

RESPIRATORY VIRUSES

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Disclosures

- **Infection Control Consultant at Deer Lodge Centre**
- **No other**

Outline

I. New Respiratory Virus

- MERS-CoV

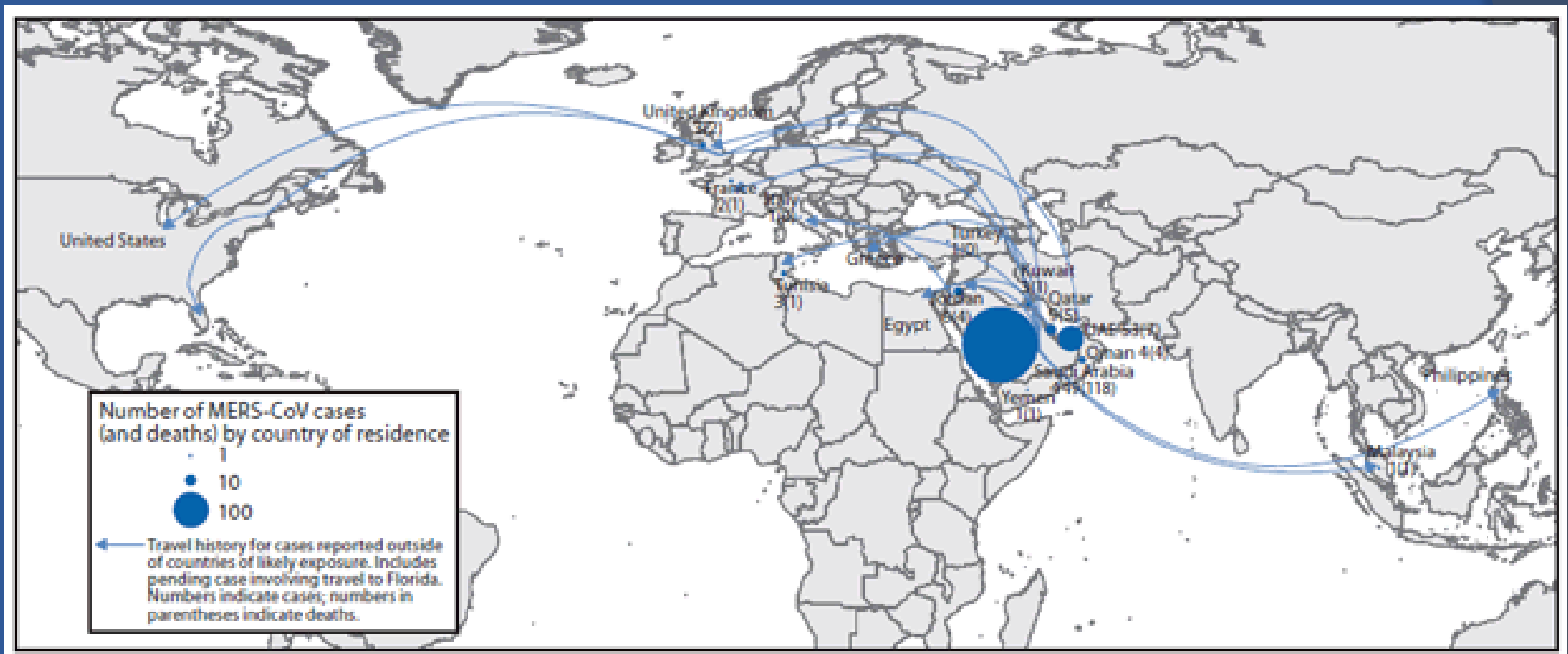
II. Influenza

- Good Vaccine News
 - Herd immunity
 - Immunizing children reduces influenza in adults
- Bad Vaccine News
 - Mismatch
 - Annual immunization
- Antiviral Drugs
 - Laninamivir
 - Oseltamivir controversy
 - Outbreak control in LTCF
- Outbreak control in WRHA, 2014-15

Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

- ⦿ A coronavirus more related to bat coronaviruses than to SARS
- ⦿ April 2012: MERS-CoV first detected in lung of fatal case in Saudi Arabia
- ⦿ Since then, global spread

By June 2015, 1154 cases, 431 deaths (37%), 25 countries





Bat origin

Major enzootic reservoir now camels

Human-human transmission

MERS-CoV

- Incubation period 3-14 days
- Presenting symptoms: fever, cough & shortness of breath
- Clinical illness is indistinguishable from other LRTI
- Virus load is highest in lung washings
- Diagnosis: PCR of respiratory tract secretions
- Only infectious when symptomatic

IP&C (Canada) Guidance for Acute Care Settings

- **Contact & droplet precautions**
- **Airborne precautions when performing aerosol-generating procedures**

Good Vaccine News (I)

