Influenza:
The evolution within and around us

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Ecology & Evolution, University of Chicago
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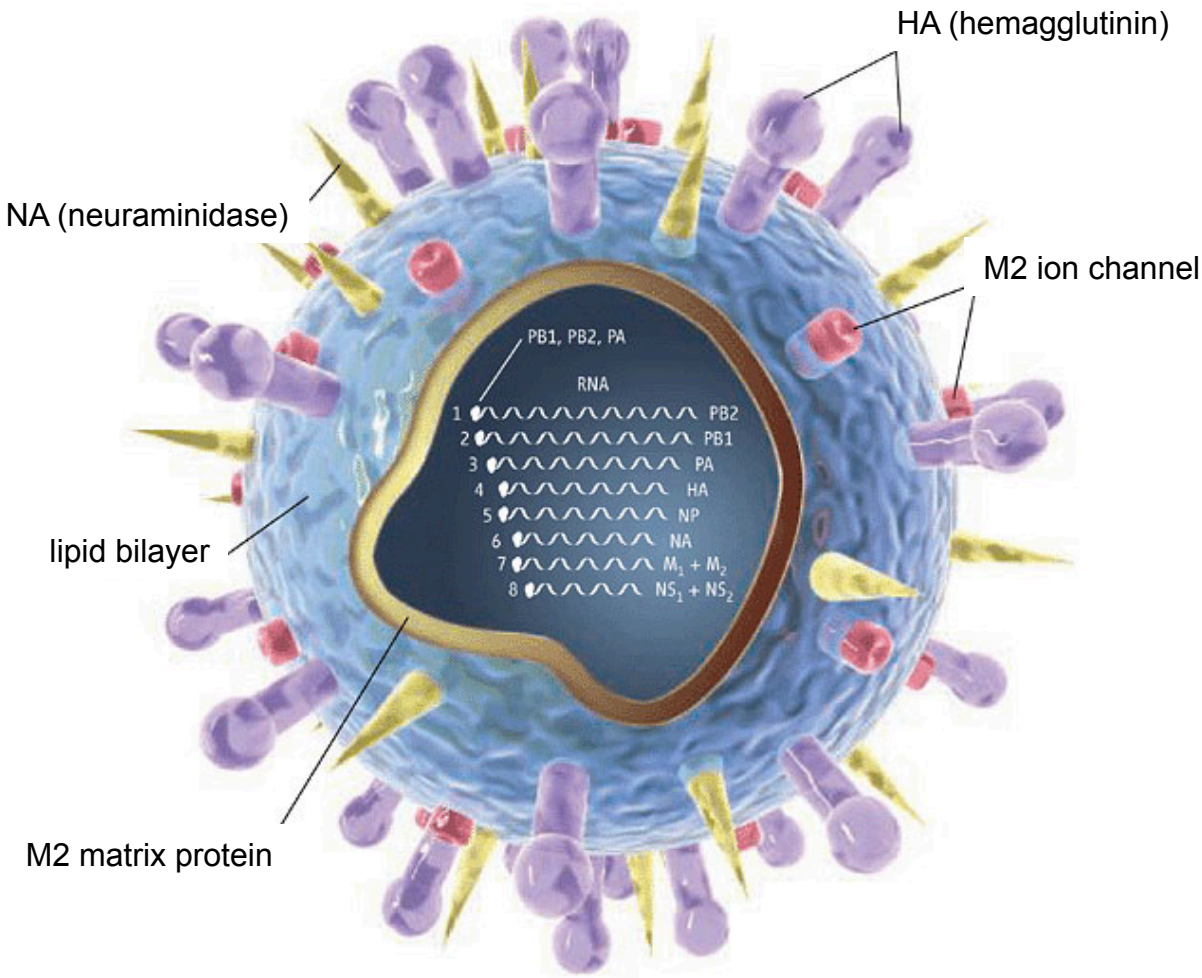
How does influenza emerge from animals?

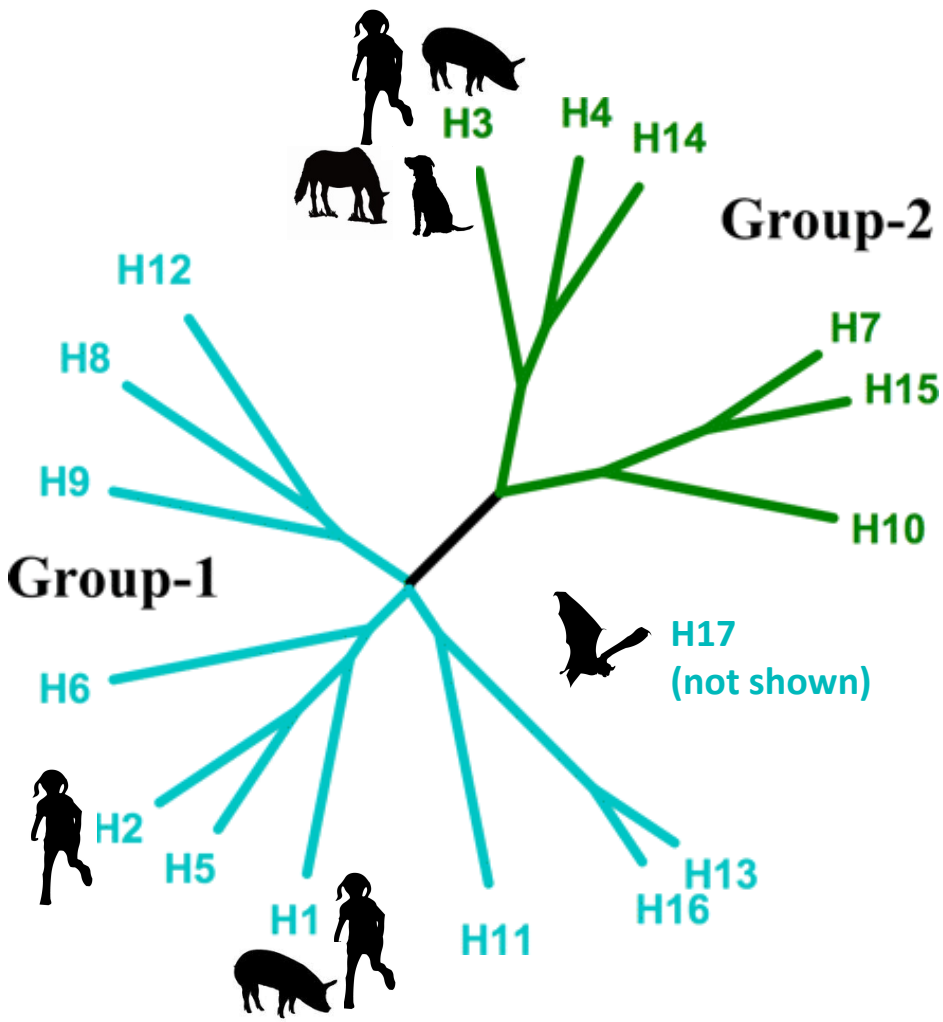
Influenza virus



Chris Bickel, *Science*, 2006

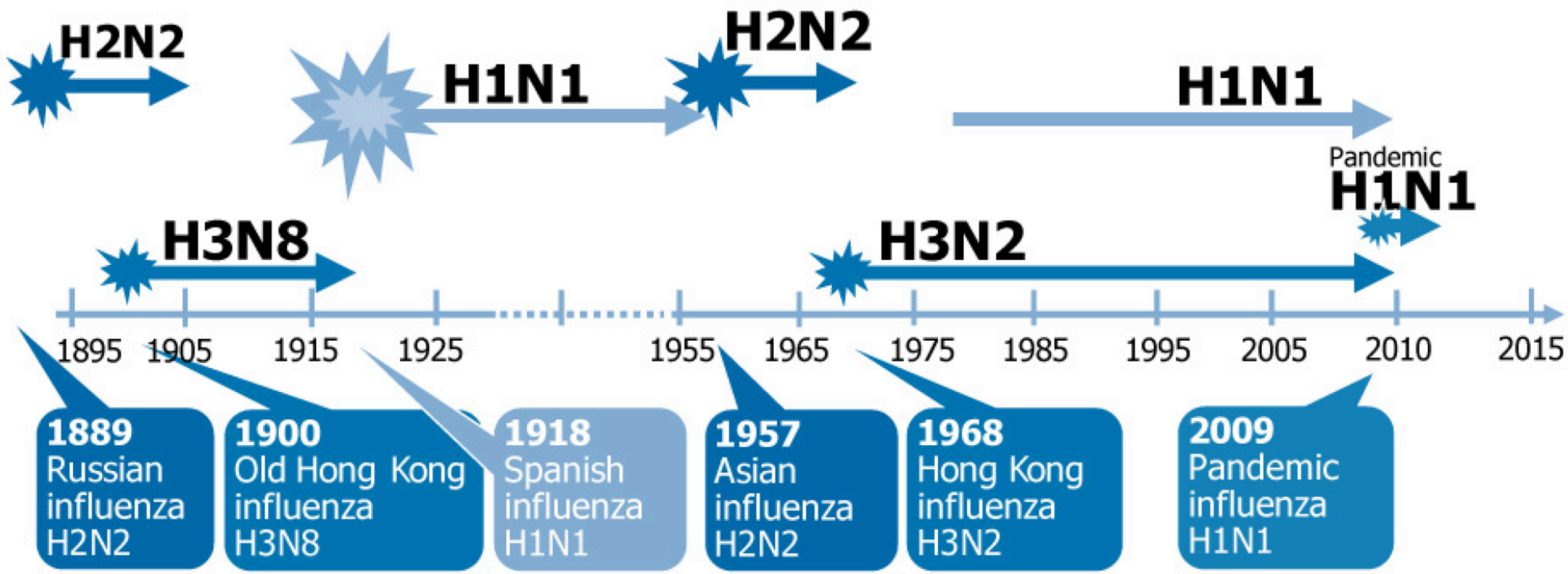
Hosts of influenza

- Birds are the main source of influenza A
- Some subtypes in mammals, e.g., dogs, horses, pigs, humans
- Types B and C are almost only in humans



History of influenza A in humans

Recorded human pandemic influenzas since 1885 (early sub-types inferred)



Source: European Centre for Disease Prevention and Control (ECDC) 2009

Reproduced and adapted (2009) with permission of Dr Masato Tashiro, Director, Center for Influenza Virus Research, National Institute of Infectious Diseases (NIID), Japan.

