Use of pneumococcal polysaccharide vaccine (PPV23) in adults aged ≥50 years

ACIP Pneumococcal Vaccines Workgroup

June 25, 2008

Outline

- Current ACIP recommendation for use of PPV23
- Estimates of vaccine uptake
- Changes in epidemiology of invasive pneumococcal disease (IPD) in adults after routine childhood pneumococcal conjugate vaccine (PCV7) use
- Considerations regarding PPV23 revaccination
- Summary of considerations related to lowering the age of universal PPV23 to 50 years
- Proposed clarification to the revaccination recommendation language

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

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MMWR™

Recommendations and Reports

MORBIDITY AND MORTALITY WEEKLY REPORT

Prevention of Pneumococcal Disease

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

TABLE 2. Recommendations for the use of pneumococcal vaccine

Groups for which vaccination is recommended	Strength of recommendation*	Revaccination†
Immunocompetent persons§		
Persons aged ≥65 years	A	Second dose of vaccine if patient received vaccine ≥5 years previously and were aged <65 years at the time of vaccination.
Persons aged 2–64 years with chronic cardiovascular disease,¶ chronic pulmonary disease,** or diabetes mellitus	A	Not recommended.
Persons aged 2–64 years with alcoholism, chronic liver disease,†† or cerebrospinal fluid leaks	B	Not recommended.
Persons aged 2–64 years with functional or anatomic asplenia§§	A	If patient is aged >10 years: single revaccination ≥5 years after previous dose. If patient is aged ≤10 years: consider revaccination 3 years after previous dose.
Persons aged 2–64 years living in special environments or social settings¶¶	C	Not recommended.

*A=Strong epidemiologic evidence and substantial clinical benefit support the recommendation for vaccine use.
B=Moderate evidence supports the recommendation for vaccine use.
C=Effectiveness of vaccination is not proven, but the high risk for disease and the potential benefits and safety of the vaccine justify vaccination.
†Strength of evidence for all revaccination recommendations is "C."
§If earlier vaccination status is unknown, patients in this group should be administered pneumococcal vaccine.
¶Including congestive heart failure and cardiomyopathies.
**Including chronic obstructive pulmonary disease and emphysema.
††Including cirrhosis.
§§Including sickle cell disease and splenectomy.
¶¶Including Alaskan Natives and certain American Indian populations.

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Immunocompromised persons aged ≥2 years, including those with HIV infection, leukemia, lymphoma, Hodgkins disease, multiple myeloma, generalized malignancy, chronic renal failure, or nephrotic syndrome; those receiving immunosuppressive chemotherapy (including corticosteroids); and those who have received an organ or bone marrow transplant.	C	Single revaccination if ≥5 years have elapsed since receipt of first dose. If patient is aged ≤10 years: consider revaccination 3 years after previous dose.

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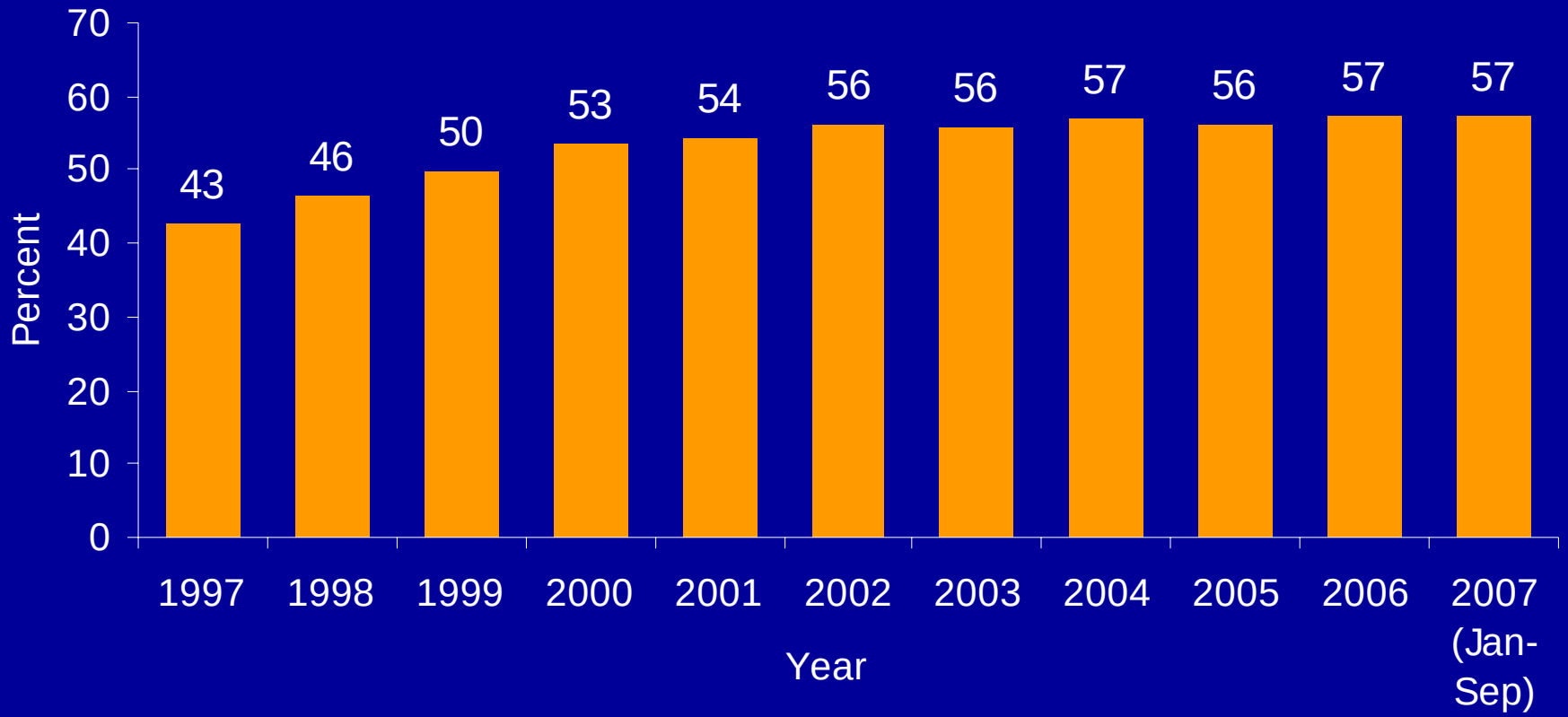
Percentage of adults aged 65 years and older who reported ever receiving PPV23, U.S.1997-2007



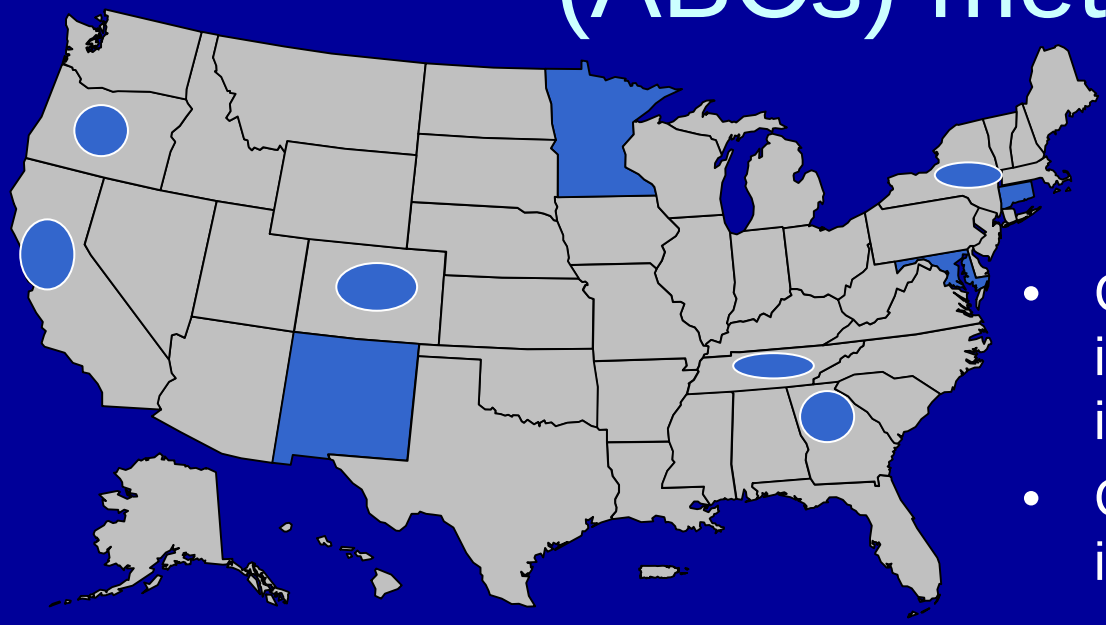
CDC/NCHS, Sample Adult Core component of the 1997-2007 NHIS.

Evaluating the need to change recommendation to include all adults aged ≥50 years – key factors

- Disease burden
- Vaccine effectiveness
- Achievable public health impact compared with current policy
- Vaccine safety
- Program issues
  - Feasibility of implementation
  - Acceptability and demand
- Cost-effectiveness
  - Information reviewed by Workgroup but will not be presented

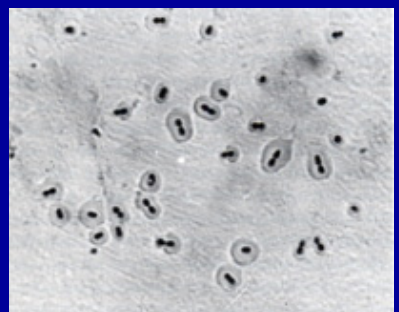
Epidemiology of IPD in adults after routine childhood PCV7 use

Active Bacterial Core surveillance (ABCs) methods



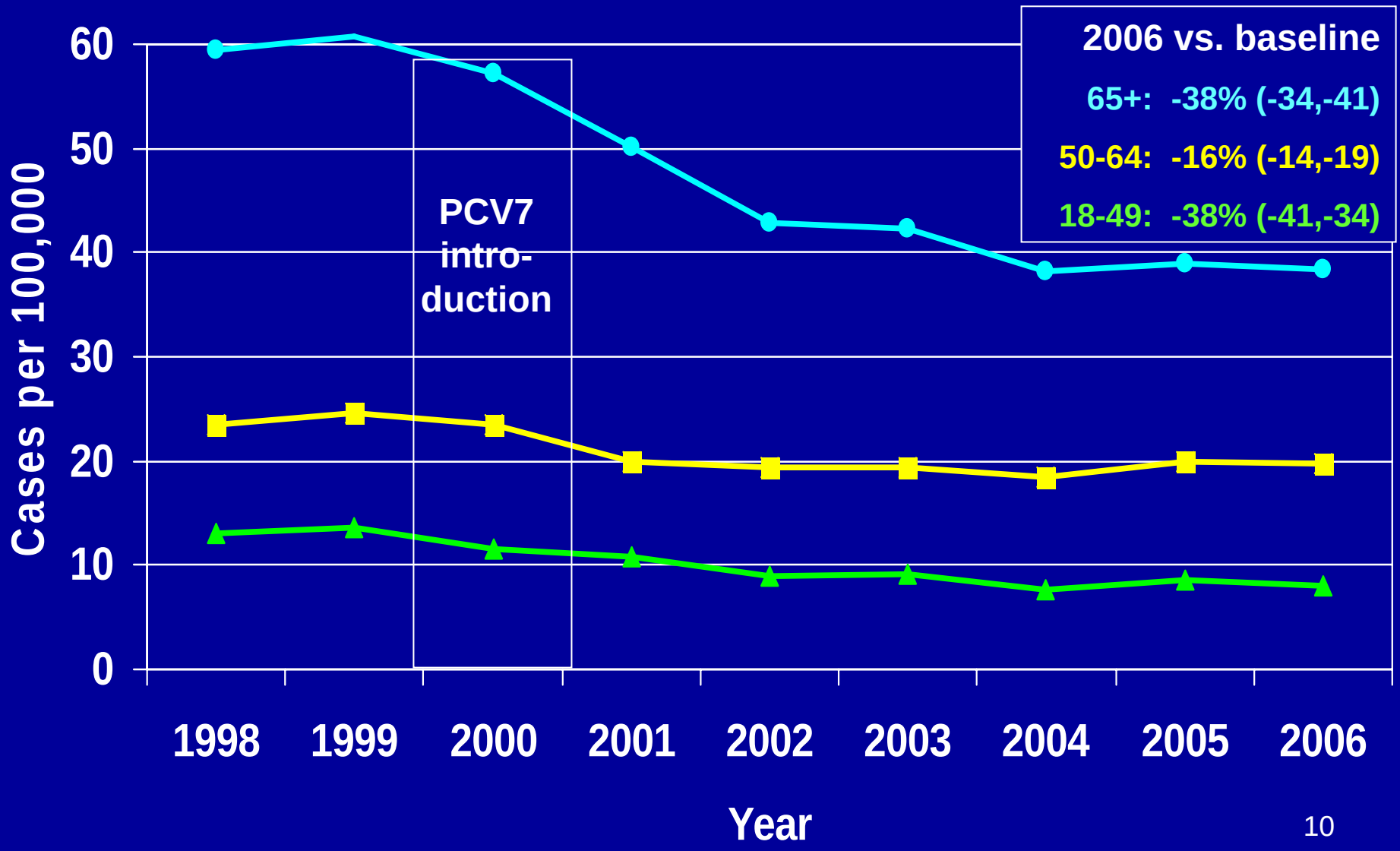
Total population

= 18.5 million



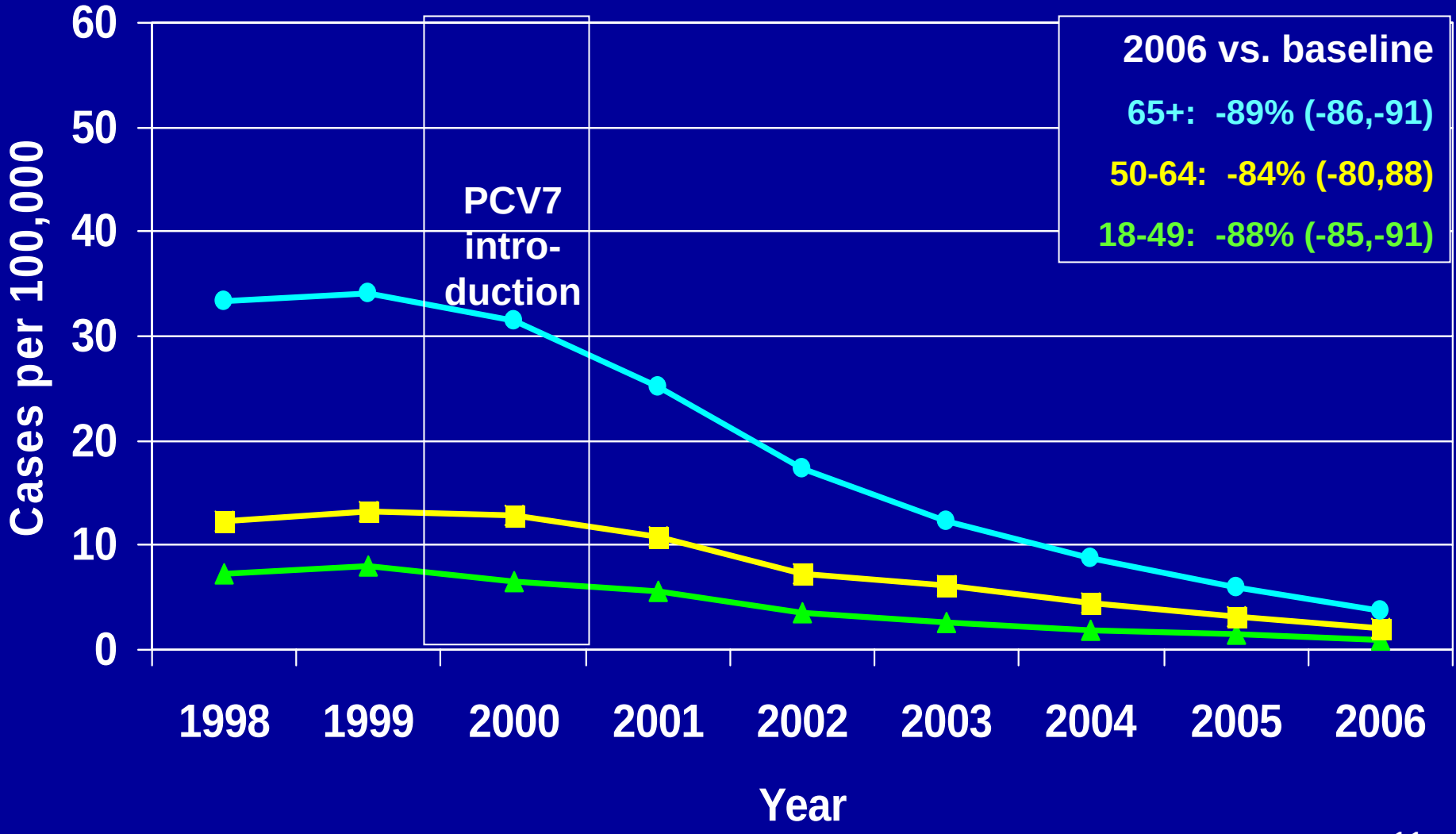
- Case definition: pneumococcus isolated from normally sterile site in a surveillance area resident
- Chart review for clinical information
- Active contact with clinical laboratories to identify cases
- Audits ensure completeness of reporting
- Isolates serotyped at reference laboratories (CDC and MDH)

Rates of invasive pneumococcal disease among adults, by age,1998/99-2006: **All serotypes**



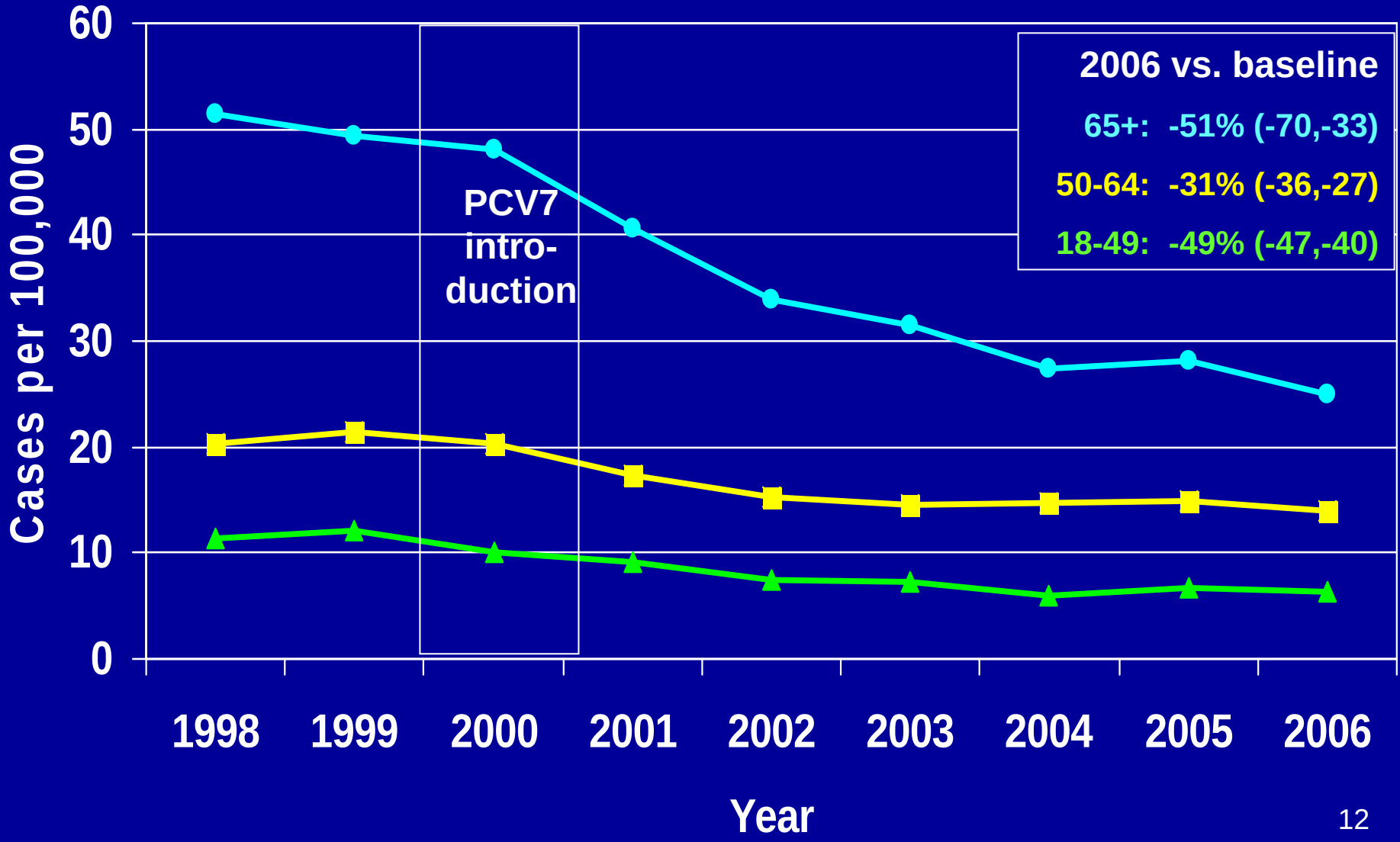
Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

Rates of invasive pneumococcal disease among adults, by age,1998/99-2006: **PCV7 serotypes**



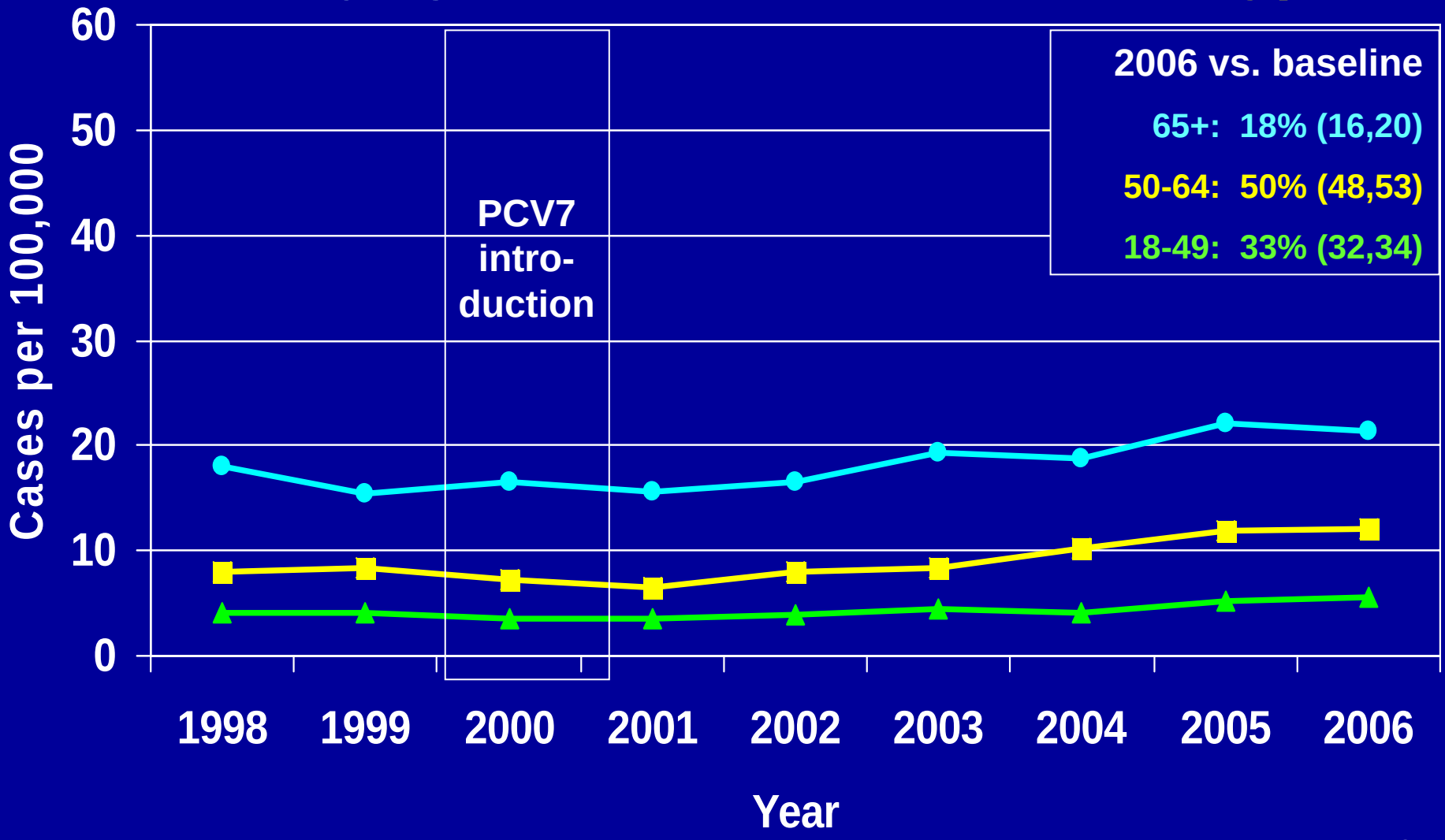
Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

Rates of invasive pneumococcal disease among adults, by age,1998/99-2006: **PPV23 serotypes**



Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

Rates of invasive pneumococcal disease among adults, by age,1998/99-2006: **PPV16 serotypes**



Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

Summary of indirect effects of childhood PCV7 on adult IPD

- After PCV7 introduction, rates of IPD in adult age-groups have decreased
  - 16%-38% for all serotypes combined
  - 84%-89% for PCV7 serotypes
  - 31%-51% for PPV23 serotypes
    - Due to PCV7 type decrease
    - Rates of PPV16 types increased 18-50%
- In adults aged 50-64 years, the overall rate has decreased from 24 to 20/100.000/year
  - Largest increase in non-PCV7 serotypes

Adults aged 50-64 years

- Differences in serotype distribution?
- Influence of the underlying medical conditions on risk of disease?
- Evaluated trends in incidence of IPD among adults with and without the underlying medical conditions that are current ACIP indications for PPV23*

*Table 2, MMWR 1997;46(No. RR-8):12

Proportion of invasive pneumococcal disease cases among adults 50-64 years-old with ACIP indications for PPV23*, 1998-2006

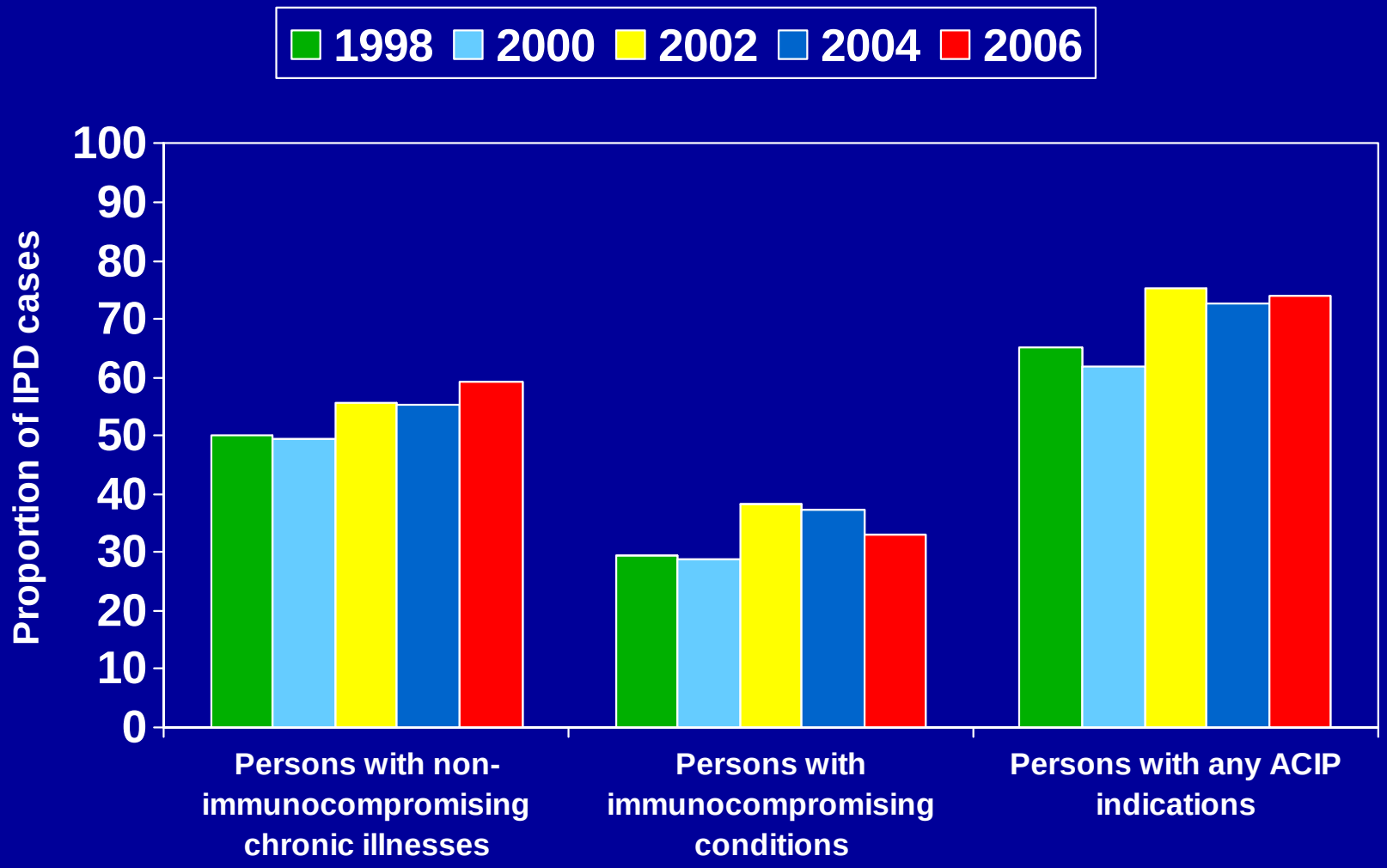
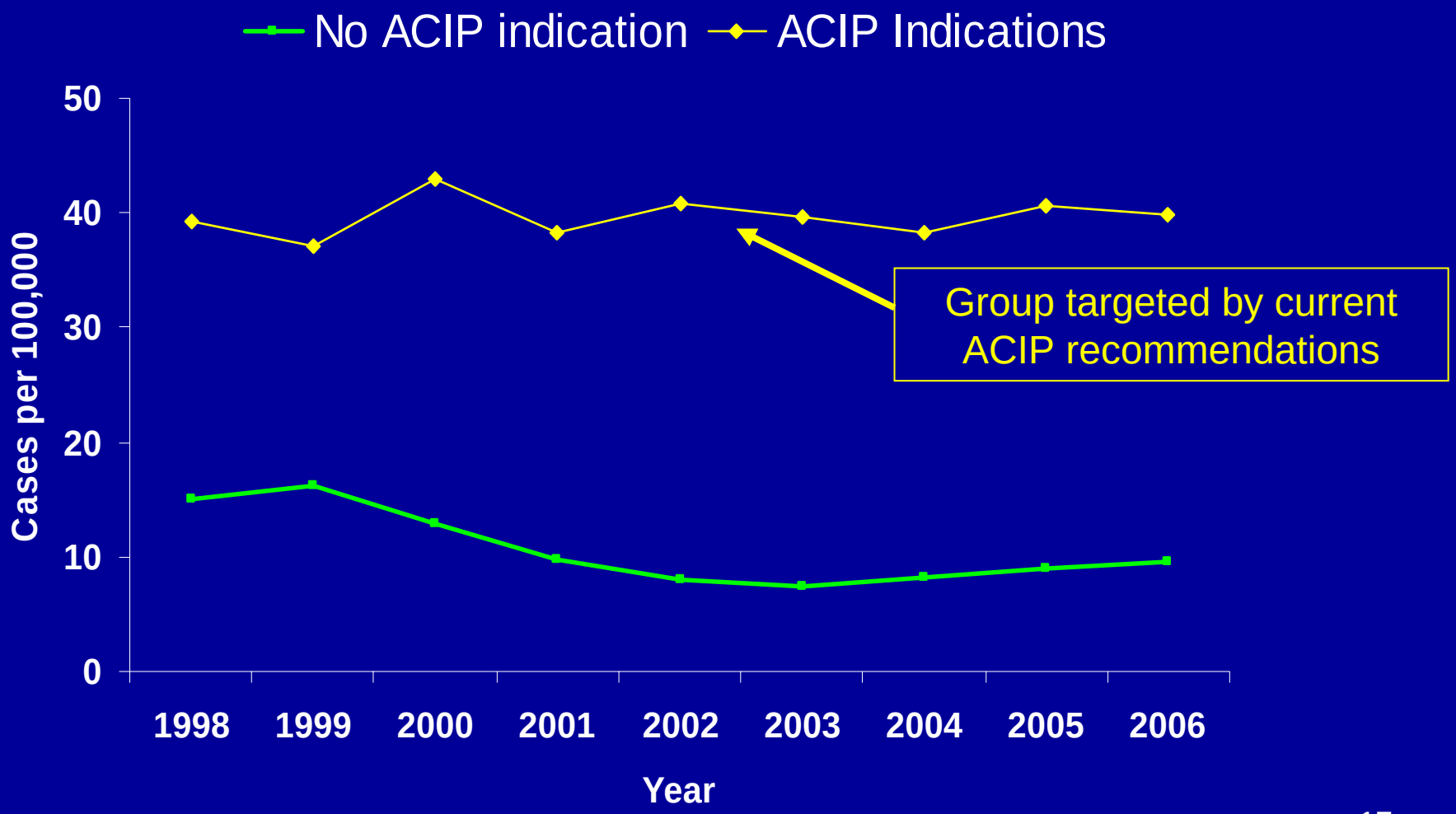


*Table 2, MMWR 1997;46(No. RR-8):12

Data source: CDC, Active Bacterial Core surveillance, unpublished, 2008

Overall rates of IPD among 50-64 year-olds, with and without current ACIP indications for PPV23



Muhammad et al; CDC Active Bacterial Core surveillance, unpublished, 2008

Summary of indirect PCV7 effects in adults aged 50-64 with and without PPV23 indications

- Substantial decreases in IPD rates among persons aged 50-64 years without current PPV23 indications
  - current rates low
- Among persons with current PPV23 indications IPD rates about 4-fold higher
  - no decrease in overall rates because of substantial increase in non-PCV7 type disease
- The proportion of persons with chronic illnesses that are current PPV23 indications has increased
  - In 2006, about ¾ of cases had a current indication
- Vaccinating high-risk groups increasingly important

Considerations related to revaccination with PPV23

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CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997;46(No. RR-8).

Considerations regarding revaccination with PPV23

- Current revaccination recommendations are based on expert opinion*
  - lowest quality of evidence and strength of recommendation “C”
- Change in age of first PPV23 vaccination would necessitate changing the revaccination regimen
- Considerations of possible revaccination strategies require evaluating
  - Safety of revaccination
  - Immunologic response to a second PPV23 dose
  - Potential clinical benefits of revaccination

*MMWR 1997;46 (No.RR-8)

Considerations regarding revaccination with PPV23

- With time since first vaccination --
  - Risk of disease and mortality increase
  - Antibody levels in older adults decline
  - Vaccine effectiveness estimates decrease[1]
- Data regarding duration of protection after first vaccination are limited and inconsisent[1,2]
- Several studies in older adults indicate that a second PPV23 vaccination given ≥5 years after first dose is well tolerated[3]
  - local reactions more frequent but self-limited
  - systemic reactions rare
- Clinical effectiveness of revaccination is unknown

[1]Shapiro N Engl J Med 1991; [2]Butler JAMA 1993
[3]Jackson JAMA 1999; Artz Clin Micro Rev 2003

Immunologic response to a second dose of PPV23

- Immunologic correlates of protection for PPV23 in adults have not been established
- Several studies have shown a significant increase in anticapsular antibody levels from pre- to post-revaccination in older adults[1]
- In most studies, the magnitude of antibody response to revaccination has been lower than with first vaccination[2]
  - Concern that administration of first dose of plain polysaccharide may blunt the immune response to subsequent doses of PPV[2] or PCV[3]
  - Clinical relevance of lower antibody response not known

[1] Artz Clin Micro Rev 2003
[2] Torling Vaccine 2003;
[3] deRoux CID 2008

Summary of Workgroup's considerations related to lowering the age of universal PPV23

Potential advantages in lowering the age of universal PPV23 to 50 years

- Programmatic simplicity and logistical considerations
- Age-based strategies may reach more groups with increased rates of IPD including those who are currently not recommended PPV23
- Harmonization with the influenza vaccine recommendation (age 50 years since 2000)

Gardner P, Ann Intern Med 2003
Sisk et al. Ann Intern Med 2003

Disadvantages in lowering the age of universal PPV23

- Due to indirect effects of childhood PCV7, rates of IPD in the majority of persons aged 50-64 years *without* current ACIP indications are very low
  - Childhood immunization with PCV13 may further reduce disease rates in these adults due to additional indirect effects
- Most persons aged 50-64 years who develop invasive pneumococcal disease already have a current PPV23 indication
- Available data do not allow determining optimal timing and frequency of PPV23 revaccination
  - Concern about potential immunologic hyporesponsiveness after repeated PPV23 doses
  - Inconsistent data on duration of antibodies
  - Lack of evidence for clinical effectiveness of revaccination

Areas of uncertainty –feasibility of program implementation

- Although most published studies have showed PPV23 effectiveness against invasive disease
  - Inconsistent results in different populations and lack of documented population impact may limit the ability to expand recommendations to new target groups
- Adequacy of vaccine supply: PPV23 target population would increase by 38.5 million people
- Acceptability of vaccination: Program would target many healthy persons at low risk of IPD
- Effectiveness of age- vs. risk-based recommendations: Relatively low coverage of influenza vaccine in 50-64 year olds

Conclusions – use of PPV23 in adults aged ≥ 50 years (1)

- The Workgroup concluded that available evidence as a whole does not favor recommending PPV23 vaccination to all adults aged ≥50 years
- Compared with the current policy of vaccinating all adults aged ≥65 years and younger adults with high risk conditions, the potentially achievable incremental public health impact of changing the recommendation appears small

Conclusions – use of PPV23 in adults aged ≥ 50 years (2)

- A program targeting all adults aged ≥50 years would substantially increase the vaccine target population
- Most of these persons are relatively healthy and at low risk of pneumococcal disease, potentially leading to reduced acceptability of the vaccine
- Targeting adults aged <65 years who have current ACIP indications for PPV23 is a high priority
- As already recommended by the ACIP*, “Persons aged 50 years should have their overall vaccination status reviewed to determine whether they have risk factors that indicate a need for pneumococcal vaccination”

*MMWR 1997;46 (No.RR-8), page 11.

Conclusions - PPV23 revaccination

- The Workgroup concluded that available data are insufficient to determine the appropriate target groups, optimal timing and frequency of PPV23 revaccination.
- Therefore, existing recommendation will not be modified - recommendation language will be clarified
- Further research is needed to guide revaccination policy, particularly regarding its clinical effectiveness, potential adverse immunological consequences of repeated PPV23 doses, long-term persistence of antibodies and the optimal sequence of PCV and PPV in adults
- Long-term immunological follow-up data may become available to re-evaluate the PPV23 revaccination recommendation during Fall of 2008

Persons with asplenia or immunocompromising conditions – proposed clarification to revaccination recommendation language

- Some providers have found the current PPV23 revaccination recommendation confusing
- The recommendations have been misinterpreted as suggesting revaccination every 5 years, although the ACIP clearly specifies only one revaccination*
- "*The ACIP does not recommend routine revaccination for most people. A second dose of vaccine is recommended 5 years after the first dose for persons with functional or anatomic asplenia or for persons with immunocompromising conditions*.
- *The ACIP does not recommend multiple revaccinations because of insufficient data concerning the degree and duration of protection and safety of PPV23 when given 3 or more times."*

*MMWR 1997;46 (No.RR-8)

Persons aged ