

Expanding Recommendations for Routine Influenza Vaccination

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Potential Time-Frame for Modifying Influenza Vaccination Recommendations*

- **2007-2008:** Consider expanding recommendations to include school-age children
- **2010-2011:** Consider expansion of recommendations to include household contacts and caregivers of school-aged children
- **2012-2013:** Consider expansion to universal vaccination

*Presented to ACIP meetings 2006-07

Assessing the Need to Change Recommendations: Critical Factors

- Vaccine supply
- Vaccine effectiveness
- Vaccine safety
- Disease burden
- Feasibility of sustained implementation
- Cost-effectiveness

Influenza Vaccine Recommendations for School-Age (5-18 Year Old) Children

A Simultaneous Individual Consultation

Convened by

Influenza Division

Centers for Disease Control and Prevention

and

Council of State and Territorial Epidemiologists

September 10-11, 2007



Meeting Objectives

- Review the evidence base supporting expansion of recommendations to include all school age children
- Identify key evidence gaps
- Identify implementation challenges and potential solutions
- Discuss methods for assessing impact

Consultation Overview

- Plenary sessions followed by panel discussions
 - Update from influenza vaccine manufacturers
 - Vaccine effectiveness and safety issues
 - Disease burden
 - Potential opportunities and challenges in various vaccination settings
 - Practical experience: immunizing children and evaluating impact
 - Economic analyses
 - Organizational perspectives and resources
- Two breakout sessions to discussion selected topics
- Final overview panel and discussion

Influenza Vaccine Supply

- Projected: 130 million total doses (all ages) this season (2007-08)
- Projected: >200 million doses (all ages) within 5 years
- All supply estimates subject to change based on
 - Selected strain growth characteristics
 - Required regulatory approval
 - Market

Influenza Vaccine Supply is Projected to be Adequate for School Age Children

Pediatric Formulations Now Available

- MedImmune (Flumist / LAIV)
 - Capacity for 20 million thimerosal-free nasal vaccine doses in 2008-09 season
 - Capacity for 35 million doses 2009-10 or later
- Novartis (Fluvirin / TIV)
 - Capacity for 55 million doses within 5 years (all ages)
 - Increasing proportion preservative-free including pediatric vaccines
- Sanofi (Fluzone / TIV)
 - Capacity for 100 million doses by 2009 (all ages)
 - Increasing proportion thimerosal-free



Other Influenza Vaccines: Pediatric Formulations in Development

- GSK (Fluarix and FluLaval / TIV)
 - Projected 35-40 million doses of adult vaccine in 2007-08
 - Pediatric vaccine planned for 2008-09
 - Capacity for 15-17 million preservative-free doses for children
 - Potential availability of 2-4 million preservative-free doses for 6-35 month olds
- CSL (Afluria / TIV)
 - New influenza vaccine approved for adults September 2007
 - 2 million doses in 2007-08
 - Both multidose and preservative-free formulations
 - Commitment to developing pediatric vaccine
 - Capacity for 20 million doses annually within 5 years