Influenza Vaccine Proven to Induce Herd Immunity



Herd immunity refers to protection of unimmunized individuals by immunization of the majority of their population

Relevant to protecting high risk nursing home residents by immunizing staff with close contact

Evidence That Influenza Vaccine Can Induce Herd Immunity:

**Effect of Influenza Vaccination of
Children on Infection Rates in
Hutterite Communities:
A Randomized Trial**

Study Design

- 46 Hutterite colonies in Manitoba, Saskatchewan & Alberta were randomly allocated to influenza or hepatitis A vaccine as control
- All children 36 mos-15 yrs in the colony were given the same vaccine
- Coverage: 83% of children in 22 colonies received flu vaccine; 79% (n = 24), control
- Only 10% of adults received flu vaccine

- **Influenza incidence was reduced by 67% from 7.6% to 3.1% ($p=0.03$)**

Conclusion: This study offered rigorous scientific proof that inactivated influenza vaccine could induce herd immunity

Corollary: Influenza Immunization of staff with close contact with residents will reduce illness in susceptible patients

Good Vaccine News (II)

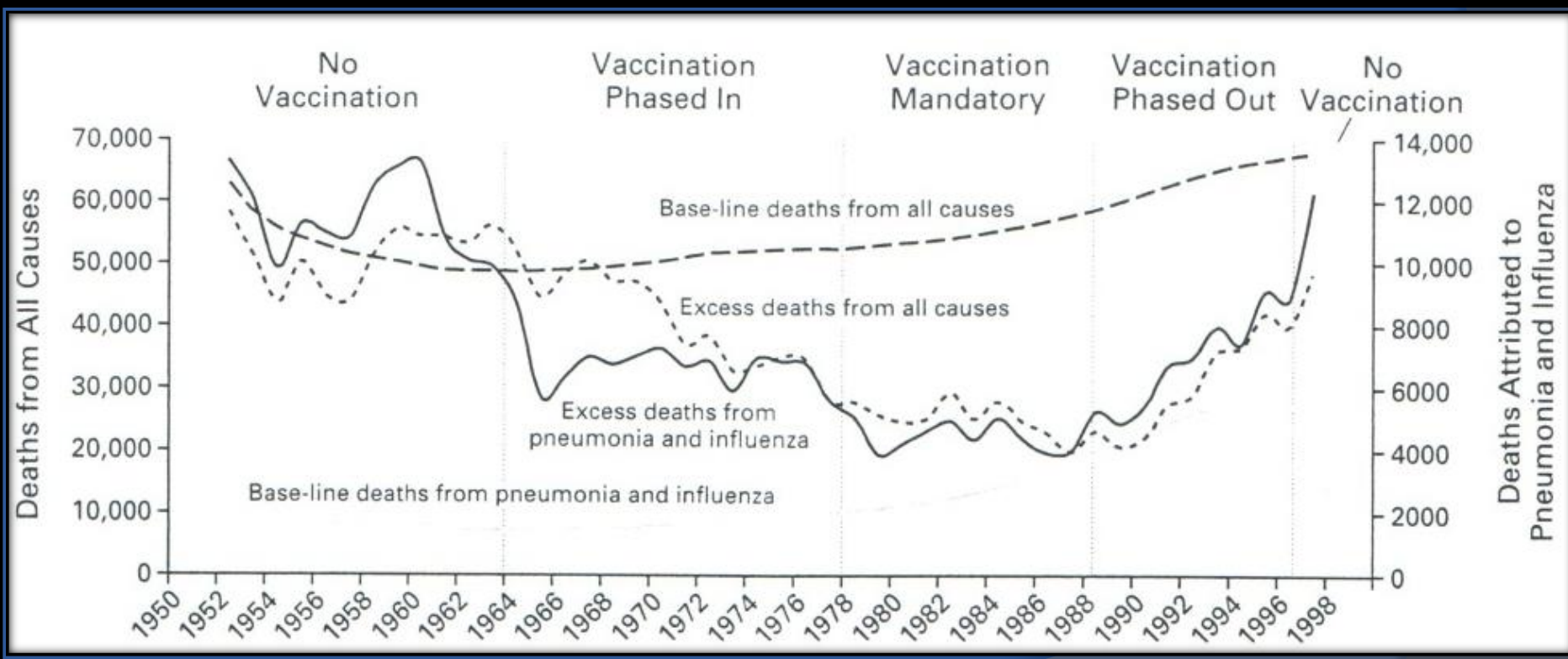
Influenza immunization of children protects adults

Hypothesis:

- Influenza is rapidly amplified each fall in the large population of susceptible children, then spreads to adults
- Immunizing children should reduce flu in adults
- Japanese experience suggests hypothesis is correct:

THE JAPANESE EXPERIENCE WITH VACCINATING SCHOOLCHILDREN AGAINST INFLUENZA

Reichert TA et al. N Engl J Med 2001; 344:889



Reichert TA et al. N Engl J Med 2001; 344:1948

- **The results of the study of influenza immunization of children in Hutterite colonies also provided direct proof of the correctness of the hypothesis that immunizing children reduces flu in adults**

Bad Vaccine News (I)

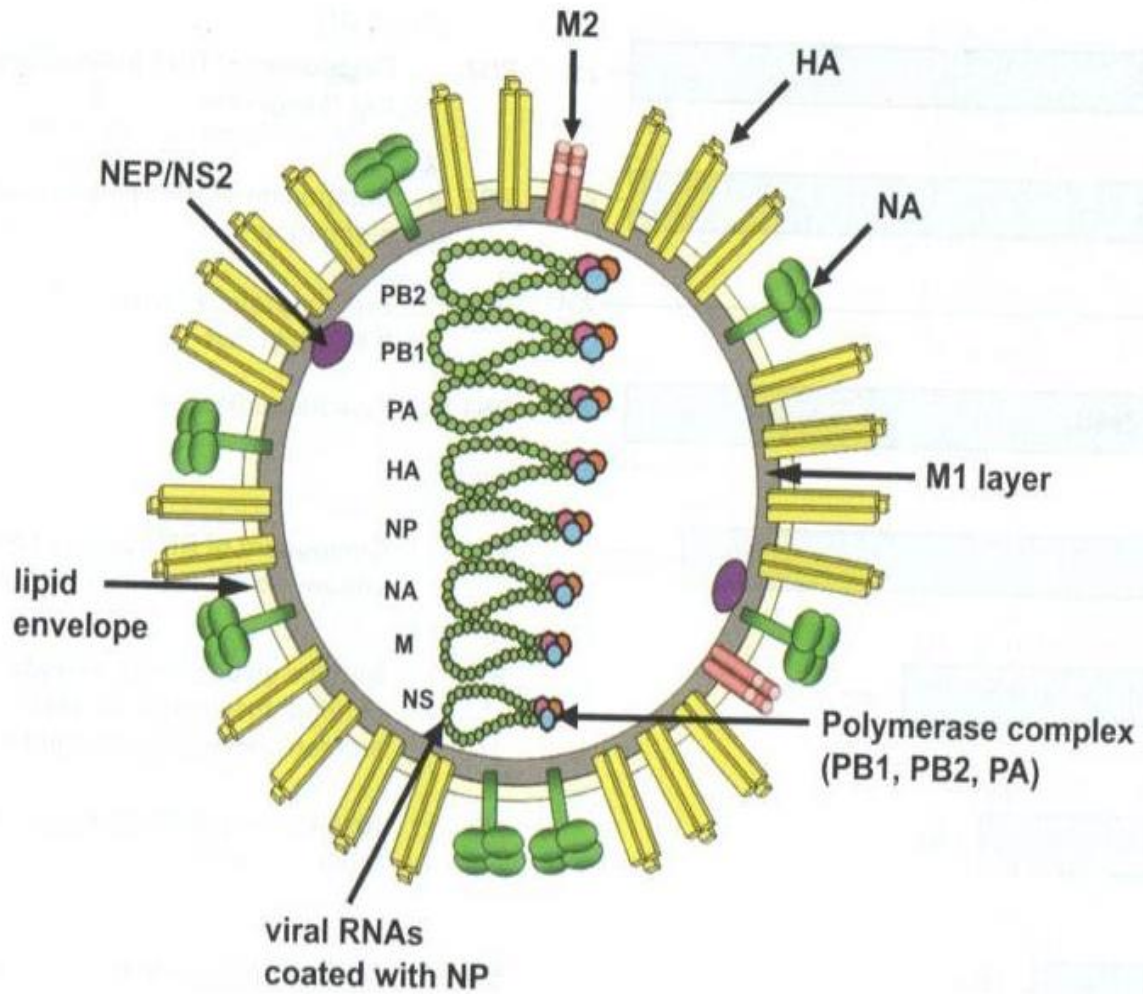
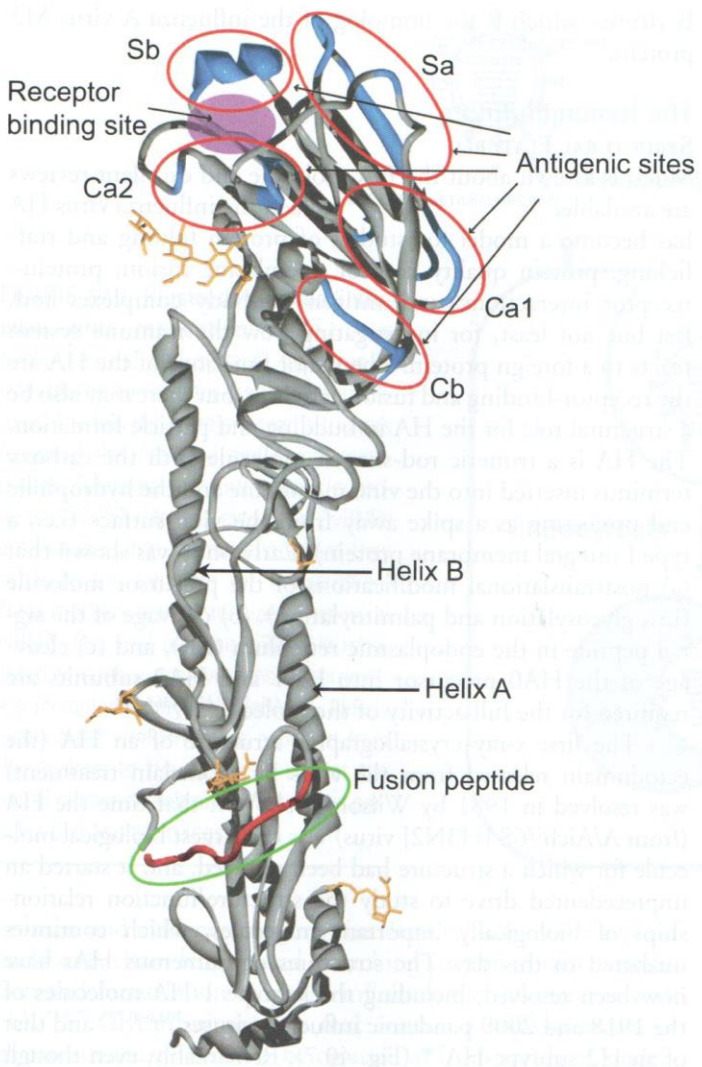
In 2014-15 unprecedented mismatch between vaccine A/H3N2 virus & circulating strain

