

How to Prevent and Control Pediatric Influenza

Clinician Outreach and
Communication Activity (COCA)
Call
October 1, 2015

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Objectives

At the conclusion of this session, the participant will be able to:

- ❑ **Describe strategies to assist in preparing for the 2015-2016 influenza season**
- ❑ **Identify gaps and opportunities to improve influenza prevention and control for children with chronic medical conditions**
- ❑ **Discuss the importance of promptly identifying children clinically presumed to have influenza disease for rapid antiviral treatment, when indicated, to reduce morbidity and mortality**
- ❑ **Identify ways to improve preparedness for infectious disease outbreaks within the office practice**

TODAY'S PRESENTER



Henry (Hank) Bernstein, DO, MHCM, FAAP
Professor of Pediatrics
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Influenza Prevention and Treatment: The Latest Paradigm



Henry (Hank) Bernstein, DO, MHCM, FAAP

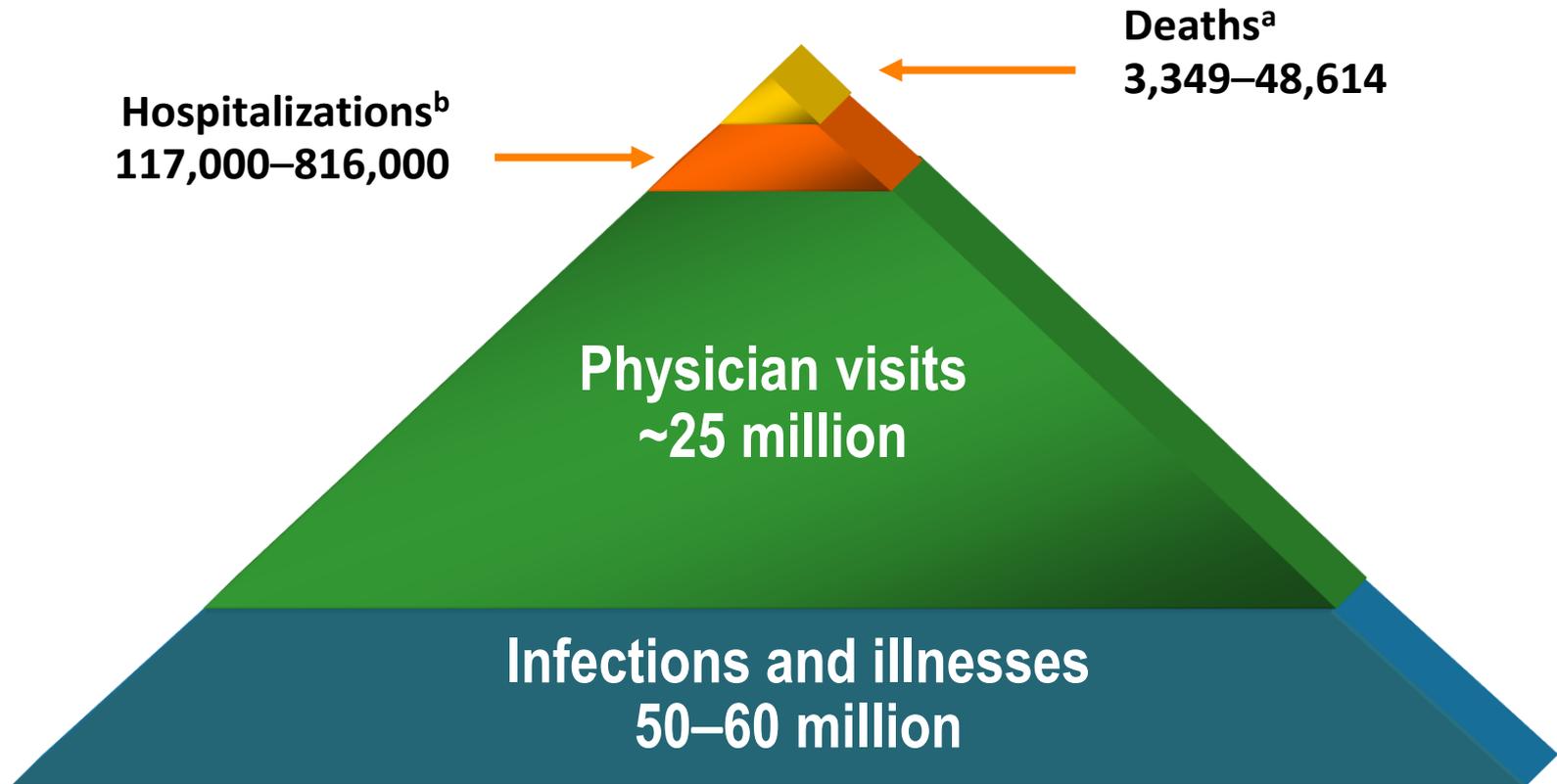
**American Academy of Pediatrics
Red Book Online Associate Editor
Ex Officio, Committee on Infectious Diseases**

**Professor of Pediatrics
Hofstra North Shore-LIJ School of Medicine**



**HOFSTRA NORTH SHORE-LIJ
SCHOOL of MEDICINE
AT HOFSTRA UNIVERSITY**

Influenza Disease Burden in the US in an Average Year

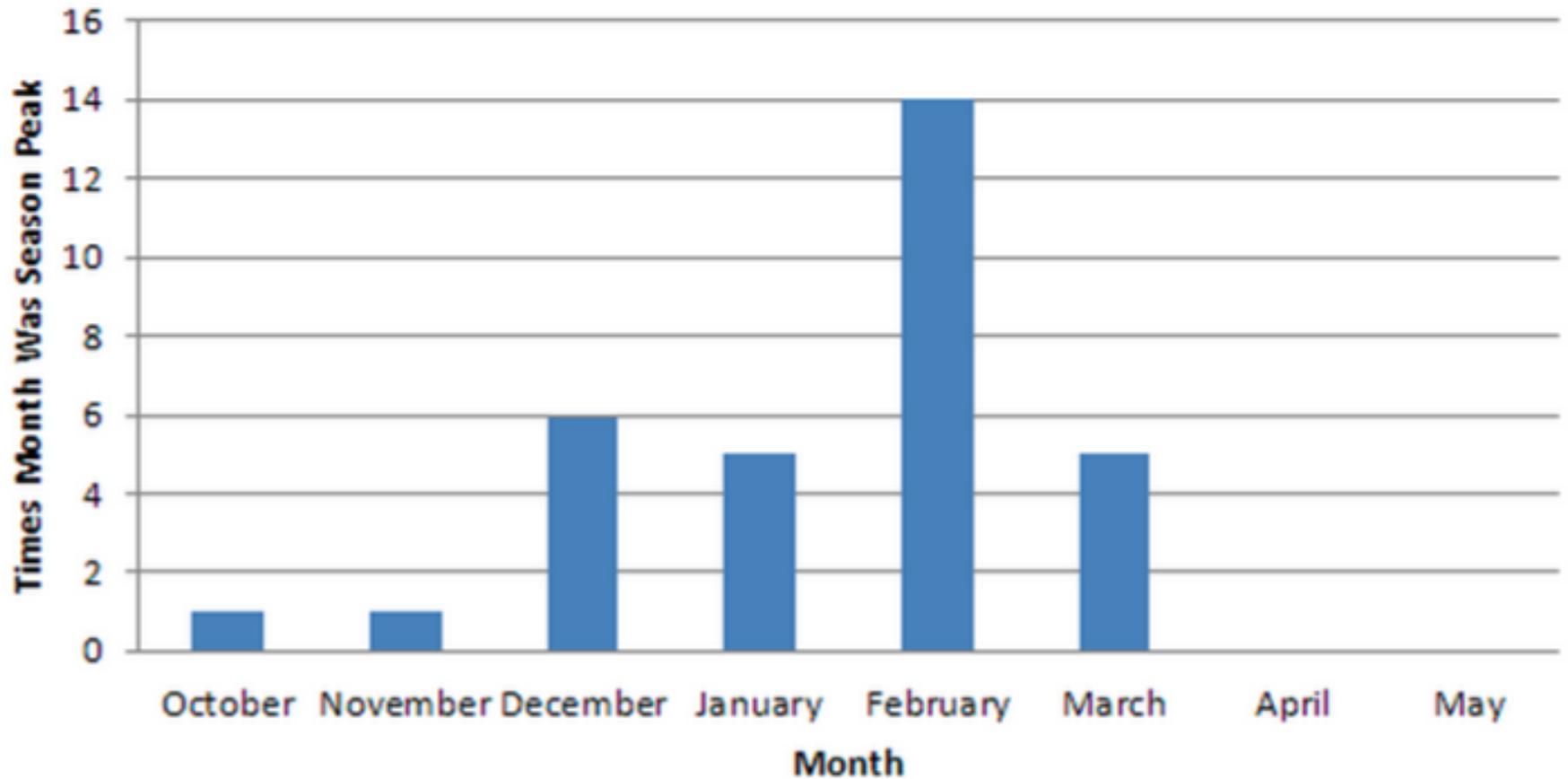


^a *MMWR*. 2010; 59(22):1057–1062.