Influenza Vaccine Effectiveness (VE) in School Age Children

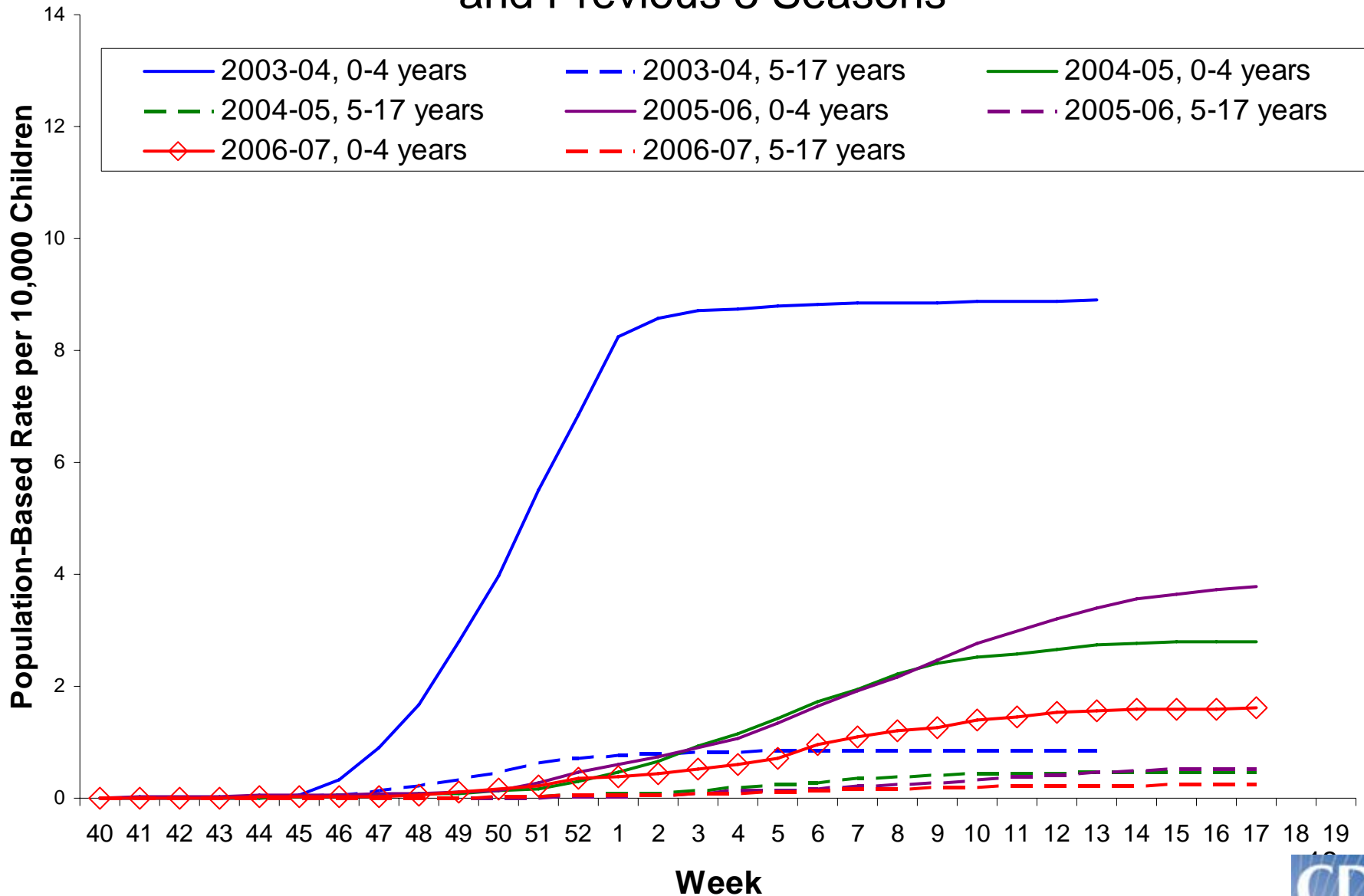
- Children develop a robust antibody response to influenza vaccine
- VE in this age group is good
 - 50-90% against laboratory-confirmed influenza
 - Best when antigenic characteristics of circulating viruses are similar to vaccine strains
- Yearly assessments of VE would be helpful
- Studies with statistical power to show VE against severe outcomes (hospitalization) would be helpful
- Limited data indicate that VE does not decline among children immunized over multiple years
 - Few studies with data beyond 5 years of immunization

Influenza Vaccine Safety in School Age Children

- Multiple established systems available for monitoring safety
 - Vaccine Adverse Events Reporting System (VAERS)
 - Vaccine Safety Datalink (VSD)
 - “Rapid cycle analysis” capacity available
 - Clinical Immunization Safety Assessment (CISA) Network
- Expected to be good based on VAERS, VSD data and clinical trials data
- Safety profile remains good among children immunized over multiple years, but data are limited
- Safety data experience for adolescents, especially for simultaneous administration with other adolescent vaccines, is limited
- Systems that can capture safety data when vaccination given outside medical settings will be needed

Burden of Influenza Illness Among School Age Children

EIP Influenza Laboratory-Confirmed Cumulative Hospitalization Rates for Children Aged 0-4 and 5-17 years, 2006-07 and Previous 3 Seasons



Prospective Study of Influenza (2000-01 Season) Among 313 Children (216 families) in a Seattle K-8 School*

Variable	Influenza-Attributable Events/100 Children
Illness Episodes	28
Total School Days Missed	63
Number Febrile Illnesses	28
Number Health Care Visits	4**
Days of Worked Missed	20
Number household members Ill in 3 days after index case	22