- ⦿ **Mismatch reduces vaccine effectiveness**
- ⦿ **Mismatch refers to differences in antigenic sites between an influenza vaccine strain & subsequent circulating strain**
- ⦿ **Arises because vaccine strains must be selected in February to preapre vaccine for October**

Influenza Vaccine & Circulating Strain Mismatches

Background

- Hemagglutinin (HA) is key antigen
- Antibody to HA protects



Hemagglutinin monomer with its 5 antigenic sites

Amino acid changes in the major antigenic sites A-E constitute antigenic “drift” = vaccine mismatch with circulating virus

Mismatches Reduce Vaccine Effectiveness (VE)

	Amino Acid Changes	VE
2012-13	} 4-8	45%
2013-14		74%
2014-15	11	23%

Skowronski et al. *Euro Surveill* 2015; 70

Conclusion

- 2014-15 vaccine mismatch compromised protective efficacy
- Raised spectre of more outbreaks in LTCF & an increased role for antiviral drugs in 2014-15

More Bad Vaccine News (II)

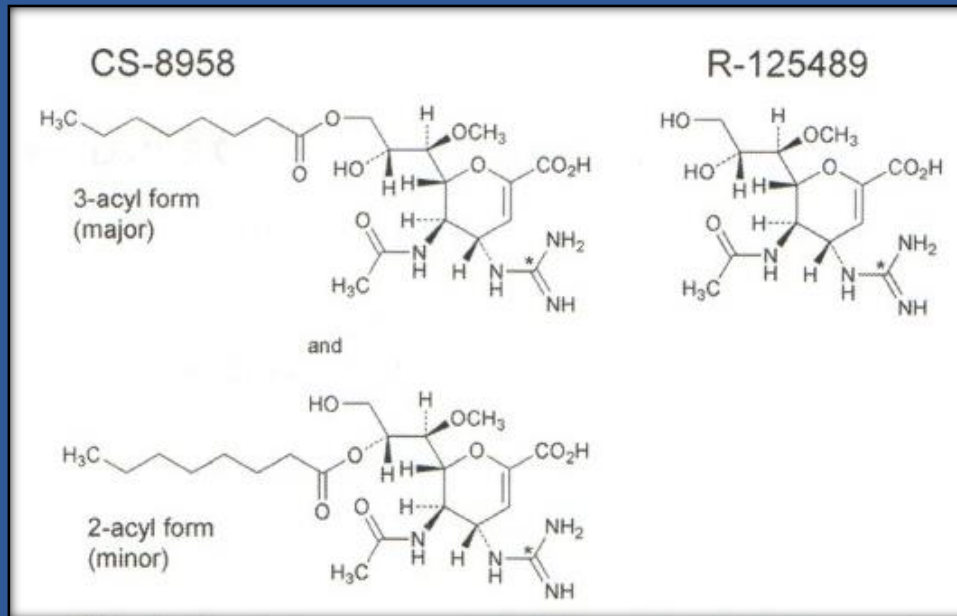
- “Influenza vaccination in the previous year is significantly associated with a modestly reduced level of protection in the current year”
- First reported by Skowronski et al (B.C. CDC) in 2014. Subsequently:
 - Observed over multiple flu seasons
 - Seen with both influenza A & B vaccines & infection
 - Not due to different antibody titres
 - Not cumulative

Vaccination Status	Cases/100 Persons, 2011–2012	Cases/100 Persons, 2012–2013	Cases/100 Persons, Both Years
2011–2012 only	1.2	5.7	6.9
2012–2013 only	10	1.2	11.2
Both years	1.2	5.3	6.5
Neither year	10	10	20

- **Highest incidence occurs in those who receive no vaccine**
- **Single vaccination is better than none**
- **Vaccination in both years prevents more disease than vaccination in a single year**
- **More multi-year prospective studies needed**

Laninamivir, a New Drug for Influenza Virus Infections

- An analogue of zanamivir – not orally bioavailable



- The acyl side-chain results in slow clearance from lungs after oral inhalation

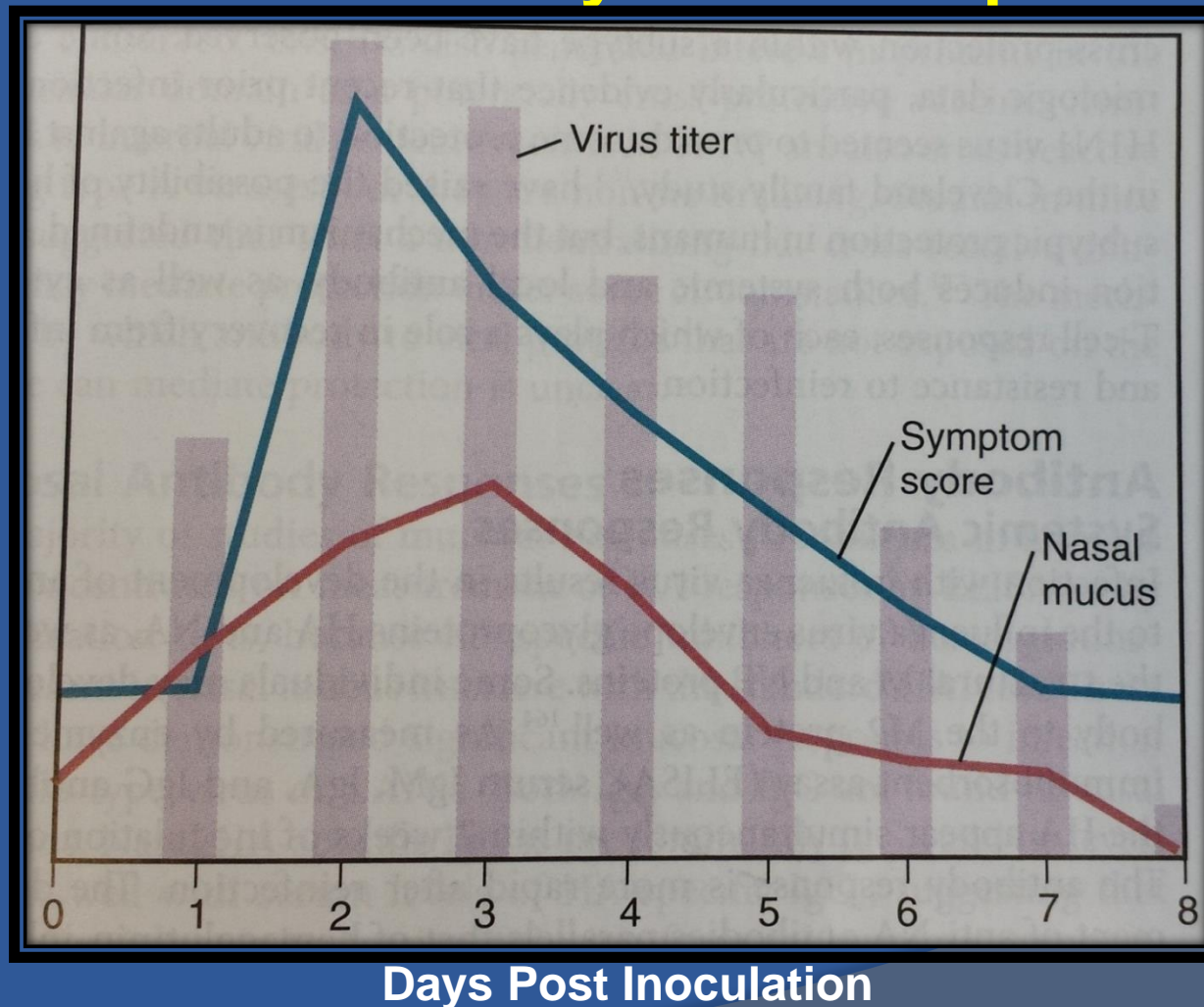
- **In mice, a single intranasal dose protected against influenza challenge 7 days later**
- **In children, a single orally inhaled dose administered \leq 48 H after influenza illness onset was as efficacious as oseltamivir BID for 5 d**

- ⦿ **Licensed in Japan for treatment**
- ⦿ **Potential for once-weekly dosing for prophylaxis not yet reported**

Oral Oseltamivir's (Os) Utility— The Controversy

- A. Treatment of mild seasonal influenza (20 randomized, placebo-controlled trials):
- Os treatment of adults begun within 48 H of symptom onset reduced the time to first symptom alleviation by 17 H, from 7 to 6.3 days, over antipyretics &/or cough medicines
 - No effect on hospitalization or pneumonia
 - Caused some nausea, vomiting & diarrhea

Time Course of Virus Shedding and Symptoms After Experimental Influenza Inoculation of Volunteers by Nasal Drops



Conclusions:

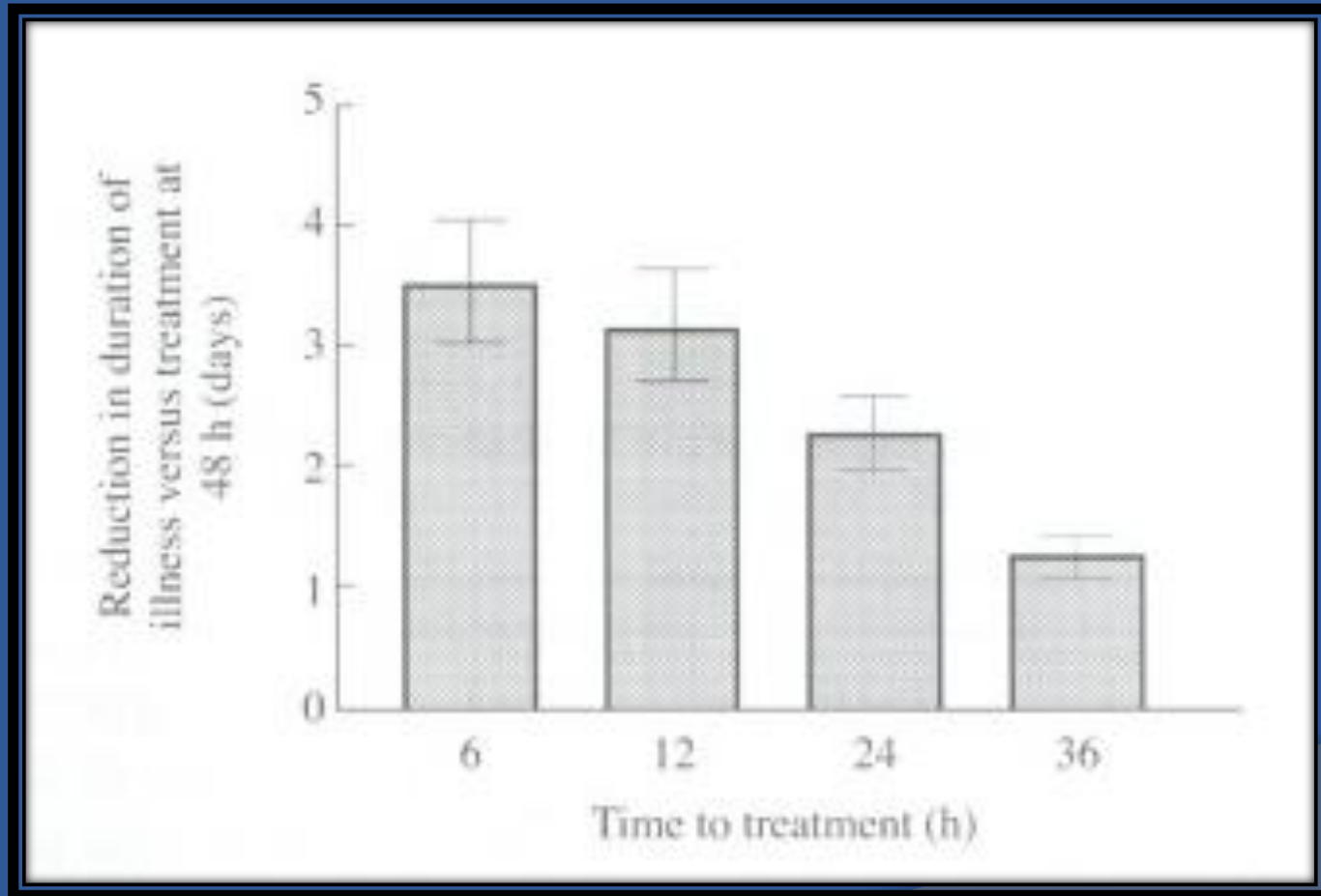
Antiviral drugs will only change the course of illness if begun before virus starts to decline naturally

Earlier treatment will be more effective

Early administration of oral oseltamivir increases the benefits of influenza treatment

Aoki FY et al. *J Antimicrob Chemother* 2003; 51:123

Reduction in Days of Influenza Illness Duration With Earlier Os Treatment Compared to Delayed Treatment at 48 H



**B. Treatment of pandemic influenza
2009-10 reduced serious outcomes:**

- **Retrospective analysis of 35,000 patients globally hospitalized with severe influenza:**
 - **About 25% had pneumonia**

- Os initiated within 2 days of onset reduced the likelihood of
 - Admission to ICU &
 - Death, by 49-65%
- Therapy was beneficial if begun up to 5 days
- Benefit was also observed in high-risk groups including pregnant women

Influenza Outbreaks

Winnipeg Regional Health Authority

Nursing Homes

2014-2015

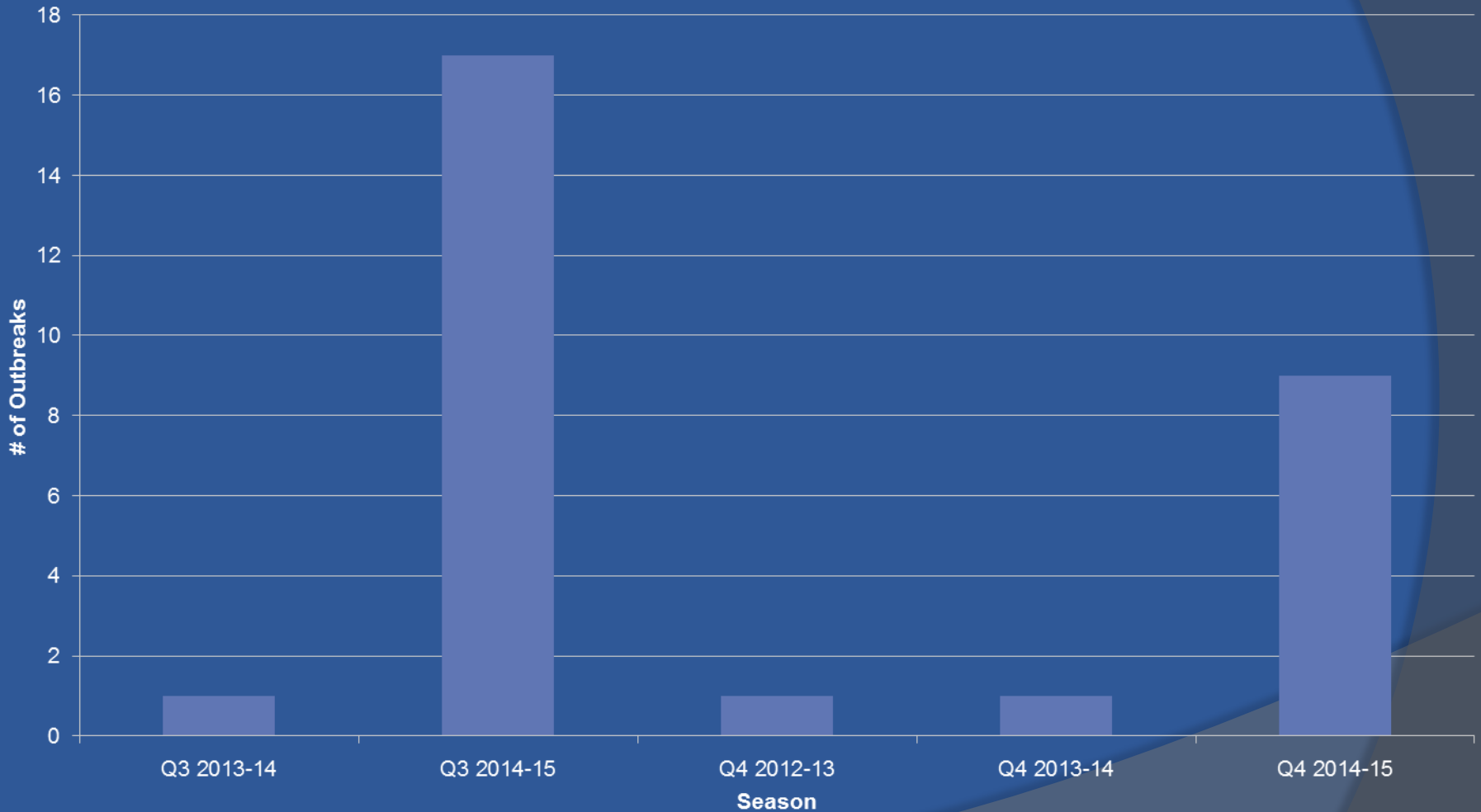
- ◎ **39 nursing homes**
 - **36 PCH + 3 hybrid like DLC**
 - **56 respiratory infection outbreaks**
 - **45 influenza**
 - **11 others (1 RSV, 1 Corona, 1 HMNV + flu; 7 unknown)**

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WINNIPEG FREE PRESS, TUESDAY, MARCH 3, 2015

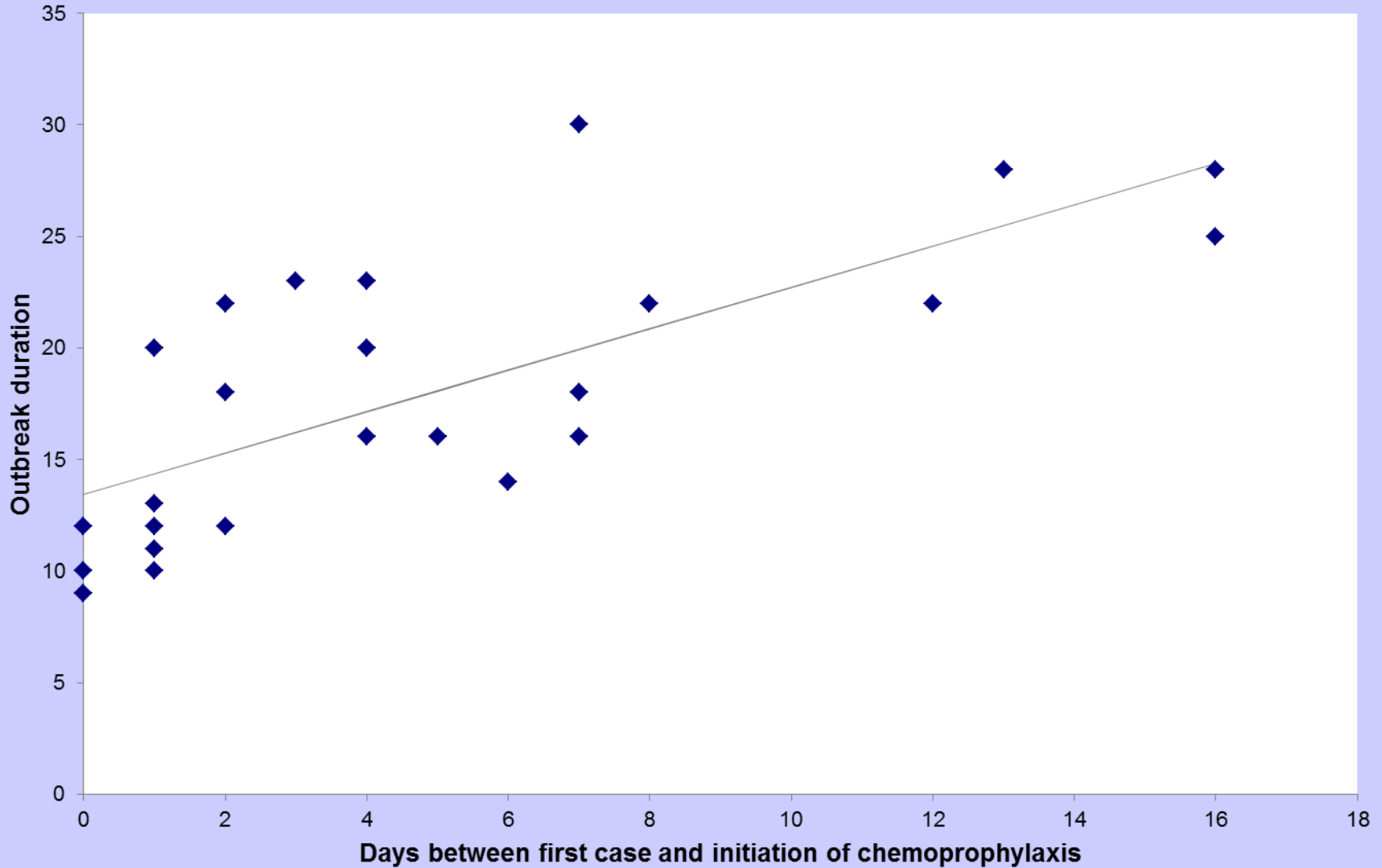
Flu ravaging nursing homes

Influenza A Outbreaks WRHA CNPHI Reported 2013-15



WRHA Nursing Home Influenza Outbreaks 2014-15 (N = 25)

Relationship between delays in chemoprophylaxis and outbreak duration



Conclusions

1. **Oseltamivir deployed at 25 sites reporting incident cases during outbreak**
2. **Median time to initiate oseltamivir 4 days (range 0 to 16 days)**
3. **Median duration of outbreak 15 days (range 9 to 32 days)**
4. **Direct relationship between time to deploy oseltamivir and duration of outbreak**