Nicoll, Eurosurveillance, 2010

Subtype success depends on immunity … and other things we don't understand!

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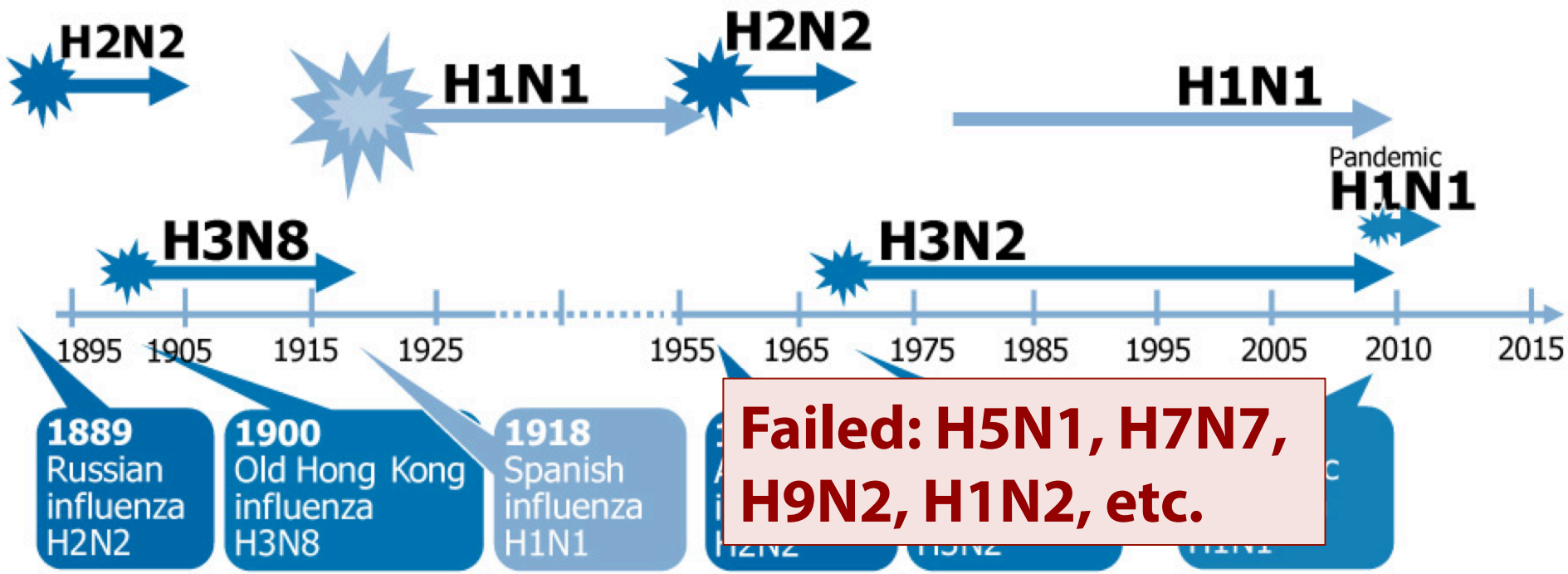

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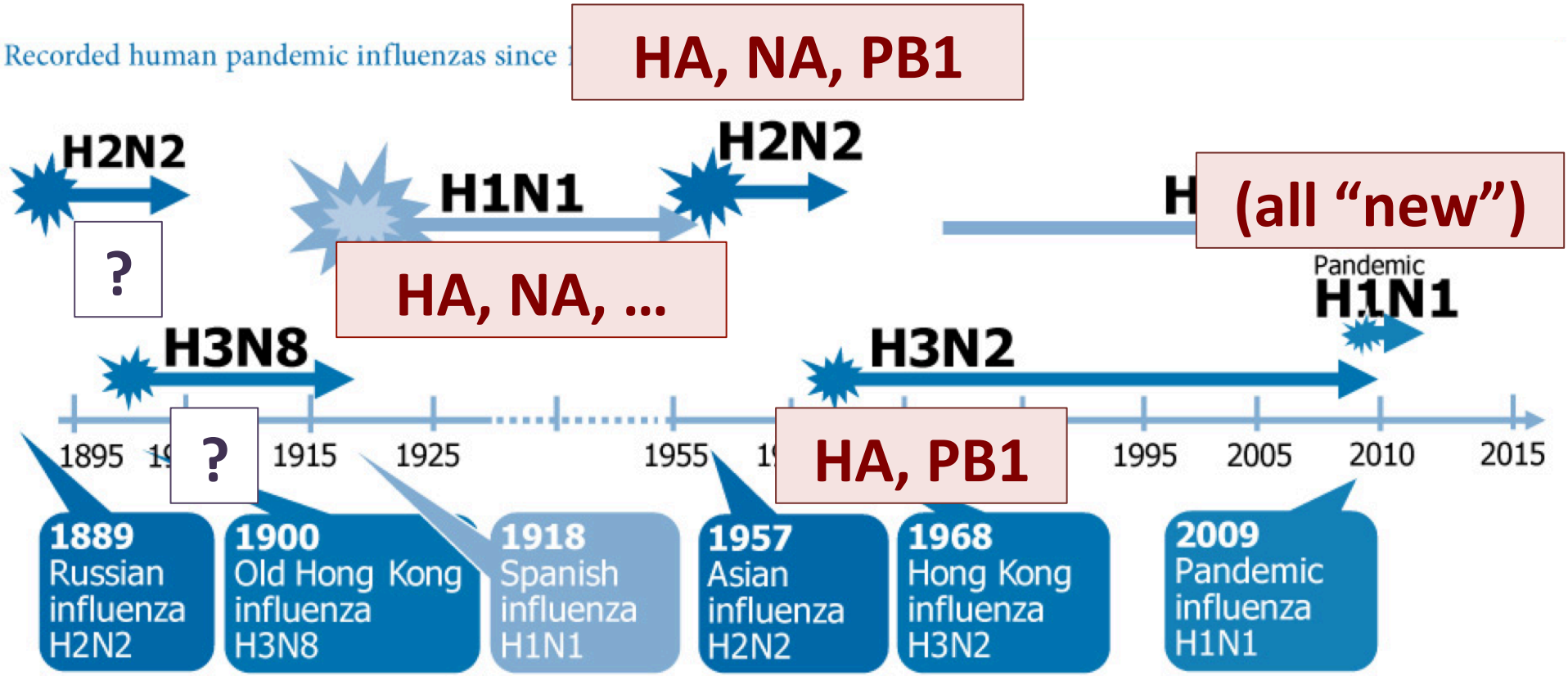
New subtypes often aren't so new



