24	45.4
5-19	6949		77	11.1	7 (13.0)	64	33.2	5	2.6
20-34	12049		67	5.6	16 (25.0)	63	30.2	13	6.2
35-49	8853		84	9.5	17 (25.8)	83	43.5	17	8.9
50-64	10218		139	13.6	26 (21.5)	127	84.4	23	15.3
65-79	9638		163	16.9	23 (16.8)	151	206.6	23	31.5
>80	6190		91	14.7	20 (25.3)	89	379.9	19	81.1
Unknown	0		267			0		0	
Ethnicity									
Māori	8103		230	28.4	24 (14.4)	202	203.1	19	19.1
Pacific peoples	12814		457	35.7	52 (14.6)	428	310.2	50	36.2
Asian	10002		109	10.9	13 (14.6)	99	47.1	11	5.2
European and Other	29257		375	12.8	57 (18.4)	329	81.9	54	13.4
Unknown	351		268	763.5		0		0	
Hospitals									
ADHB	35635	1911	756 (39.6)	21.2	91 (18.1)	467	107.0	81	18.6
CMDHB	24911	1673	682 (40.8)	27.4	56 (13.0)	590	125.7	53	11.3
Sex									
Female	32072		570	17.8	72 (16.1)	518	111.4	66	14.2
Male	28471		596	20.9	72 (15.3)	534	121.2	66	15.0
Unknown	3		273			6		2	

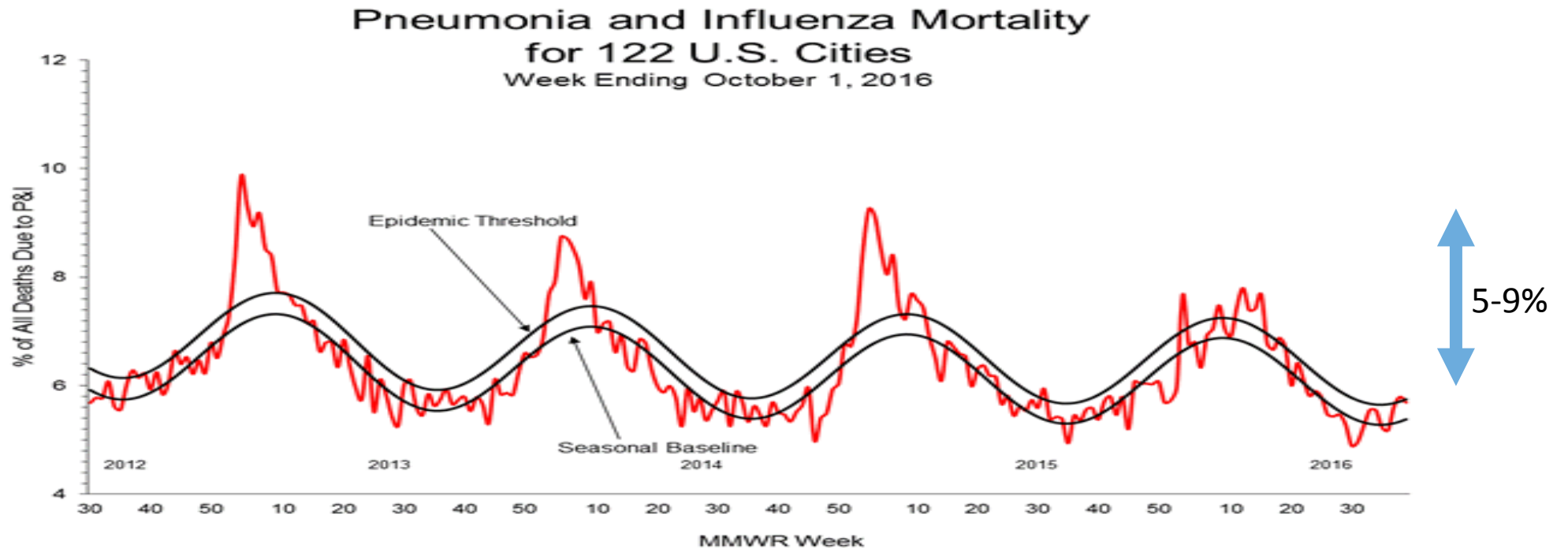
¹Proportion of cases tested which were positive for influenza viruses

https://surv.esr.cri.nz/PDF_surveillance/Virology/FluWeekRpt/2016/FluWeekRpt201639.pdf

