UR MEDICINE
GOLISANO CHILDREN'S HOSPITAL

UNIVERSITY of ROCHESTER
NYICE
New York Influenza Center of Excellence

Influenza Vaccines:
The science, the myths, and looking towards the future

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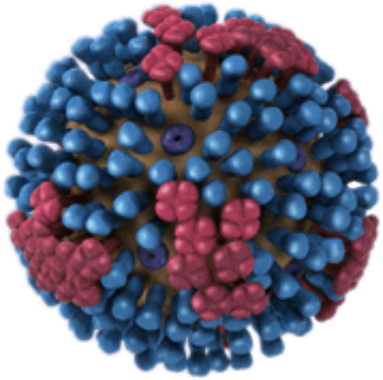
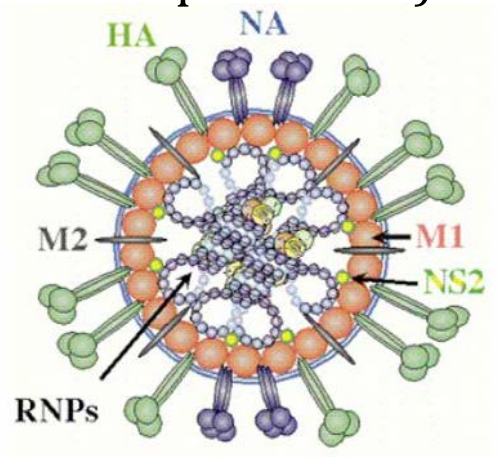


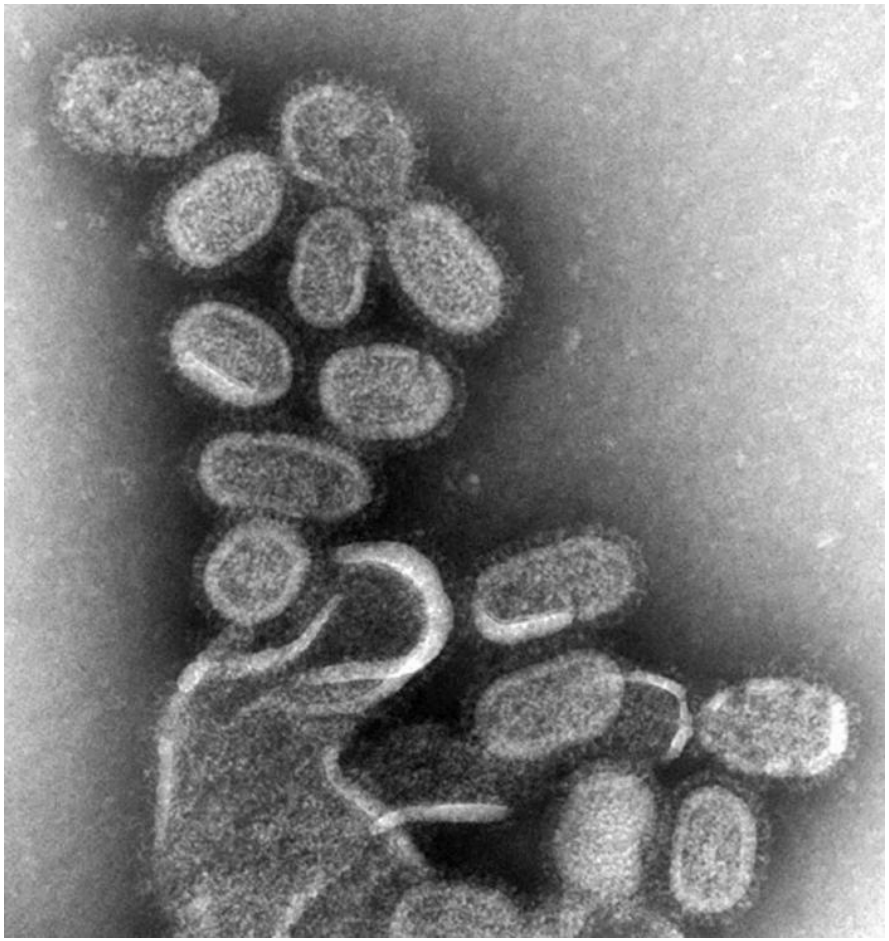
Overview of Discussion

- Brief discussion of influenza pathogenesis
- Overview of current influenza vaccination strategies and recommendations
- What happened to LAIV?
- Discussion of vaccine refusal
- Future goals

Influenza virus

- Enveloped negative strand RNA virus with a segmented genome
- Family Orthomyxoviridae
- Surface envelope contains the HA (sialic acid binding) and NA (sialic acid cleavage) proteins
- Spread mainly through respiratory droplets
- Some antibodies to HA can block viral uptake and thus can be neutralizing (major known correlate of protection)





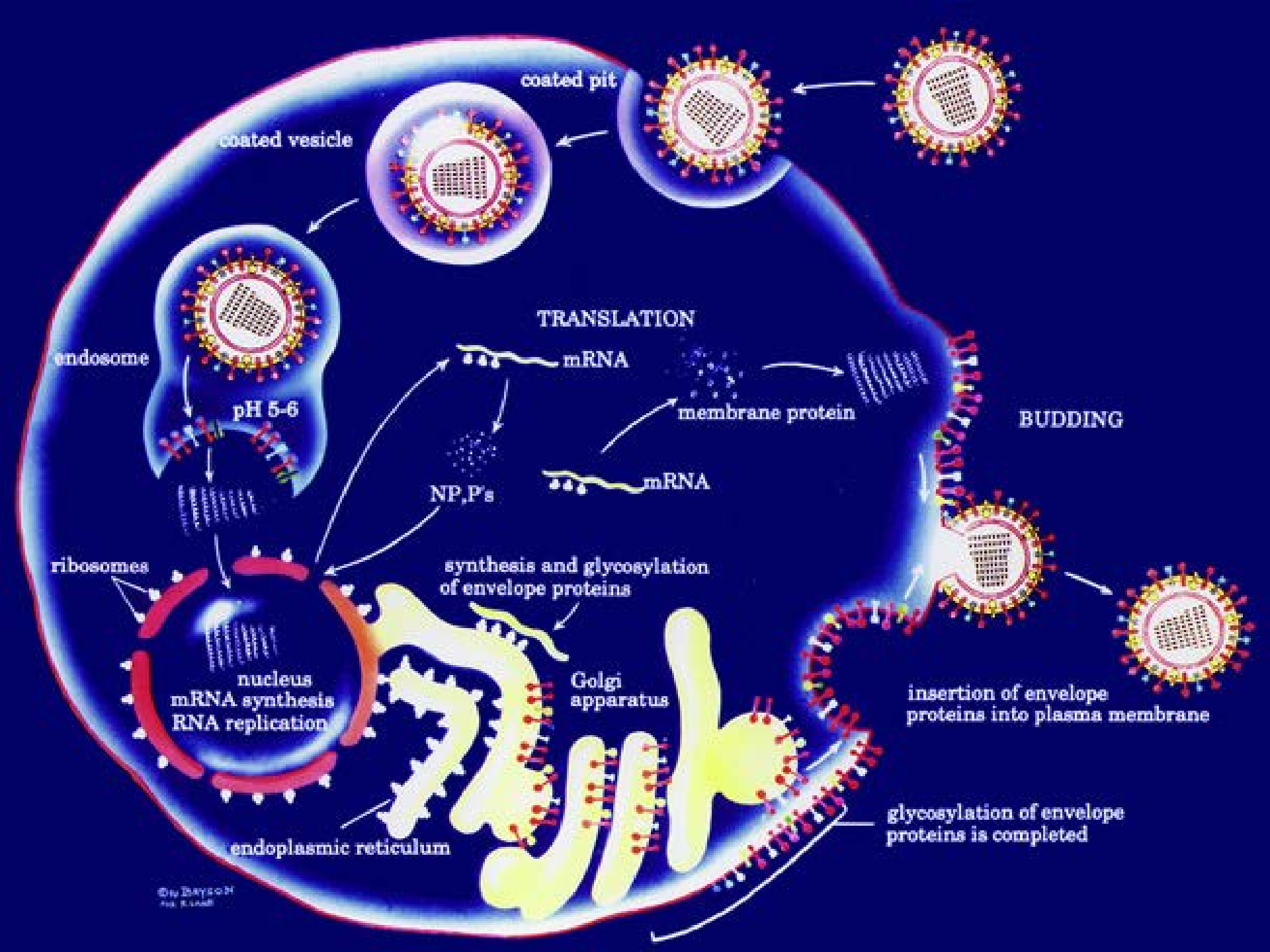
Background information

- Influenza A viruses infect a wide range of avian and mammalian species, including humans
- Influenza B viruses predominantly infect humans
- Influenza C known to infect humans and pigs
  - Infections more rare compared to types A or B





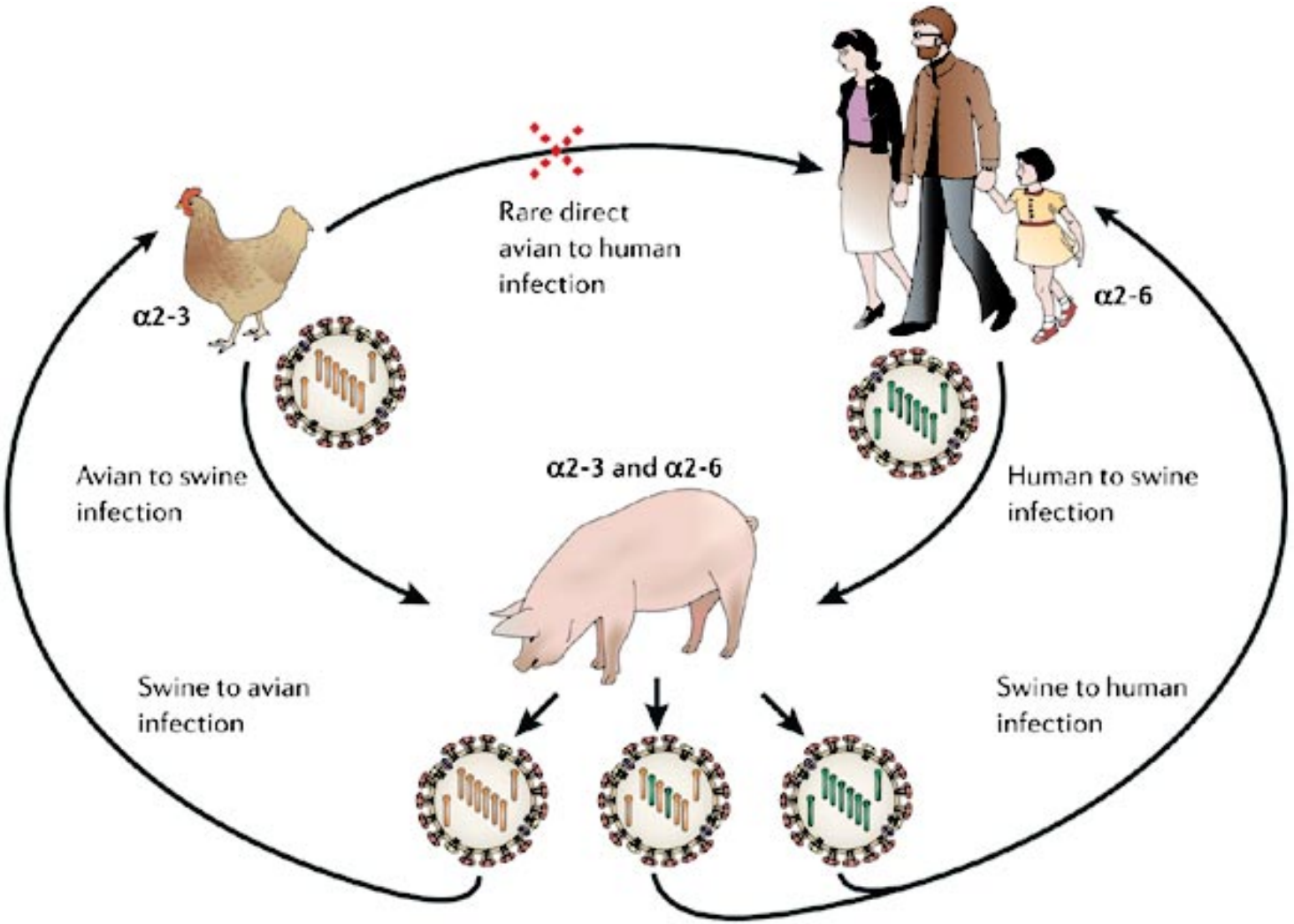


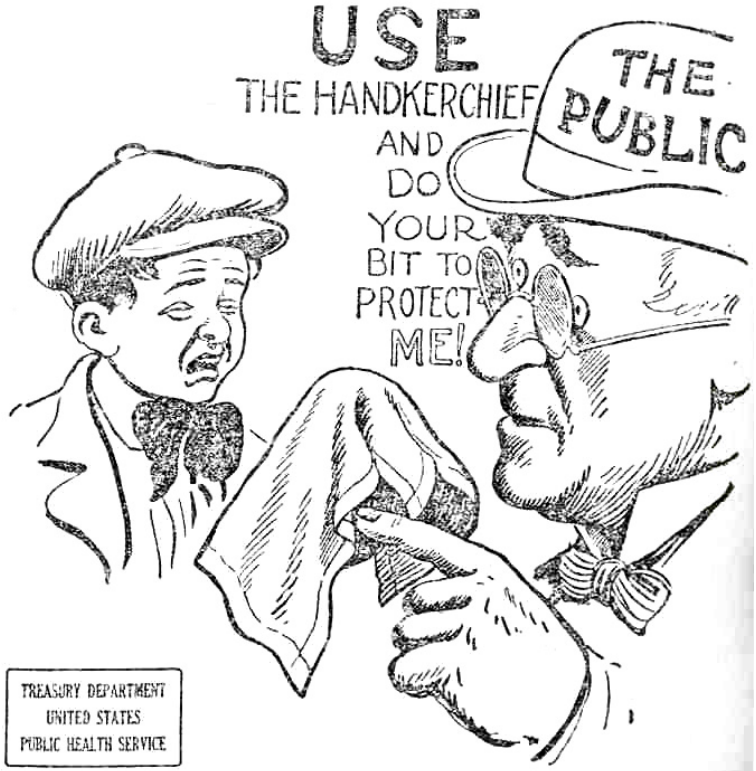

coated pit
coated vesicle
endosome
pH 5-6
TRANSLATION
mRNA
membrane protein
BUDDING
NP, P's
mRNA
ribosomes
synthesis and glycosylation
of envelope proteins
nucleus
mRNA synthesis
RNA replication
Golgi
apparatus
insertion of envelope
proteins into plasma membrane
endoplasmic reticulum
glycosylation of envelope
proteins is completed

Antigenic Drift vs. Shift

- Antigenic drift: Selection of viruses with point mutations in the HA or NA genes by antibody prevalent in the population
  - Occurs with both influenza A and B viruses.
- Antigenic shift: Reassortment of gene segments in a host co-infected with two different strains of influenza
  - Can result in the introduction of pandemic viruses with completely novel hemagglutinin molecules (eg novel H1N1 virus)
  - May cause severe world-wide epidemics or pandemics.
  - Antigenic shift is seen only in influenza A viruses as only this viral subtype can infect hosts of diverse species.

Antigenic Shift





COLDS, INFLUENZA, PNEUMONIA, AND TUBERCULOSIS ARE SPREAD THIS WAY

12 Oct. 1918

PROVINCIAL SECRETARY'S DEPARTMENT

ONTARIO
PROVINCIAL BOARD OF HEALTH

INFLUENZA

PRECAUTIONS

Warning to Health Authorities

"'Health authorities have the power under Section 54, ss. 2, of the Public Health Act to close schools, churches, theatres and other places of assemblage if it is deemed advisable to do so.' Asked what the Board advises regarding this measure, we have said: 'The weight of public health authority is against closing such places, except perhaps in country districts, for the following reasons, viz.: In cities and towns it is impossible to prevent children commingling in the streets and playgrounds where they are without the supervision found in the schools. Hence closing schools is more effective in country districts. Closing schools is economically wasteful, and usually has no influence on the course of an outbreak of disease like influenza. Children are less likely to infect one another in the class-room than in the home or on the playground.'

"As a rule better results will be achieved by a daily inspection of school children, such as for example is maintained in cities like Toronto.

"There is no great danger of spreading the disease in churches, theatres and other assemblages, if these places are well ventilated. In any case, the good derived from closing places of assemblage is more than counterbalanced by the conditions in crowded street cars, railway cars, in large shops and in restaurants where food and dishes may be handled by persons having the disease. It would be just as rational and much more effective to stop all travel on street cars and trains and to stop people from entering shops, eating places, etc., as to close schools, churches, theatres, etc.

"Health officers should do nothing consistent with the welfare of the public, likely to dislocate business or the ordinary affairs of life. They should not be moved from their duty by public clamor, to adopt fussy and ill-advised measures, which only serve to irritate the public and accomplish no useful purpose. If, however, the health officer of any municipality deems it his duty to utilize the section of the Act referred to the Provincial Board will not interfere with him, but the Board does not, for the reasons given, propose to ask its endorsement."

Ontario is confronted by an epidemic of influenza which will in all probability affect more than half of our population. There is a shortage of physicians, nurses, and hospital accommodation. The health and efficiency of the civilian population must be maintained. It is the patriotic duty of every citizen to avoid influenza and keep in good health. To avoid influenza:

Avoid contact with other people so far as possible. Especially avoid crowds indoors, in street cars, theatres, motion-picture houses, and other places of public assemblage.

Avoid persons suffering from "colds," sore throats and coughs.

Avoid chilling of the body or living in rooms of temperature below 65 deg. or above 72 deg. F.

Sleep and work in clean, fresh air.

Keep your hands clean, and keep them out of your mouth.

Avoid expectorating in public places, and see that others do likewise.

Avoid visiting the sick.

Eat plain, nourishing food and avoid alcoholic stimulants.

Cover your nose with your handkerchief when you sneeze, your mouth when you cough. Change handkerchiefs frequently. Promptly disinfect soiled handkerchiefs by boiling or washing with soap and water.

Don't worry, keep your feet warm. Wet feet demand prompt attention. Wet clothes are dangerous and must be removed as soon as possible.

What to do for Influenza and Colds

Oftentimes it is impossible to tell a cold from mild influenza. Therefore:

If you get a cold go to bed in a well ventilated room. Keep warm.

Keep away from other people. Do not kiss anyone. Use individual basins, and knives, forks, spoons, towels, handkerchiefs, soap, wash plates and cups.

Every case of influenza should go to bed at once under the care of a physician. The patient should stay in bed at least three days after fever has disappeared and until convalescence is well established.

The patient must not cough or sneeze except when a mask or handkerchief is held before the face.

He should be in a warm, well ventilated room.

There is no specific for the disease. Symptoms should be met as they arise.

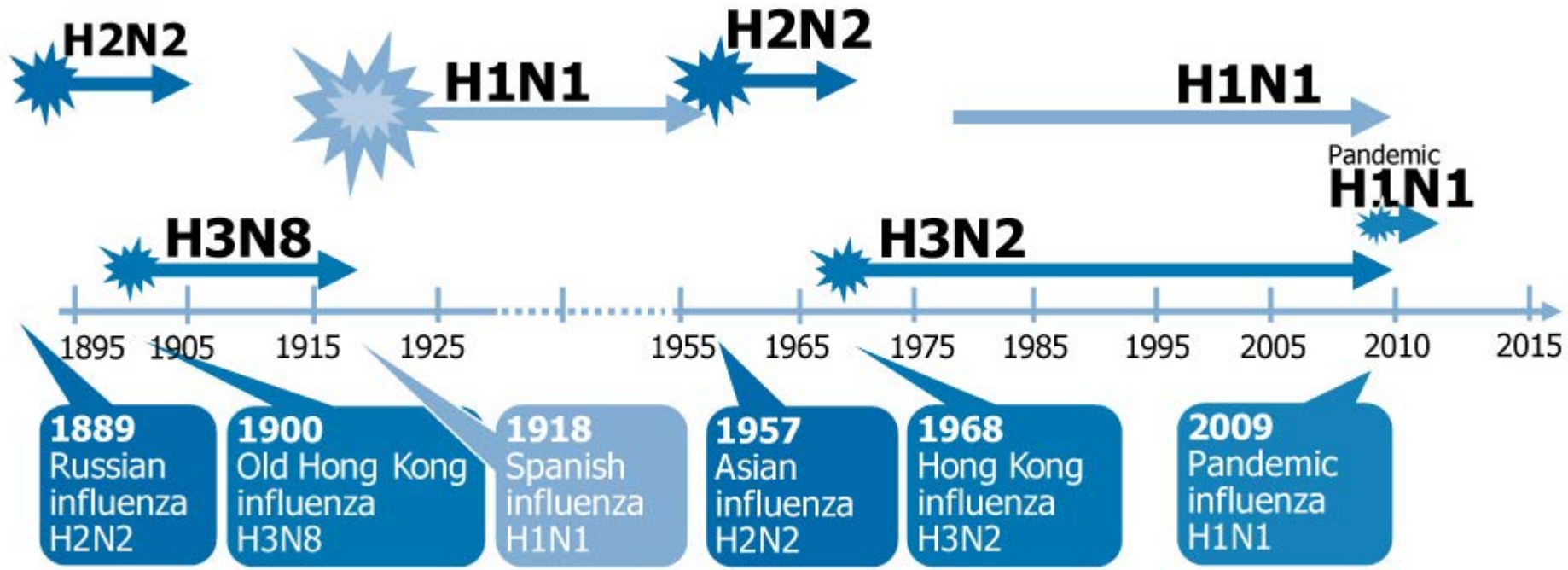
The great danger is from pneumonia. Avoid it by staying in bed while actually ill and until convalescence is fully established.

The after effects of influenza are worse than the disease. Take care of yourself.

Novel H1N1 Influenza (AKA The Swine Flu…)

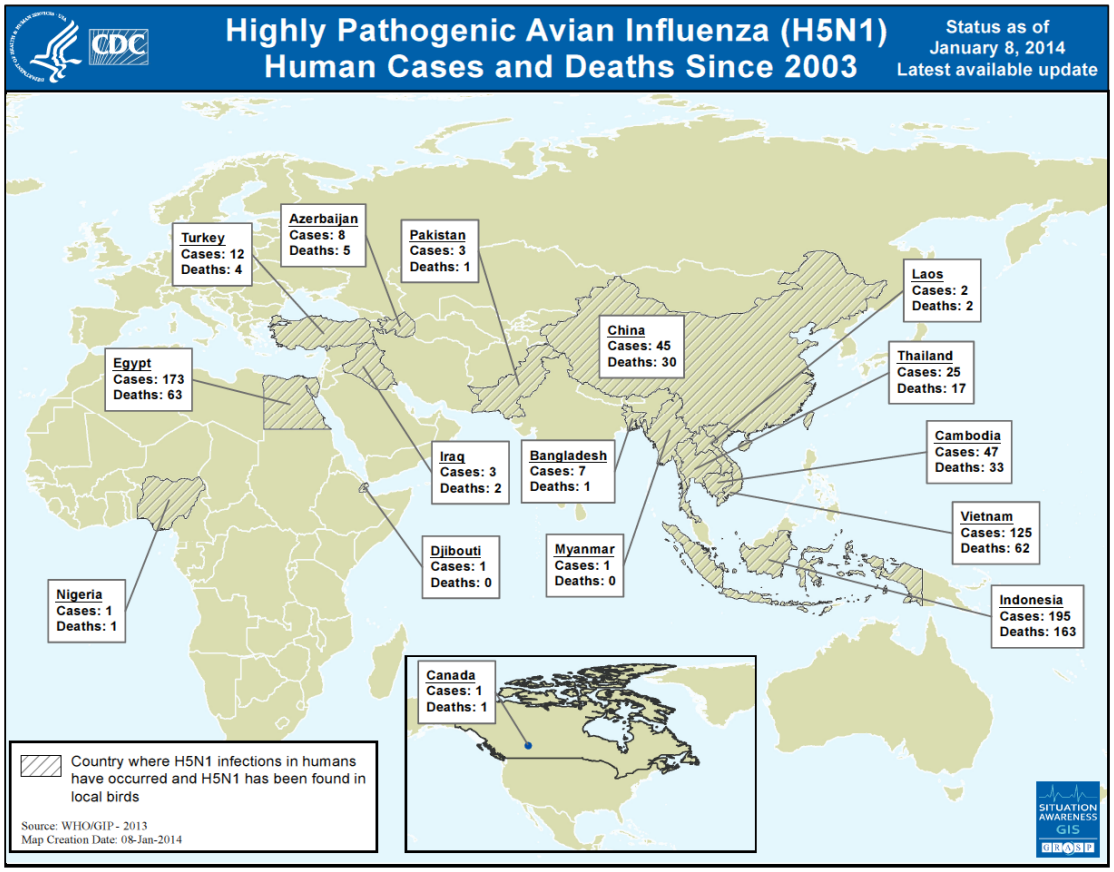
The start of swine influenza…..

History of recent influenza pandemics

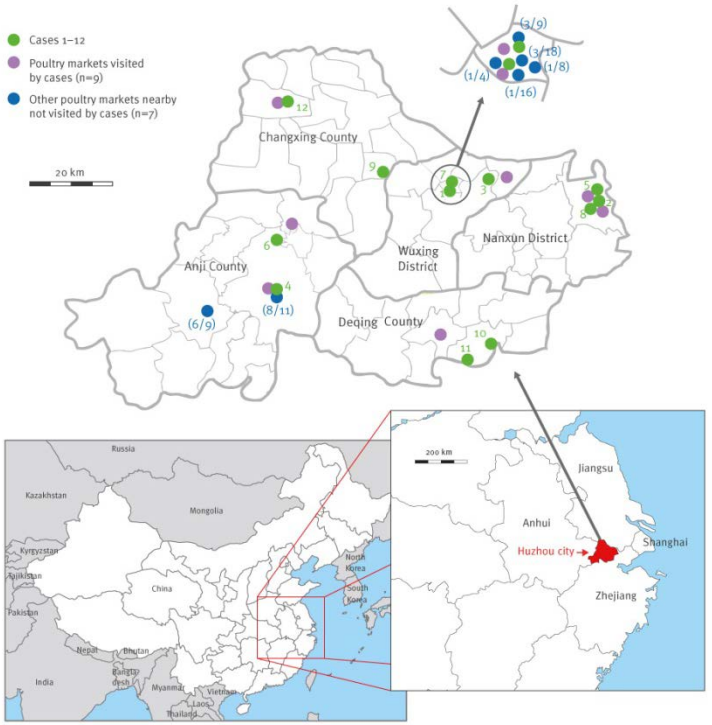


Source: European Centre for Disease Prevention and Control (ECDC) 2009

Potentially pandemic influenza strains



Avian Flu Human World Summary CDC SA-GRASP since 2003 (2013-JAN-08b)

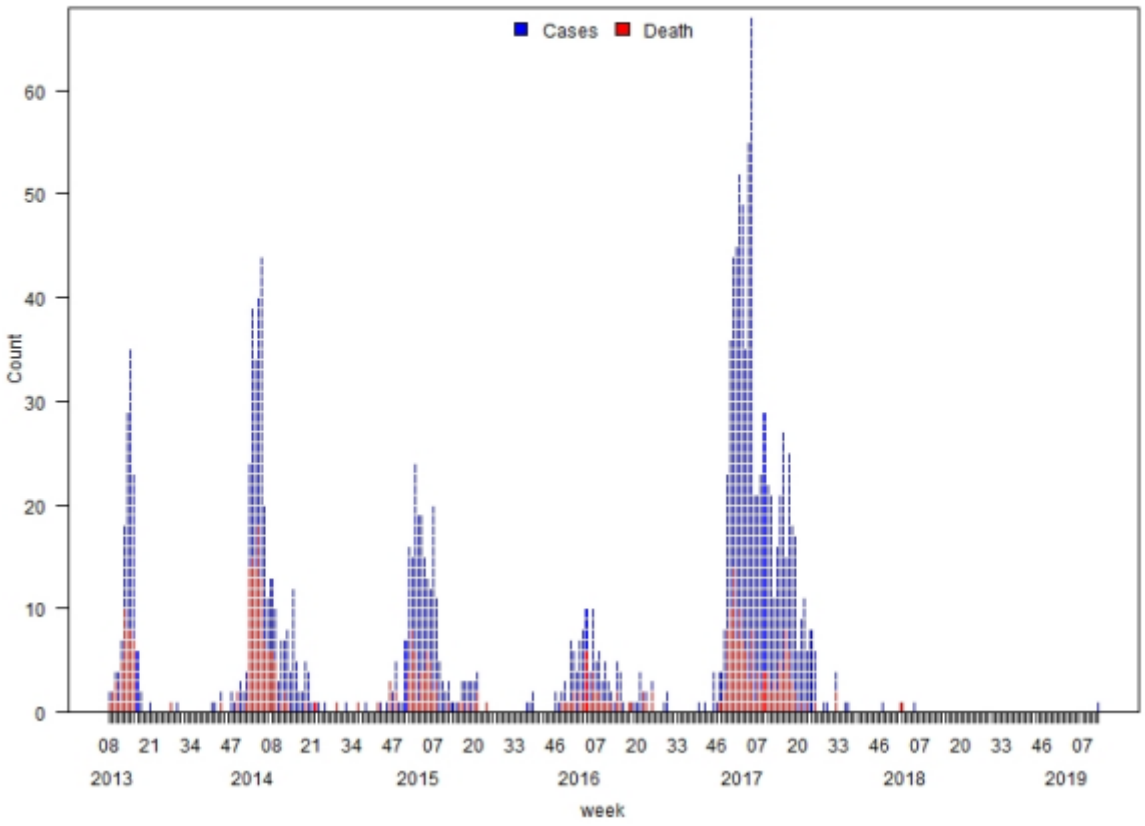


H5N1

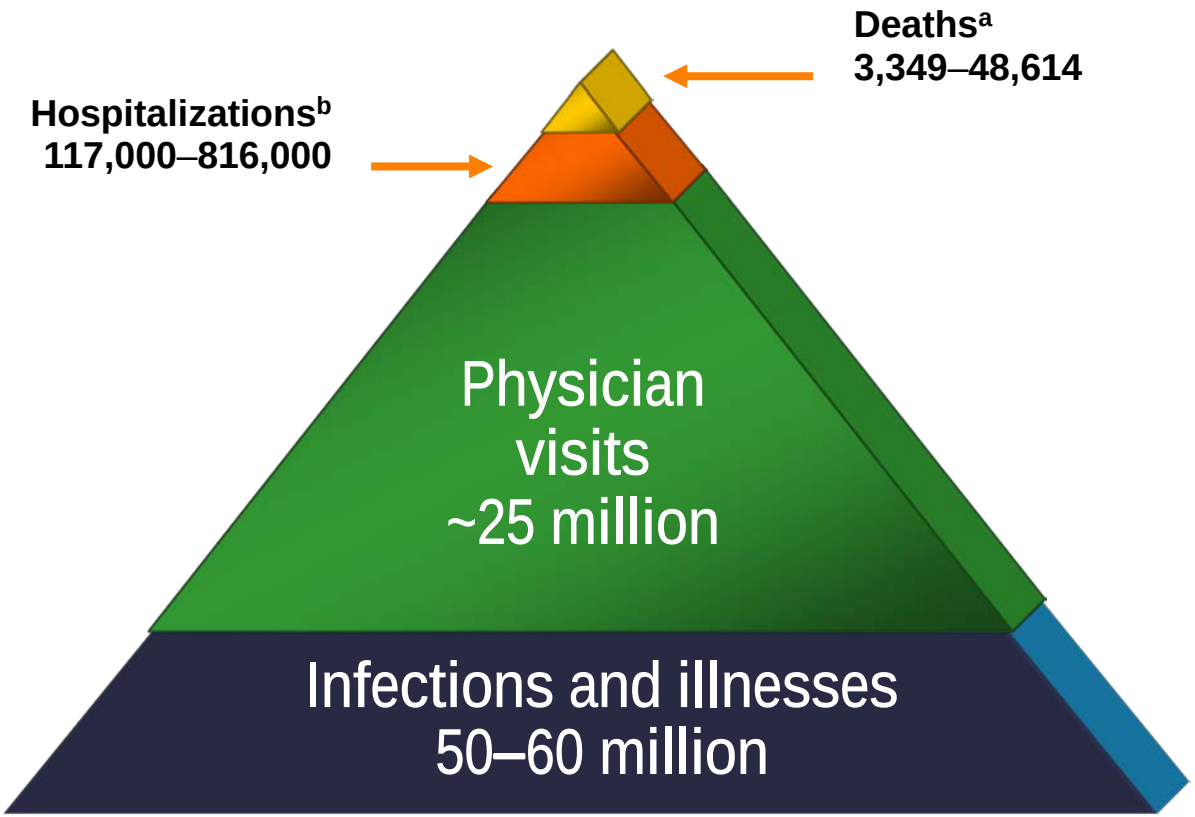
H7N9

Potentially pandemic influenza strains

Figure 1: Epidemiological curve of avian influenza A(H7N9) cases in humans by week of onset, 2013-2019.



While "pandemic influenza" evokes a great deal of fear, seasonal influenza leads to a high annual burden of disease



[a] *MMWR.* 2010: 59(22):1057-1062.; Reed C, Chaves SS, Daily Kirley P, et al. (2015) Estimating Influenza Disease Burden from Population-Based Surveillance Data in the United States. PLoS ONE 10(3): e0118369.

[B] All-cause hospitalization and mortality associated with influenza virus infection.
Thompson WW, et al. *JAMA.* 2003;289:179; Thompson WW, et al. *JAMA.* 2004;292:1333; Couch RB. *Ann Intern Med.* 2000;133:992; Patriarca PA. *JAMA.* 1999;282:75;ACIP. *MMWR.* 2004;53(RR06):1.; Reed C, Chaves SS, Daily Kirley P, et al. (2015) Estimating Influenza Disease Burden from Population-Based Surveillance Data in the United States. PLoS ONE 10(3): e0118369.

Estimated Vaccine-Preventable Disease Incidence and Deaths in the US

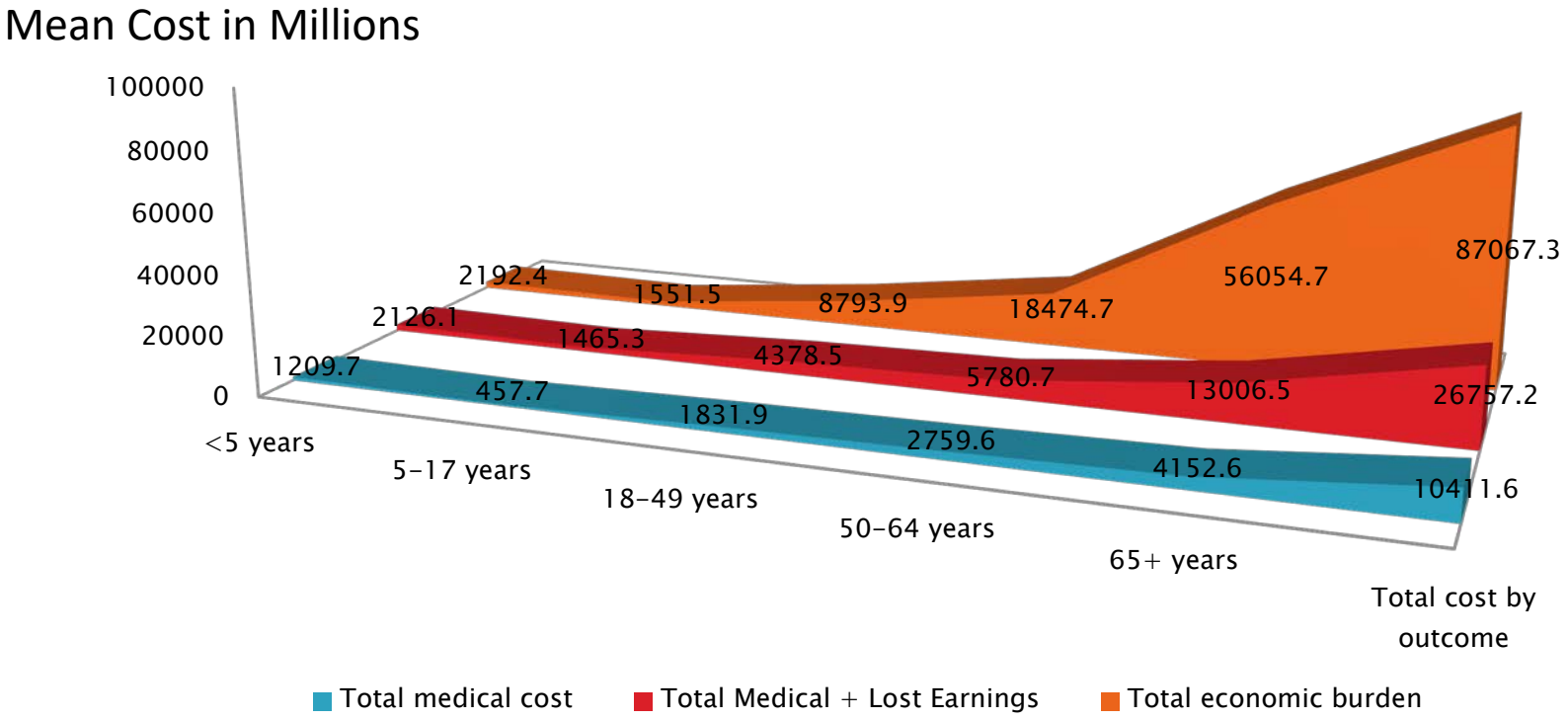
Disease	Annual Cases	Annual Deaths
Influenza	61,000,000[a] ('09)	3,349–48,614[b,c] ('76–'13)
Pneumococcal disease, invasive (bacteremia & meningitis)[d]	33,900 ('13)	3,700 ('13)
HPV[e] (cervical cancer)	12,900 ('15)	4,100 ('15)
Hepatitis B	3,050[f] ('13)	1,873[g] ('13)
Meningococcal disease[f]	556 ('13)	26 ('11)
Hepatitis A	1,781[f] ('13)	80[g] ('13)
Varicella[f] (chickenpox)	11,359 ('13)	14 ('11)
Pertussis[f]	28,639 ('13)	13 ('13)

[a] Data based on CDC estimates of 2009 H1N1 cases using statistical modeling.
[b] Reed C, Chaves SS, Daily Kirley P, et al. (2015) Estimating Influenza Disease Burden from Population-Based Surveillance Data in the United States. PLoS ONE 10(3): e0118369.
[c] MMWR. 2010: 59 (22): 1057–62. [d]CDC. ABCs Report: *Streptococcus pneumoniae*, 2013 Available at https://www.cdc.gov/abcs/reports-findings/survreports/spneu13.pdf
[e] American Cancer Society. Cancer Facts and Figures 2015. Available at http://m.cancer.org/acs/groups/content/@editorial/documents/document/acspc-

How much does Influenza Cost YOU?

Total economic burden 87.1 billion

Annual burden per capita: $284.53



US Population: 306 Million

http://www.census.gov/main/www/popclock.html

Created Using Table 5 of Noelle-Angelique, et al. Vaccine 25 (2007) 5086-5096

How "was" the 2018–19 influenza season?

CDC estimates that, from **October 1, 2018,** through **May 4, 2019**, there have been:

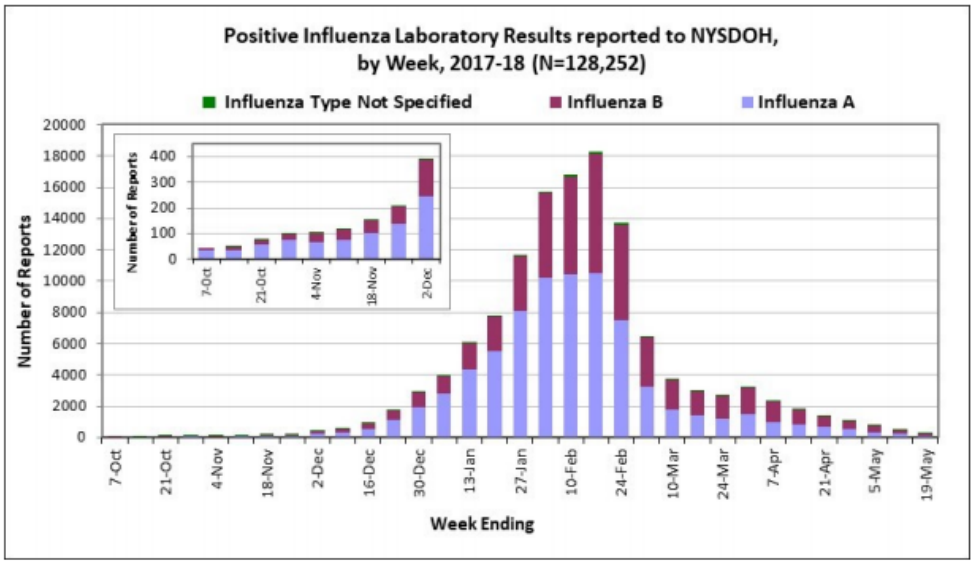
37.4 million – 42.9 million
flu illnesses

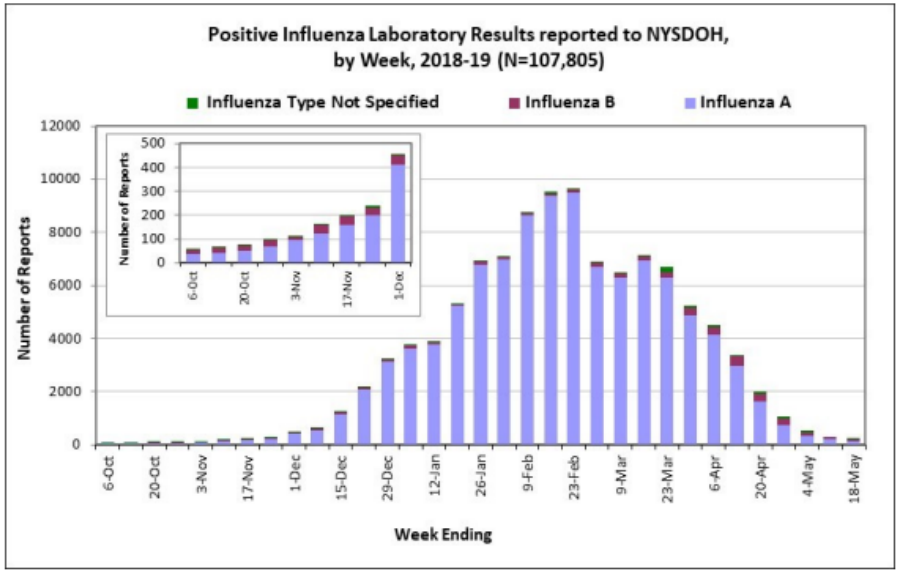
17.3 million – 20.1 million
flu medical visits

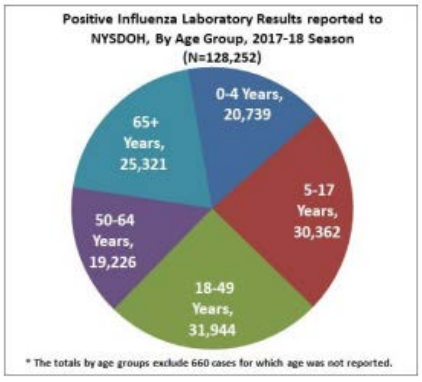
531,000 – 647,000
flu hospitalizations

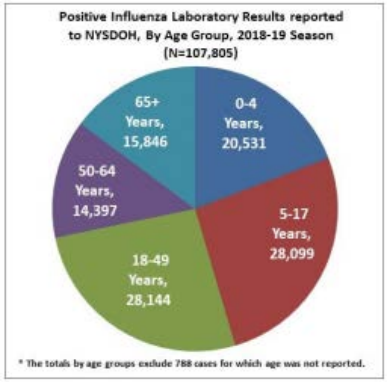
36,400 – 61,200
flu deaths

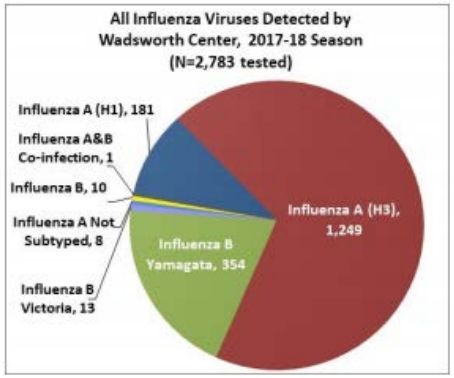
How have 2 recent influenza seasons in NYS compared?

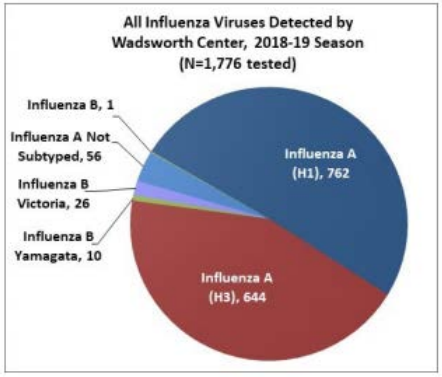








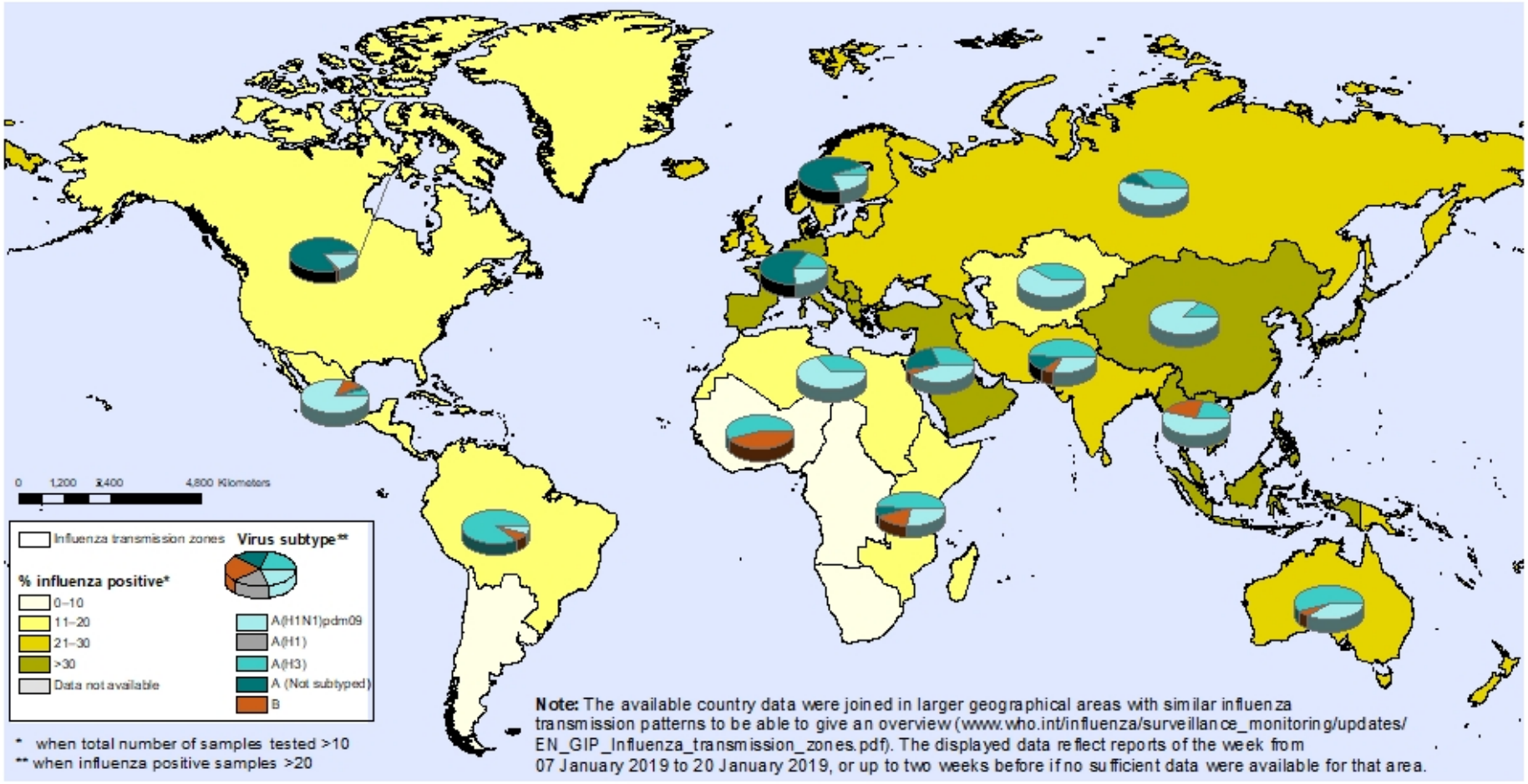




Seasonal Influenza early 2019

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

Status as of 01 February 2019



* when total number of samples tested >10
** when influenza positive samples >20

Note: The available country data were joined in larger geographical areas with similar influenza transmission patterns to be able to give an overview (www.who.int/influenza/surveillance_monitoring/updates/EN_GIP_Influenza_transmission_zones.pdf). The displayed data reflect reports of the week from 07 January 2019 to 20 January 2019, or up to two weeks before if no sufficient data were available for that area.

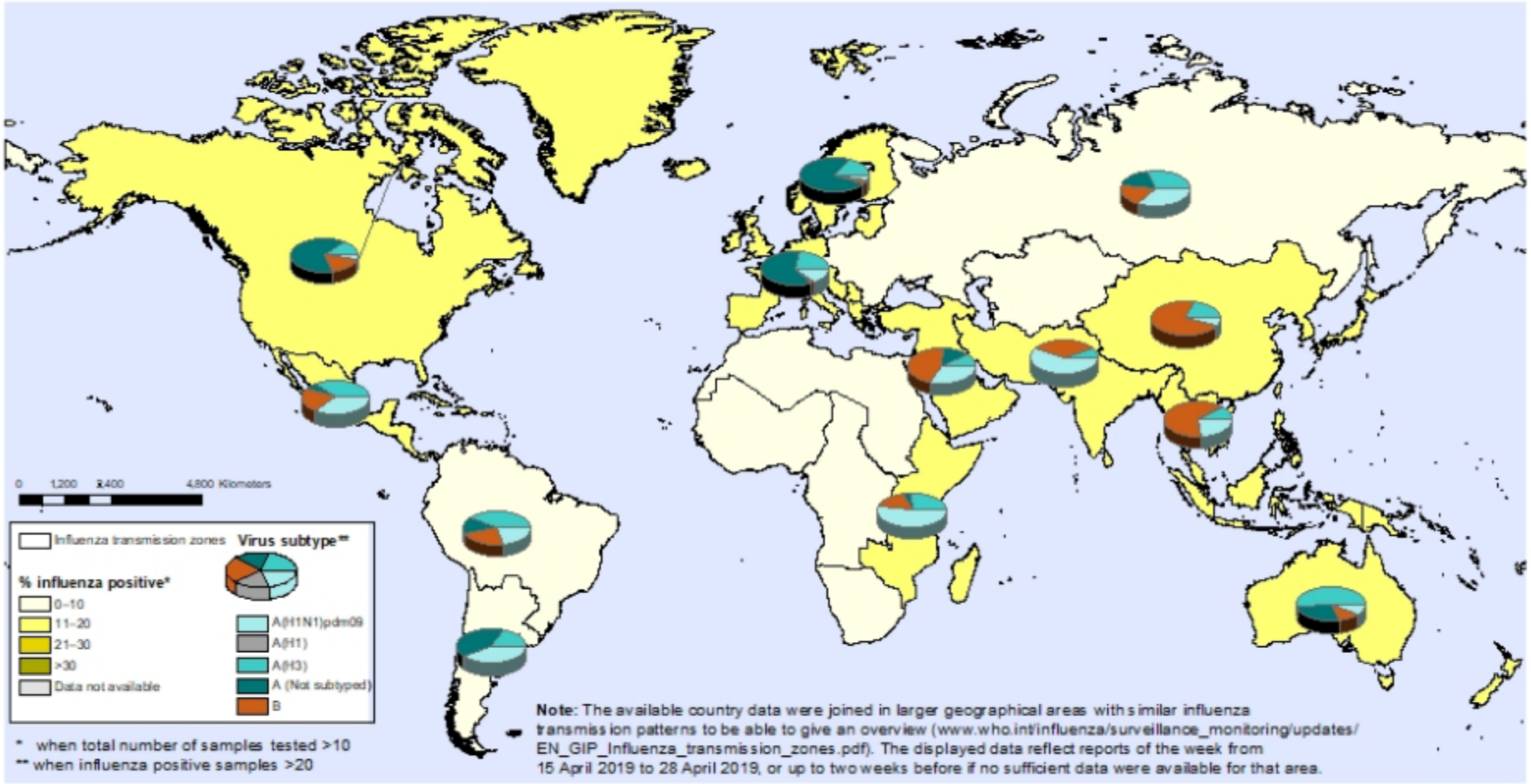
Data Source:
Global Influenza Surveillance and Response System (GISRS),
FluNet (www.who.int/flunet)

World Health Organization

Seasonal Influenza late 2019

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

Status as of 10 May 2019



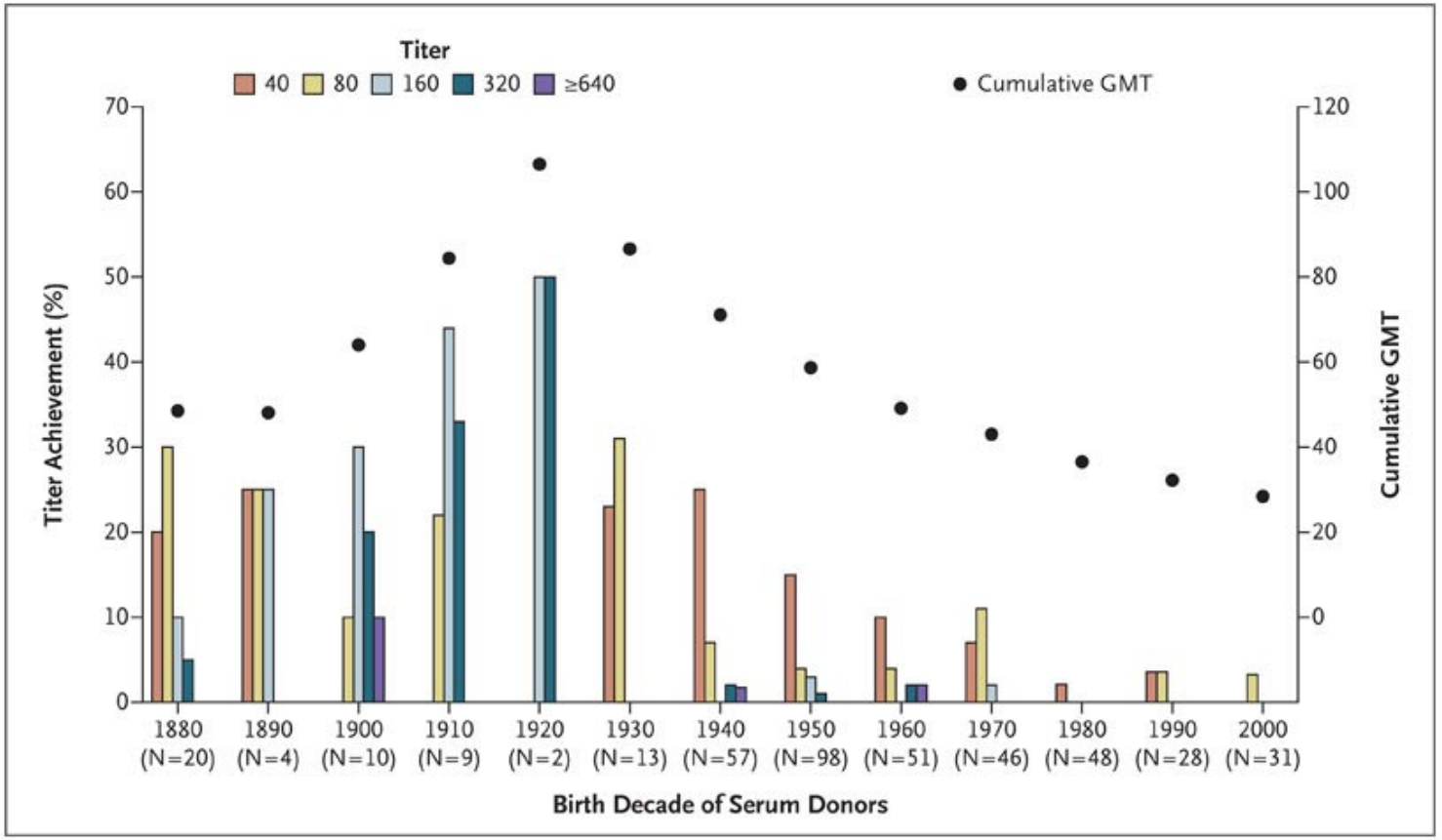
* when total number of samples tested >10
** when influenza positive samples >20

Note: The available country data were joined in larger geographical areas with similar influenza transmission patterns to be able to give an overview (www.who.int/influenza/surveillance_monitoring/updates/EN_GIP_Influenza_transmission_zones.pdf). The displayed data reflect reports of the week from 15 April 2019 to 28 April 2019, or up to two weeks before if no sufficient data were available for that area.

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

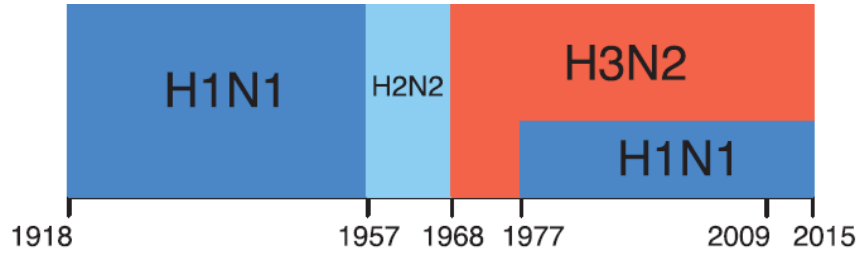
World Health Organization

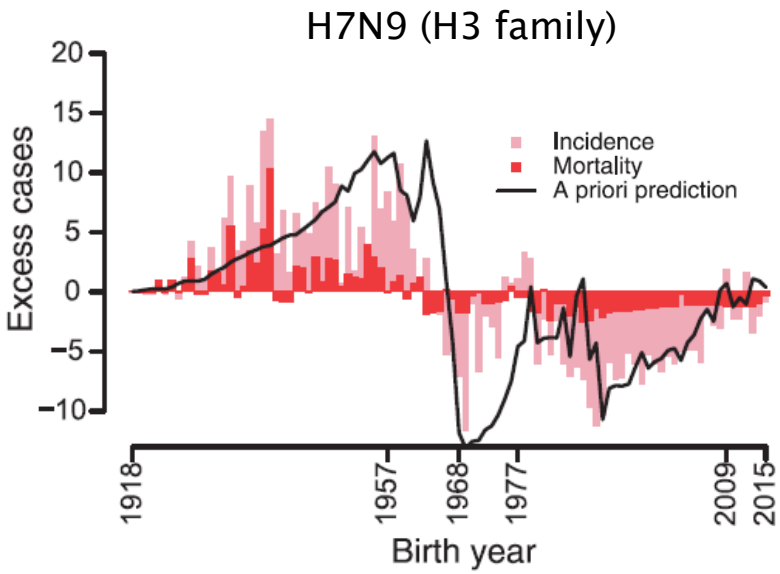
Does early childhood exposure matter? Neutralizing antibody titers against 2009 Pandemic H1N1 virus according to birth decade

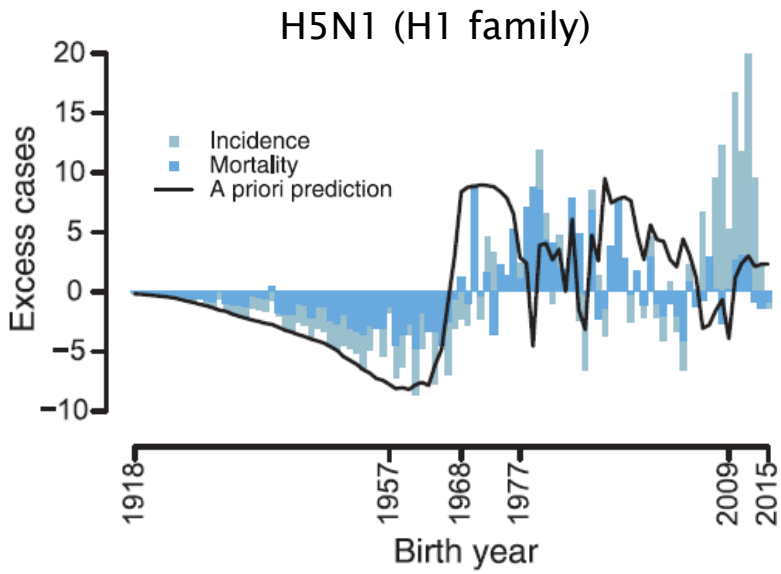


Hancock K et al. N Engl J Med 2009;10.1056/NEJMoa0906453

Does early childhood exposure matter?



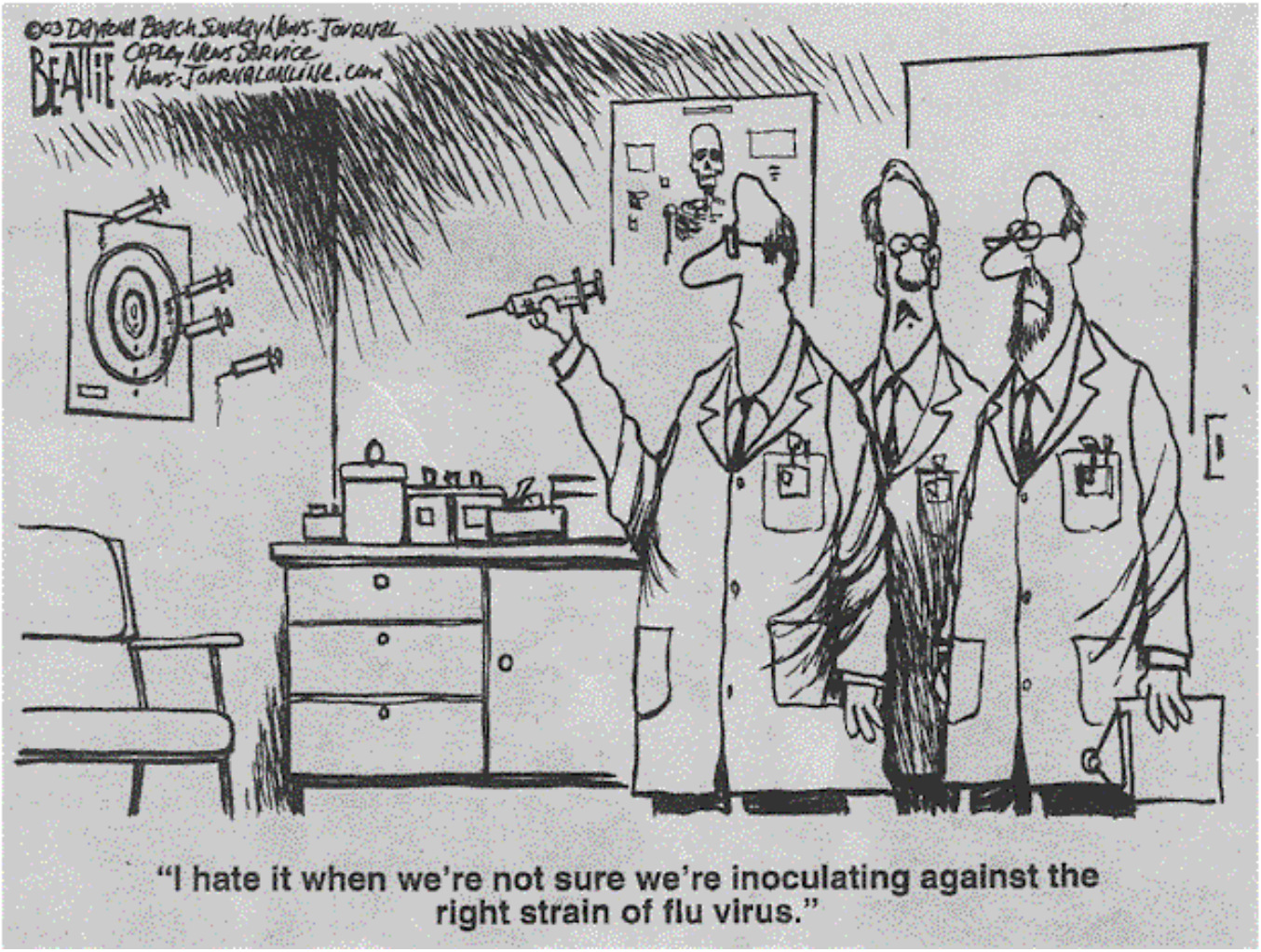




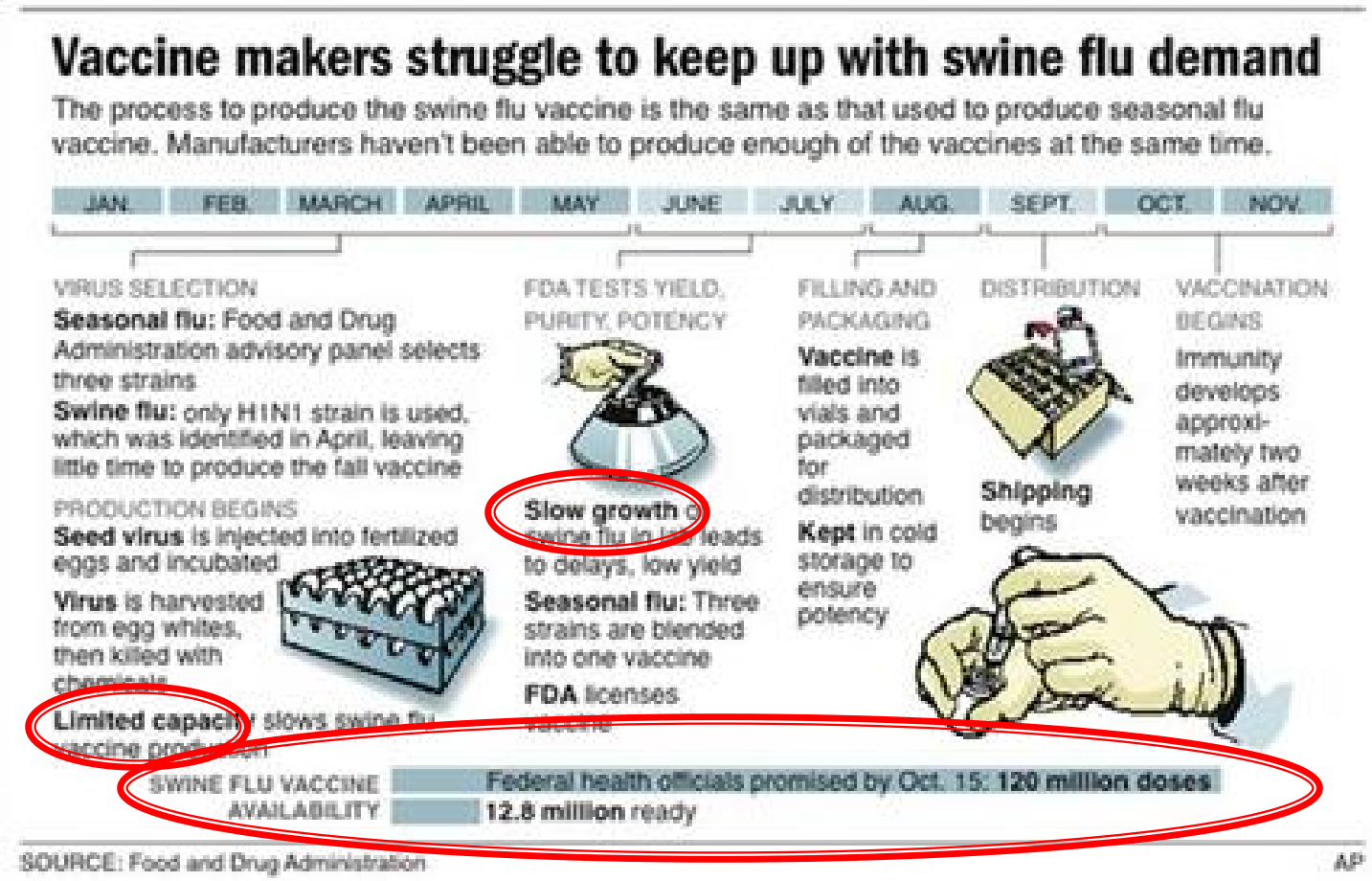
- Gostic et al: Epidemiologic study looking at the effect of birth year on pandemic disease
- Case data normalized to demographic age distribution from appropriate countries and case observation years
- Conclusions: Incidence and mortality risk for pandemic strains closely linked to early childhood exposure using birth year as surrogate marker

Gostic 2016

Influenza Vaccine



Vaccine development: significant challenges



- The viral strain that will circulate each year is unpredictable
- Time lag between pandemic initiation and vaccine production is lengthy

1) Ongoing risk of vaccine mismatch

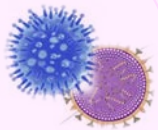
2) In the setting of a pandemic, vaccine not available until after significant viral spread has occurred

Overview: Vaccine production

Licensed methods of vaccine production include
Egg-Based (Traditional), Cell-Based, and Recombinant (SF9 Baculovirus)

Egg-Based
(6 months +)

- A hybrid virus is created that grows well in eggs.



- The hybrid is tested in ferrets to determine antigenicity.

- Optimum growth conditions are determined in egg.

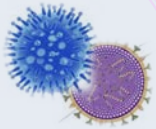
- The virus is injected into many fertilized eggs.

- The virus is then collected, inactivated, split and purified to produce antigen.

- The chosen strains are combined for that year.

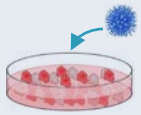
Cell-Based
(age 4+)

- A hybrid virus is created that grows well in cells.



- The hybrid is tested in ferrets to determine antigenicity.

- Mammalian cells (MDCK) are infected with virus.



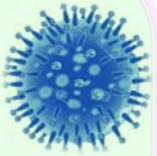
- The virus is collected, inactivated, split, and purified to produce surface antigen.

- The viral potency is checked.

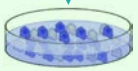
- The chosen strains are combined for that year.

Recombinant Protein
Age 18+

- Genes specific for HA proteins selected by the WHO are cloned into baculovirus vectors.



- Insect cells (SF9) are infected with the vectors, and express HA.



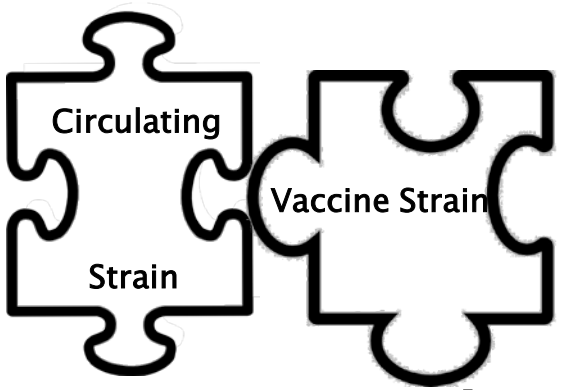
- HA is harvested and purified.

- HA for the chosen strains are combined for that year.

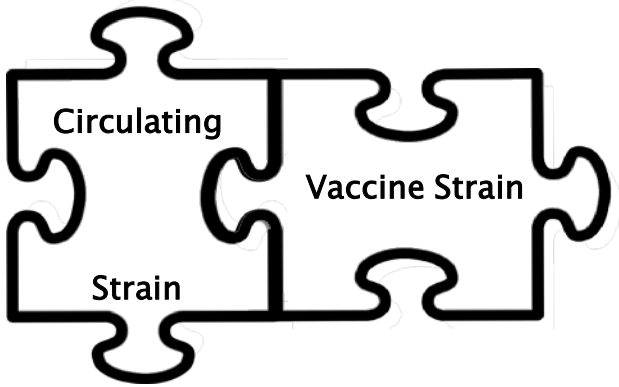
- The vaccine is tested, packaged, and distributed.

Circulating and Vaccine Viruses

Influenza Season	Adjusted vaccine effectiveness*
2018–19	47%
2017–18	38%
2016–17	40%
2015–16	48%
2014–15	19%



Mismatch



Match

2019-2020 Seasonal Influenza Vaccine Strains

- A/Brisbane/02/2018 (H1N1)pdm09-like virus (Updated)
- A/Kansas/14/2017 (H3N2)-like virus (Updated)
- B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)
- B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage)

The H1 and H3 strains were updated for the upcoming influenza season

The H3 strain recommendation was delayed until March!

Human Vaccines & Immunotherapeutics 8:1, 81–88; January 2012; © 2012 Landes Bioscience

The rationale for quadrivalent influenza vaccines

Christopher S. Ambrose[1,*] and Myron J. Levin[2]

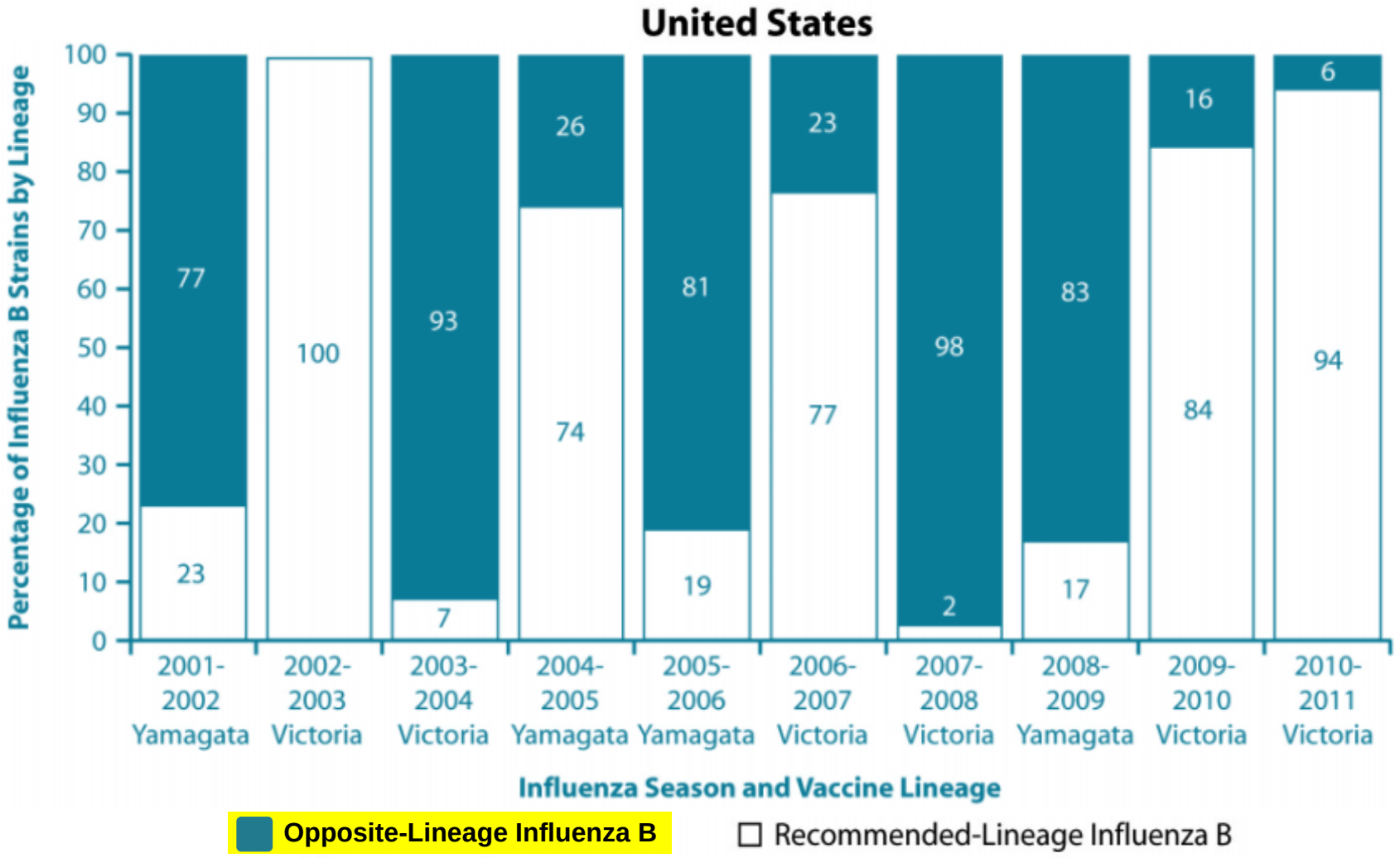
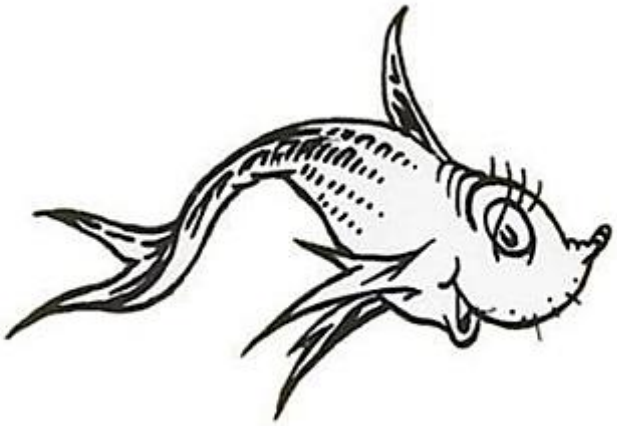


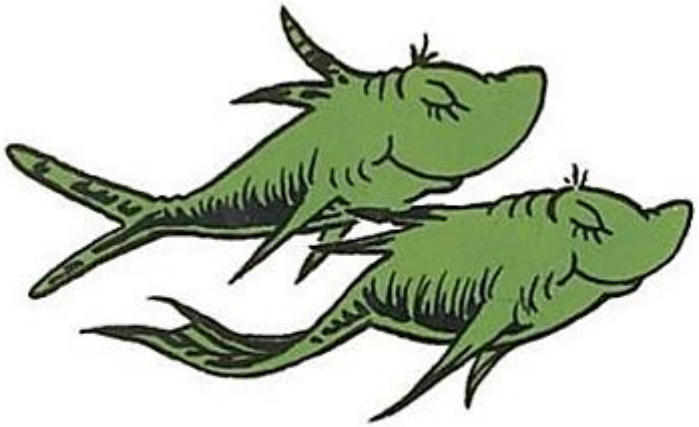
Figure: Influenza B Circulation by Lineage: US for 2001 to 2011. The influenza B lineage (Victoria or Yamagata) recommended for inclusion in trivalent vaccine shown on x-axis.

Influenza vaccine recommendations

- Everyone 6 months of age and older should receive a flu shot
- Vaccine should be offered throughout the year, starting as soon as possible and continuing through late spring
- Special populations:
  - Children
  - Age >65 years
  - High risk populations
  - Pregnant women
  - Individuals in contact with children or other high risk populations

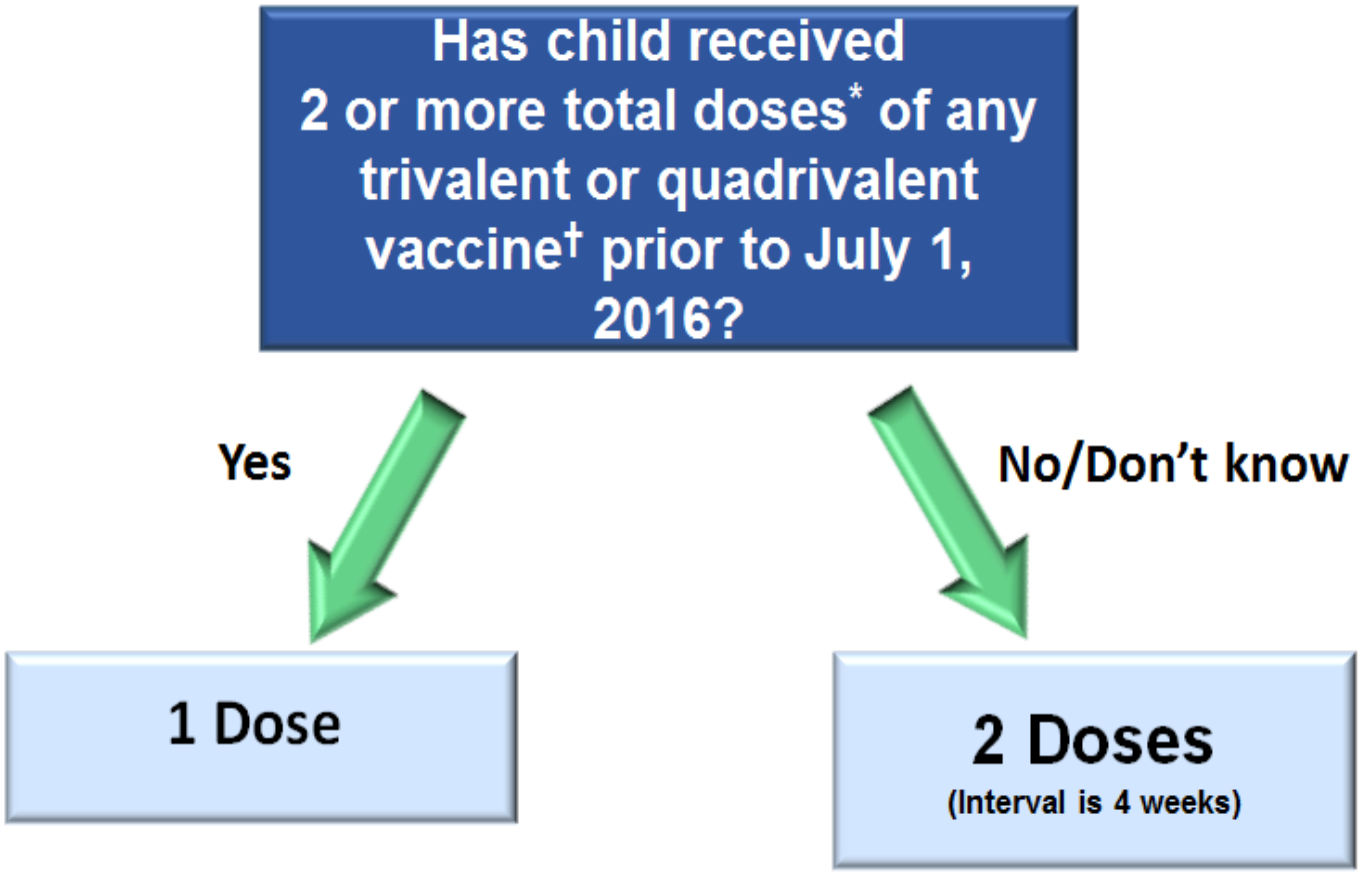


One Dose



Two Dose

Number of Seasonal Influenza Doses for Children 6 Months – 8 Years



* 2 doses need not have been received during the same season or consecutive seasons

† Receipt of LAIV4 in the past is still expected to have primed a child's immune system, despite recent evidence for poor effectiveness. There currently are no data that suggest otherwise.

Egg allergy: Evidence-Based Practice

- **28** studies
- **4315** egg-allergic subjects (656 with severe allergies)
- **No** serious allergic reactions (respiratory distress or hypotension) after receiving the influenza vaccine

Amount of egg protein:

- Lowest provoking dose: **130 mcg**
- Per 0.5mL vaccine dose: **<1 mcg**

Des Roches A, et al. Egg-allergic patients can be safely vaccinated against influenza. *J Allergy Clin Immunol* 2012;130:1213-1216.
Greenhawt MJ, Spergel JM, Rank MA, et al. Safe administration of the seasonal trivalent influenza vaccine to children with severe egg allergy. *Ann Allergy Asthma Immunol.* 2012;109:426—430.
Kelso, JM. Influenza Vaccine and Egg Allergy: Nearing the End of an Evidence-Based Journey. *J Allergy Clin Immunol.* 2015;;3:140-1.=

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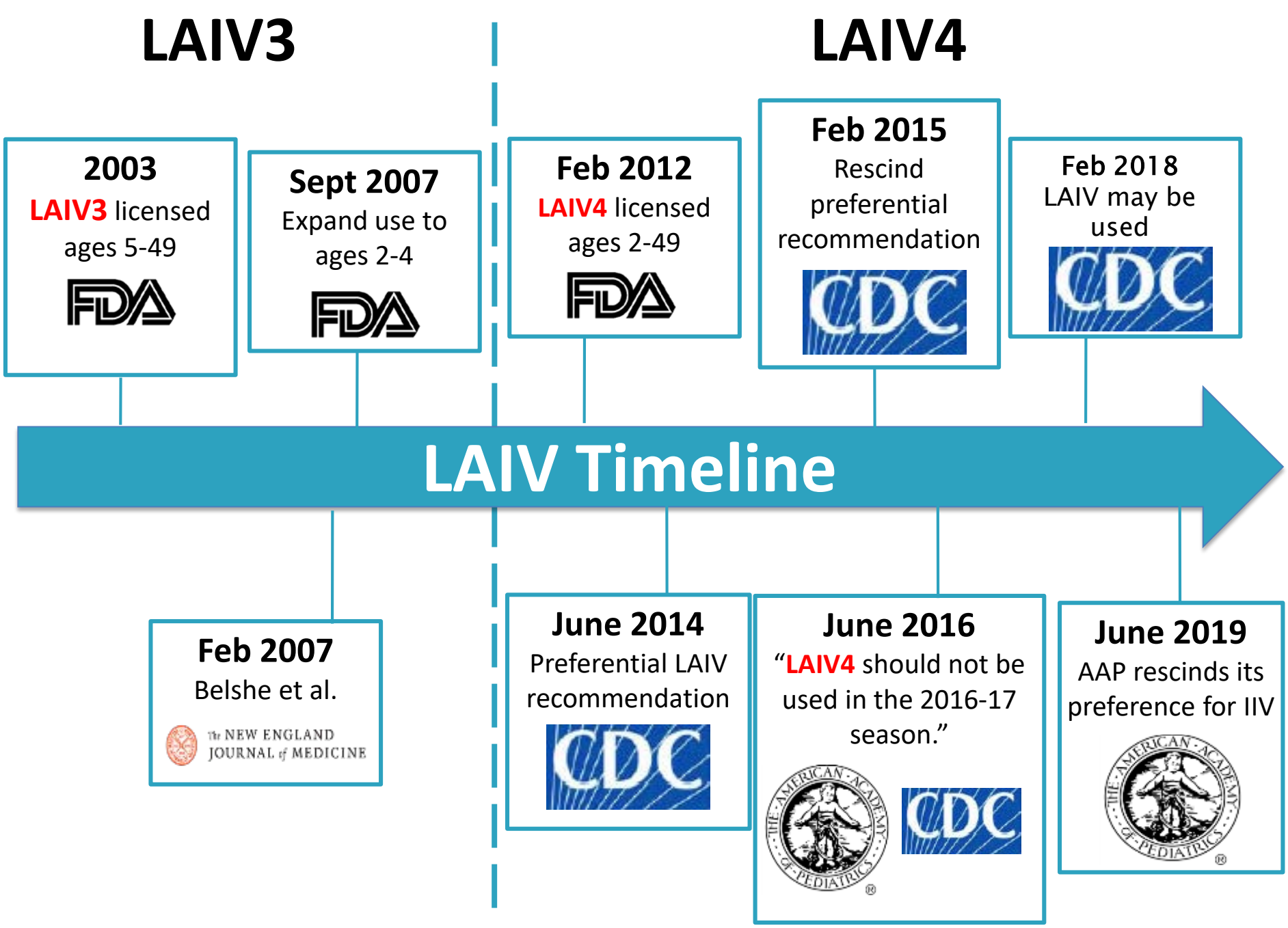
AAP Influenza Policy Recommendation

All children with egg allergies can receive the influenza vaccine with no special precautions than those recommended for routine vaccines.

Recommendations for Prevention and Control of Influenza in Children, 2016–2017. COMMITTEE ON INFECTIOUS DISEASES. Pediatrics Sep 2016, e20162527; **DOI**: 10.1542/peds.2016-2527

So what about LAIV?


LAIV3
LAIV4
2003
LAIV3 licensed
ages 5-49
FDA
Sept 2007
Expand use to
ages 2-4
FDA
Feb 2012
LAIV4 licensed
ages 2-49
FDA
Feb 2015
Rescind
preferential
recommendation
CDC
Feb 2018
LAIV may be
used
CDC
LAIV Timeline
Feb 2007
Belshe et al.
The NEW ENGLAND
JOURNAL of MEDICINE
June 2014
Preferential LAIV
recommendation
CDC
June 2016
"LAIV4 should not be
used in the 2016-17
season."
THE AMERICAN ACADEMY OF PEDIATRICS
CDC
June 2019
AAP rescinds its
preference for IIV
THE AMERICAN ACADEMY OF PEDIATRICS

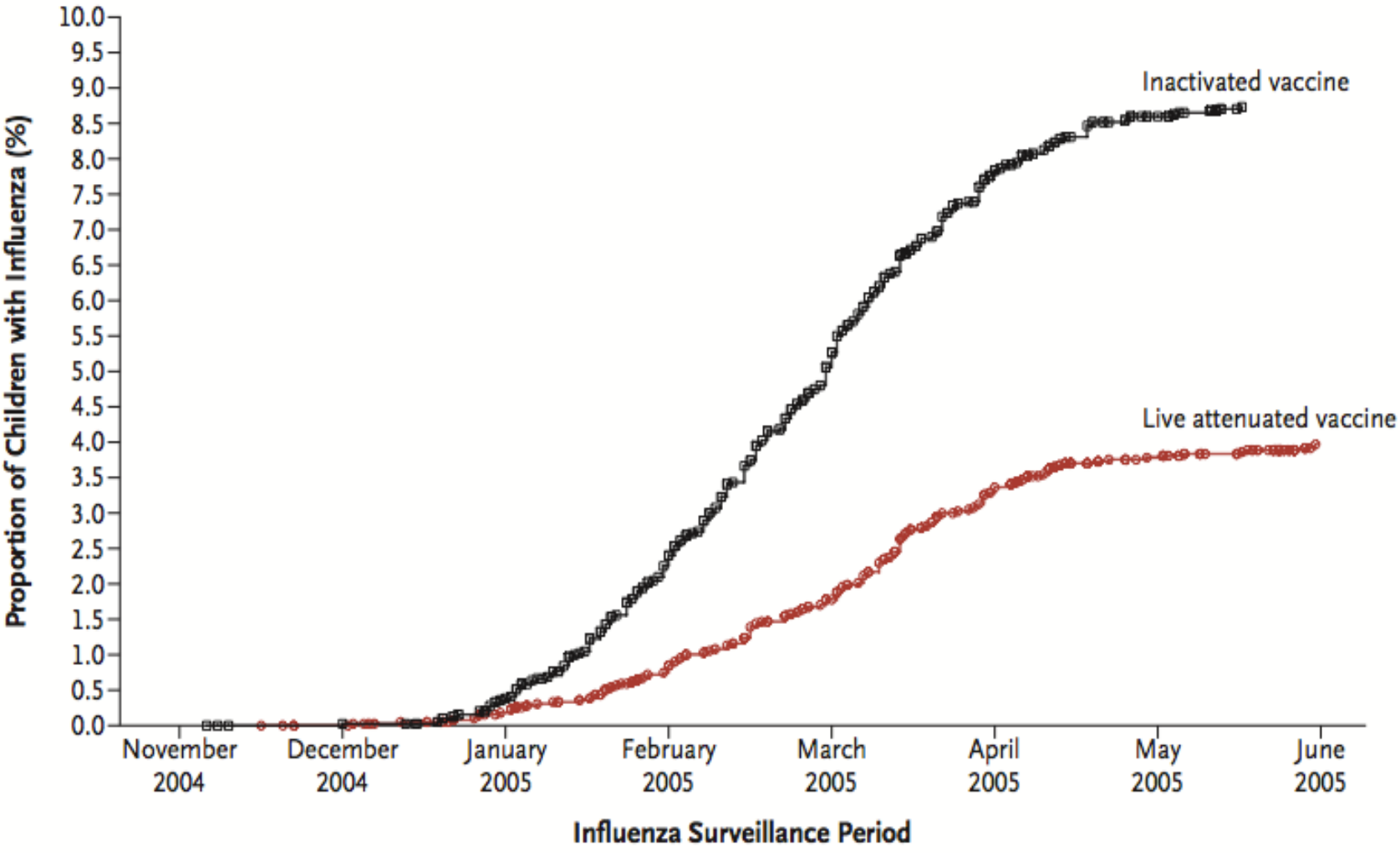


Figure 1. Kaplan–Meier Curves for the Time to the First Culture-Confirmed Report of Influenza in the Two Vaccine Groups.

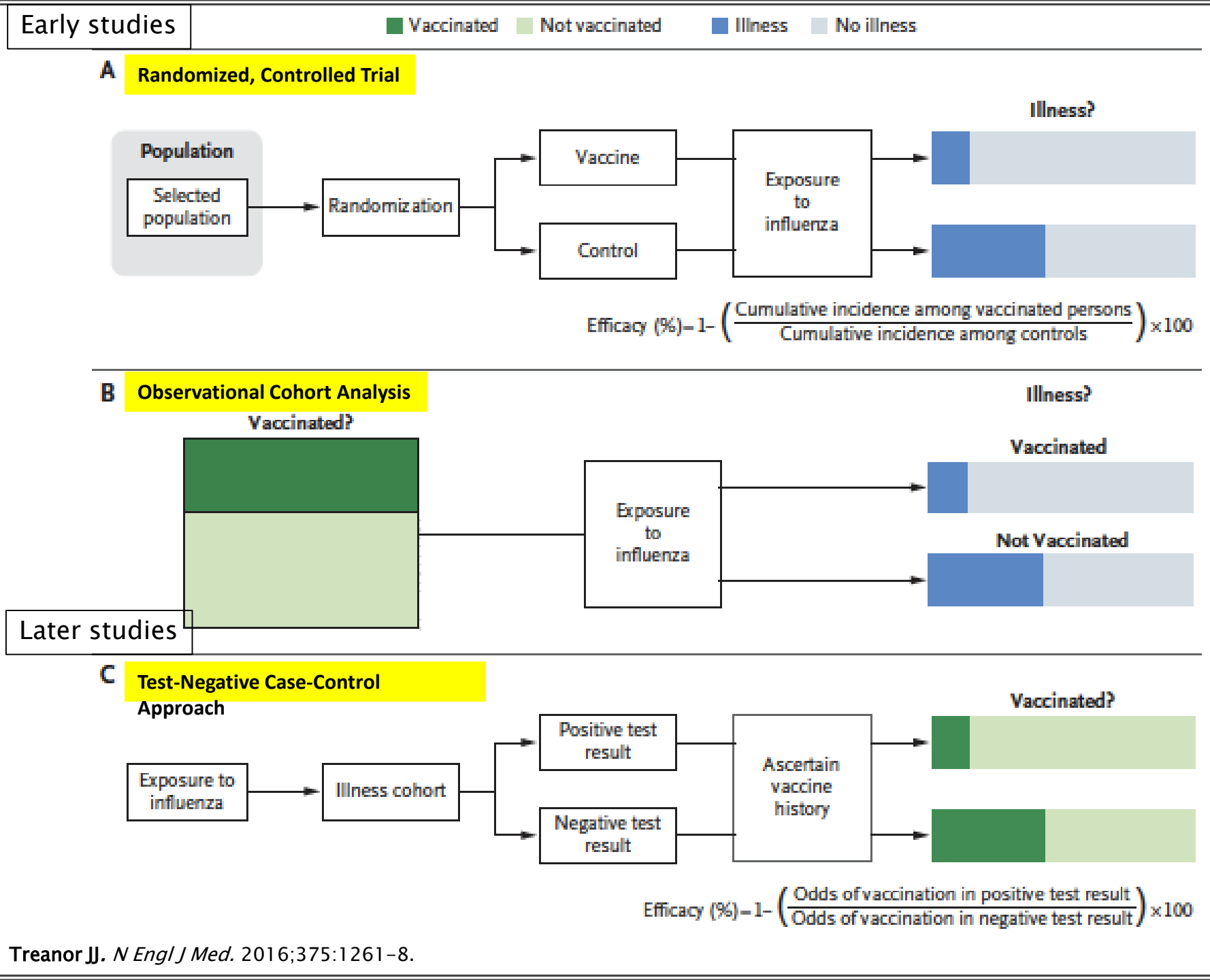
Belshe RB, et al. Live attenuated versus inactivated influenza vaccine in infants and young children. N Engl J Med. 2007 Feb 15;356(7):685-96.

Historically LAIV performed better against both matched and unmatched viral strains

Table 2. Influenza Attack Rates in the According-to-Protocol Population.*

Variable	Similarity to Vaccine†	Live Attenuated Vaccine (N=3916)‡		Inactivated Vaccine (N=3936)§		Reduction in Attack Rate with Live Vaccine¶
		Cases	Attack Rate	Cases	Attack Rate	
		no.	%	*no.*	%	% *(95% CI)*
Virus	Well matched	53	1.4	93	2.4	44.5 (22.4 to 60.6)
A/H1N1		3	0.1	27	0.7	89.2 (67.7 to 97.4)
A/H3N2		0	0	0	0	—
B		50	1.3	67	1.7	27.3 (–4.8 to 49.9)
Virus	Not well matched	102	2.6	245	6.2	58.2 (47.4 to 67.0)
A/H1N1		0	0	0	0	—
A/H3N2		37	0.9	178	4.5	79.2 (70.6 to 85.7)
B		66	1.7	71	1.8	6.3 (–31.6 to 33.3)
Virus	Regardless of match	153	3.9	338	8.6	54.9 (45.4 to 62.9)
A/H1N1		3	0.1	27	0.7	89.2 (67.7 to 97.4)
A/H3N2		37	0.9	178	4.5	79.2 (70.6 to 85.7)
B		115	2.9	136	3.5	16.1 (–7.7 to 34.7)

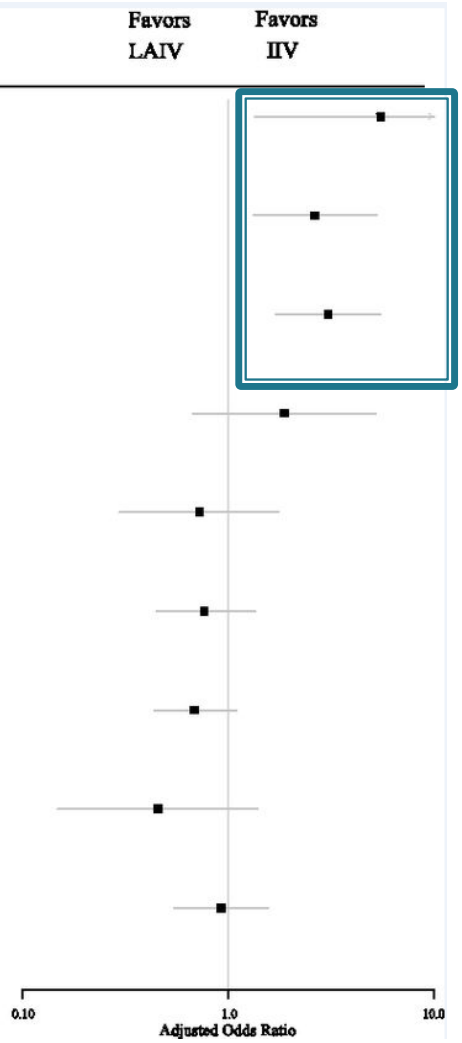
Belshe RB, et al. Live attenuated versus inactivated influenza vaccine in infants and young children. N Engl J Med. 2007 Feb 15;356(7):685-96.



Treanor JJ. *N Engl J Med.* 2016;375:1261–8.

LAIV and IIV Vaccine Effectiveness Ages 2-17 Years, By Influenza Type/Subtype

Influenza Type/ Subtype	Influenza Season	Vaccine Type	Total	No. (%) Positive	aOR
A/H1N1pdm09	2010–2011	LAIV	102	7 (9)	5.53
		IIV	420	9 (2)	REF
	2013–2014	LAIV	154	24 (16)	2.65
		IIV	459	27 (6)	REF
	Combined*	LAIV	256	31 (12)	3.08
		IIV	879	36 (4)	REF
A/H3N2	2010–2011	LAIV	103	8 (8)	1.89
		IIV	431	20 (5)	REF
	2011–2012	LAIV	150	10 (7)	0.73
		IIV	490	42 (9)	REF
	2012–2013	LAIV	171	27 (16)	0.77
		IIV	523	99 (19)	REF
	Combined*	LAIV	321	37 (12)	0.69
		IIV	1013	141 (14)	REF
B	2010–2011	LAIV	100	5 (5)	0.46
		IIV	448	37 (8)	REF
	2012–2013	LAIV	174	30 (17)	0.93
		IIV	520	96 (18)	REF



Chung et al Pediatrics 2016

Poor VE of LAIV4

- Current Medimmune hypothesis: H1 virus overall less virulent based on cell culture results
  - In 2018-19 A/Slovenia/2903/2015 virus included, which may have greater shedding and immunogenicity compared
- Increased susceptibility to thermal degradation
  - But a new, more stable A(H1N1)pdm09 virus substituted without benefit in 2015-16
- Viral interference with adding 4th strain
  - A(H1N1)pdm09 issue first noted in 2010, predating switch to quadrivalent vaccine
- Pre-existing immunity due to more years of annual influenza vaccination or natural infection
  - This could be an overall issue affecting LAIV

H. Caspard et al. / Vaccine 34 (2016) 5066–5072

Why do parents refuse vaccinations?

- Religious reasons
  - Most states accept exemptions for this reason
- Personal beliefs or philosophical reasons
- Safety concerns
- Desire for more information from healthcare providers.

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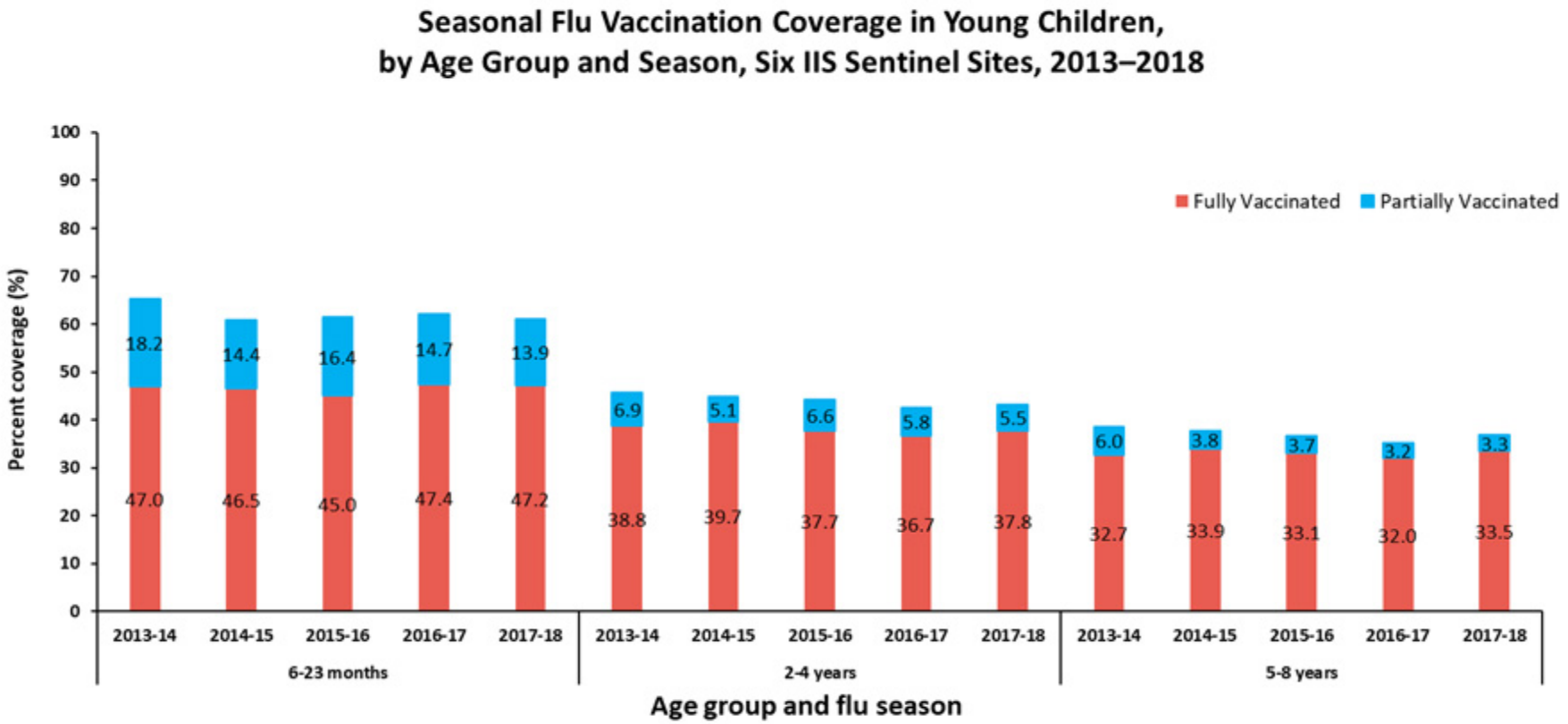
Medical Versus Nonmedical Immunization Exemptions for Child Care and School Attendance

"…legitimate medical exemptions to immunization requirements are important to observe. However, **nonmedical exemptions to immunization requirements are problematic** because of medical, public health, and ethical reasons and create unnecessary risk to both individual people and communities."

Pediatrics. 2016; e20162145; doi: 10.1542/peds.2016-2145

Influenza Vaccination Rates for Children



- Flu vaccination coverage 47.2% (6–23 month), 37.8% (2–4 year), and 33.5% (5–8 year) in 2017–18
- Flu vaccination coverage of ≥1 dose declined from 2013–14 season, then remained largely unchanged in the 6–23 month age group
- Flu vaccination coverage of ≥1 dose showed a slightly but consistently declining trend over the first four seasons in the 2–4 year and 5–8 year age groups, but increased slightly in the most recent season.

The changing face of vaccine exemptions in NYS

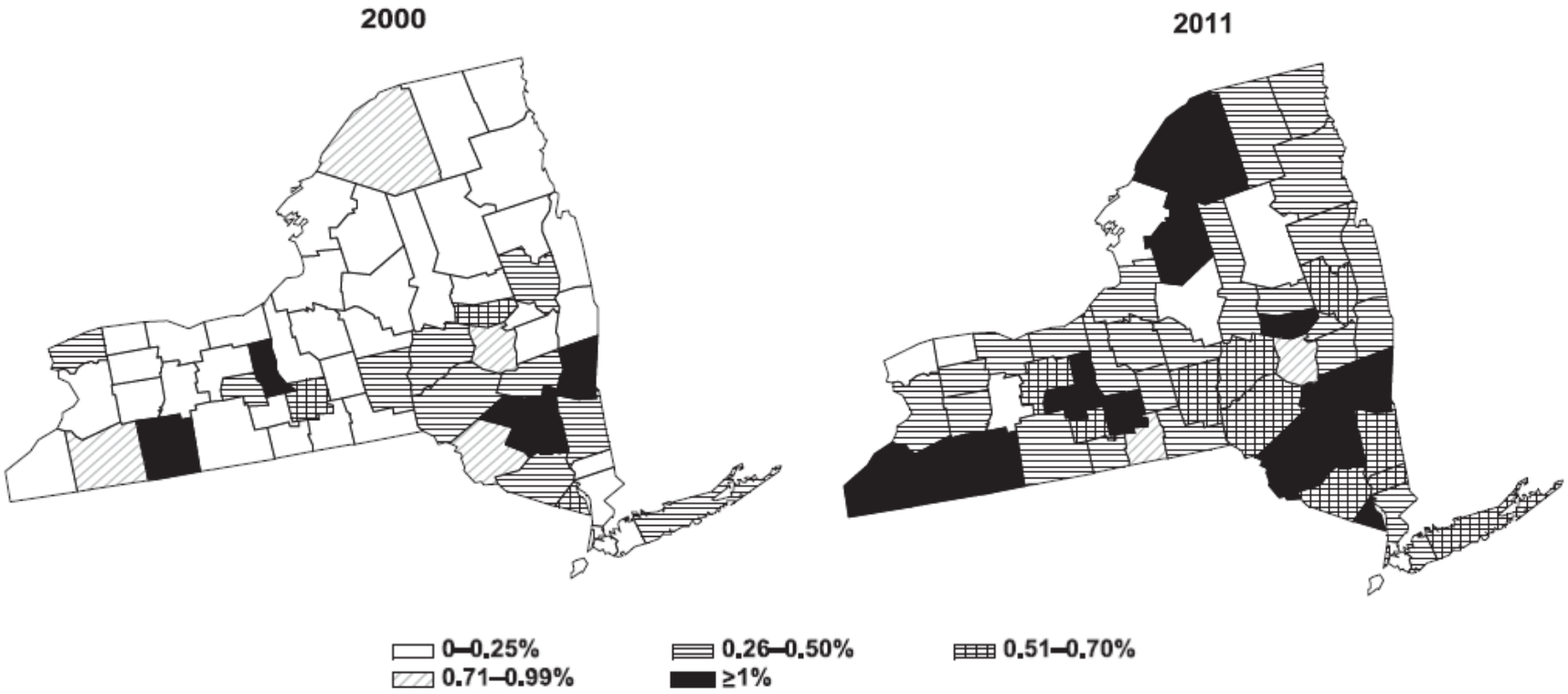
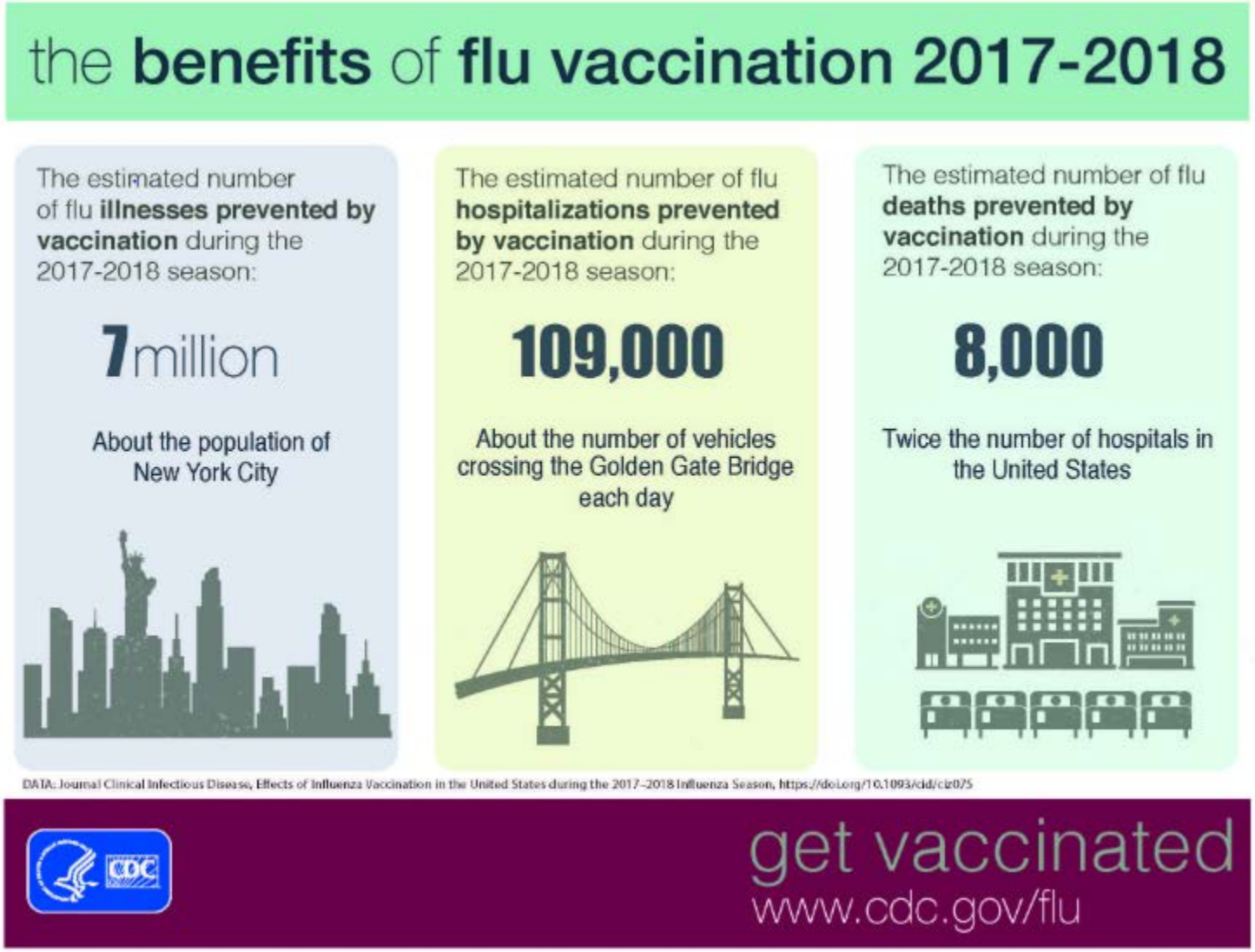


FIGURE 1
County religious exemption rates in NYS schools in 2000 and 2011.

Imdad, A et al. *Pediatrics*. 2013.

Myth:

"Why bother – influenza vaccine doesn't work anyways"



Myth:

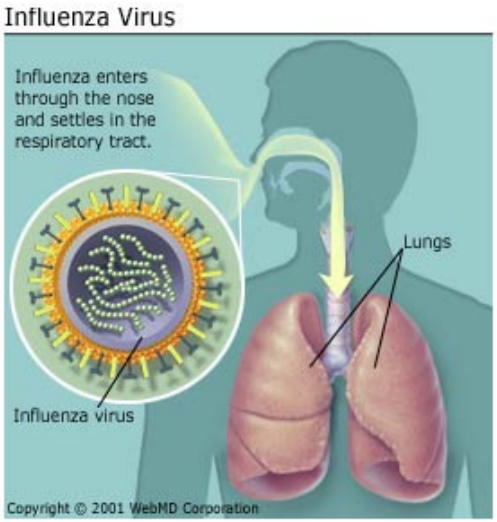
"But every time I get the flu shot I get sick!"

Sanofi Pasteur

Fluzone® Quadrivalent INFLUENZA VACCINE

Initially approved by US FDA in 1980

An inactivated split-virus influenza vaccine prepared in chicken eggs.
Produced by inactivation with formaldehyde to chemically disrupt the virus, followed by purification via a linear sucrose density gradient using continuous flow centrifuge and further disrupted by Triton X-100.



Myth:

"What about thimerosal? Is there truly a link to autism?"

- Thimerosal: Ethyl mercury-based preservative used in vials that contain more than one dose of a vaccine
- American Academy of Pediatrics and the U.S. Public Health Service issued a joint statement in 1999 recommending the removal of thimerosal from vaccines
  - Based solely on the fact that a child received approximately 200 mcg of ethylmercury from vaccines and this exceeded the EPA's maximal allowable amount of orally ingested methylmercury (eliminated more slowly)
- Multiple studies have failed to substantiate a link between thimerosal and autism
  - No link found in 2004 paper from the IOM reviewing >200 studies
  - Autism rates have continued to increase despite removal of thimerosal from childhood vaccines
- Pediatric formulations of influenza vaccine are single dose vials with trace or no thimerosal

Offit, P. Autism's False Profits
IOM. Immunization Safety Review: Vaccines and Autism 2004
Hurley AM et al. Thimerosal-Containing Vaccines and Autism: A Review of Recent Epidemiologic Studies. 2010

Myth:

"Natural immunity is better for children than is immunity acquired through vaccinations"

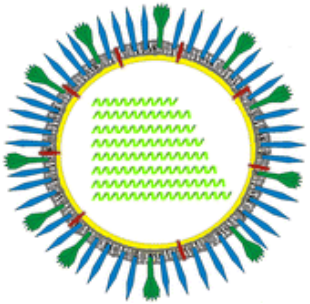
- While immunity via vaccination may not be as durable, in all cases natural immunity comes with the risk of significant adverse effects
  - We have all seen complicated cases of influenza and Pertussis
- Many of today's parents have never seen measles and only remember "simple" cases of diseases like influenza or chicken pox
  - Personal stories are powerful – this is a situation where sharing them (in a HIPAA compliant manner) can convince skeptical parents

Exploring the Reasons Behind Parental Refusal of Vaccines. 2016.

Myth:

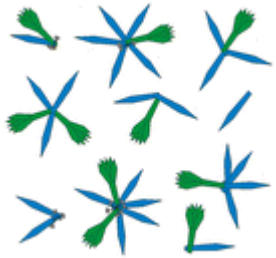
"Too many antigens will overload the immune system"

Whole virus



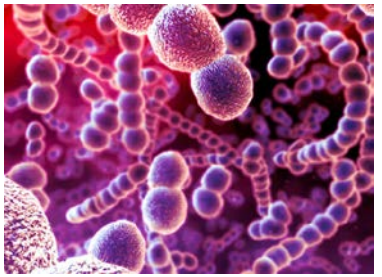
About 10 protein antigens

Split or subunit vaccine



About 2-3 protein antigens

Bacteria



>40-50 protein antigens

- With the exception of live vaccines, an infection with any given microbe contains many more antigens than a protein or subunit vaccine
- "Typical" childhood illness provide much greater stimulation of the immune system than the current vaccination regimen
- Multiple studies have demonstrated that vaccines can be safely administered together

Talking to vaccine hesitant parents

- Understand parental concerns
  - Uninformed but educable, misinformed but correctable, well read and open minded, convinced and contented, and missionary anti-vaxers
- Discuss with respect and without jargon
  - Physicians and scientist struggle against the scientific method when discussing vaccines
- Include ancedotes and visual imagery, not just data
- Ensure ongoing communication
  - Alternative schedules are not scientifically sound, increase the risk of noncompliance, and leave children vulnerable to vaccine preventable diseases

Healy CM and Pickering LK. Pediatrics 2011

Provide scientifically sound resources

TABLE 1 Recommended Online Resources

Organization	Web-Site Address
Albert B. Sabin Vaccine Institute	www.sabin.org
Allied Vaccine Group	www.vaccine.org
American Academy of Family Physicians	www.familydoctor.org
American Academy of Pediatrics	www.aap.org
American Academy of Pediatrics Childhood Immunization Support Program	www.cispimmunize.org
American College of Physicians	www.acponline.org
American Immunization Registry Association	www.immregistries.org
American Medical Association	www.ama-assn.org
American Nurses Association	www.nursingworld.org
Association of State and Territorial Health Officials	www.astho.org
Association of Teachers of Preventative Medicine	www.atpm.org
Baby 411	www.windsorpeak.com/baby411
Canadian Paediatric Society	www.caringforkids.cpc.ca
Centers for Disease Control and Prevention	www.cdc.gov/vaccines
Center for Vaccine Awareness and Research, Texas Children's Hospital	www.vaccine.texaschildrens.org
Vaccine Resource Library	www.path.org/vaccineresources
Every Child by Two	www.ecbt.org
Families Fighting Flu	www.familiesfightingflu.org
Global Alliance for Vaccines and Immunization	www.gavialliance.org
Group on Immunization Education, Society of Teachers and Family Medicine	www.immunizationed.org
Health on the Net Foundation	www.hon.ch
Infectious Diseases Society of America	www.idsociety.org
Immunization Action Coalition	www.immunize.org
Institute for Vaccine Safety (Johns Hopkins University Bloomberg School of Public Health)	www.vaccinesafety.edu
Institute of Medicine	www.iom.edu/Global/Search.aspx?q=immunizations&output=xml_no_dtd&client=default_frontend&site=default_collection&proxyreload=1
Meningitis Angels	www.meningitis-angels.org
National Alliance for Hispanic Health	www.hispanichealth.org
National Foundation for Infectious Diseases	www.nfid.org
National Institutes of Allergy and Infectious Diseases	www3.niaid.nih.gov/dmid/vaccines
National Medical Association	www.nmanet.org
National Meningitis Association	www.nmaus.org
National Network for Immunization Information	www.immunizationinfo.org
Parents of Kids with Infectious Diseases	www.pkids.org
Vaccine Education Center (Children's Hospital of Philadelphia)	www.vaccine.chop.edu
US Food and Drug Administration	www.fda.gov/cber/vaccines.htm
World Health Organization	www.who.int/en

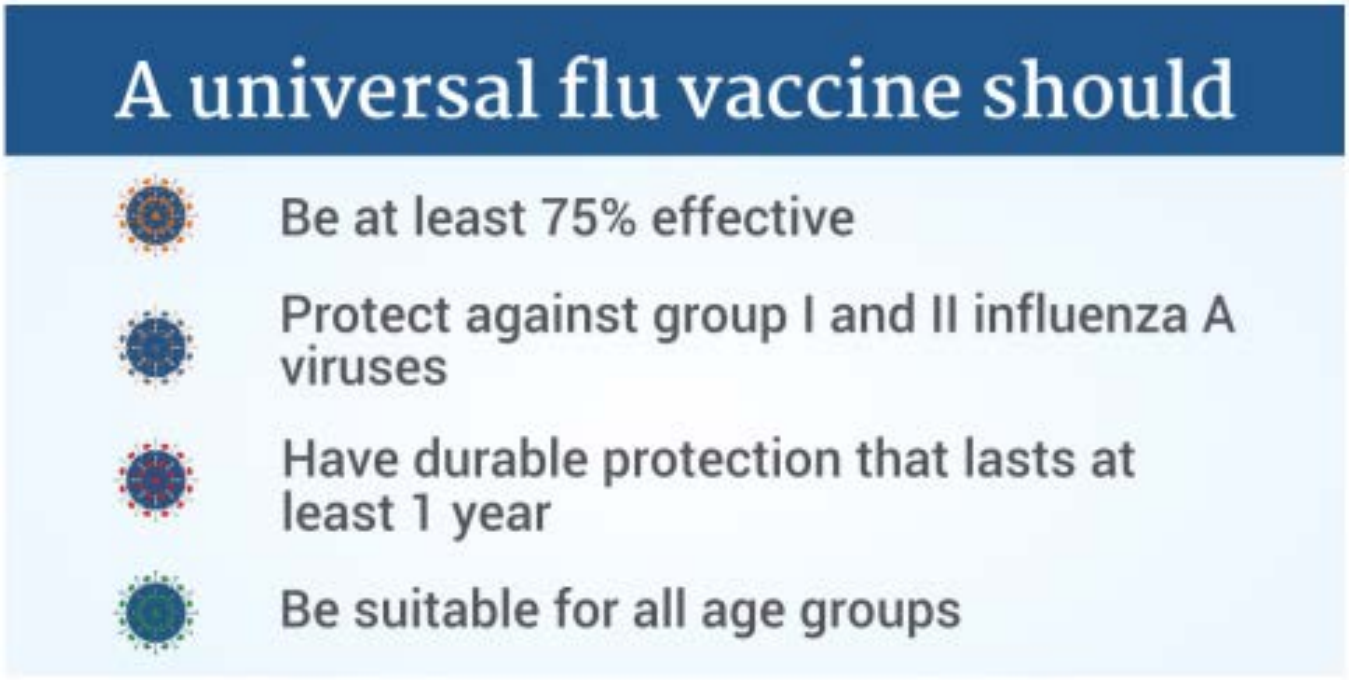
Healy CM and Pickering LK. Pediatrics 2011

In most cases, physicians are more trusted than celebrities and media personalities. However, we need to have our voice heard.

https://www.urmc.rochester.edu/news/story/5496/ur-medicine-community-pediatricians-team-up-to-encourage-vaccinations.aspx

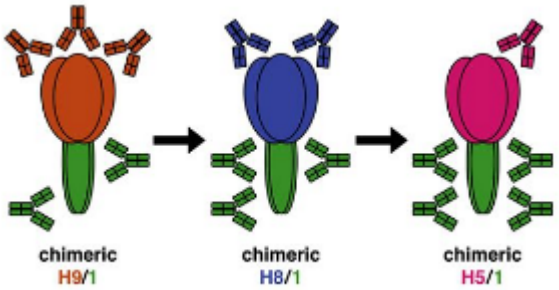
Where do we go from here?

New NIAID strategic plan addresses the research areas essential to creating a safe and effective universal influenza vaccine



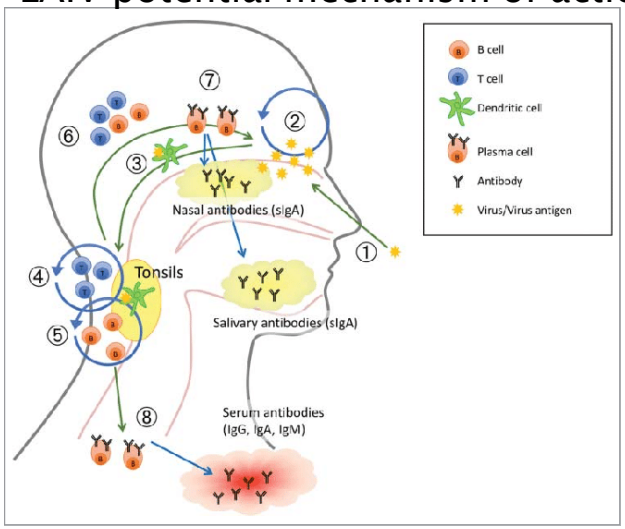
NIH National Institutes of Health
Turning Discovery Into Health

Potential novel universal influenza vaccines

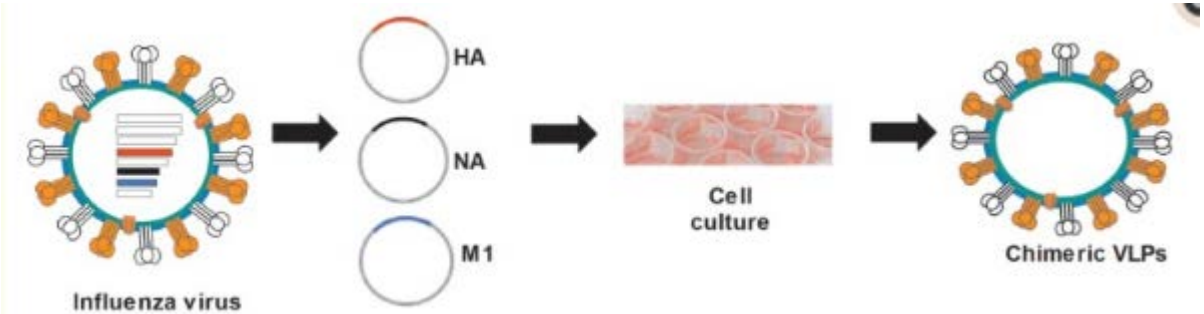


- Chimeric influenza vaccines promote increased stalk (more cross reactive) immunity
- Peptide –based vaccines could promote heterosubtypic immunity
- DNA priming may increase potency and durability of seasonal influenza vaccines

LAIV potential mechanism of action

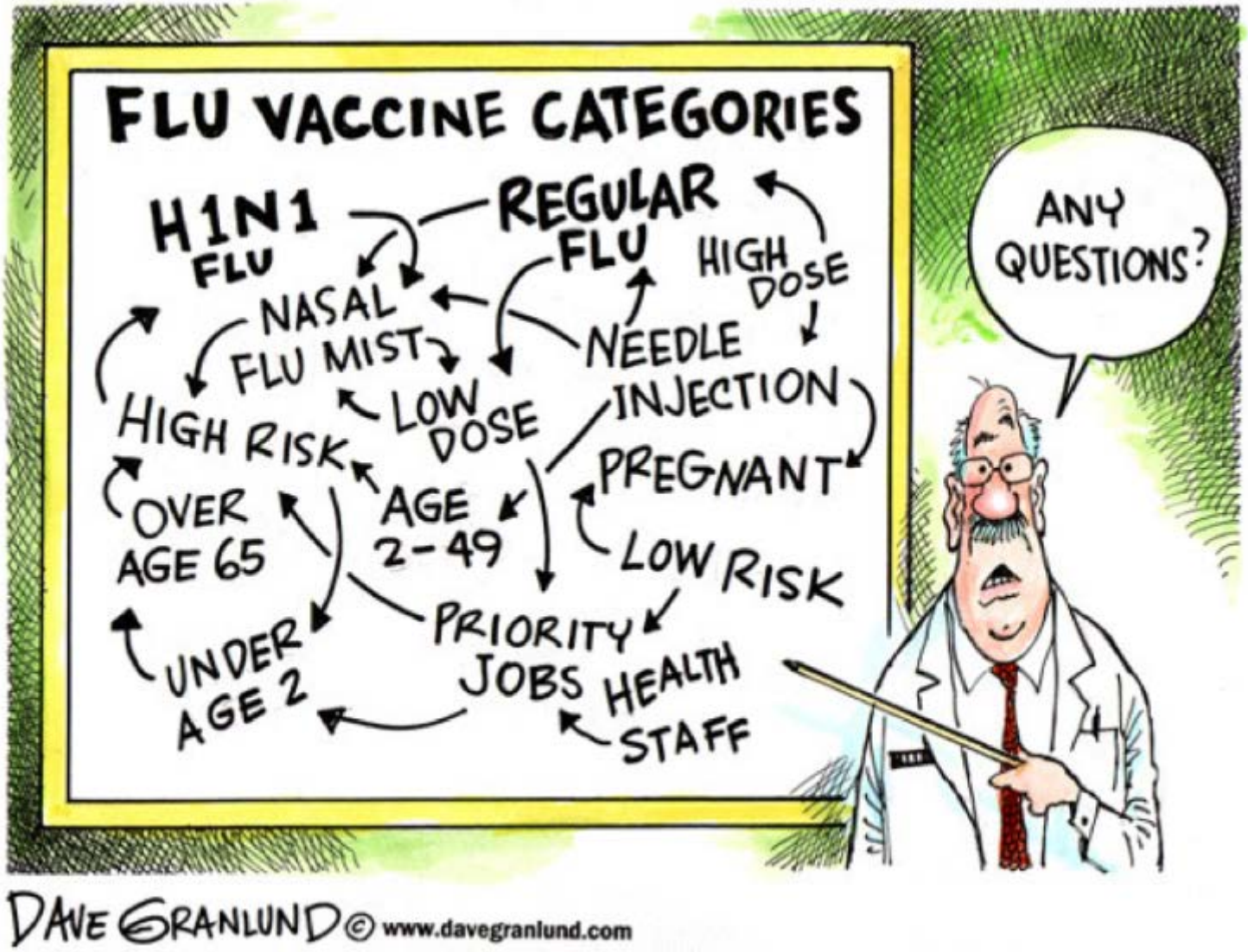


- Novel LAIVs could increase the safety and immunogenicity of current LAIV



- VLP and nanoparticle vaccine formulations aim to increase vaccine immunogenicity and promote cross reactive immunity

Thank you!!!


FLU VACCINE CATEGORIES
H1N1 FLU
REGULAR FLU
HIGH DOSE
NASAL FLU MIST
NEEDLE INJECTION
LOW DOSE
HIGH RISK
PREGNANT
OVER AGE 65
AGE 2-49
LOW RISK
PRIORITY JOBS
UNDER AGE 2
HEALTH STAFF
ANY QUESTIONS?
DAVE GRANLUND © www.davegranlund.com