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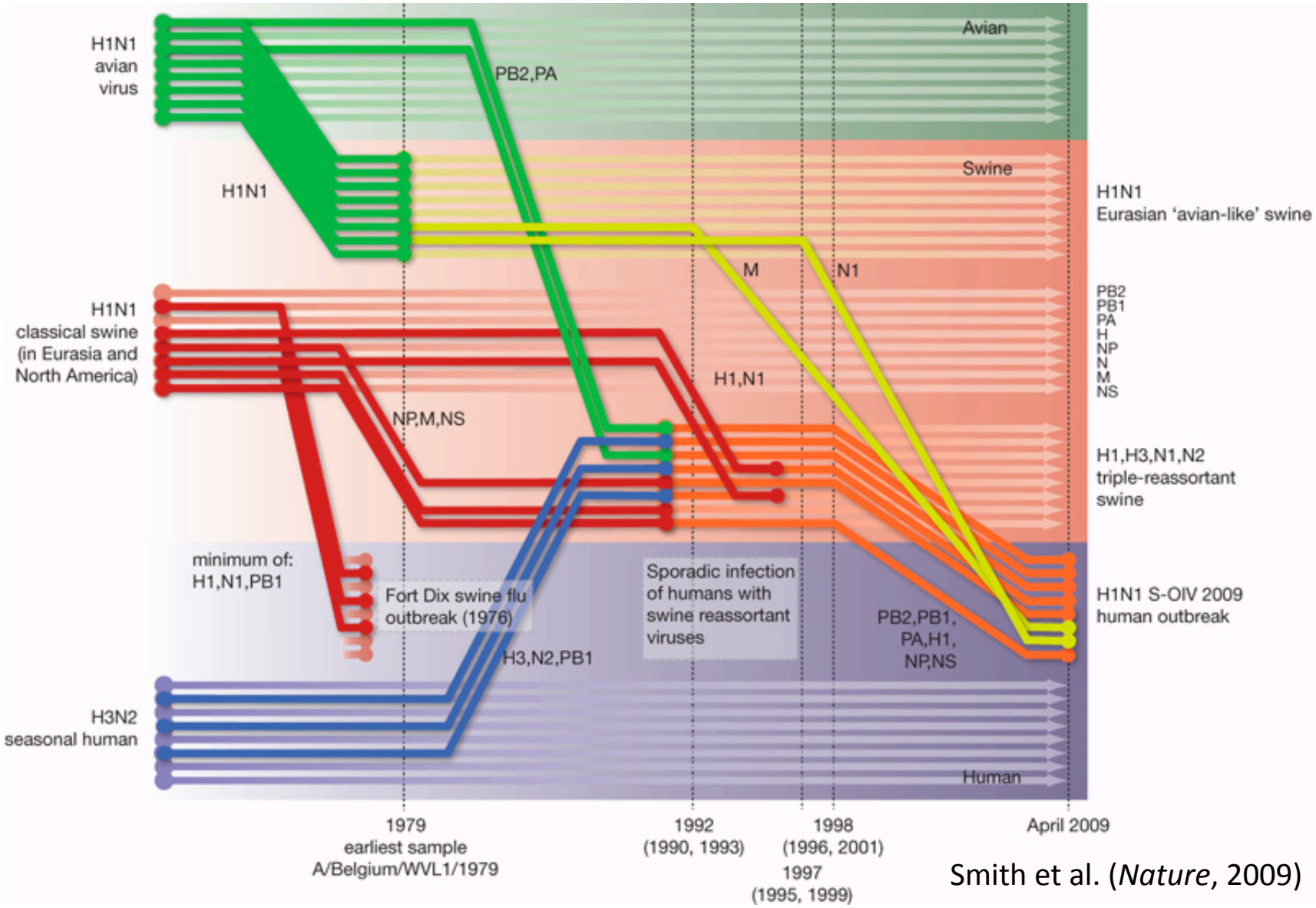
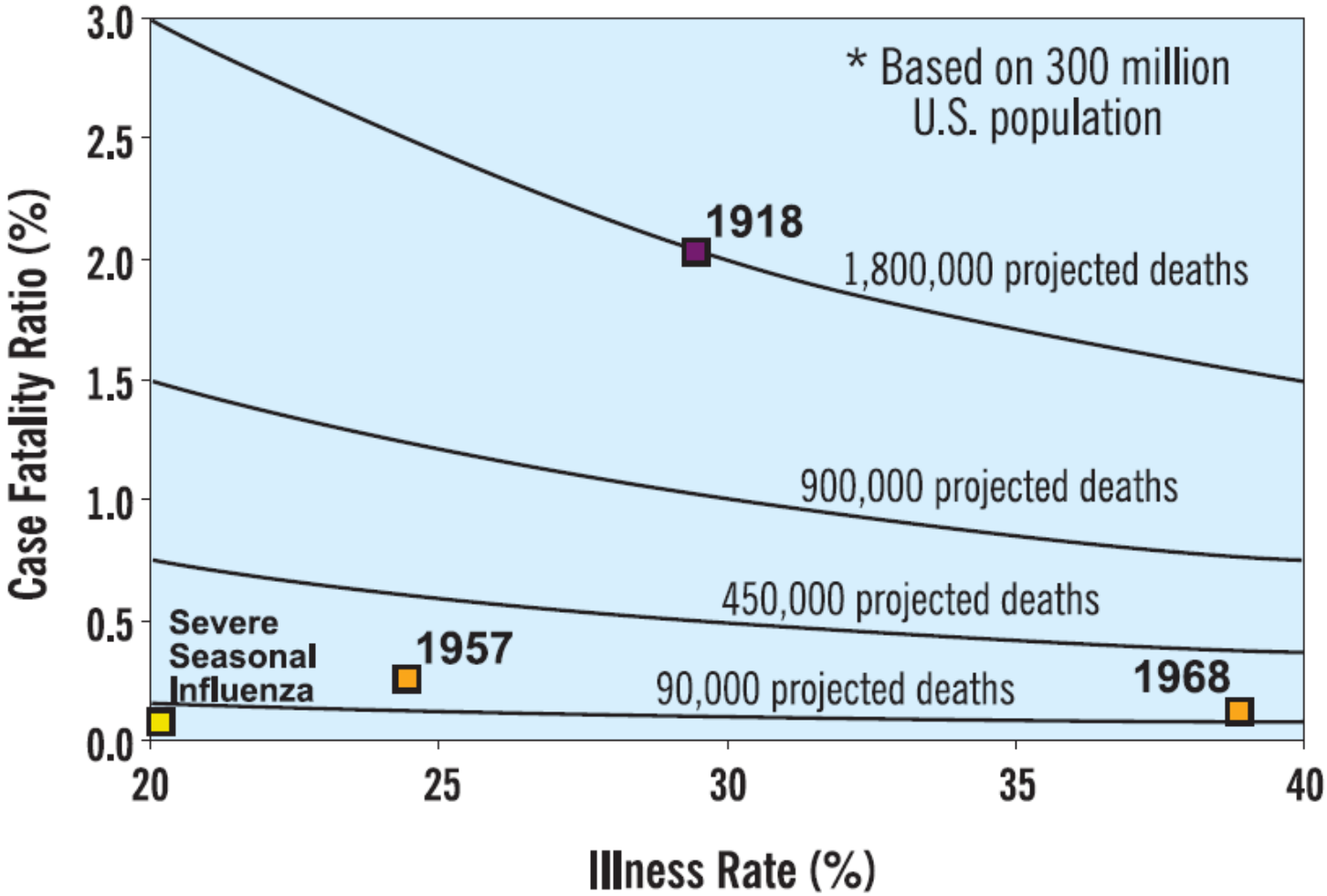
Ancestry of 2009 pandemic H1N1



Smith et al. (*Nature*, 2009)

Current controversy: Should we try to create pandemic strains to study them?

Pandemic flu: High incidence & severity



US Govt, *Community Strategy for Pandemic Influenza Mitigation*

How is influenza transmitted?

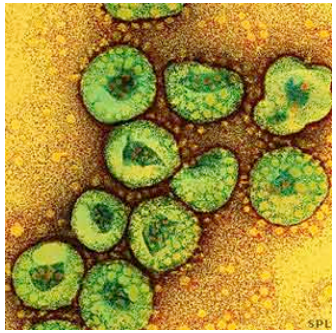
Fun facts about flu
(why flu is hard to study)

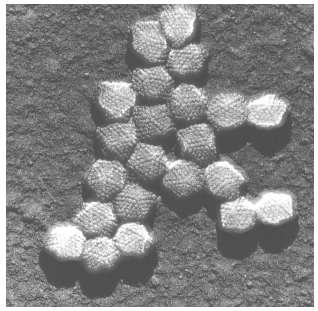
- Most people with flu-like illnesses do not have the flu!

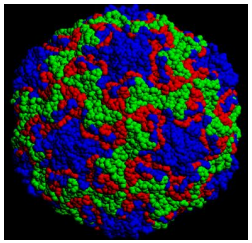
  (rhinovirus, adenovirus, coronavirus, respiratory syncytial virus, metapneumovirus, etc.)

- Mortality from influenza does not come directly from influenza

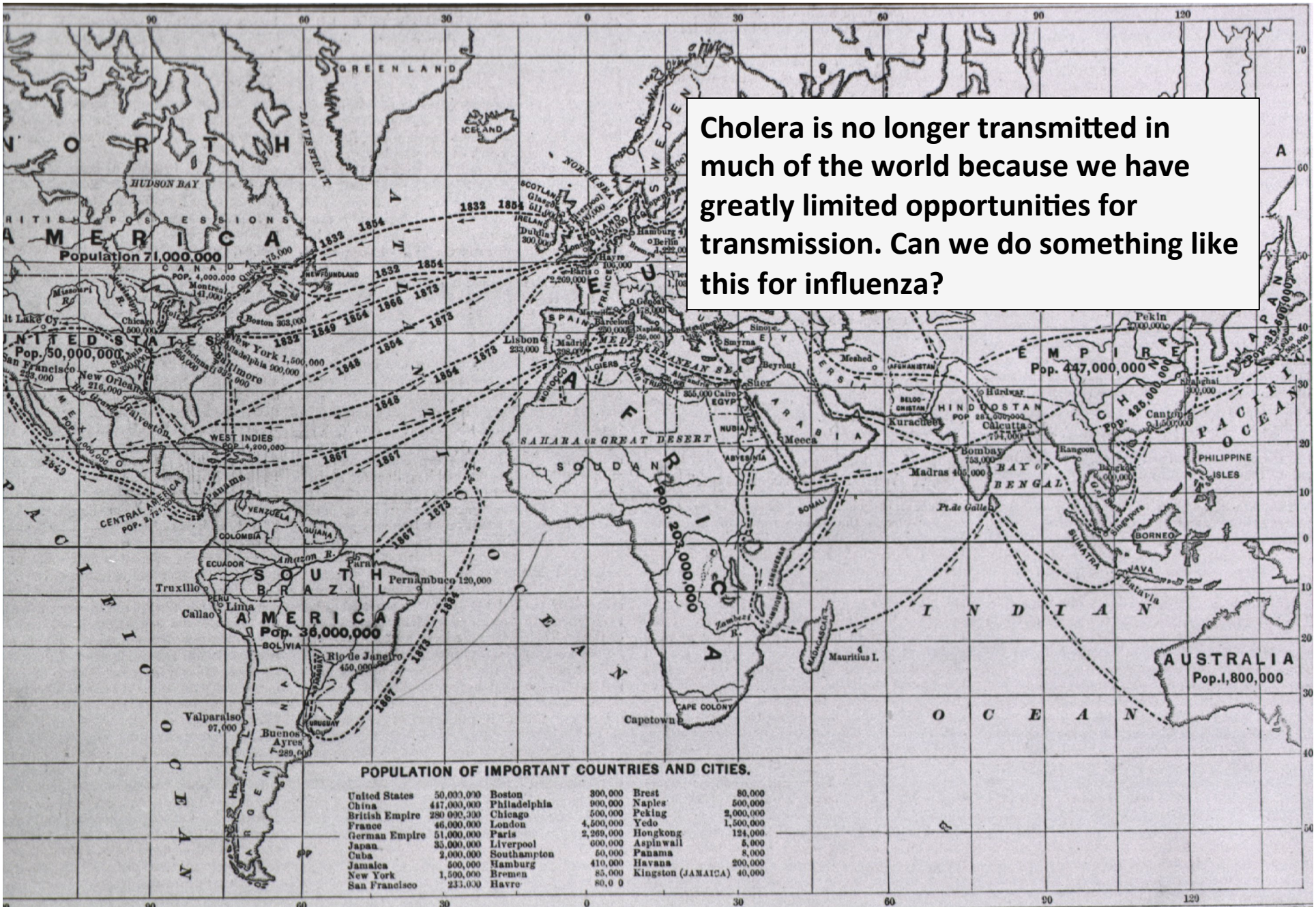
  (often *Streptococcus pneumoniae*)







Cholera is no longer transmitted in much of the world because we have greatly limited opportunities for transmission. Can we do something like this for influenza?