^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.

Peak Month of Influenza Activity from 1982-83 through 2013-14



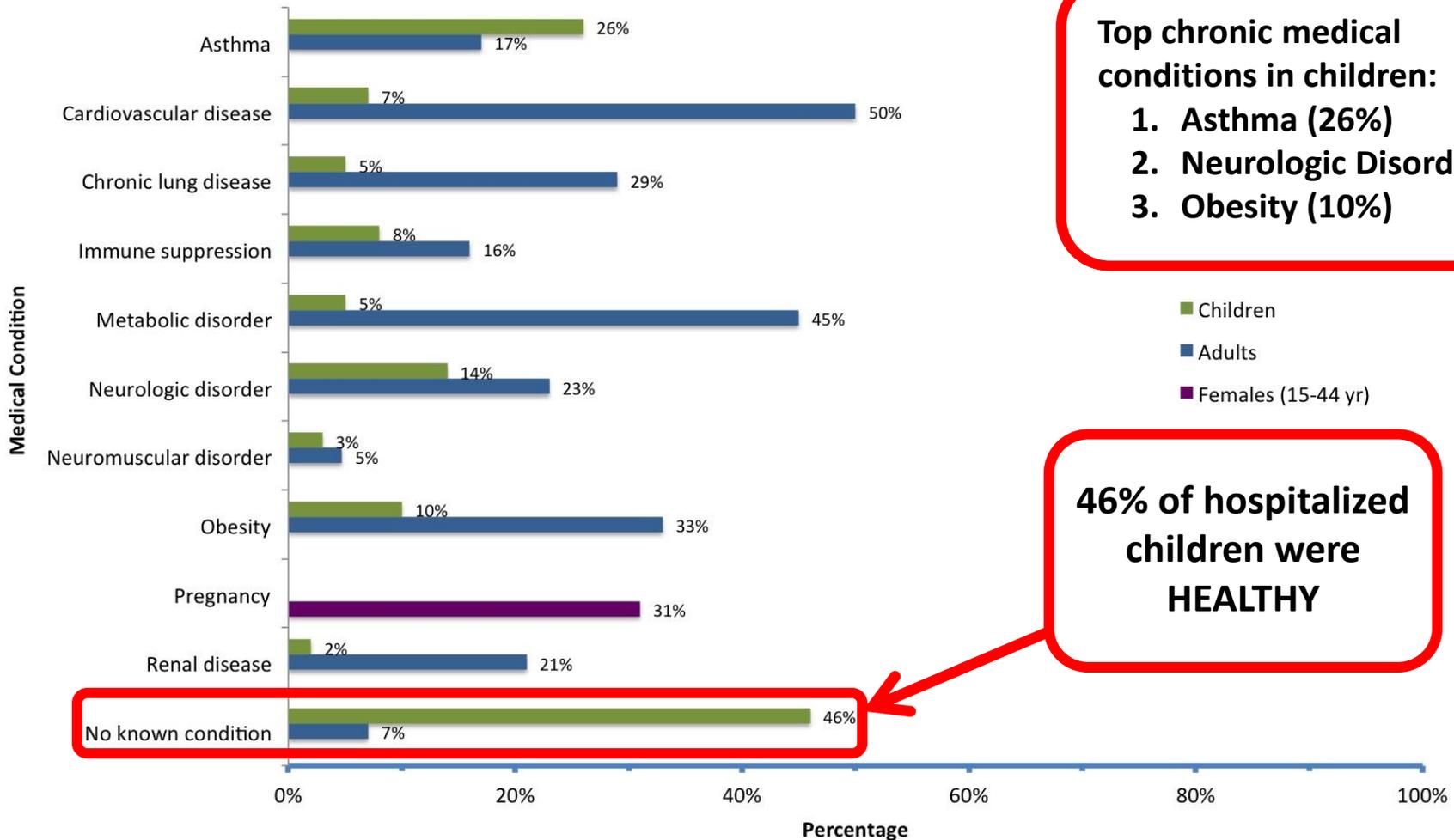
Pediatric Deaths and Hospitalizations By Season and Predominant Strain

Influenza Season	Predominant Strain	Pediatric Deaths	Hospitalizations (0-4 years old) per 100,000	Hospitalizations (5-17 years old) per 100,000
2014-2015*	H3N2	145	57.2	16.8
2013-2014	pH1N1	111	47.3	9.4
2012-2013	H3N2	171	67	14.6
2011-2012*	H3N2	37	16	4
2010-2011	H3N2	123	49.5	9.1
2009-2010	pH1N1	288	77.4	27.2
2008-2009	H1N1	137	28	5
2007-2008	H3N2	88	40.3	5.5
2006-2007	H1N1	77	34.6	2.3
2005-2006	H3N2	46	28	4

*No change in vaccine strains from previous influenza season

Selected Underlying Medical Conditions in Patients Hospitalized w/ Influenza 2014-2015

Selected Underlying Medical Conditions in Laboratory-Confirmed Influenza Hospitalizations: 2014-15 Season



Top chronic medical conditions in children:

- 1. Asthma (26%)**
- 2. Neurologic Disorder (14%)**
- 3. Obesity (10%)**

46% of hospitalized children were HEALTHY

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Recommendations for Prevention and Control of Influenza in Children, 2015–2016

Committee on Infectious Diseases



2015-16 Seasonal Influenza Vaccine Strains

Trivalent

- A/California/7/2009 (H1N1)-like virus
- A/Switzerland/9715293/2013 (H3N2)-like virus
- B/Phuket/3073/2013-like virus

Quadrivalent

- Adds B/Brisbane/60/2008-like virus (B/Victoria lineage)

Strains that changed from last season

	H1N1-like strain	H3N2-like strain	B-like strain
1986-'87	A/Chile/1/83 and A/Singapore/6/86	A/Christchurch/4/85-A/Mississippi/1/85	B/Ann Arbor/1/86
1987-'88	A/Singapore/6/86	A/Leningrad/360/1986	B/Ann Arbor/1/86
1988-'89	A/Singapore/6/86	A/Sichuan/2/87	B/Beijing/1/87
1989-'90	A/Singapore/6/86	A/Shanghai/11/87	B/Yamagata/16/88
1990-'91	A/Singapore/6/86	A/Guizhou/54/89	B/Yamagata/16/88
1991-'92	A/Singapore/6/86	A/Beijing/1/87	B/Yamagata/16/88
1992-'93*	A/Singapore/6/86		B/Yamagata/16/88
1993-'94	A/Singapore/6/86		B/Yamagata/16/88
1994-'95			B/Yamagata/16/88
1995-'96			B/Beijing/184/93
1996-'97			B/Beijing/184/93
1997-'98			B/Beijing/184/93
1998-'99			B/Beijing/184/93
1999-2000*			B/Beijing/184/93
2000-'01			B/Beijing/184/93
2001-'02		A/Moscow/10/99	B/Sichuan/379/99
2002-'03		A/Moscow/10/99	B/Hong Kong/330/2001
2003-'04*	A/New /20/99	A/Moscow/10/99	B/Hong Kong/330/2001
2004-'05	A/New /20/99	A/Fujian/411/2002	B/Shanghai/361/2002
2005-'06	A/New /20/99	A/California/7/2004	B/Shanghai/361/2002
2006-'07	A/New /20/99	A/Wisconsin/67/2005	B/Malaysia/2506/2004
2007-'08	A/Solomon Islands/3/2006	A/Wisconsin/67/2005	B/Malaysia/2506/2004
2008-'09	A/Brisbane/59/2007	A/Brisbane/10/2007	B/Florida/4/2006
2009-'10	A/Brisbane/59/2007	A/Brisbane/10/2007	B/Brisbane/60/2008
Pandemic	A/California/07/2009		
2010-'11	A/California/07/2009	A/Perth/16/2009	B/Brisbane/60/2008
2011-'12*	A/California/07/2009	A/Perth/16/2009	B/Brisbane/60/2008
2012-'13	A/California/07/2009	A/Victoria/361/2011	B/Wisconsin/1/2010
2013-'14	A/California/07/2009	A/Texas/50/2012	B/Massachusetts/2/2012**
2014-'15*	A/California/07/2009	A/Texas/50/2012	B/Massachusetts/2/2012**
2015-'16	A/California/07/2009	A/Switzerland/9715293/2013	B/Phuket/3073/2013**

**Influenza is unpredictable:
Only 5 times in past 30 years
have vaccine strains not
changed from previous season**

• No change in vaccine strains from previous season
** Quadrivalent vaccine with add'l B lineage available

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

Has child received
2 or more total doses* of
tri- or quadrivalent vaccine
prior to July 1, 2015?

