

CE IN THE MORNINGS

An Ounce of Prevention: The Importance of Adult Vaccines in Clinical Care

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Faculty and Planner Disclosures

The faculty listed below report relationships pertinent to this activity:

- Dennis M. Williams, Pharm.D., BCPS, AE-C, FASHP, FCCP, FAPhA, declares that his spouse is employed by and owns stock from GlaxoSmithKline.


The following planners report no relationships pertinent to this activity:


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ASHP staff has no relevant financial relationships to disclose.

Learning Objectives

- Discuss the various options for vaccinating adults against influenza virus during the 2013-14 influenza season.
- Consider approaches to improve vaccination rates against pneumococcal, tetanus, and pertussis infections.
- Describe the national strategies for managing the risks of a pandemic influenza epidemic.
- Assess the impact of changes in health care policy and laws on efforts to improve immunization rates among adults.






National Immunization Rates and Goals


Vaccine	Population	2011 Rates from NHIS	2020 National Goal
Pneumococcal	High Risk Persons, age 19 to 64 years	20.1%	60%
Pneumococcal	age ≥ 65 years	62.3%	90%
Tdap	Ages 19 to 64 years	12.5%	N/A
Hepatitis B	Health Care Workers	63.8%	90%
Hepatitis B	Diabetes, age 19 to 59 years	26.9%	N/A
Herpes Zoster	age ≥ 60 years	15.8%	30%

MMWR. 2013; 62: 66-72 and
Healthy People 2020. Summary of objectives. URL in Ref List.

NHIS = National Health Interview Survey




Seasonal Influenza Vaccine



Strategies to Reduce Impact of Annual Influenza Seasons

- Increasing public awareness about staying home when experiencing possible 'flu' symptoms
- 'Cover your cough' and 'Sneeze in your sleeve' messages
- Frequent handwashing
- Influenza vaccine for everyone 6 months of age and older




Test Your Vaccine Knowledge!

Which of the following seasonal influenza vaccine products should a 44-year-old man who is HIV positive receive?

Live, intranasal influenza vaccine


High-dose, inactivated, intramuscular vaccine

Standard dose, inactivated intramuscular vaccine



New Terminology for Influenza Vaccines

- Previously referred to as TIV and LAIV
- New designations based on complexity of available vaccines
 - IIV (inactivated influenza vaccine)
 - IIV₃ (egg-based or cell culture-based trivalent)
 - IIV₄ (egg-based quadrivalent)
 - ccIIV₃ (cell-culture-based trivalent)
 - LAIV (live, attenuated influenza vaccine)
 - LAIV₄ (quadrivalent)
 - RIV (recombinant hemagglutinin influenza vaccine)
 - RIV₃ (trivalent)



2013-14 Vaccine

- Trivalent
 - A/California/7/2009 (H1N1)-like virus
 - A/Texas/50/2012 (H3N2) virus
 - This is antigenically like the cell-propagated A/Victoria/361/2011 virus
 - B/Massachusetts/2/2012-like (B/Yamagata lineage) virus
- Quadrivalent
 - B/Brisbane/60/2008-like (B/Victoria lineage) virus

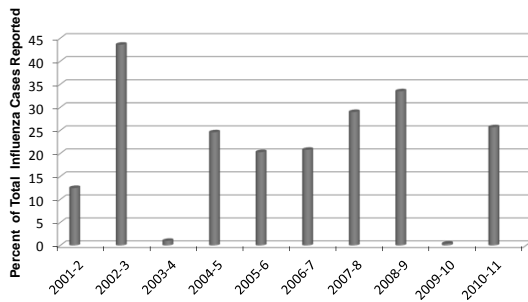
MMWR. 2013; 62: 473-9.

Anticipated Influenza Vaccine Supply 2013-14

- Six new products have been approved as influenza vaccine since early 2012
- 138-145 million doses expected for this influenza season
 - 30 to 32 million doses available as quadrivalent

CDC. Quadrivalent influenza Vaccine: questions and answers. URL in Ref List.
 CDC. Seasonal influenza vaccine supply for the U.S. 2013-14 influenza season. URL in Ref List.

Influenza Type B - United States



Ambrose CS et al. *Hum Vaccin Immunother*. 2012; 8:81-8.