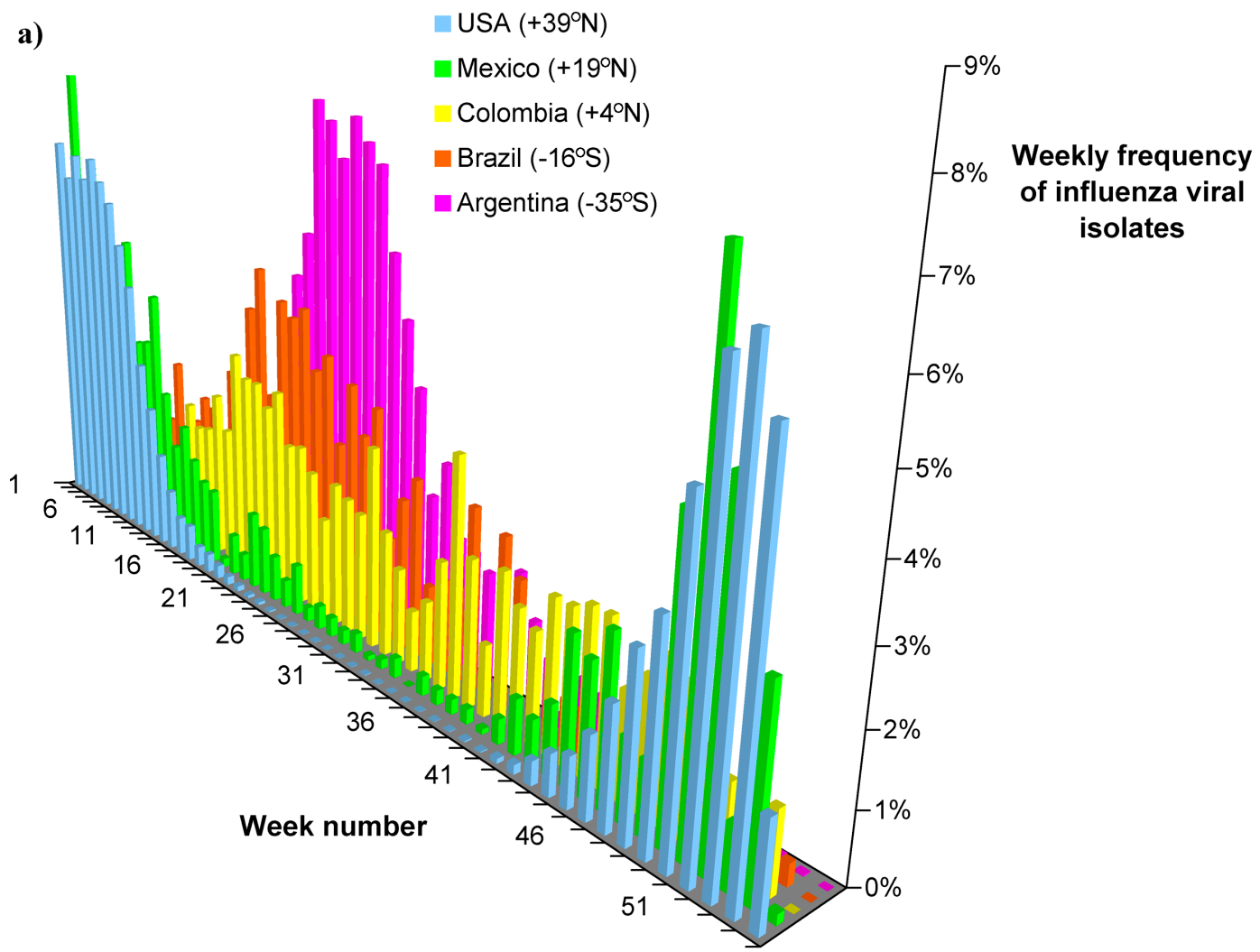


ROUTES OF ASIATIC CHOLERA.—By Dr. John C. Peters.—[See Page 267.]

How is flu transmitted?

- Three potential modes: droplets, aerosols, fomites/direct contact
- Strong support for aerosol and droplet modes
- Relative contributions of different modes of transmission could vary by age group, location, and time of year!

All flu by latitude

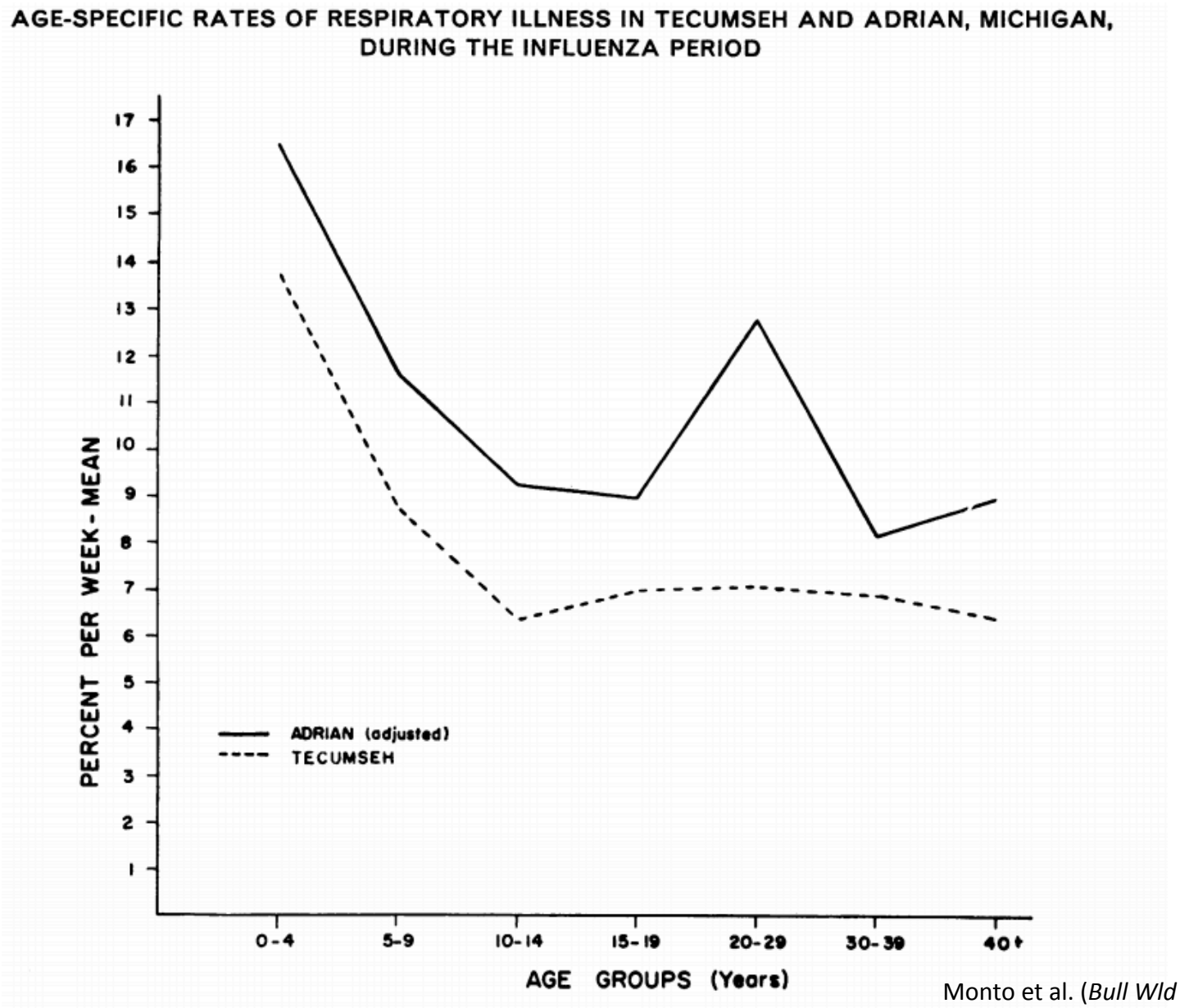


Viboud et al. (*PLoS Med*, 2006)

Why does flu peak in the winter?

- Low absolute humidity
- School terms (kids!)
- Vitamin D deficiency?