Understanding the impact of seasonal influenza



Seasonal influenza mortality

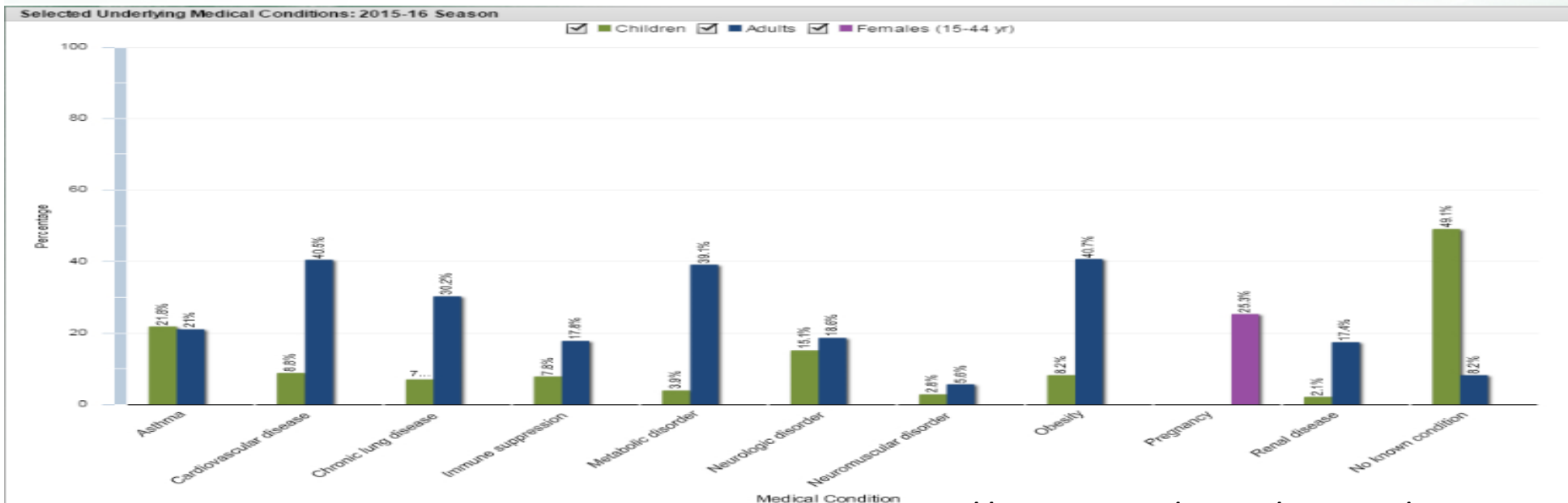
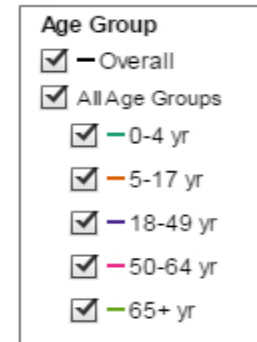
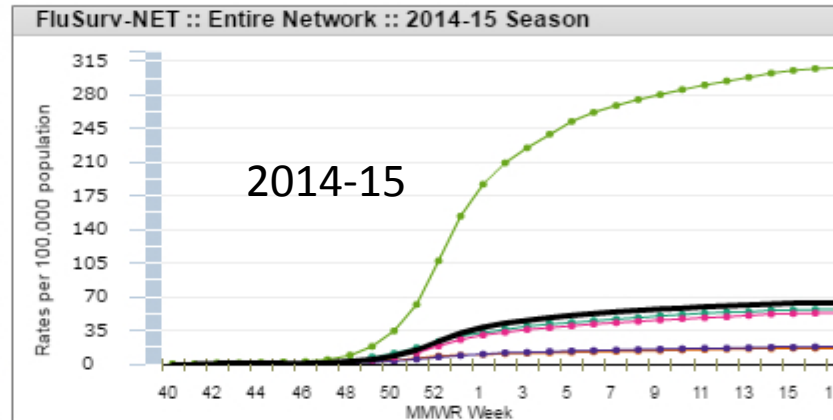
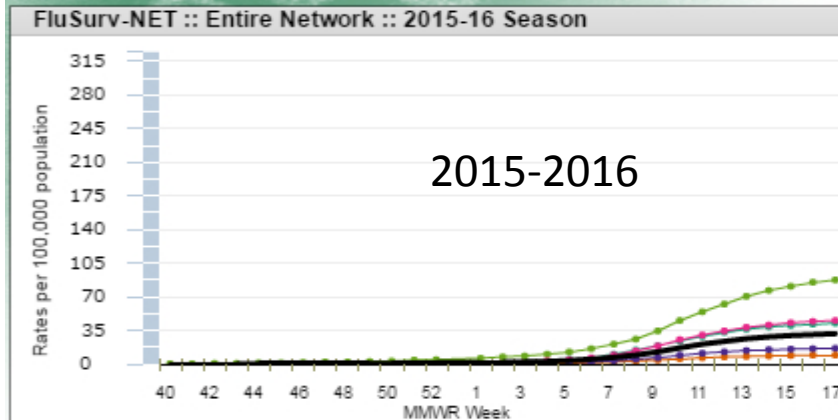


- In temperate parts of the world influenza is a seasonal disease peaking in the winter months
- In tropical and subtropical areas it has more variable pattern
- Each year seasonal influenza kills a large number of people
- Bad seasonal influenza can have as great an impact as a mild pandemic