Influenza Type B

- Hospitalization rates generally higher than that observed with Influenza A (H1N1)
 - 81.4 per 100,000 vs. 55.9 per 100,000
- During 1990s, accounted for 15% of all influenza-associated deaths, including 27% of respiratory-related deaths in children less than one year of age
- Most prominent in older children and young adults
- Commonly associated with myalgias, myositis, and leukopenia

Ambrose CS et al. *Hum Vaccin Immunother*. 2012; 8:81-8.

Influenza B: Match Between Circulating Strain and Vaccine Strain

Year	% Infections caused by B	Primary Lineage (% Total B)	Vaccine Lineage	Year	% Infections caused by B	Primary Lineage (% Total B)	Vaccine Lineage
2000-1	46	Yamagata (100)	Y	2006-7	21	Victoria (77)	V
2001-2	13	Victoria (77)	Y	2007-8	29	Yamagata (98)	V
2002-3	43	Victoria (99.6)	V	2008-9	33	Victoria (83)	Y
2003-4	1	Yamagata (93)	V	2009-10	0.2	Victoria (88)	V
2004-5	25	Yamagata (74)	Y	2010-11	30	Victoria (94)	V
2005-6	19	Victoria (78)	Y	2011-12	14	Yamagata (51)	V

C Reed, et al. Vaccine 2012;30:1993-8 and www.cdc.gov/flu/weekly/fluactivitysurv.htm

Influenza Type B

- Experts estimate that inclusion of antigens against two common strains during 2001-8 would have resulted in:
 - 2.1 million fewer cases of influenza infection
 - 20,000 fewer hospitalizations
 - 1,200 fewer deaths

Ambrose CS et al. *Hum Vaccin Immunother*. 2012; 8:81-8.

Influenza Vaccine and Cardiovascular Outcomes

- Meta-analysis performed for ~60 year period of RCTs
- 5 RCTs involving 6469 subjects included
- Demographics
 - Mean age 67 years
 - 51.3% women
 - 36.2% with cardiac history
 - Mean follow-up 7.9 months
- Primary outcome was composite of CV events

Udell JA et al. *JAMA*. 2013;310: 1711-20.

Influenza Vaccine and Cardiovascular Outcomes

- Vaccine associated with a lower risk of composite CV events (2.9% vs. 4.7%)
 - RR of 0.64 (CI 0.48-0.86)
- Treatment interaction detected for patients with recent Acute Coronary Syndrome (ACS)
 - RR 0.45 (CI 0.32-0.63)
 - Patients with stable CAD had a non-statistically significant reduction
 - RR 0.94 (CI 0.55-1.61)

Udell JA et al. *JAMA*. 2013;310: 1711-20.

Benefits of Influenza Vaccine on CV Outcomes

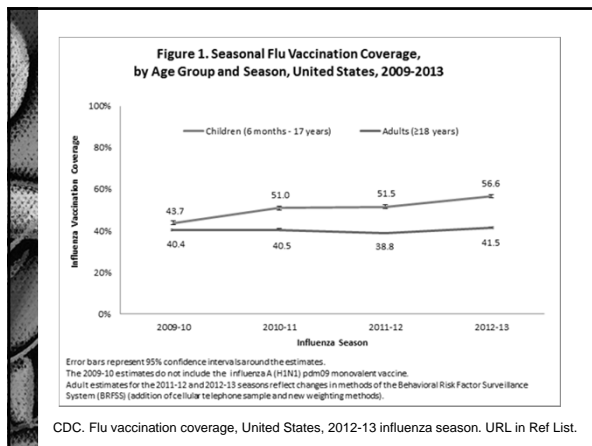
- Editorialist promotes 100% vaccination against influenza based on
 - Influenza infection rates of 5 to 20%
 - Vaccine efficacy of 40 to 70% in older adults
- Concluded that 2 to 14 cases of influenza could be prevented for every 100 persons vaccinated
- 1.7 major CV events could be prevented for every 100 persons vaccinated

Neuzil KM. *JAMA*. 2013;310: 1681-2.

ACIP Influenza Vaccine Recommendations 2013-14

- Routine and annual influenza vaccination is recommended for all persons age ≥ 6 months of age
- No preferential recommendation is made for one product over another for persons in whom multiple specific products may be appropriate

MMWR. 2013; 62(RR-07): 1-43.