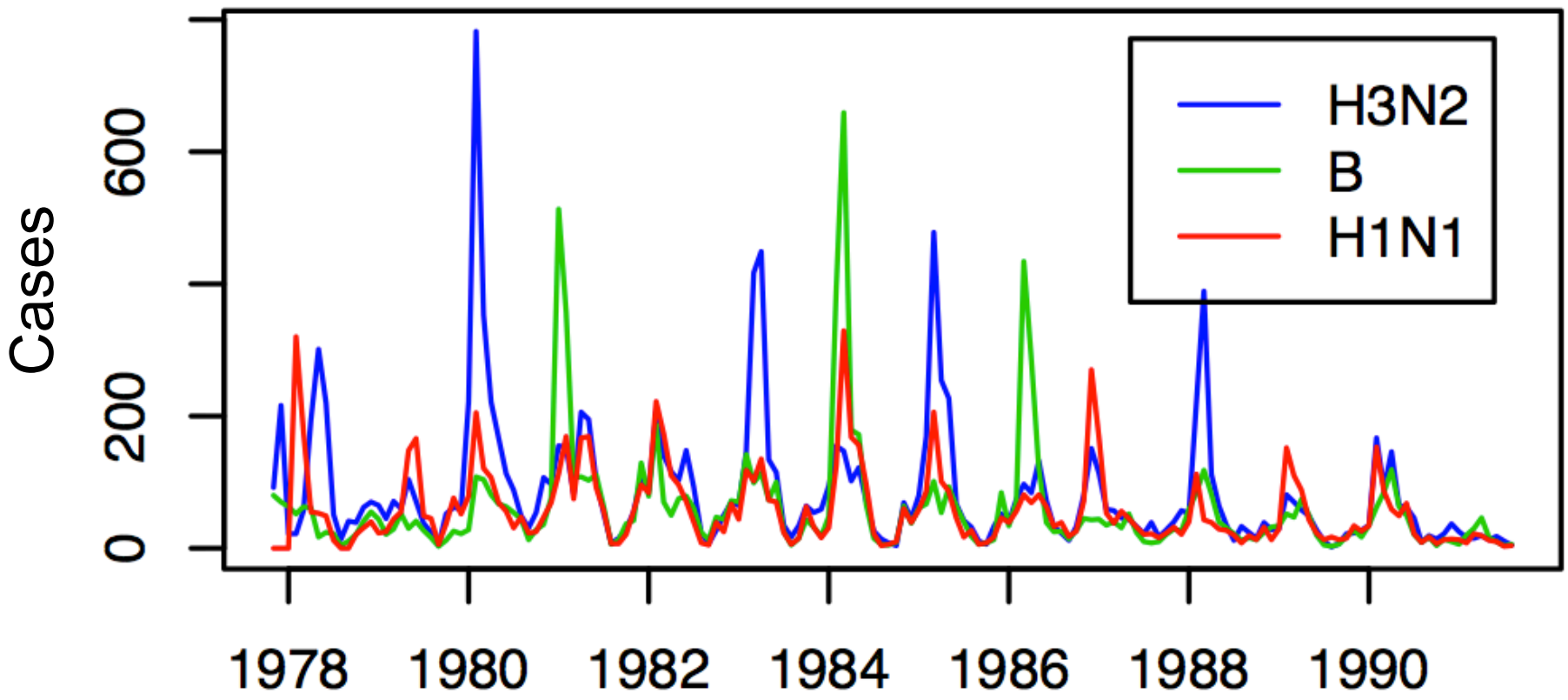
Tecumseh study (1968-1969)



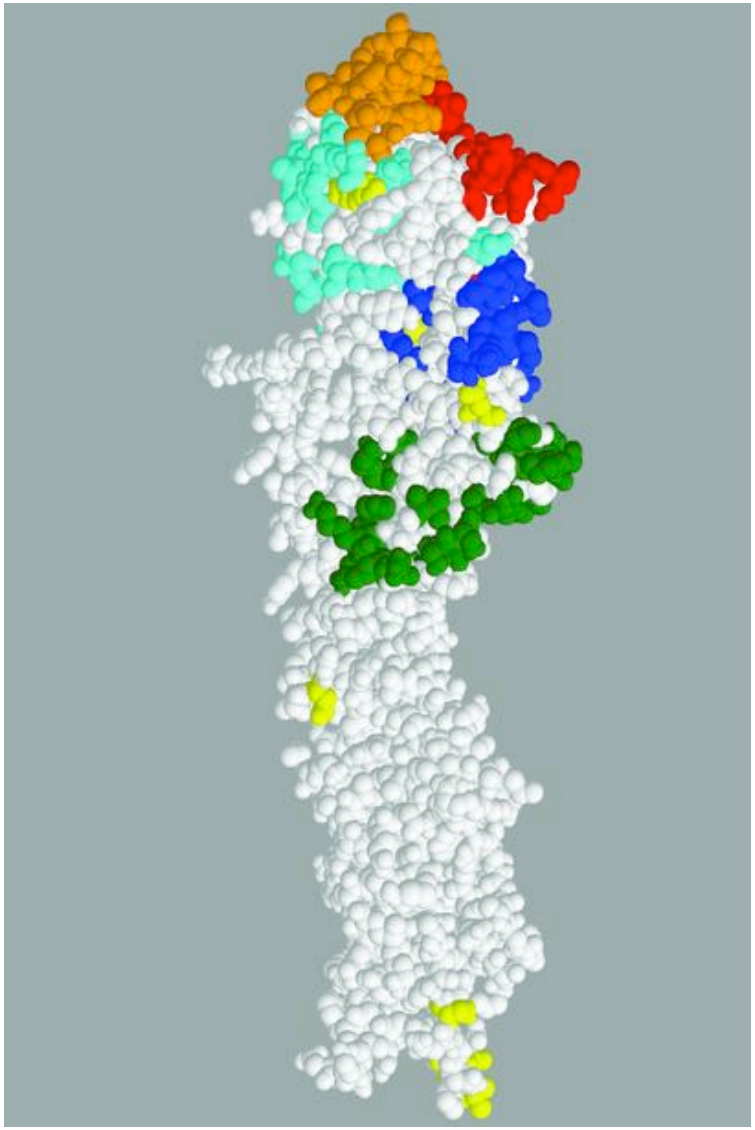
Monto et al. (*Bull Wld Hlth Org*, 1969)

How does influenza persist globally?

Influenza keeps coming back!