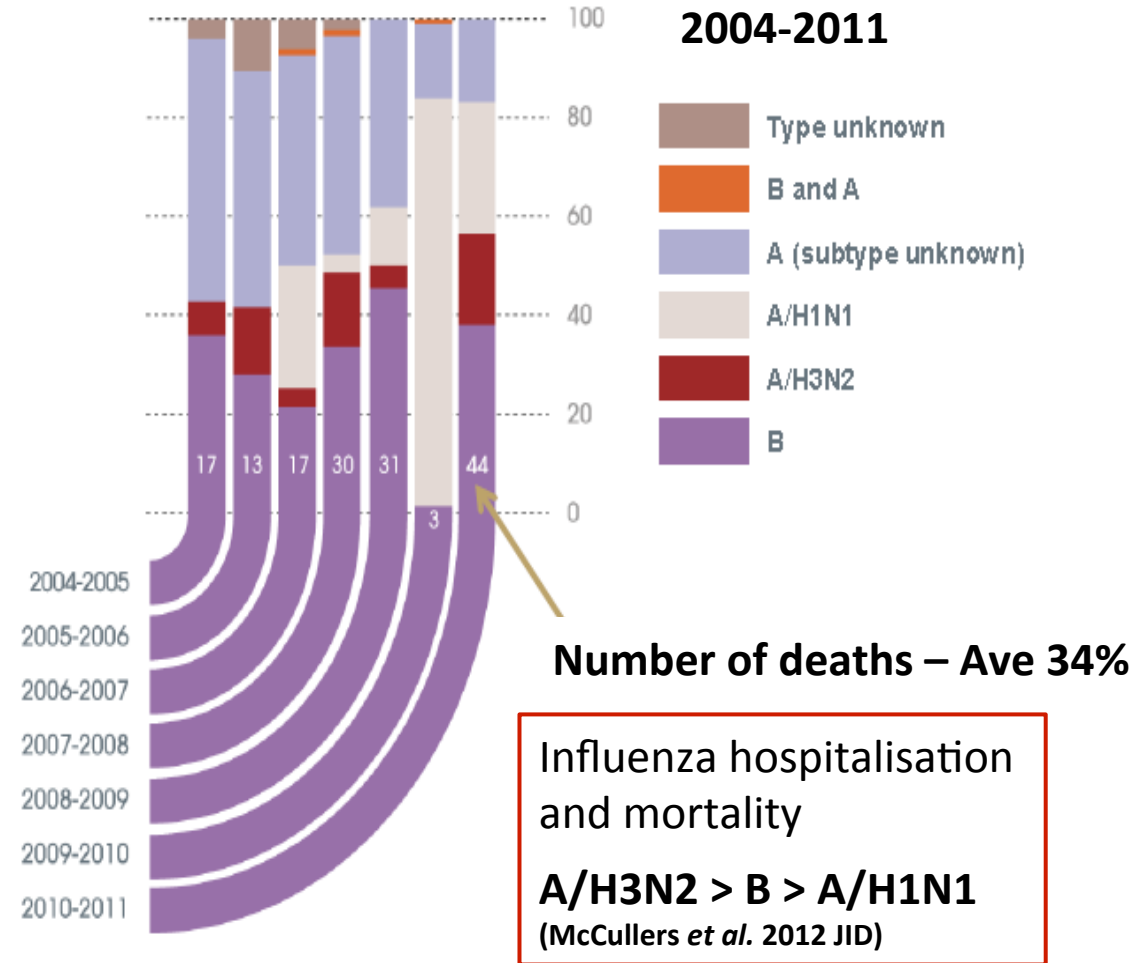
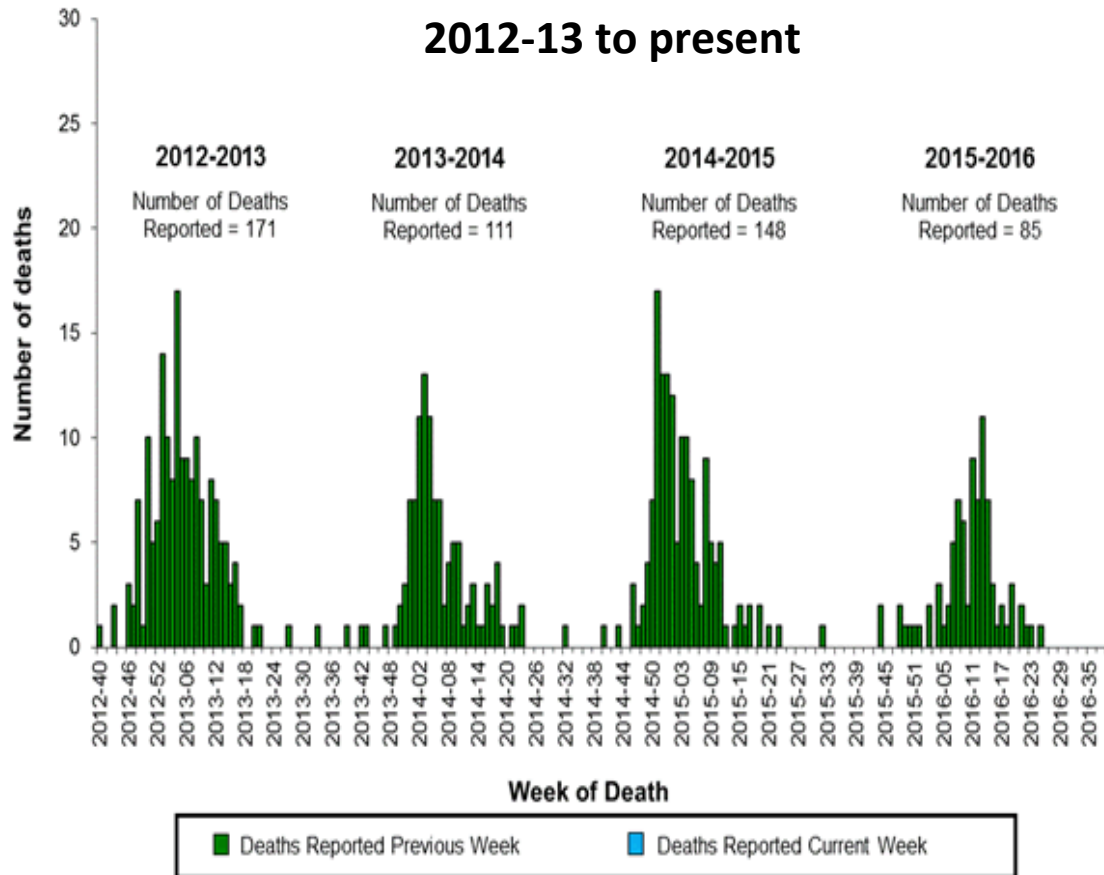
US influenza hospitalisations



Laboratory-Confirmed Influenza Hospitalizations Preliminary cumulative rates as of Sep 24, 2016



Paediatric influenza-associated deaths



<http://gis.cdc.gov/GRASP/Fluview/FluHospRates.html>

Ambrose CS, Levin MJ. Human Vaccines & Immunotherapeutics. 2012;8: 1-8; www.cdc.gov/flu/pastreports.htm