*Neuzil et al. Arch Adoles Med 2002

**Not significantly different from non-influenza winter season

Slide source: K Edwards, CDC/CSTE Consultation, September 10, 2007

Summary of Influenza Burden in School Aged Children

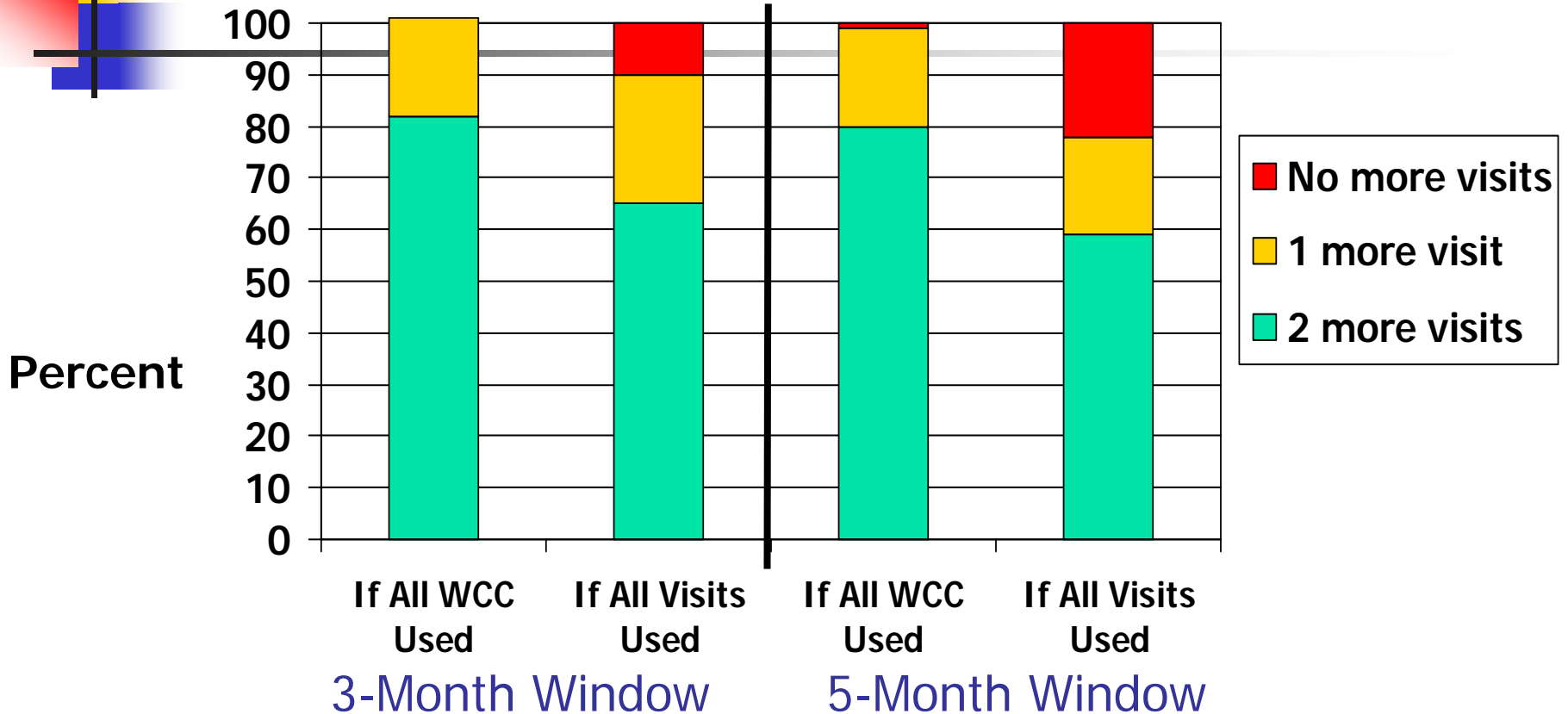
- Few deaths and hospitalizations compared to younger children, elderly, or chronically ill
- 5-7 outpatient visits per 100 children annually, frequently receive antibiotics
- 10-30 illnesses per 100 children –frequently associated with school absenteeism

Implementation Issues: Vaccinating School Age Children

Implementation Challenges: Experience with Current Recommendations

- Approximately 50% of school age children already have an indication
- Inconsistent public interest
 - Media interested in rare severe outcomes but not low coverage
- Providers and programs slow to adopt strategies to improve coverage
 - Reminder / recall systems
 - Enhanced access
 - Reducing missed opportunities
 - Advocating vaccination
 - Leading by example
- Logistical challenges
 - Some providers near capacity to provide influenza vaccination with current recommendations

Percent of Children 5-8 Years Old Needing More Visits for Flu Vaccinations



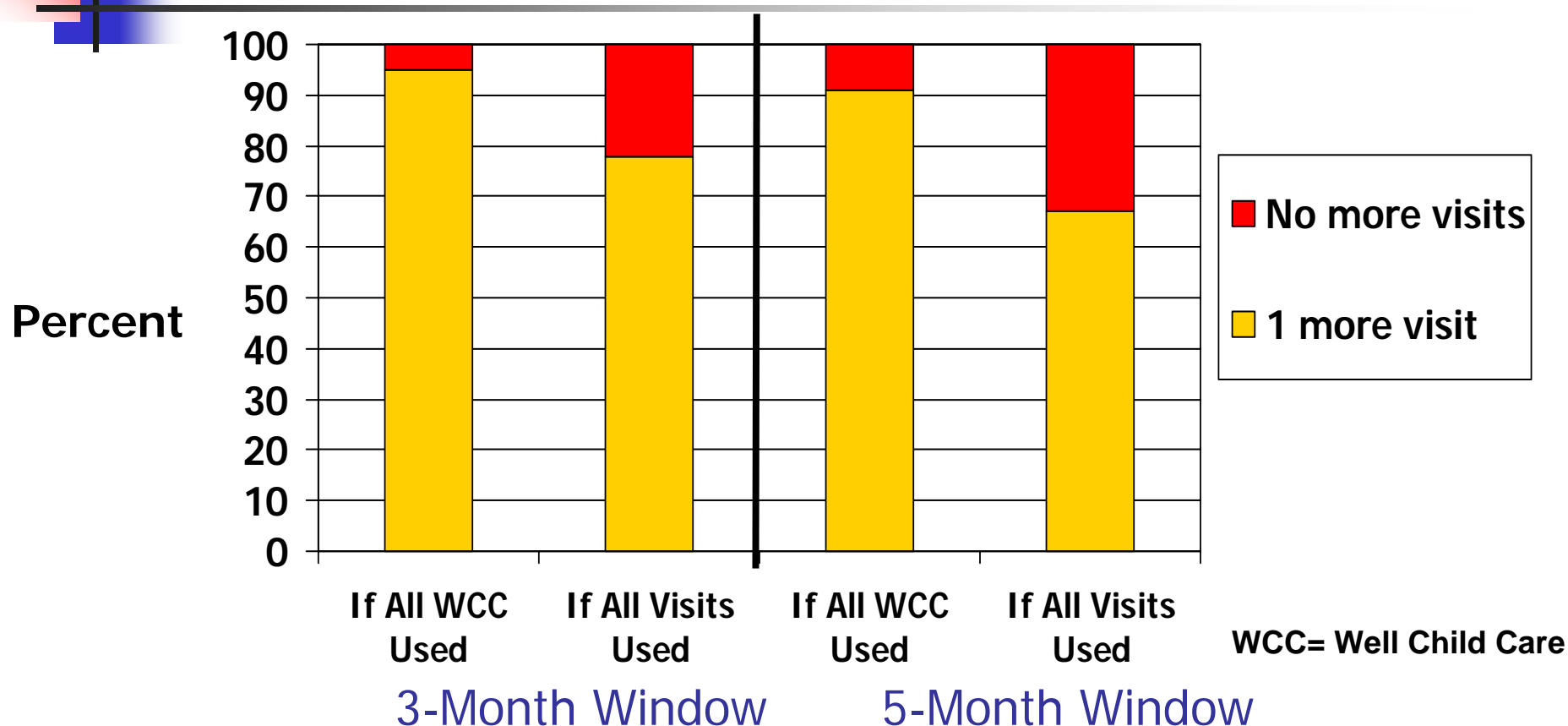
WCC= Well Child Care

Most will need 1-2 additional healthcare visits.

Use all visits as for vaccination, and long windows

Slide source P Szilagyi, CDC/CSTE Consultation, September 10, 2007

Percent of Children 9-18 Years Old Needing More Visits for Flu Vaccinations



Most will need 1 additional healthcare visit.

Use all visits as for vaccination, and long windows

Slide source P Szilagyi, CDC/CSTE Consultation, September 10, 2007

School-based Vaccination

- Schools and public health share goal of improving the lives of children
- School administrators might be intrigued by potential benefits of reducing influenza
 - Reduce absenteeism
 - Help children to be “ready to learn”
- Most school systems do not have robust school health infrastructure
- Considerable outside assistance would be required
- Schools under local control – district by district uptake

Example: School Influenza Campaign 2005 and 2006 Influenza Seasons, Knox County, TN

2005

- 31,160 - Total Vaccinations
- 81 - Public Schools (x2 Phases)
- 0 - Private Schools
- 0 - Weekend Clinics
- 45% of Children Fully Vaccinated
- 63% of School Faculty Vaccinated

2006

- 35,148 - Total Vaccinations
- 81 - Public Schools (x2 Phases)
- 13 - Private Schools (x2 Phases)
- 6 - Weekend Clinics
- 48% of Children Fully Vaccinated
- 47% of School Faculty Vaccinated

Slide Source: J Lott, CDC/CSTE Consultation, September 10, 2007.

Used donated vaccine (LAIV). grant money for school coordinators

Selected Remarks from Consultants: Implementation Issues

- Implementation will not be planned until recommendations made
- Low expectations for coverage in first few years of implementation
- Local solutions to implementation will vary
- The medical home does not have capacity to deliver influenza vaccinations to all school age children
- Immunization programs and providers must maintain focus on children at higher risk for influenza complications
- School systems might be interested but lack means



Economic Issues: Vaccinating School Age Children

C/E Results (\$/QALY)

Mean C/E Ratios*

	TIV, High Risk	TIV, Low Risk	LAIV, Low Risk
6-23 months	Cost Saving	\$12,000	\$9,000
2 years	Cost Saving	\$18,000	\$15,000
3-4 years	\$1,000	\$28,000	\$25,000
5-11 years	\$7,000	\$79,000	\$72,000
12-17 years	\$10,000	\$119,000	\$109,000

Current strategy 

Slide source L Prosser, CDC/CSTE Consultation,
September 11, 2007. Reference: Emerg Infect Dis, 2006

***2003 estimates**

Vaccinating School Age Children: Indirect Effects

Indirect Effects as a Basis for Influenza Vaccination Recommendations

- Rationale for current influenza vaccine recommendations
 - Reduce influenza and influenza complications in groups with the highest rates of:
 - Hospitalizations
 - Medical or ER Visits
 - Mortality
 - Vaccinate anyone who wants to be vaccinated
- Paradigm shift: A primary goal of vaccinating school age children would be to achieve indirect effects (reduce transmission to contacts and in the community)

Evidence for Indirect Effects

- Growing literature on reductions in illness among contacts of school age vaccinees in community demonstration projects
 - Coverage levels among children typically have not exceeded 50%
 - Most common model has been large-scale school-based vaccination program using LAIV for most children
- Evidence for reductions in school or work absenteeism in some studies
- Reductions in severe outcomes among contacts not demonstrated but might not be achievable without larger samples

Summary: Indirect Effects

- Few studies designed specifically to examine issues of indirect protection.
- Studies use various designs: blinded assignment to vaccine or placebo, vaccination of all eligibles in specific age groups, observational.
- Difficult to use standards applied to RCTs to interpretation of results.
- Evidence suggest indirect protection has been produced, but precise quantification difficult.

Evaluating Direct and Indirect Effects: Challenges

- Historical comparisons are problematic
 - Season-to-season variability in influenza activity and vaccine effectiveness
 - Patterns of circulation of specific viruses
 - Timing, duration, and intensity of activity
- Existing community-level studies in the U.S. could be expanded and adapted to evaluate direct impact
- Estimating community-level indirect effects will require large multi-year studies that are beyond current existing capacity
- Assessments of indirect effects should include
 - Lab-confirmed outcomes (in at least a subset)
 - Data from >1 influenza season



Selected Remarks from Consultants: Direct and Indirect Effects of Vaccinating School Age Children

- Recommendation could be justified by direct benefit to children even if indirect effects are uncertain
- Indirect effects on contacts/community expected but hard to prove
- Influenza vaccination of school-age children yields cost-effectiveness ratios at the higher end of the range for currently recommended vaccines
- Economic studies should also take indirect effects on illness among contacts or in the community into account if possible
- Planning of studies to measure impact must accompany implementation
- Extending interval between recommendations vote and implementation might be helpful for planning assessments and engaging providers and the public



Summary: Routine Vaccination of School Age Children (Ages 5-18)

- School age children
 - Frequently infected (highest influenza attack rates)
 - Major source of community transmission
 - Respond well to the vaccine with few adverse events
 - Already are recommended for vaccination in many instances (50%)
 - Are at low risk for severe influenza complications
 - Costs to vaccinate per QALY saved (>\$100,000 per QALY) higher than for young children or children at higher risk for influenza complications
- Vaccinating school age children (full implementation, good coverage)
 - Will be difficult to accomplish in traditional medical settings
 - Should reduce influenza illness among contacts but might be difficult to measure
 - Could have an impact on rates of influenza in the community but these will be difficult to assess without careful planning and multiple years of observation

Consultation Follow-up

- Draft summary of consultation
 - Publication planned
- Additional presentations at upcoming ACIP meetings
- Continued efforts to harmonize recommendations timeline with provider organizations, public health, and immunization programs
- ACIP workgroup discussions