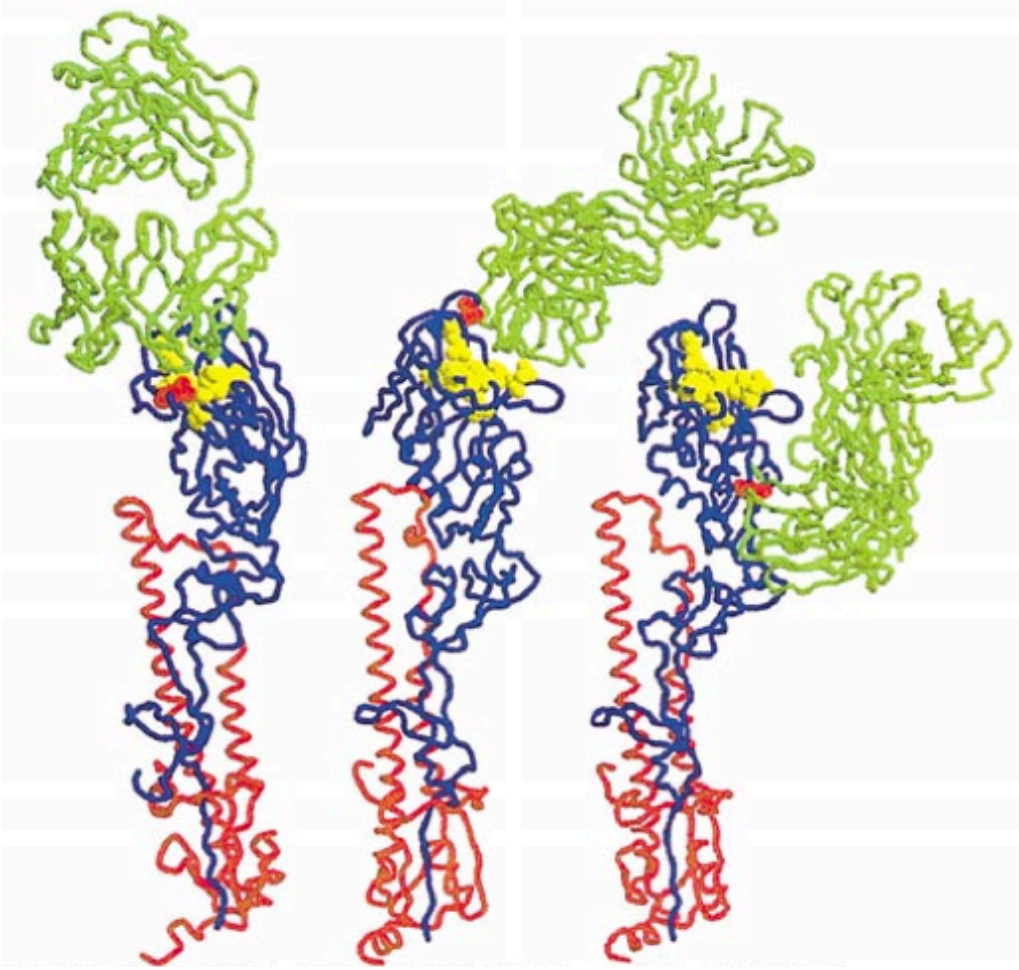


Evolving surface of the H3 hemagglutinin



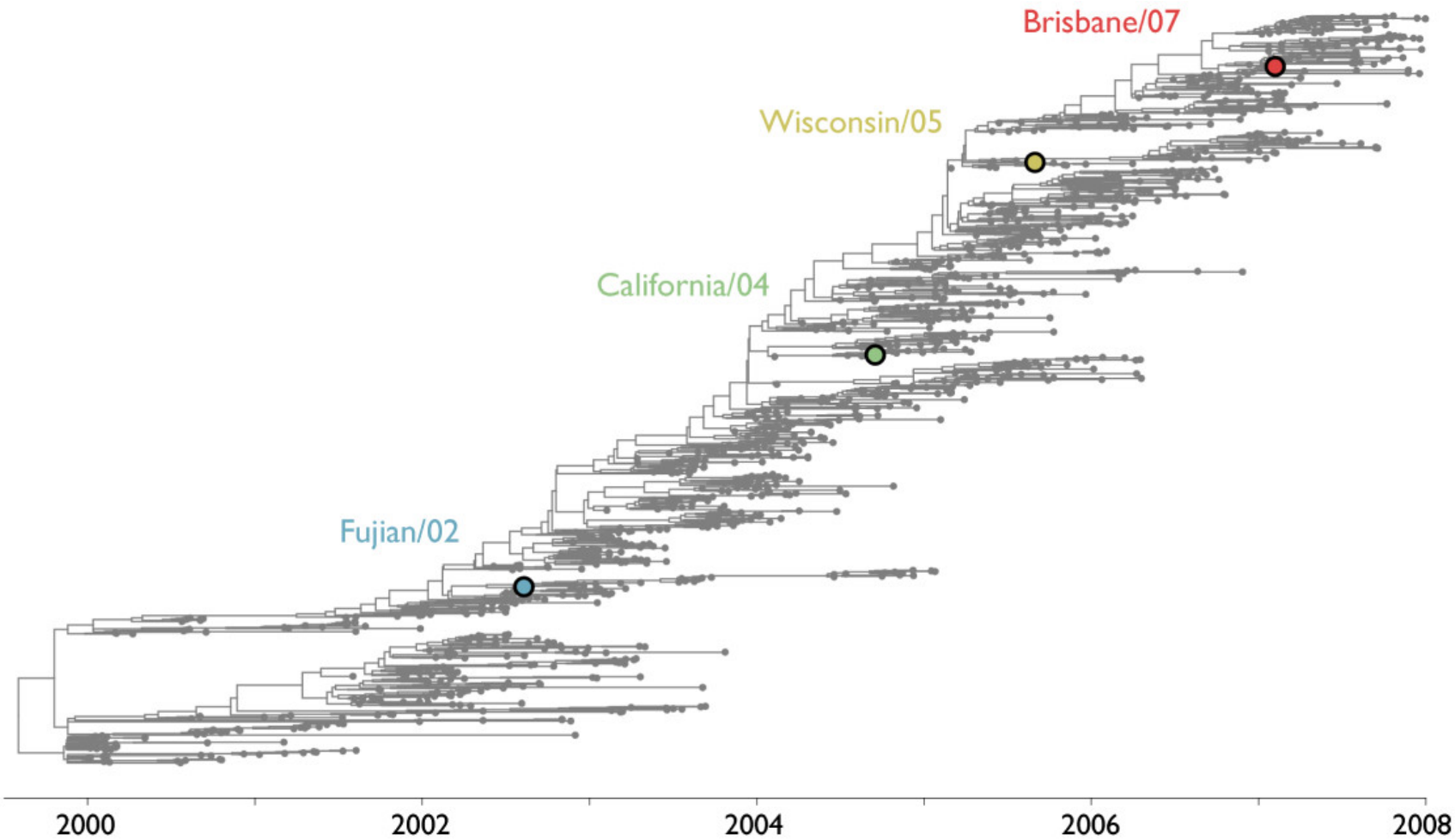
Plotkin & Dushoff 2004 *PNAS*

Antibodies drive flu evolution



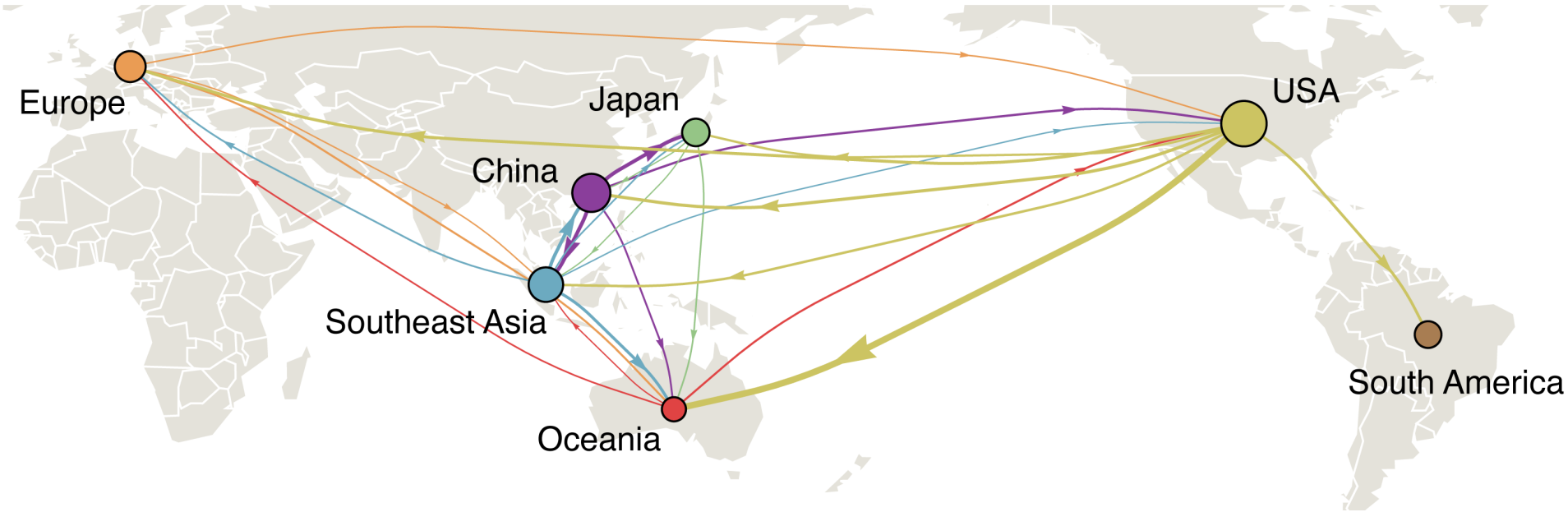
Knossow et al. (2002, *Virology*)

Current flu population is only 2-4 years old



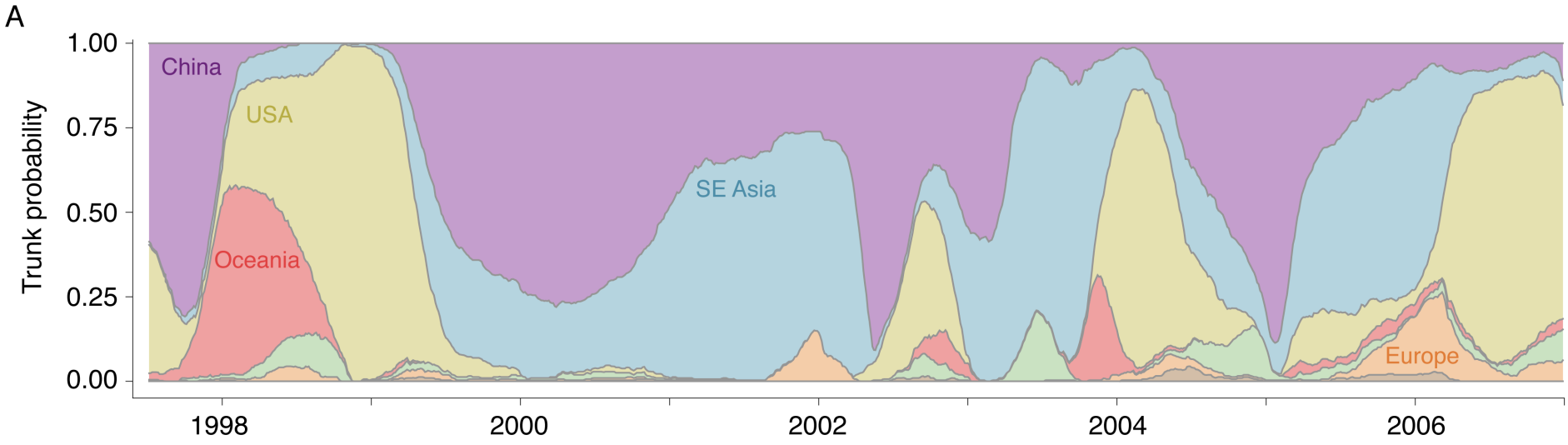
Bedford et al. (*BMC Evol Biol*, 2011)