Yes



1 Dose

No/Don't know



2 Doses
(Interval is 4 weeks)

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

Special Populations to Reach



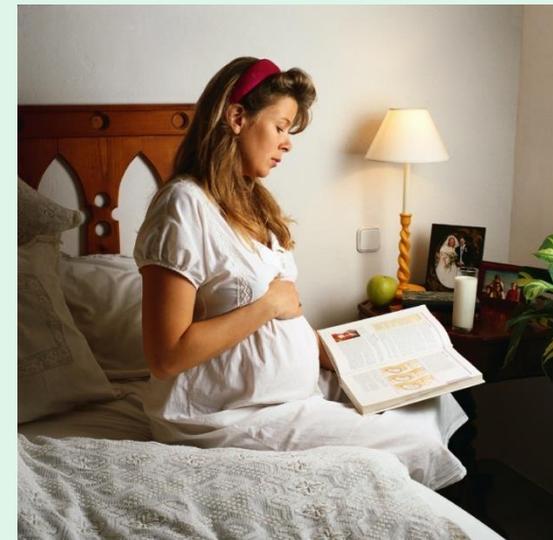
Children



Health Care Personnel



***Household Contacts of High Risk Children
and All Children <5***



Pregnant Women

Offer Vaccine Throughout Year

August 14

M	T	W	Th	F	Sa	S
4	5					
11	12					
18	19	20	21	22	23	24
25	26	27	28	29	30	31

September 14

M	T	W	Th	F	Sa	S
22	23	24	25	26	27	28
29	30					

October 14

M	T	W	Th	F	Sa	S
23	24	25	26	27	28	29
30	31					

November 14

M	T	W	Th	F	Sa	S
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30

Start as soon as available

December 14

M	T	W	Th	F	Sa	S
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

January 15

M	T	W	Th	F	Sa	S
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

February 15

M	T	W	Th	F	Sa	S
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	

March 15

M	T	W	Th	F	Sa	S
30	31					1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29

April 15

M	T	W	Th	F	Sa	S
		1	2	3	4	5
6	7					
13	14					
20	21					
27	28	29	30			

May 15

M	T	W	Th	F	Sa	S
				1	2	3
25	26	27	28	29	30	31

June 15

M	T	W	Th	F	Sa	S
		1	2	3	4	5
6	7					
13	14					
20	21					
27	28					
29	30					

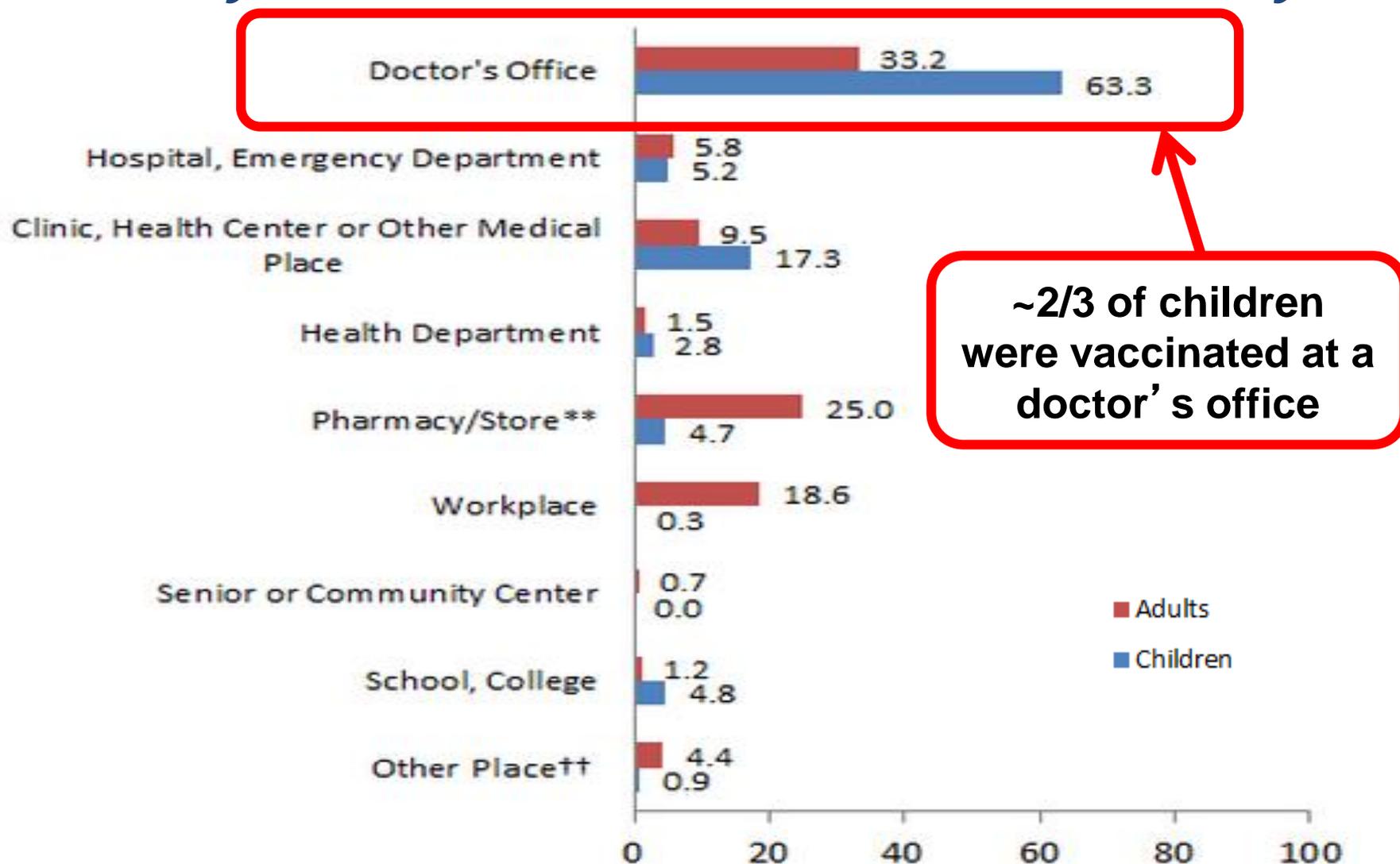
July 15

M	T	W	Th	F	Sa	S
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

Continue into late spring

Place of Vaccination for Children and Adults

Early 2014-15 season, National Flu Survey



‡ includes hospitals, clinics or health centers, local health departments, and other.

Source: CDC. Available online at: <http://stacks.cdc.gov/view/cdc/26550>

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BEATIE



"I hate it when we're not sure we're inoculating against the right strain of flu virus."

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.	%	
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)
Age at first vaccination (any influenza virus)	Well matched					
6–23 mo		23	1.3	32	1.7	29.1 (-21.2 to 59.1)
24–35 mo						32.6 (-25.8 to 64.5)
36–59 mo						65.6 (36.3 to 82.4)
Previous vaccination (any influenza virus)						
Yes		18	1.9	29	3.1	39.3 (-9.2 to 66.9)
No		35	1.2	64	2.1	46.9 (20.0 to 65.2)
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)

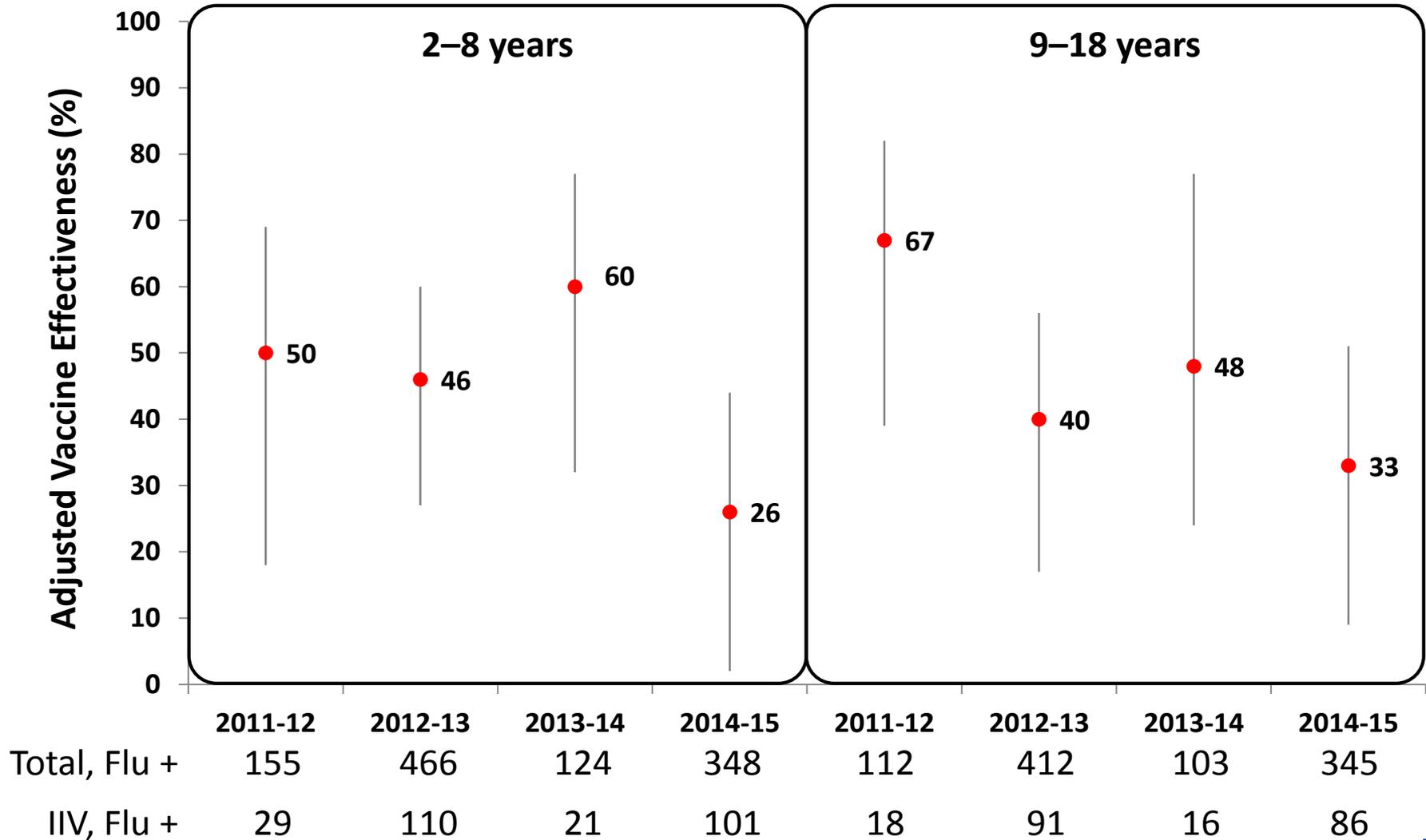
LAIV had higher efficacy for both well matched and drifted strains

Effectiveness of IIV vs. LAIV

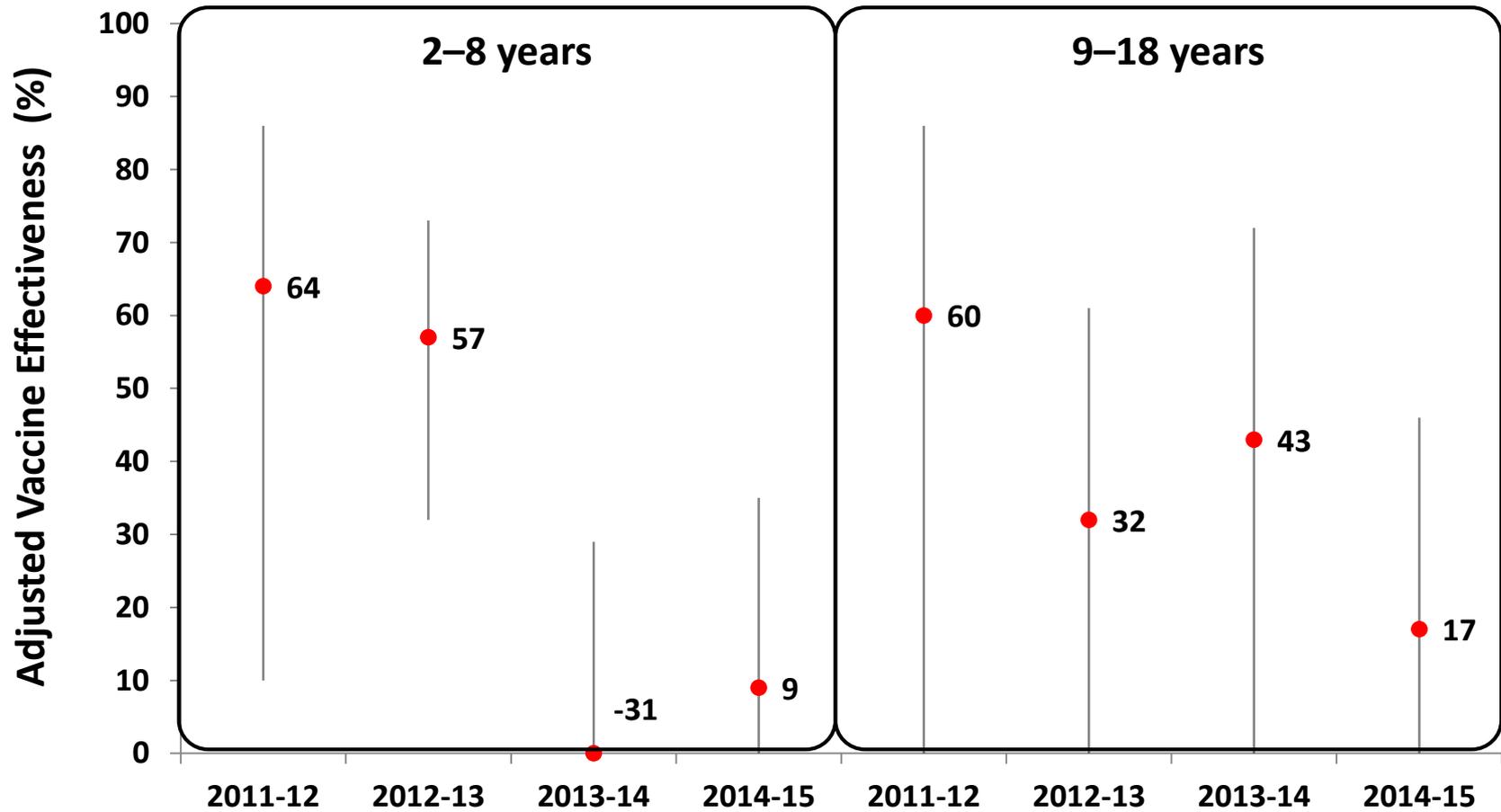
- **Healthy children ages 2 through 8 years may be immunized with either IIV or LAIV (no preference)**
- **Vaccination should not be delayed to obtain a specific product**



IIV effectiveness against medically-attended influenza, by season and age category



LAIIV effectiveness against medically-attended influenza, by season and age category



Total, Flu +	168	391	127	316	100	347	99	307
LAIIV, Flu +	6	35	22	70	6	26	12	49

Take Home Messages

- **Immunize everyone 6 months of age and older, especially close contacts of children at high risk of influenza-related complications**
- **Vaccine composition has changed**
- **Dosing algorithm for children 6 months through 8 years reflects H1N1 pandemic virus no longer believed antigenically novel**
- **Vaccine effectiveness can vary**
- **Neuraminidase inhibitors continue to be important in influenza control**

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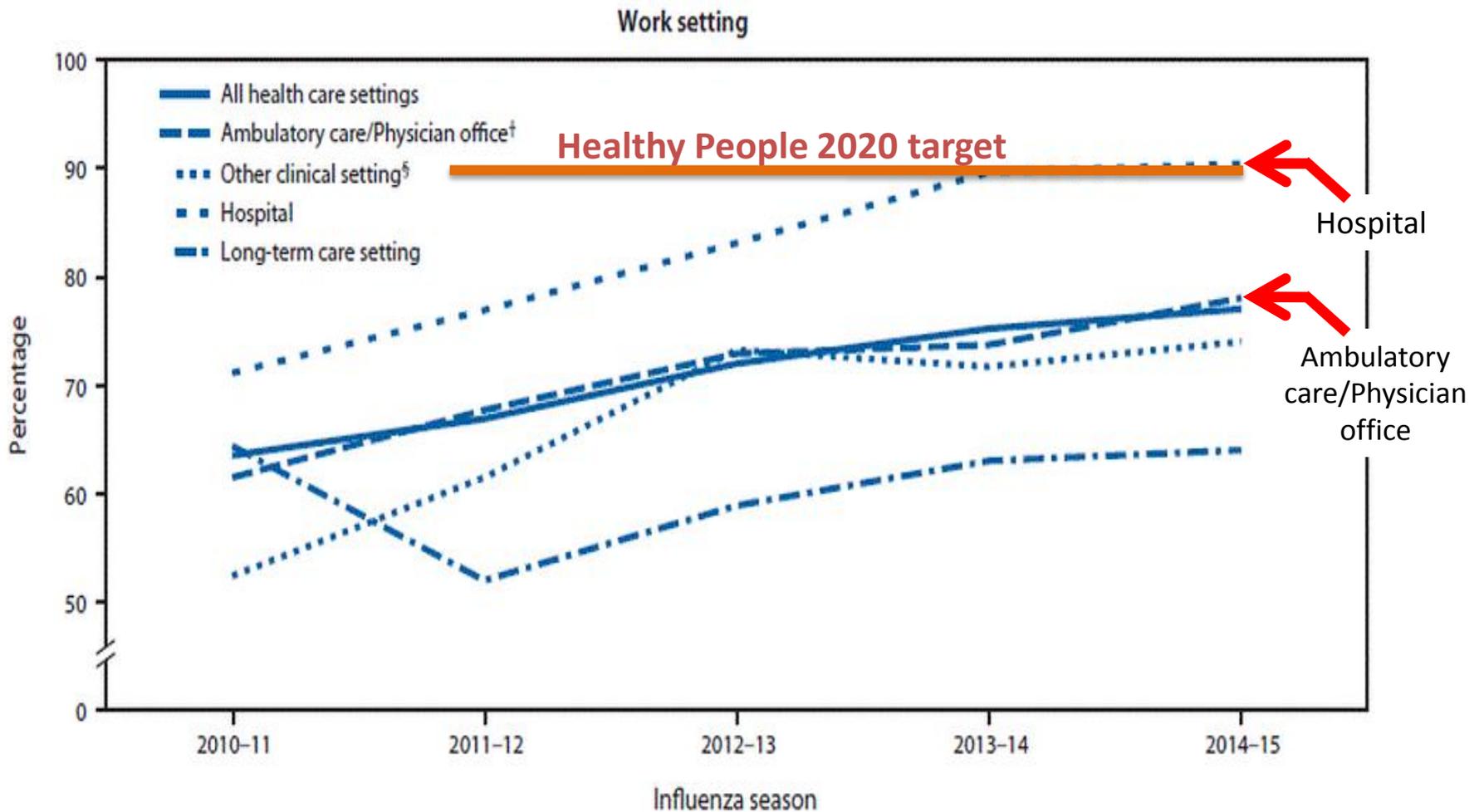
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Influenza Immunization for All Health Care Personnel: Keep It Mandatory

COMMITTEE ON INFECTIOUS DISEASES



Percentage of HCP who received influenza vaccination by work setting



Effect of influenza vaccination of healthcare personnel on patient outcomes: forest plots of cluster randomized trials

Study or Subgroup	Risk Ratio for All-Cause Mortality		
	IV, Random	95% CI	Year
Potter 1997	0.59	0.34, 1.03	1997
Carman 2000	0.61	0.42, 0.88	2000
Hayward 2006	0.73	0.54, 0.99	2006
Lemaitre 2009	0.87	0.59, 1.27	2009
Total (95% CI)	0.71	0.59, 0.85	

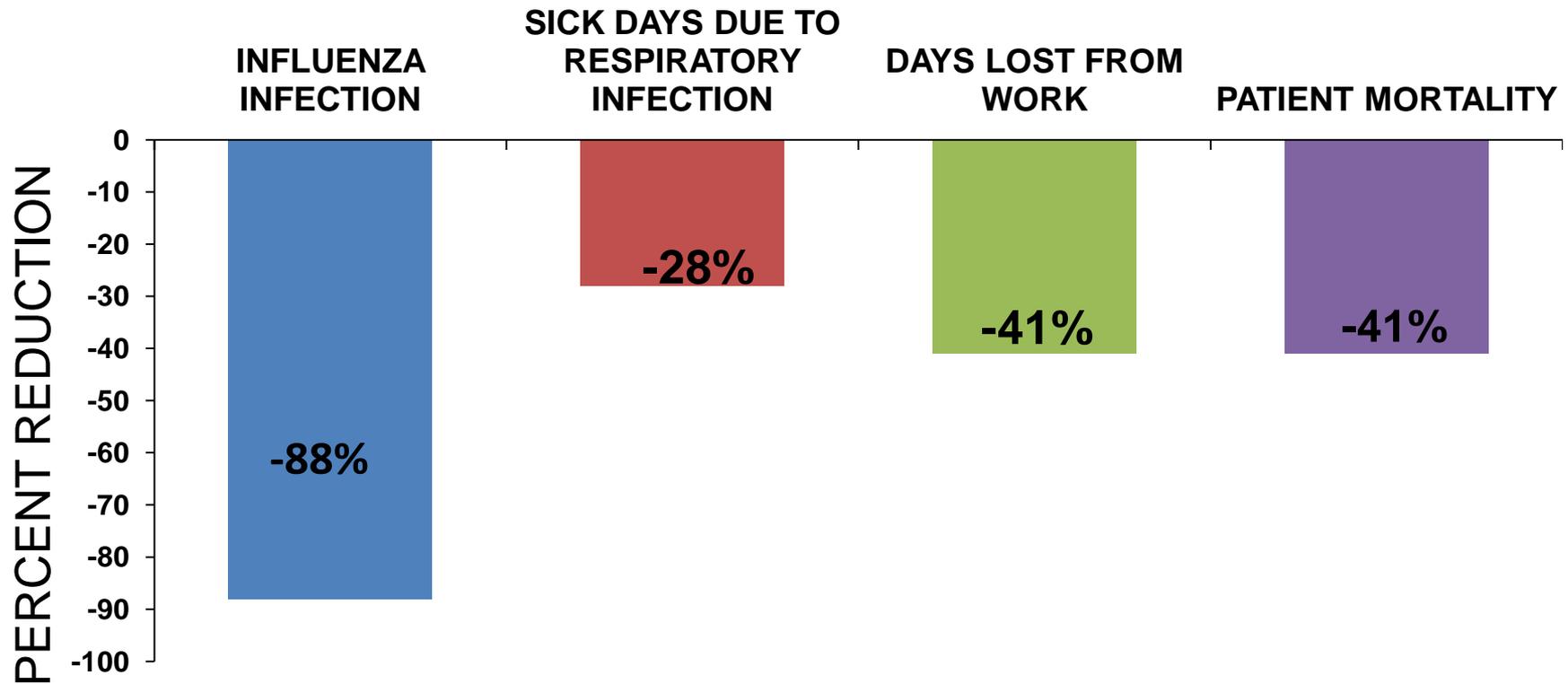
29% reduction in all-cause death

Study or Subgroup	Risk Ratio for Influenza-like-Illness		
	IV, Random	95% CI	Year
Potter 1997	0.61	0.26, 1.45	1997
Hayward 2006	0.50	0.38, 0.66	2006
Lemaitre 2009	0.69	0.51, 0.95	2009
Total (95% CI)	0.58	0.46, 0.73	

42% reduction in influenza-like illness

Importance of Influenza Vaccine for HCP

REDUCTION OF FLU AND RELATED OUTCOMES IN HCP RECEIVING VACCINE

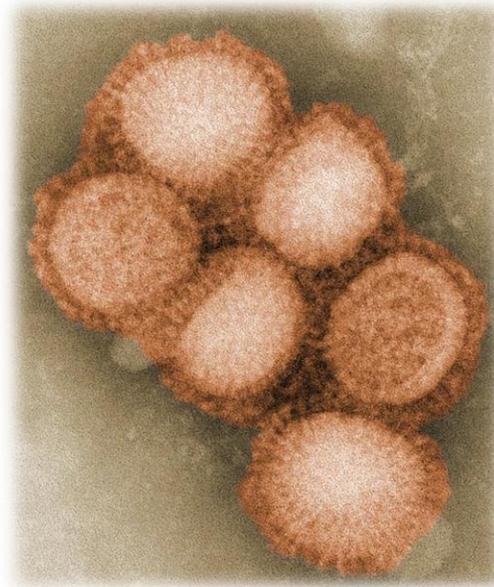
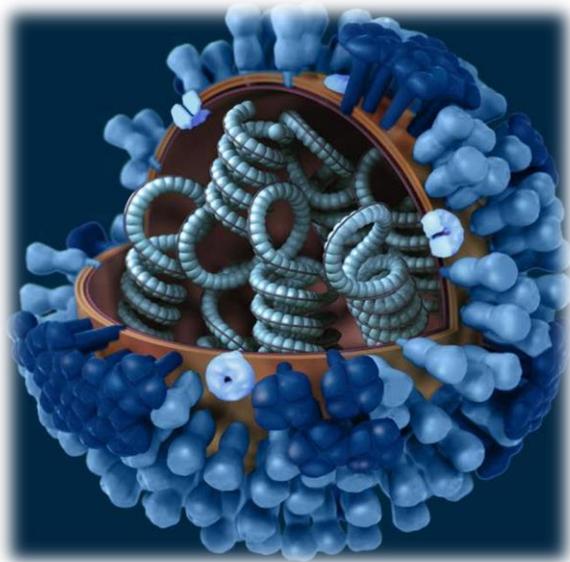


Adapted from: Talbot TR, Bradley SF, Cosgrove SE, et al. Influenza vaccination of healthcare workers and vaccine allocation for healthcare workers during vaccine shortages. *Infect Control Hosp Epidemiol* 2005;26:882–890.

Take Home Messages

- **Voluntary efforts to improve and sustain HCP immunization rates have failed**
- **A mandate is ethical, just, and necessary**
- **Mandatory vaccine programs**
 - **have been successful**
 - **would cut costs**
- **Concept has growing widespread support**

Influenza Antiviral Therapy



Diagnostic Tests

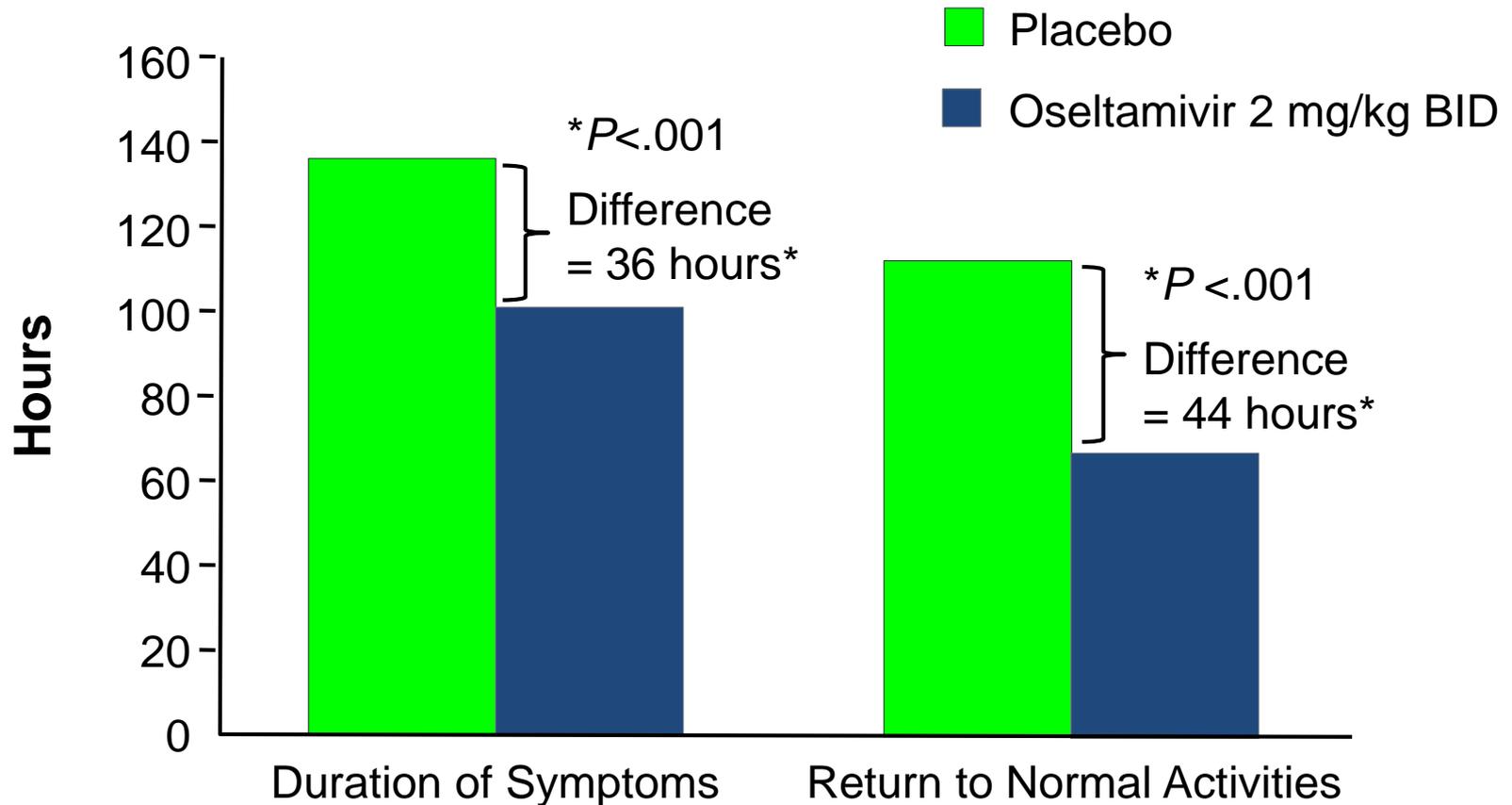
Influenza Diagnostic Test	Method	Availability	Typical Processing Time	Sensitivity	Distinguishing Subtype Strains of Influenza A	Cost
Rapid influenza diagnostic tests (RIDTs)	Antigen detection	Wide	<30 minutes	10-80%	No	\$
Direct and indirect immunofluorescence assays (DFA and IFA)	Antigen detection	Wide	1-4 h	70-100%	No	\$
Viral cell culture	Virus isolation	Limited	3-10 d	100%	Yes	\$\$
Rapid cell culture (shell vials and cell mixtures)	Virus isolation	Limited	1-3 d	100%	Yes	\$\$
Nucleic acid amplification tests (including rRT-PCR)	RNA detection	Limited	1-6 h	86-100%	Yes	\$\$\$
Rapid Influenza molecular assays	RNA detection	Wide	<15 minutes	86-100%	No	\$\$\$

Adapted from the Centers for Disease Control and Prevention (CDC) Guidance for clinicians on the use of rapid influenza diagnostic tests. http://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm Accessed September 24, 2014.

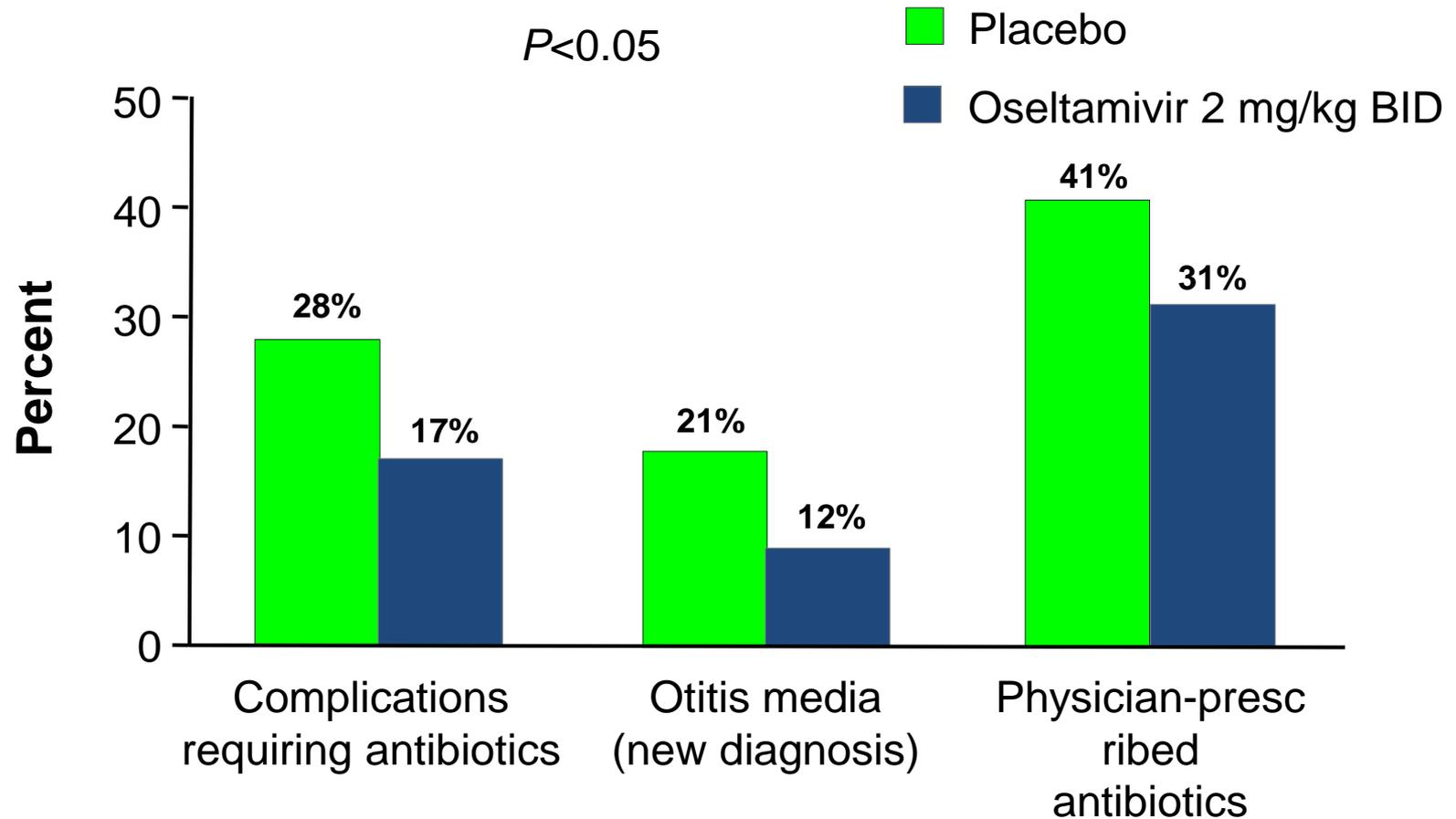
Influenza Antiviral Medications

	Adamantanes (Amantadine /Rimantadine)	Oseltamivir (Tamiflu)	Zanamivir (Relenza)	Peramivir (Rapivab)
2015–2016 Viruses				
Influenza A (H1N1) (derived from 2009 pandemic)	Resistant	Susceptible	Susceptible	Susceptible
Influenza A (H3N2)	Resistant	Susceptible	Susceptible	Susceptible
Influenza B (both lineages)	Resistant	Susceptible	Susceptible	Susceptible

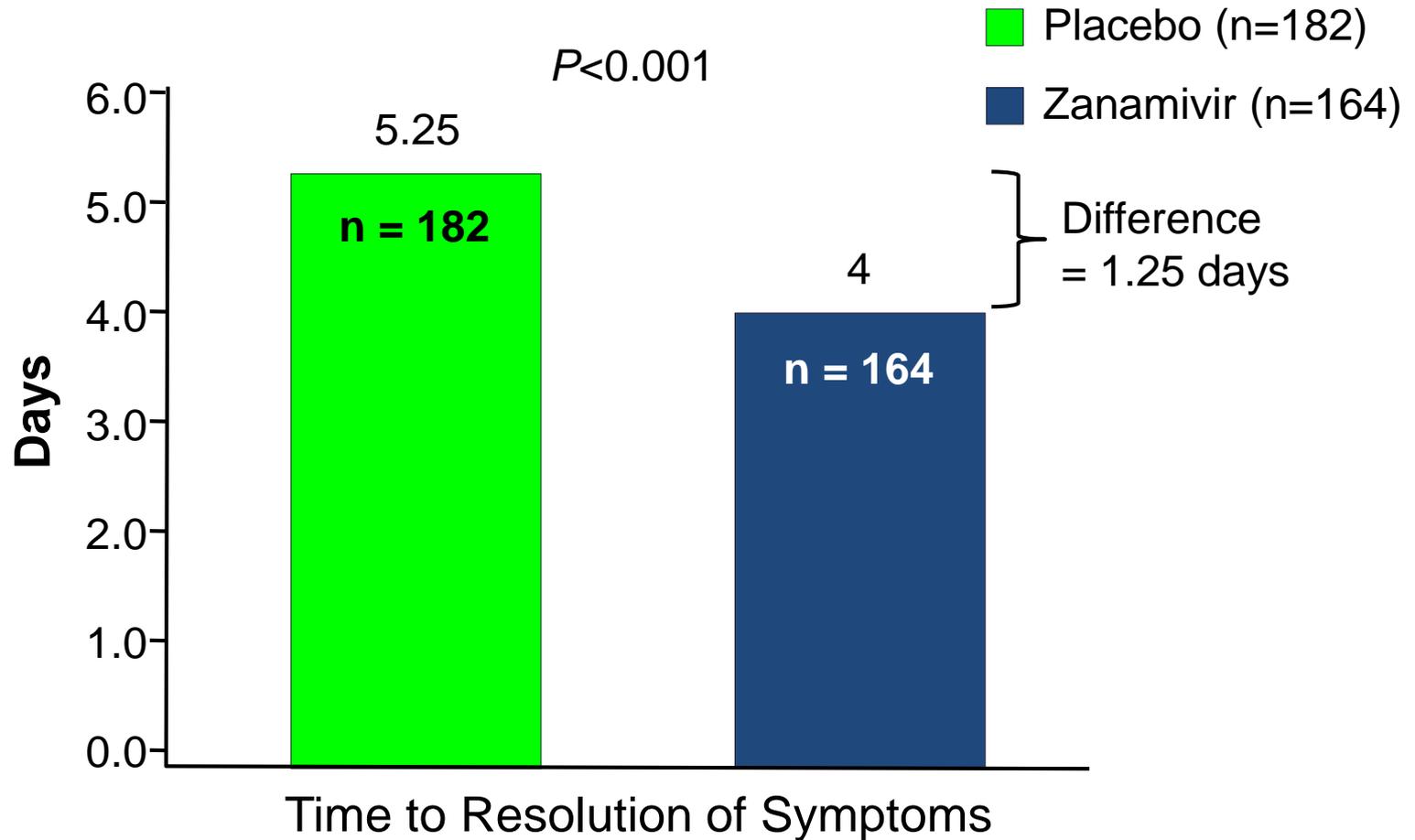
Oseltamivir Treatment Clinical Efficacy in Children



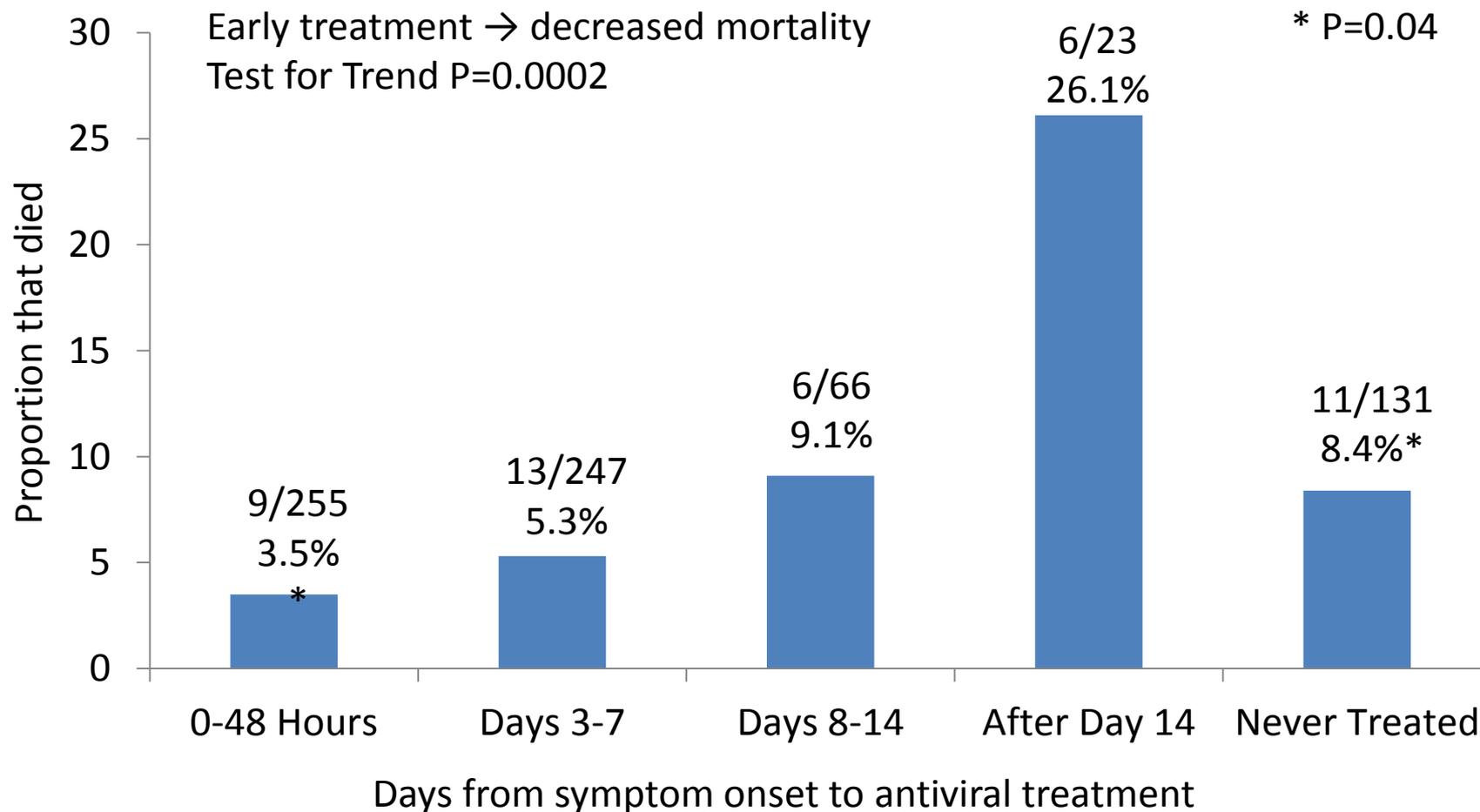
Oseltamivir Treatment Clinical Efficacy in Children



Zanamivir Treatment Clinical Efficacy in Children



NAIs and Mortality in Children California Surveillance Data (n=784)



Adverse Effects of Oseltamivir in Children 1-12 Years Old

Adverse Event [‡]	Treatment Trials*	
	Placebo N=517	TAMIFLU 2 mg/kg twice daily N=515
Vomiting	48 (9%)	77 (15%)
Diarrhea	55 (11%)	49 (10%)
Otitis media	58 (11%)	45 (9%)
Abdominal pain	20 (4%)	24 (5%)
Asthma (including aggravated)	19 (4%)	18 (3%)
Nausea	22 (4%)	17 (3%)
Epistaxis	13 (3%)	16 (3%)
Pneumonia	17 (3%)	10 (2%)

OFFER treatment ASAP to children

- **Hospitalized for:**
 - **presumed influenza**
 - **severe, complicated, or progressive illness attributable to influenza**
- **With influenza (any severity) at high risk of complications**

CONSIDER treatment for clinical influenza if...

- **Otherwise healthy child where decreasing symptoms is felt to be warranted**
- **Siblings at home:**
 - **< 6 months old**
 - **with underlying medical conditions that predispose to flu complications**



Commentary and Society Support for Influenza Antiviral Treatment

- **No placebo-controlled RCTs available for NAI treatment of hospitalized influenza patients**
- **Challenging to undertake RCTs with mortality and severe morbidity as outcomes**
- **Observational studies consistently report clinically meaningful benefits of NAI treatment that creates large body of evidence for benefit**

Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis – U.S., 2015-2016

Medication	Treatment (BID x5 days)	Chemoprophylaxis (QD x10 days)
Oseltamivir^a		
Adults	75 mg	75 mg
Children ≥12 mo		
Body weight		
≤15 kg (≤33 lb)	30 mg	30 mg
>15 kg–23 kg (33 lb–51 lb)	45 mg	45 mg
>23 kg–40 kg (>51 lb–88 lb)	60 mg	60 mg
>40 kg (>88 lb)	75 mg	75 mg
Infants 9–11 mo^b	3.5 mg/kg per dose	3.5 mg/kg per dose
Term infants 0–8 mo^b	3 mg/kg per dose twice daily	3 mg/kg per dose once daily for infants 3–8 mo; not recommended for infants <3 mo old, unless situation judged critical, because of limited safety and efficacy data in this age group
Preterm infants	See details in footnote ^c	
Zanamivir^d		
Adults	10 mg (two 5-mg inhalations)	10 mg (two 5-mg inhalations)
Children (≥7 y for treatment, ≥5 y for chemoprophylaxis)	10 mg (two 5-mg inhalations)	10 mg (two 5-mg inhalations)

Oseltamivir Dosing for Term and Preterm Infants Younger Than 1 Year

Age	Treatment (mg/kg/dose po BID x 5 days)	Chemoprophylaxis (mg/kg/dose po QD x 10 days)
<u>Term</u> 0 to <9 mo	3.0	<ul style="list-style-type: none"> • 3.0 for infants 3 - 8 mo • Not recommended for infants <3 mo
<u>Term</u> 9 to <12 mo	3.5	3.5
<u>Preterm</u>	Varies based on postmenstrual age*	Not recommended

*Gestational age + chronological age (in weeks)

Double vs. Standard Dose Oseltamivir Therapy in Children and Adults

	Double Dose	Standard Dose	P-value
RT-PCR negative on treatment day 5 [N (%; 95% CI)]	115/159 (72%) (CI 65%,79%)	105/154 (68%) (CI 61%,75%)	0.42
Mortality [N (%; 95% CI)]	12/165 (7%) (CI 4%,12%)	9/161 (6%) (CI 3%,10%)	0.54
Median days on supplemental oxygen [N (interquartile range)]	3 (2-5)	3.5 (2-7)	0.48
Median days in ICU [N (interquartile range)]	4.5 (3-6)	5 (2-11)	0.66
Median days on mechanical ventilation [N (interquartile range)]	2.5 (1-16)	8 (1-16)	0.58

Take Home Messages

- **Annual influenza outbreaks cause significant morbidity and mortality in children**
- **Antiviral treatment of influenza is indicated in young children, hospitalized patients, and patients at higher risk of complications**
- **Oseltamivir dosing down to 2 weeks of age now determined; OK for newborns**
- **No benefit of doubling oseltamivir dose**

Improve Office Preparedness for Seasonal and Pandemic Influenza

- AAP offers resources to help pediatric office practices prepare for seasonal and pandemic influenza outbreaks
- Having a vaccine handling and storage plan for power outages/disasters is beneficial
- Talking with office staff about infection control practices for influenza and other outbreaks is a critical part of an office preparedness plan

Improve Office Preparedness for Seasonal and Pandemic Influenza

- Develop a written office management plan that includes:
 - An Office Respiratory Protection Plan (i.e. use of gloves, masks, hand sanitizers, tissues, etc.)
 - Strategies to Address Office Flow Issues
 - Segregating patients with influenza-like illness
 - Postponing less critical visits
 - Rapid Triage of Patients
 - Enhanced Cleaning and Disinfection Strategies

Office Preparedness Resources

Preparedness Checklist for Pediatric Practices

www.aap.org/disasters/checklist

Pediatric Preparedness Resource Kit

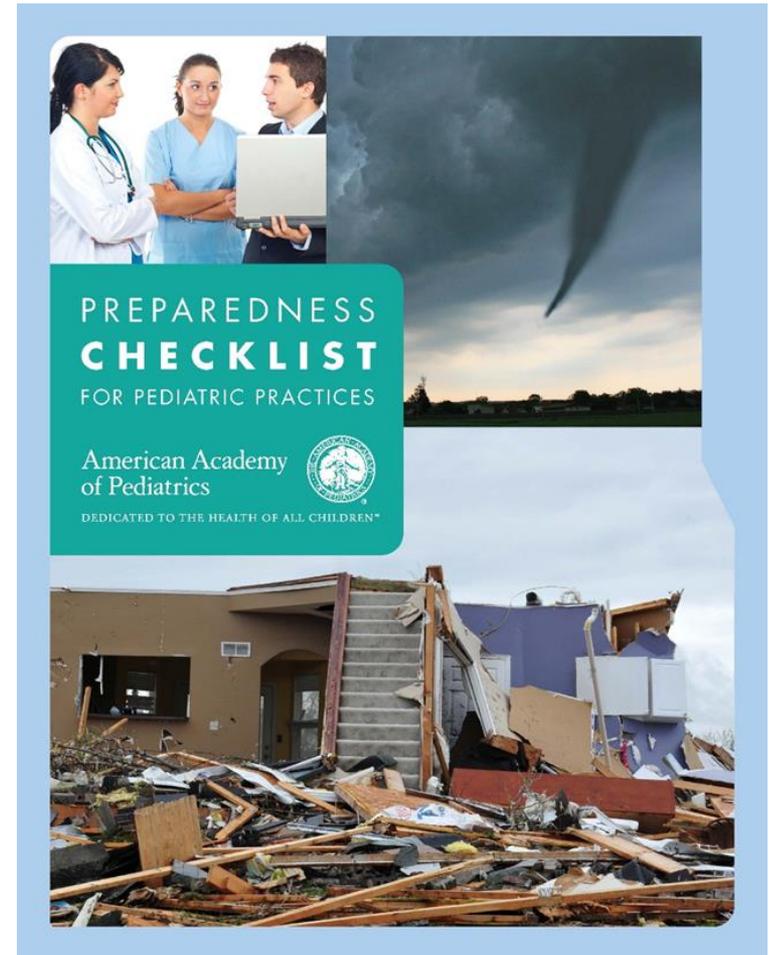
www.aap.org/disasters/resourcekit

Ready.gov

www.ready.gov/business/index.html

Vaccine Storage and Handling

www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/immunization/Pages/vaccine-storage-and-handling.aspx



To Ask a Question

□ Using the Webinar System

- “Click” the Q&A tab at the top left of the webinar tool bar
- “Click” in the white space
- “Type” your question
- “Click” ask

□ On the Phone

- Press Star (*) 1 to enter the queue
- State your name
- Listen for the operator to call your name
- State your organization and then ask your question

Thank you for joining!
Please email us questions at
coca@cdc.gov



Centers for Disease Control and Prevention
Atlanta, Georgia

<http://emergency.cdc.gov/coca>

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