Asia-Pacific excess mortality

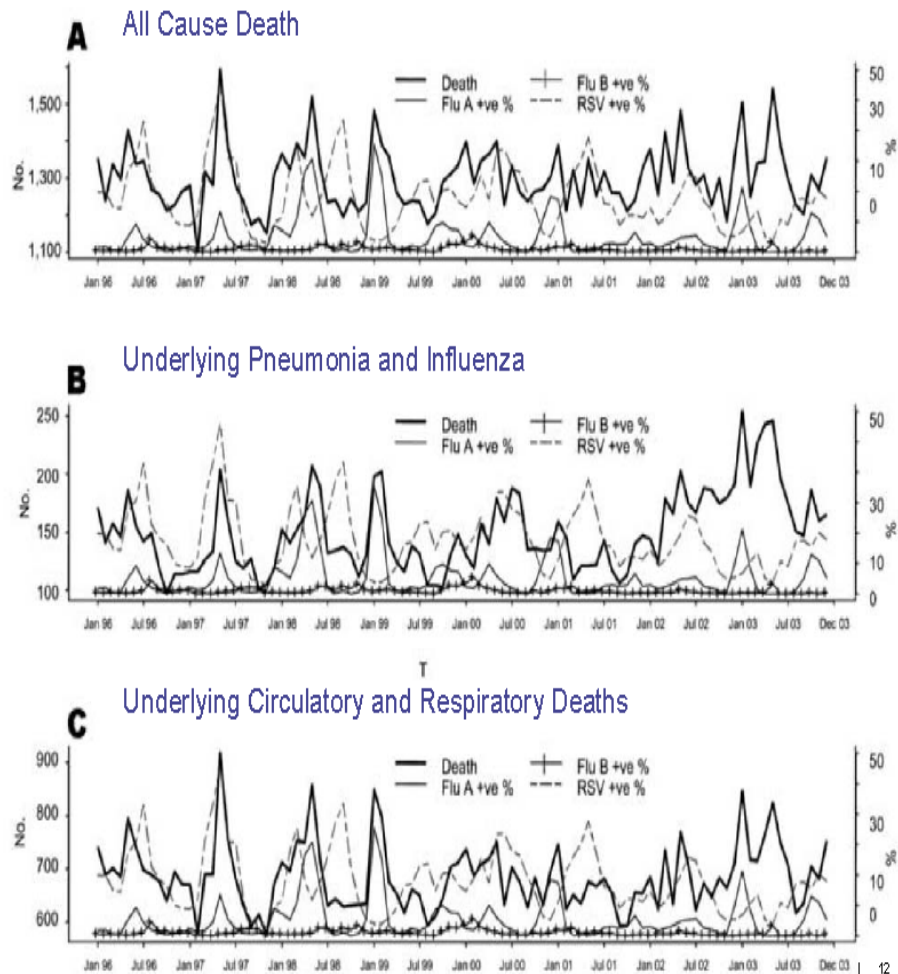


Table 5. Estimated influenza-associated excess deaths in Singapore, 1996–2003

Mortality outcome/age group (y)	Deaths (%) associated with influenza (95% CI)*	No. excess deaths per year (95% CI)	Excess mortality rate/100,000 person-years (95% CI)
All-cause deaths			
All ages	3.8 (2.5–5.0)	588 (396–782)	14.8 (9.8–19.8)
≥65	4.2 (2.7–5.6)	421 (273–571)	167.8 (107.0–229.5)
20–64	2.3 (0.9–3.7)	114 (42–186)	4.2 (1.6–6.8)
Underlying pneumonia and influenza deaths			
All ages	6.5 (2.2–10.5)	116 (40–196)	2.9 (1.0–5.0)
≥65	7.7 (3.5–11.7)	118 (50–189)	46.9 (20.3–74.6)
20–64	9.6 (3.0–15.7)	23 (7–39)	0.8 (0.2–1.4)
Underlying circulatory and respiratory deaths			
All ages	5.8 (4.0–7.5)	475 (324–629)	11.9 (8.3–15.7)
≥65	6.2 (4.4–8.1)	390 (270–512)	155.4 (108.8–203.0)
20–64	4.6 (2.5–6.7)	88 (47–131)	3.2 (1.7–4.8)

*CI, confidence interval.

Influenza causes mortality in the tropics!