Flu routinely travels between continents



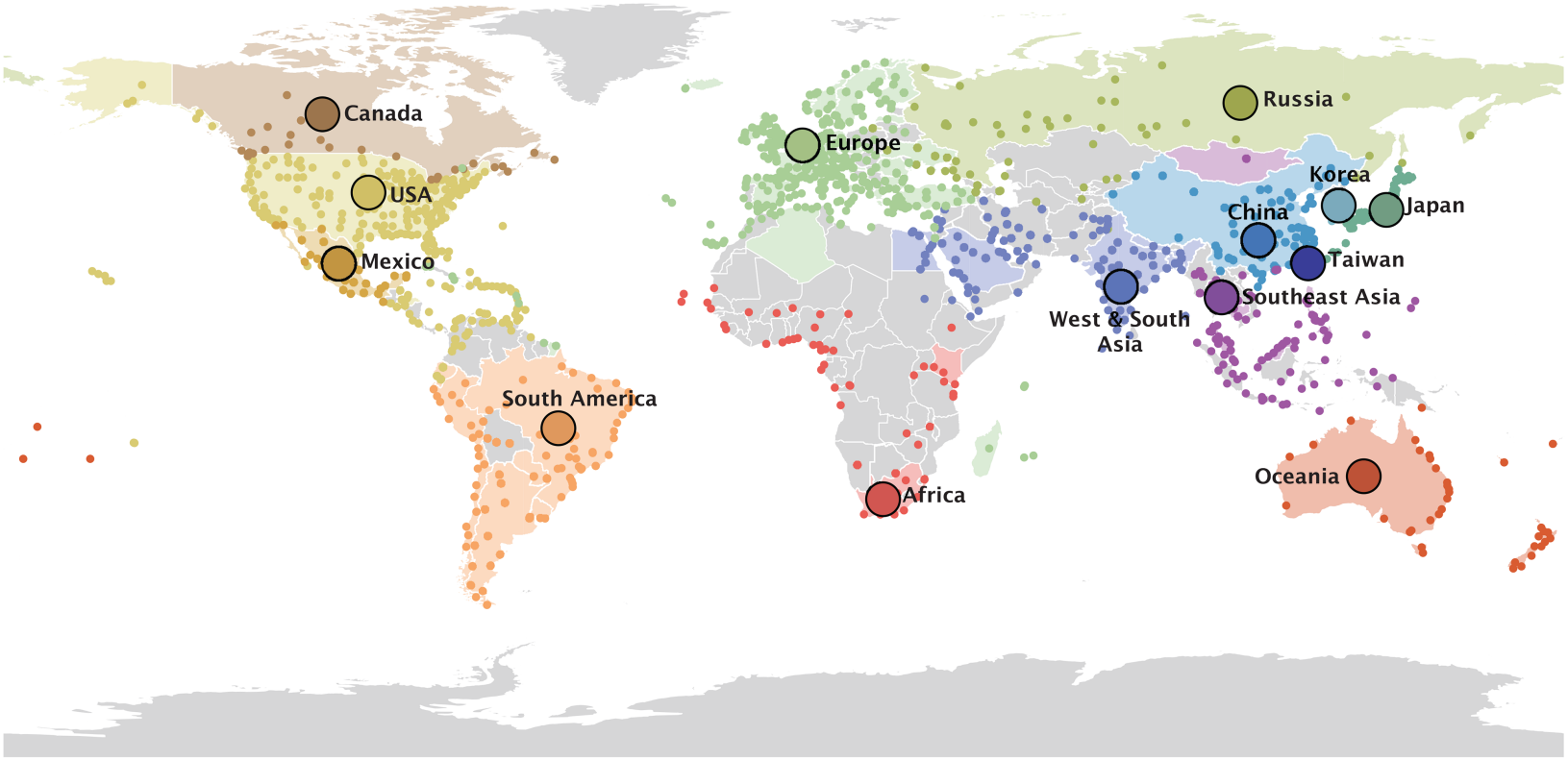
Bedford et al. (*PLoS Path*, 2010)

Roughly 2/3 of successful strains originate in Asia



Bedford et al. (*PLoS Path*, 2010)

Air travel “communities” shape flu migration

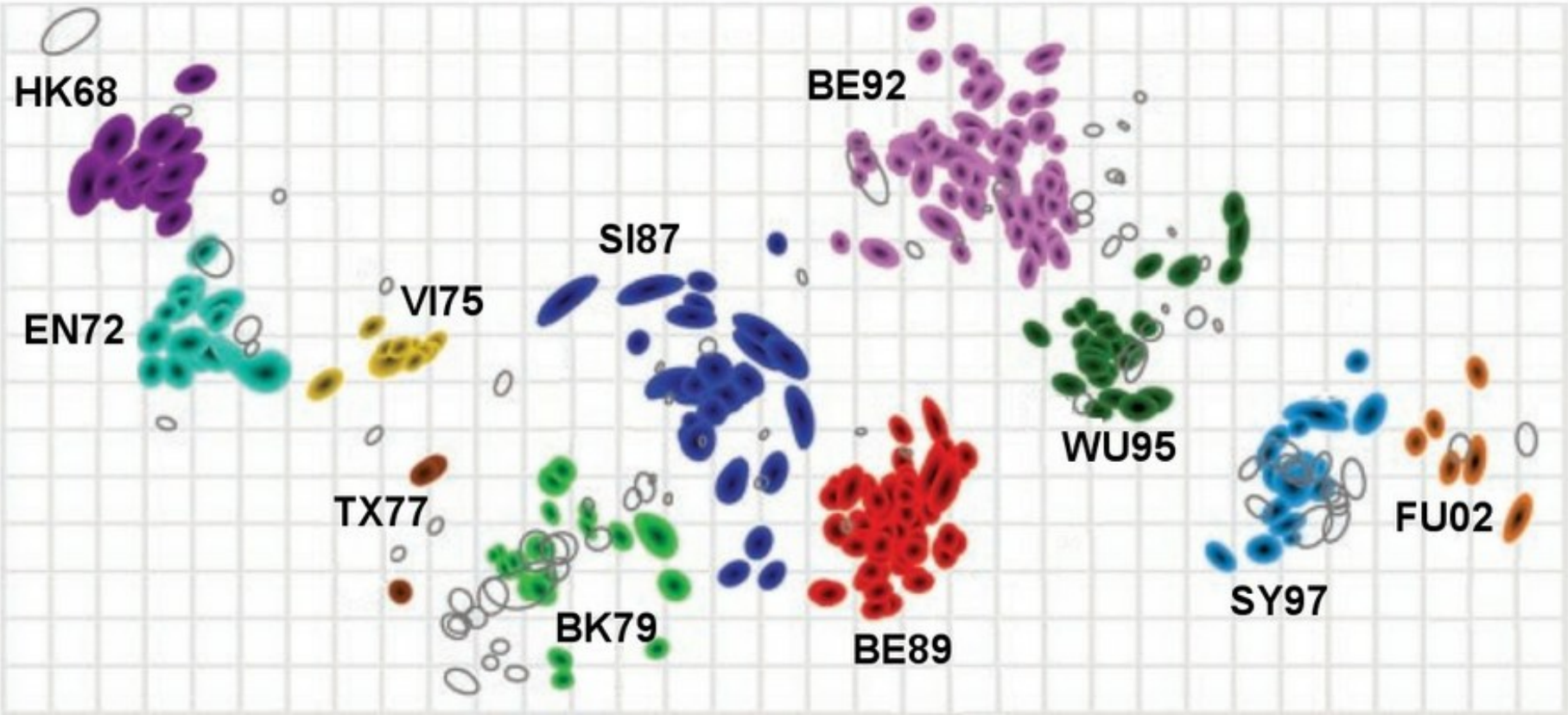


Lemey et al. (*PLoS Path*, 2014)

How do flu vaccines work?
(And why are they so lousy sometimes?)

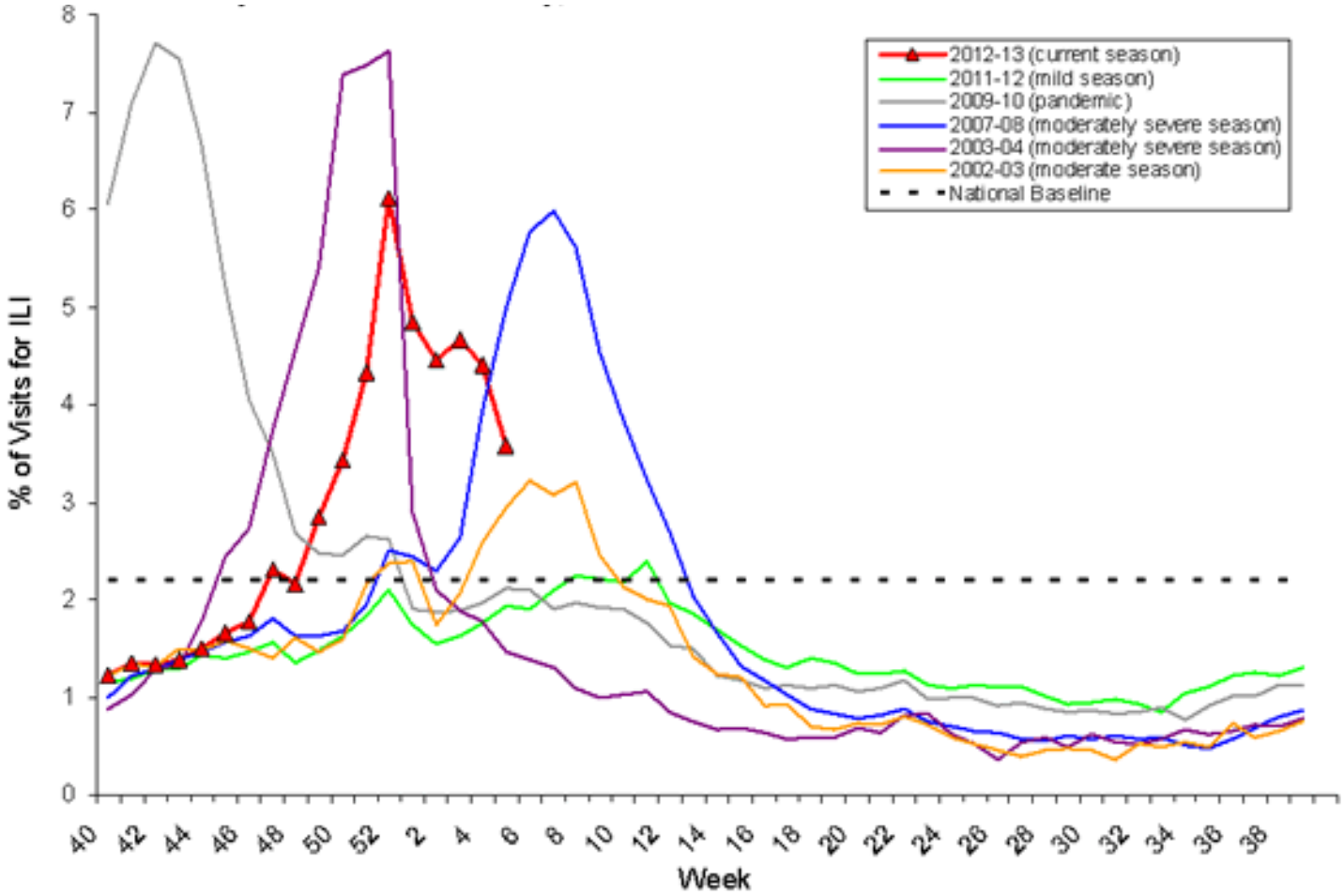
Influenza is a moving target, and vaccine strategy is a hot topic