Influenza Vaccine Coverage by Age Group 2012-13


Age Group	Unweighted Sample Size	% ^a ±95% CI ^b	Difference from the 2011-12 Season ±95% CI
≥18 years	348,686	41.5 ± 0.4	2.7 ± 0.6 ⁽¹⁾
18-64 years	232,856	35.7 ± 0.6	2.6 ± 0.8 ⁽¹⁾
18-64 years at high risk ^{***}	47,017	47.0 ± 1.4	1.8 ± 1.8
18-49 years	120,286	31.1 ± 0.8	2.5 ± 1.0 ⁽¹⁾
18-49 years at high risk	17,296	39.8 ± 2.2	3.0 ± 3.0 ⁽¹⁾
50-64 years	112,570	45.1 ± 0.8	2.4 ± 1.1 ⁽¹⁾
≥65 years	115,830	66.2 ± 0.8	1.3 ± 1.1 ⁽¹⁾

CDC. Flu vaccination coverage, United States, 2012-13 influenza season. URL in Ref List.


Influenza Vaccination Rates among Health Care Workers (HCW) 2012-13

• All HCW	72%	• Mandated	96.5%
• Physicians	92.3%	• No mandate, but promoted	76.9%
• Pharmacists	89.1%	• Neither mandated nor promoted	50.4%
• Nurse Practitioners	88.5%	• No cost versus cost	86.2% vs. 55.3%
• Nurses	84.8%		
• Other Clinical Personnel	68.6%		

MMWR. 2013; 62: 781-6.




Pandemic Influenza Threats



Emerging Strain of Avian Influenza Virus (H7N9)

- In March 2013, China CDC reported 3 cases of human infection with avian Influenza A (H7N9) not previously reported
 - Each patient had severe pneumonia, developed ARDS, and died
 - Cases not linked epidemiologically
- In April follow-up, 126 confirmed cases of H7N9 (in China) with 19% mortality
- Majority of confirmed exposures were to chickens (76%) and ducks (20%)

MMWR. 2013; 62: 366-71.



Pandemic Influenza Threat (H7N9)

- Epidemiologic Predictions of 3 patterns
 - Virus could disappear from animal reservoir
 - Virus could persist in animal reservoir, causing sporadic human infections
 - Virus could mutate or reassort, and become readily transmissible between humans

Osterholm MT et al. JAMA. 2013; 309: 2557-8.

Pandemic Influenza Threat (H7N9)

- Strategies for managing pandemics
 - Vaccines
 - Antiviral medications
 - Respiratory protection
 - Social distancing
- WHO focuses on vaccine efforts and has ongoing research with several strains possessing pandemic potential (H5N1, H9N2, and H7N9)

Osterholm MT et al. *JAMA*. 2013; 309: 2557-8.

Test Your Vaccine Knowledge!

Which of the following is accurate regarding how candidate vaccines against pandemic influenza are assessed for their effectiveness prior to use?

- ☐ Prevention of clinical influenza infection in normal volunteers
- ☐ Achieving acceptable inhibitory titers in a majority of study subjects
- ☐ Documentation of adequate antigen concentrations in product

Methods for Developing Pandemic Vaccines

- Dose ranging is performed to determine the amount of antigen required
 - to achieve a hemagglutination inhibition titer of 1:40 in at least 70% of subjects less than 65 years of age,
 - or the dose that results in a 4-fold increase in the titer in at least 40% of subjects.
- Based on past experiences, it is likely that an adjuvant will be required in the vaccine

Osterholm MT et al. *JAMA*. 2013; 309: 2557-8.

More Challenges in Developing Pandemic Influenza Vaccines

- Dose required for response is a limiting factor
- Typically requires 17 to 22 weeks for production
- Manufacturing not likely to start until pandemic declared
- Pandemic vaccine product will compete with seasonal vaccine production
- Limited quantities likely available during early phases of pandemic

Osterholm MT et al. *JAMA*. 2013; 309: 2557-8.

Future for Pandemic Vaccine Production

- Another influenza pandemic is inevitable
- Advances in manufacturing capacity are beneficial but likely not enough to meet demand
- Efforts should focus on novel influenza vaccines that provide protection against multiple strains of influenza

Osterholm MT et al. *JAMA*. 2013; 309: 2557-8.

Pneumococcal Vaccine Recommendations

Pneumococcal Vaccine

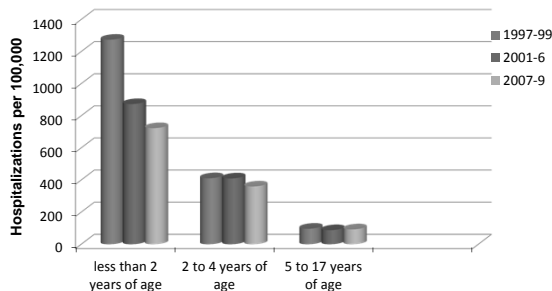
- Available as
 - PPSV23 (Polysaccharide), Recommended for
 - All patients ≥ 65 years of age
 - Some patients age 2-64 years with selected chronic diseases
 - Patients > 18 years with asthma or who smoke
 - PCV13 (Conjugate), Recommended for
 - All infants as part of primary immunizing series (4 doses completed by age 15 months)
 - FDA approved for patients > 50 years of age to prevent pneumonia and invasive infections from *S. pneumoniae*

Pneumococcal Conjugate Vaccine

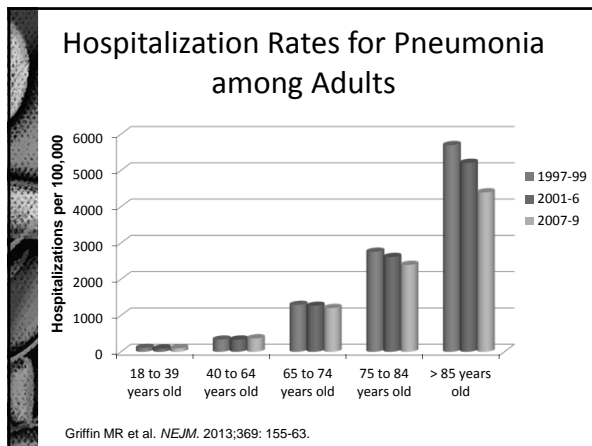
- PCV7 introduced in 2000
 - Within 7 years, invasive pneumococcal infections in children less than 5 years of age were virtually eliminated
- *Streptococcus pneumoniae* estimated to cause 20 to 60% of community-acquired pneumonias
- PCV13 introduced in 2010

Griffin MR et al. *NEJM*. 2013;369: 155-63.

Hospitalization Rates for Pneumonia among Children and Adolescents



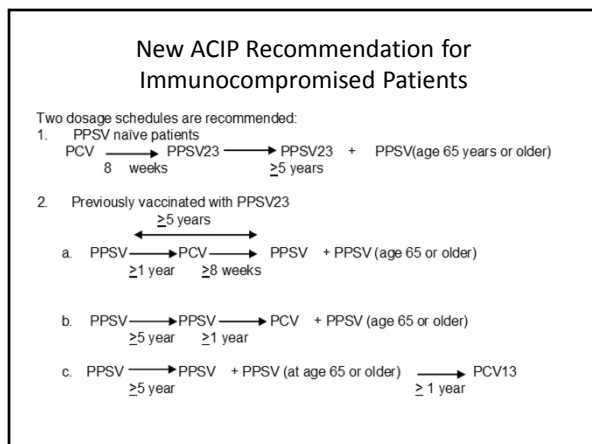
Griffin MR et al. *NEJM*. 2013;369: 155-63.




Pneumococcal Vaccine Recommendations for Adults from the CDC*

Risk group	Underlying medical condition	PCV13	PPSV23	
		Recommended	Recommended	Revaccination 5 yrs after first dose
Immunocompetent persons	Chronic heart disease ¹		✓	
	Chronic lung disease ²		✓	
	Diabetes mellitus		✓	
	Cerebrospinal fluid leak	✓	✓	
	Cochlear implant	✓	✓	
	Alcoholism		✓	
	Chronic liver disease, cirrhosis		✓	
	Cigarette smoking		✓	
Persons with functional or anatomic asplenia	Sickle cell disease/other hemoglobinopathy	✓	✓	✓
	Congenital or acquired asplenia	✓	✓	✓
Immunocompromised persons	Congenital or acquired immunodeficiency ³	✓	✓	✓
	Human immunodeficiency virus infection	✓	✓	✓
	Chronic renal failure	✓	✓	✓
	Nephrotic syndrome	✓	✓	✓
	Leukemia	✓	✓	✓
	Lymphoma	✓	✓	✓
	Hodgkin disease	✓	✓	✓
	Generalized malignancy	✓	✓	✓
	Iatrogenic immunosuppression**	✓	✓	✓
	Solid organ transplant	✓	✓	✓
	Multiple myeloma	✓	✓	✓

* Expanded in 2013 to include Children, ages 6 through 18 years





Core (Quality) Measures

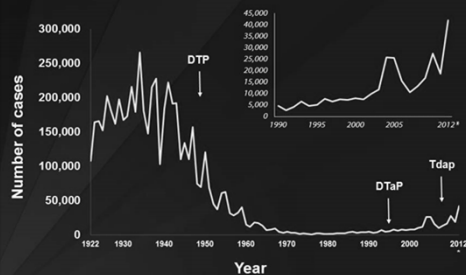
- Mandated by the Centers for Medicare & Medicaid Services (CMS) and The Joint Commission (TJC) to monitor specific hospital clinical processes and how well hospitals provide recommended care
- Evidence-based best practice
- All major payors moving toward using Core Measure results to benchmark & for contract negotiations
- Basis for Medicare Pay-for-Performance/Value-Based Purchasing
- Pneumococcal and Influenza vaccines (When appropriate and indicated) are included as Core Measures

Global Immunization	
Indicator	Documentation Requirements
Pneumococcal Vaccination	<ul style="list-style-type: none"> •Includes: <ul style="list-style-type: none"> Inpatients age 65 & older; Inpatients age 6 to 64 with a High Risk Diagnosis (High Risk Diagnosis - Diabetes, Nephrotic syndrome, ESRD, CHF, COPD, HIV or Asplenia) Inpatients age 19-64 years with Asthma •Contraindications: <ul style="list-style-type: none"> Hypersensitivity to components of the vaccine Bone marrow transplant within the past 12 months Received chemo or radio therapy during this hospitalization or within 2 weeks prior Received Shingles vaccine within 4 weeks prior to arrival Pt 6 years of age who received a conjugate vaccine within the previous 8 weeks •Screening questions in the RN admission and discharge assessments must be completed •Patients have the option of declining the vaccine

Global Immunization	
Indicator	Documentation Requirements
Influenza Vaccination	<ul style="list-style-type: none"> •Includes inpatients age 6 months and older •Contraindications: <ul style="list-style-type: none"> -Hypersensitivity to eggs or other components of the vaccine -Bone marrow transplant within the past 6 months -History of Guillain-Barre' Syndrome within 6 weeks after a previous influenza vaccination -Anaphylactic latex allergy •Screening questions in the RN admission and discharge assessments must be completed •Patients have the option of declining the vaccine

Updates to the Pertussis Epidemic

Reported NNDSS pertussis cases: 1922-2012*



*2012 data are provisional.
SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1945, passive reports to the Public Health Service.

CDC. Pertussis (whooping cough): surveillance and reporting. URL in Ref List.

Test Your Vaccine Knowledge!

A 29-year-old woman, in her third trimester of pregnancy, reports that she received the Tdap vaccine three years ago during a pregnancy. Which of the following recommendations is appropriate at this time?

- ☐ Administer another Tdap dose
- ☐ Administer the adult Td vaccine
- ☐ No additional vaccines are needed

Pertussis

- 18,719 cases in 2011; 48,277 cases in 2012
- 18 deaths in 2012

Age	% of Cases
Less than 1 year	10.8
1 to 6 years	17.5
7 to 10 years	19.9
11 to 19 years	29.8
20 years and older	21.2

CDC. Pertussis cases by year, 1992-2012. <http://www.cdc.gov/mmwr/preview/mm6152md.htm>

Safety of Tdap in Elderly Patients (≥65 years of age)


- Matched cohort study
- Patients received Tdap or Td between Jan 2006 and Dec 2010
- Involved 7 HMOs and ~120,000 subjects in each group
- Analysis suggested a small increased risk of 'medically attended inflammatory or allergic events' in 1 to 6 days following Tdap, but no more commonly than following Td
- Results support the safety of Tdap in this elderly population

Tseng HF et al. *CID*. 2013;56: 315-21.


Tetanus-containing Vaccines 'Something for everyone'

Age	Vaccine	Recommendation
Birth through 6 years	DTaP	5 dose series: 2, 4, 6, 15 to 18 months, and 4 to 6 years
7 through 10 years	Tdap	Administer one dose if child has not completed pediatric series
11 through 18 years	Tdap	Administer as first 'tetanus' booster at any time if not received
19 years and older	Tdap or Adult Td	Administer Tdap if not yet received, and Adult Td every 10 years as tetanus booster
Pregnancy	Tdap	Administer during each pregnancy, preferably between 27 and 36 weeks gestation
Health Care Personnel	Tdap or Adult Td	Administer Tdap if not yet received, and Adult Td every 10 years as tetanus booster

Bridges CB et al. *MMWR*. 2013; 62:9-19.




New Vaccine Research



Investigational Vaccine against
Staphylococcus aureus

- A vaccine to protect against infections from *S. aureus* would represent a significant advance; however, development has been challenging
- Vaccine development has targeted development of opsonic antibodies but humoral immunity responses may be lacking
- Most recent candidate (V710) has elicited adequate humoral responses


Fowler VG et al. JAMA. 2013; 309: 1368-78.



Investigational Vaccine against
Staphylococcus aureus

- RCT conducted 12/2007 to 8/2011, involving 8031 subjects, ages 18 and older, scheduled to undergo median sternotomy within 14 to 60 days
- Subjects received single dose of V710 vaccine or placebo
- Primary efficacy endpoint: Prevention of *S. aureus* bacteremia or deep sternal wound infection through POD 90


Fowler VG et al. JAMA. 2013; 309: 1368-78.




Investigational Vaccine against *Staphylococcus aureus*

- Study terminated at ~7200 subjects
 - Nonsignificant reduction in infections (2.6 per 100 person-yr vs. 3.2 per person yr) (RR 0.81; CI 0.44-1.48) despite good antibody response
 - Adverse reactions higher in vaccine group at 14 days (injection site reactions and serious adverse reactions)
 - Significantly higher mortality rate in patients who developed *S. aureus* infections in vaccine group

Fowler VG et al. JAMA. 2013; 309: 1368-78.




Vaccine Storage and Handling Resources




CDC Vaccine Storage and Handling Toolkit

- Comprehensive document addressing strategies for optimal storage and handling of vaccines
- Recommends stand-alone units (refrigerators or freezers)
 - Refrigerators should maintain temperatures between 35 and 46°F (2 to 8°C)
 - Freezers should maintain temperatures between -58 and +5°F (-50 to -15°C)
- Recommends calibrated thermometer with a Certificate of Traceability and Calibration Testing
- Recommends continuous temperature monitoring device

<http://www.cdc.gov/vaccines/recs/storage/toolkit/storage-handling-toolkit.pdf> (published November 2012)




Health Care Law and Vaccines



ACA and Vaccines


- Access to the vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) prior to September 2009 with no co-payments or other cost-sharing requirements when those services are delivered by an in-network provider.
- New health plans required to cover new ACIP recommendations made after September 2009 without cost sharing in the next plan year that occurs one year after the date of the recommendation.

ACA = Affordable Care Act





ACA and Vaccines

- Provides authority to states to purchase adult vaccines with state funds from federally-negotiated contracts
- Reauthorizes an Immunization Grant Program, which makes available federally purchased vaccines to provide immunization services to priority populations
- Requires a General Accountability Office (GAO) study and report to Congress about Medicare beneficiary access to recommended vaccines under the Medicare Part D benefit



Resources for Vaccine-Related Information

- National Vaccine Advisory Committee
- Affordable Care Act and Immunizations
- Healthy People 2020 Immunization Goals
- Advisory Committee for Immunization Practices (ACIP)



Summary

- Vaccine development and recommendations are dynamic processes that warrant periodic review and assessment to stay current
- Ongoing research should provide insights into effective strategies and health outcomes for vaccine-preventable diseases
- Access to vaccines are an important component of changing health care policies
- Clinicians should engage in multidisciplinary efforts to ensure safe and effective use of vaccines