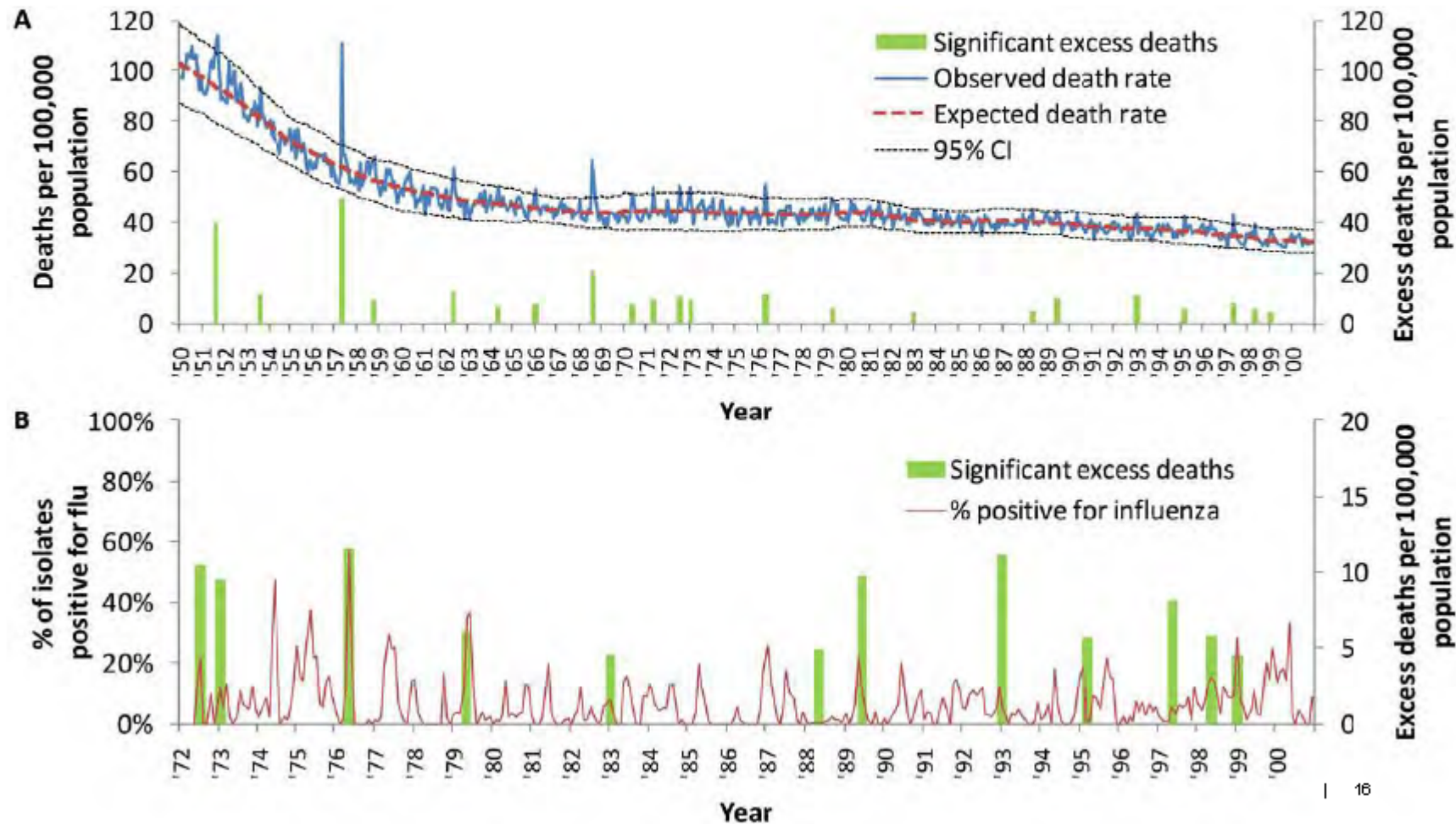
Excess mortality parallels influenza peaks

OPEN ACCESS Freely available online

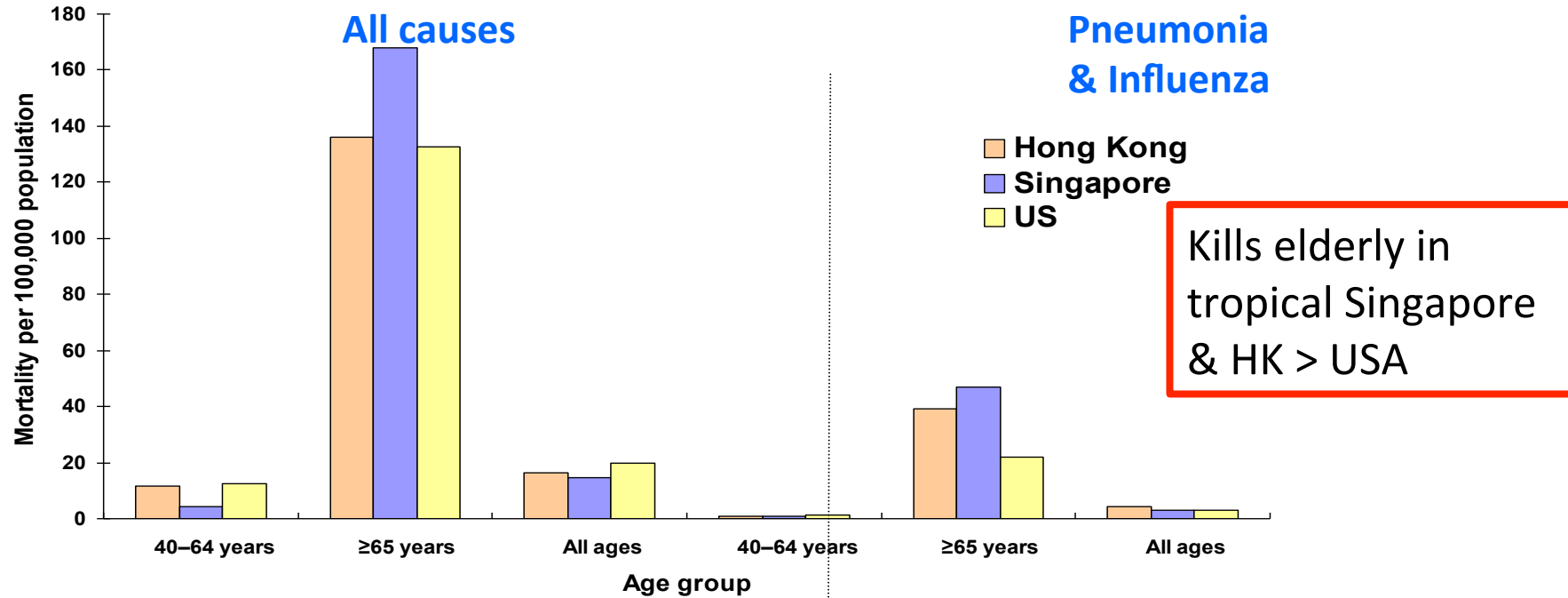


Influenza Excess Mortality from 1950–2000 in Tropical Singapore

Vernon J. Lee^{1,2,3,4*}, Jonathan Yap¹, Jimmy B. S. Ong², Kwai-Peng Chan⁵, Raymond T. P. Lin⁶, Siew Pang Chan⁷, Kee Tai Goh⁶, Yee-Sin Leo⁸, Mark I-Cheng Chen^{2,3,9}



Influenza associated excess mortality in Hong Kong, Singapore and US



Wong et al. 2004; HK data: 1996-1999 ; Chow et al. 2006: SG data:1996-2003; Thompson et al, 2003: US data: 1976-1999

Thailand

OPEN ACCESS Freely available online

PLoS one

Incidence, Seasonality and Mortality Associated with Influenza Pneumonia in Thailand: 2005–2008

James Mark Simmerman^{1*}, Malinee Chittaganpitch³, Jens Levy¹, Somrak Chantra³, Susan Maloney¹, Timothy Uyeki², Peera Areerat³, Somsak Thamthitawat¹, Sonja J. Olsen⁴, Alicia Fry², Kumnuan Ungchusak³, Henry C. Baggett¹, Supamit Chunsuttiwat³

China: Influenza associated excess mortality

Study area	Model	Study period	Proportion of influenza seasons by:		Excess deaths (per 100 000 people)						
			A(H3N2)	B	All ages			Age ≥ 65 years			
					P&I	R&C	AC	P&I	R&C	AC	
Australia ¹⁵	Poisson	1997–2004	NA	NA	NA	NA	NA	NA	15.2	80.4	101.2
China (Guangzhou) ²¹	Poisson	2004–2006	2/3	0/3	1.0	9.9	10.6	NA	104.1	111.3	111.3
China (northern cities) ^b	Negative binomial	2003–2008	2.5/6	1/6	0.4	12.4	18.0	3.1	106.0	150.8	150.8
China (northern cities) ^b	Serfling	2003–2008	2.5/6	1/6	0.4	13.4	17.0	2.6	108.1	131.3	131.3
China (southern cities) ^b	Negative binomial	2003–2008	2.5/6	1/6	0.5	8.8	11.3	3.6	64.3	75.4	75.4
China (Hong Kong SAR) ¹⁹	Poisson	1996–1999	4/4	0/4	4.1	12.4	16.4	39.3	102.0	136.1	136.1
Italy ^{11,12}	Serfling	1970–2001	21/31	5/31	1.9–2.2	NA	11.6–18.6	12.7–14.2	NA	71.2–115.7	71.2–115.7
Mexico ¹⁶	Serfling	2000–2008	6/9	1/9	1.5	12.7	15.7	10.4 ^c	115.6 ^c	147.4 ^c	147.4 ^c
Singapore ²²	Negative binomial	1996–2003	8/8	0/8	2.9	11.9	14.8	46.9	155.4	167.8	167.8
United States ⁴	Poisson	1990–1999	6/9	2/9	3.1	13.8	19.6	22.1	98.3	132.5	132.5
United States ³	Poisson	1976–2002	14/27	9/27	NA	9.9	NA	NA	72.4	NA	NA
United States ⁵	Poisson	1976–2007	17/31	9/31	2.4	9.0	NA	17.0	66.1	NA	NA
United States ¹⁰	Serfling	1980–2001	12/21	6/21	2.9	NA	15.0	22.0	NA	100.0	100.0

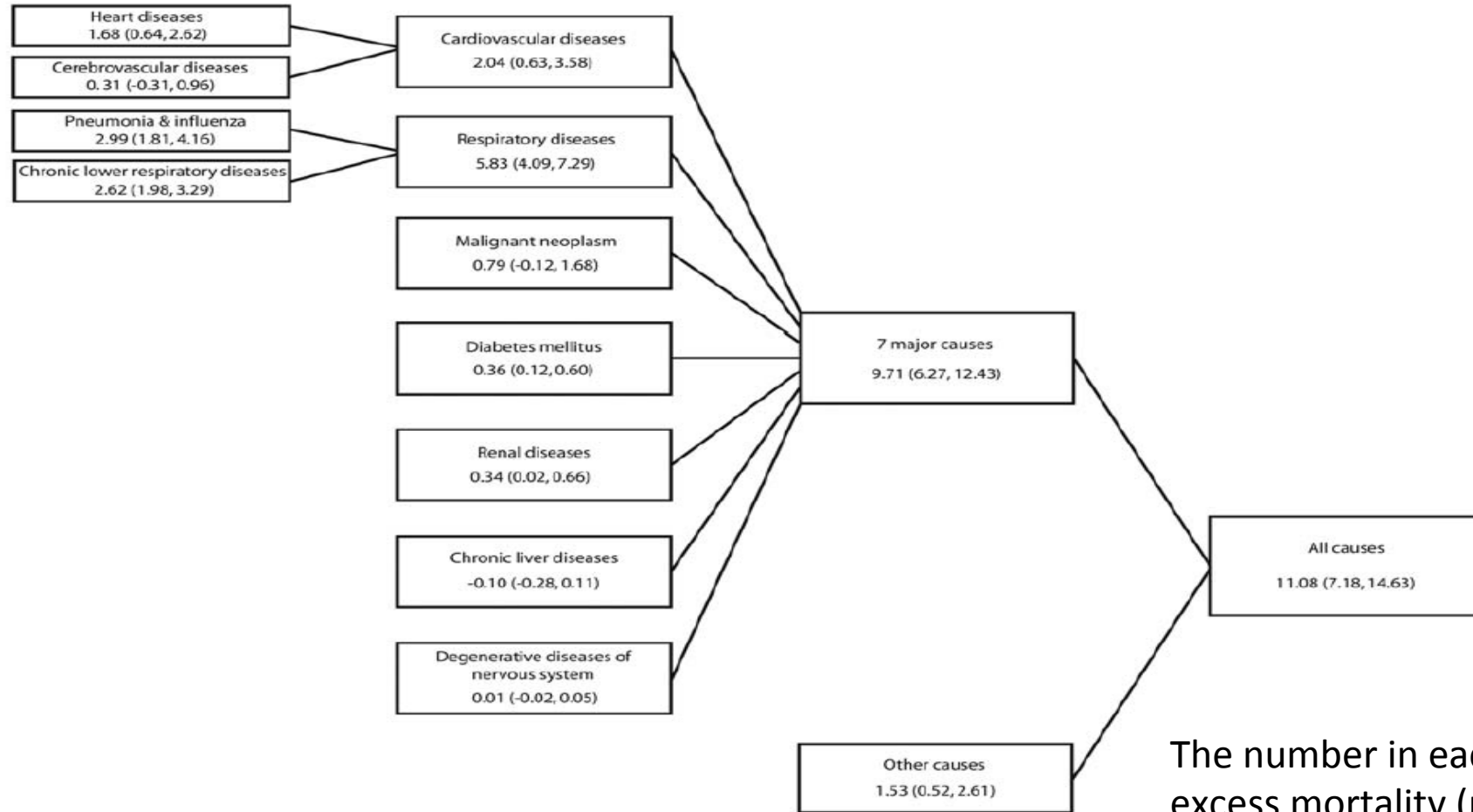
- Excess mortality for respiratory & circulatory diseases:
 - Northern temperate cities: 12.4 (7.4-22.2) deaths/100,000
 - Southern subtropical cities: 8.8 (5.5-13.6) deaths/100,000
 - Most (86%) occurred among people aged ≥ 65 years
 - Higher in B-dominant seasons than H3N2 or H1N1 predominated

Annual excess influenza-associated mortality rates in Hong Kong

Average type/subtype-specific annual excess all-cause mortality rates by age in Hong Kong 1998-2009

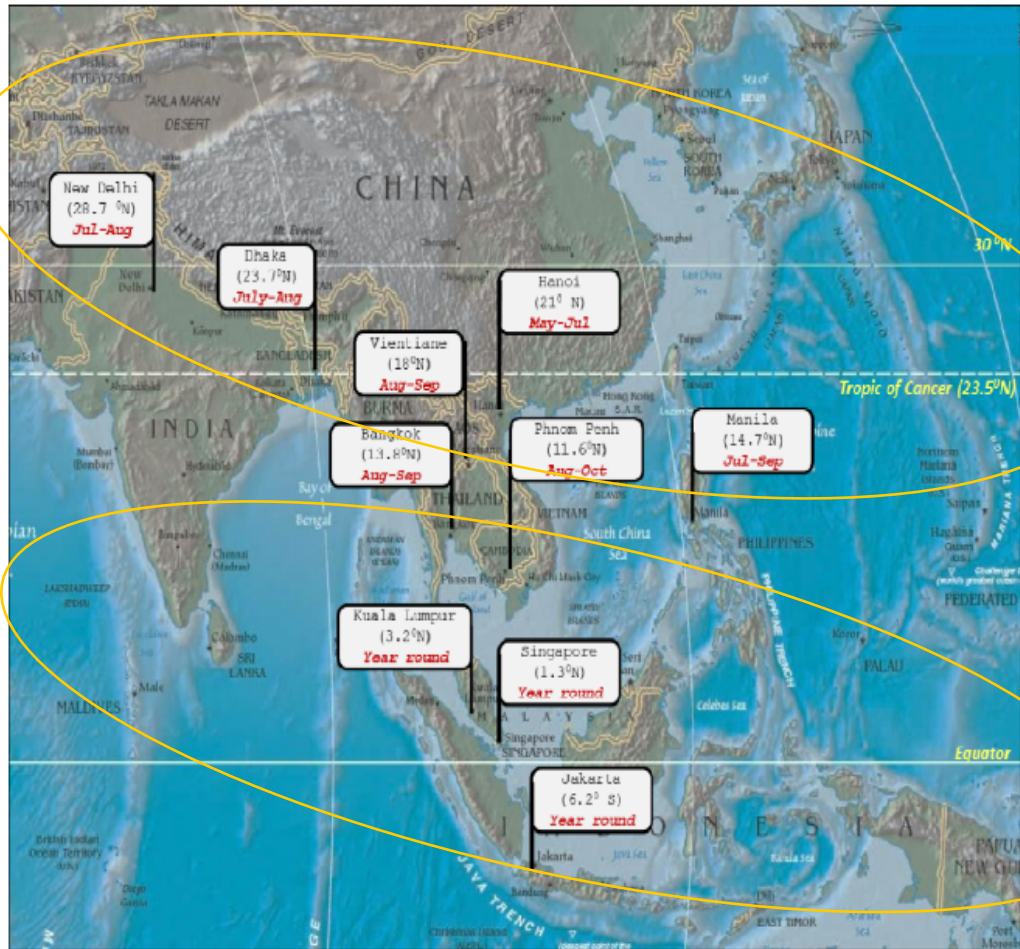
Age	Average excess mortality rate (per 100,000 population per year)									
	sH1N1	(95% CI)	sH3N2	(95% CI)	pH1N1	(95% CI)	B	(95% CI)	All	(95% CI)
0-4y	0.9	(-0.3, 2.4)	0.2	(-1.7, 2.2)	-3.0	(-7.6, 2.5)	-1.5	(-4.0, 0.8)	-0.7	(-3.7, 2.4)
5-14y	0.1	(-0.2, 0.5)	-0.1	(-0.5, 0.4)	-0.7	(-1.9, 0.7)	-0.3	(-0.8, 0.3)	-0.2	(-1.0, 0.5)
15-44y	0.8	(0.1, 1.3)	0.6	(0.0, 1.4)	-0.8	(-2.6, 1.0)	0.0	(-0.8, 0.9)	1.3	(0.3, 2.4)
45-64y	0.2	(-1.5, 1.8)	1.9	(-0.1, 3.9)	-0.8	(-6.4, 5.3)	1.3	(-1.3, 3.6)	3.3	(0.1, 6.1)
≥65y	8.4	(-6.0, 21.7)	58.8	(40.5, 76.0)	23.4	(-23.7, 75.7)	20.3	(0.1, 41.5)	89.7	(61.8, 113.7)
All	1.6	(-0.3, 3.3)	6.9	(4.3, 9.4)	2.2	(-4.8, 8.8)	2.5	(-0.5, 5.3)	11.1	(7.2, 14.6)

Excess mortality by cause in Hong Kong

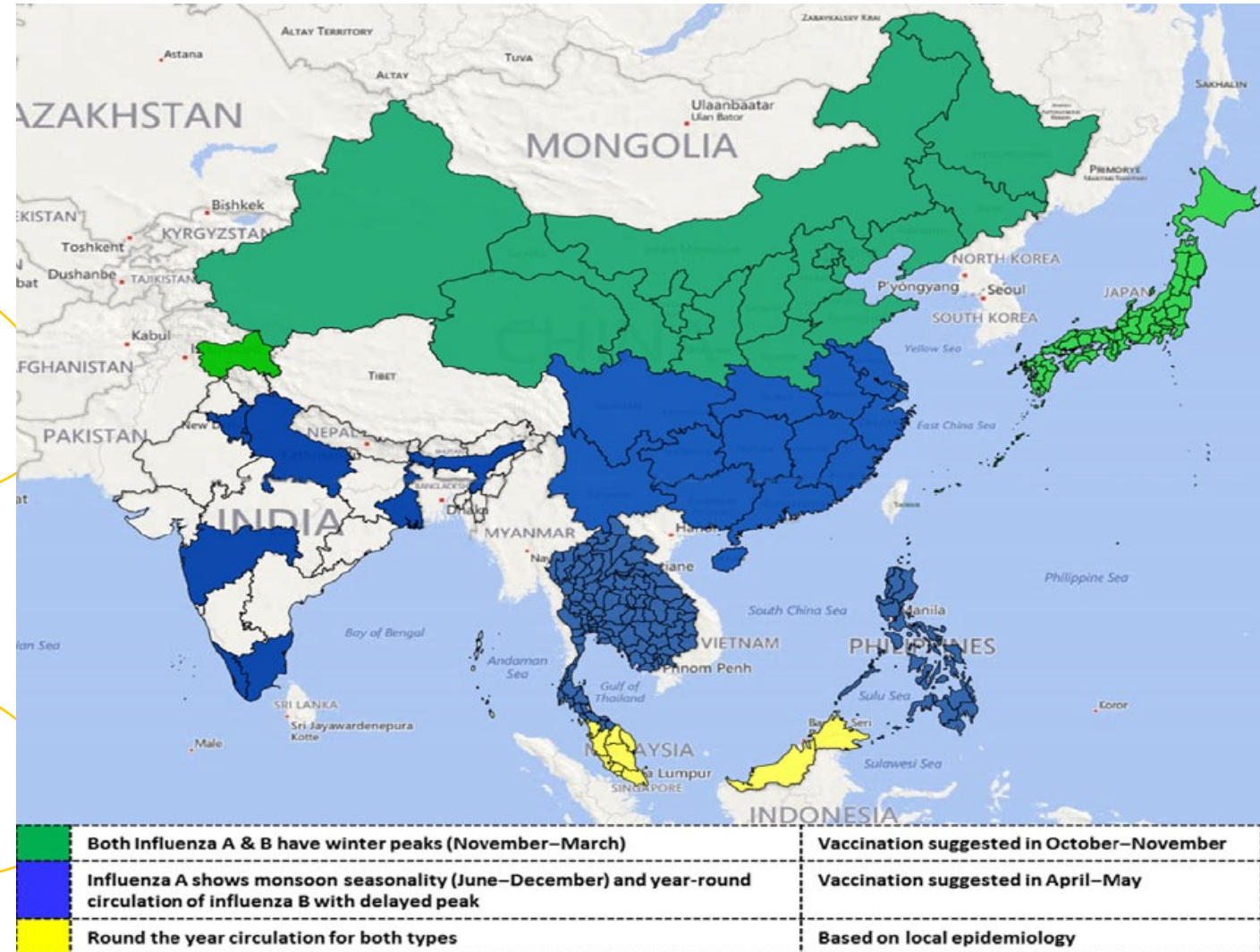


The number in each box represents the excess mortality (rate/100,000 pop/year) from that cause associated with influenza A and B

Influenza activity in S- & SE-Asia countries, 2006-2013



Saha S et al. Bull WHO, 2014;



Saha S et al. JIORV 2016;10(6);176-184

Influenza must be a public health priority

- WHO Global initiatives on influenza: GISRS; GAP; PIP
- The burden of influenza is also substantial globally
 - including Asia-Pacific countries/tropical & sub-tropical regions
- Influenza is an important leading cause of hospitalization and death in the extremes of age.
- Measurement of the disease burden is pivotal
 - Most data on disease burden come from a small number of locations in the region.
- Influenza is preventable by vaccination.

**Thank
you**