Influenza is always evolving to avoid immune recognition



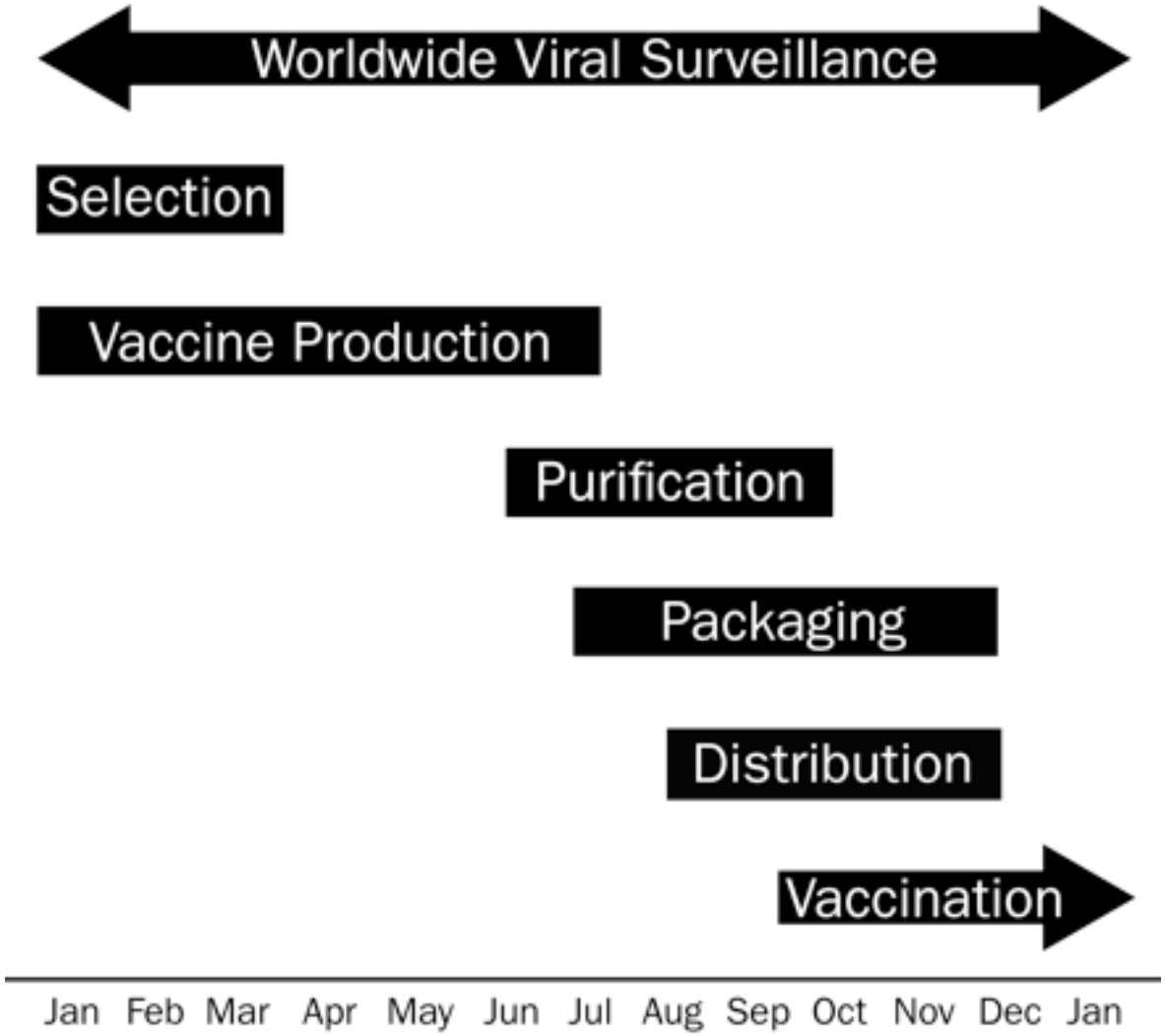
Smith et al. (*Science*, 2004)

Rate of change determines severity of flu season



CDC, 2013

Vaccine development timeline



P Tosh et al. *Mayo Clin Proc* 2010

How are vaccine strains chosen? It's complicated…

- Use data collected by the WHO Global Influenza Surveillance and Response System (GISRS), which includes:
  - 135 National Influenza Centers (NICs)
  - 6 WHO Collaborating Centers (WHOCCs)
  - 4 WHO Essential Regulatory Laboratories (ERLs)
- Essentially, semi-quantitative heuristics developed by the WHO vaccine strain selection committee. Vaccine updates recommended on basis of:
  - Antigenic novelty, mostly based on hemagglutination inhibition (HI) assay – NA antigenic data not widely used
  - Evidence of geographic spread and association with disease—sampling biased toward N. America, Europe, and E & SE Asia
  - Phylogenetic patterns, including substitutions at exposed sites, to help resolve antigenic changes
  - Ability of reassortant to grow well in eggs (problem for H3N2)
- Since 1998, biannual recommendations (Feb. and Sept.)

New vaccine may be needed every year for at least one subtype

Year	A/H1N1	A/H3N2	B
2010	A/California (pdm)	A/Perth	B/Brisbane
2009	A/Brisbane	A/Brisbane	B/Brisbane
2008	A/Brisbane	A/Brisbane	B/Florida
2007	A/Solomon Isl	A/Wisconsin	B/Malaysia
2006	A/New Caledonia	A/Wisconsin	B/Malaysia
2005	A/New Caledonia	A/California	B/Jiangsu
2004	A/New Caledonia	A/Fujian / A/ Wyoming	B/Shanghai / B/ Jiangsu
2003	A/New Caledonia	A/Panama*	B/Hong Kong

Wikipedia: verified with
http://www.who.int/csr/disease/influenza/vaccinerecommendations1/en/index.html

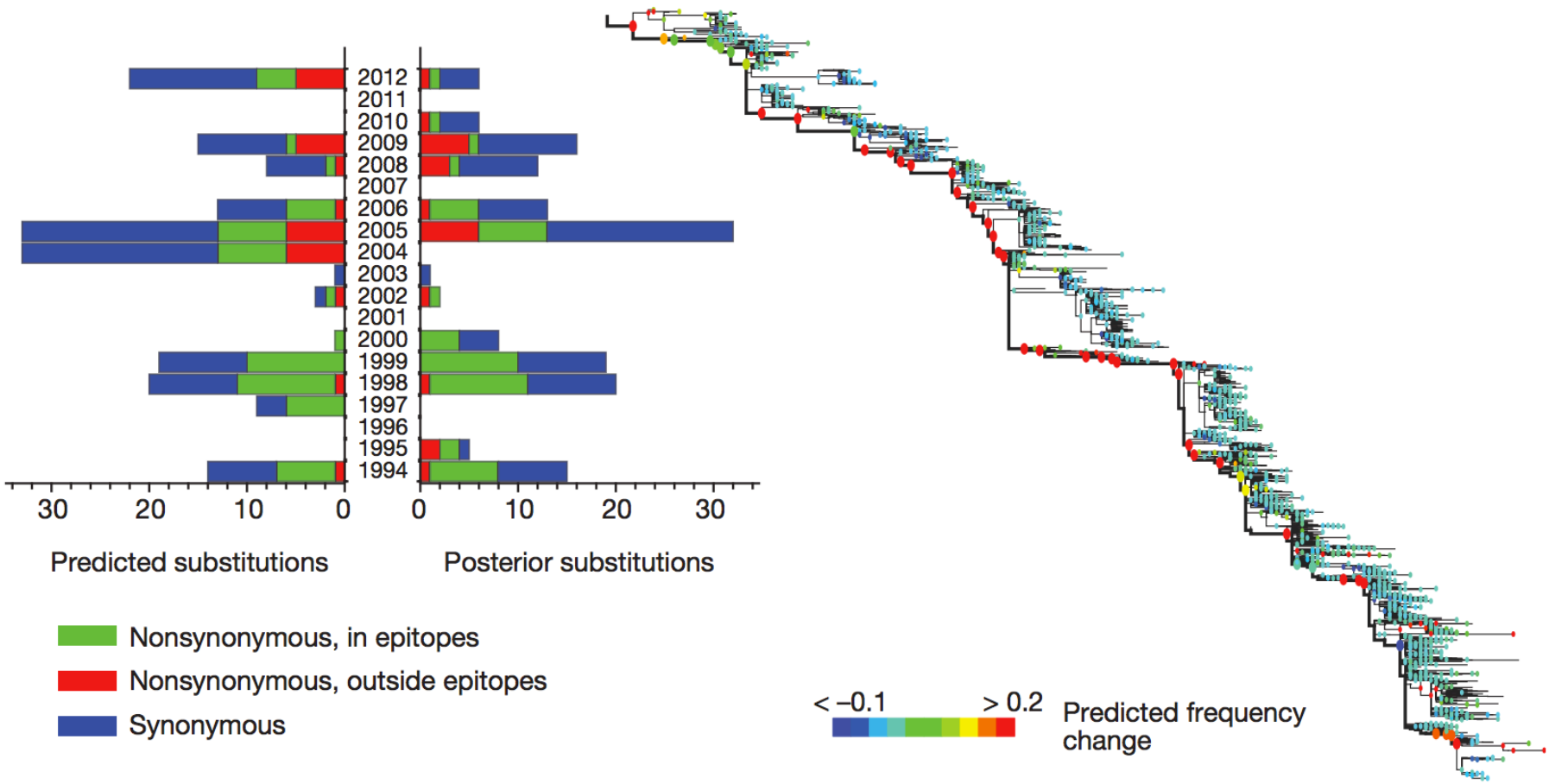
Flu vaccines are, *on average*, efficacious

In children, the live attenuated vaccine works best.

In adults*, both work equally well.

*Older adults need special formulation.

Models can predict evolution



Luksza & Lassig *Nature* 2014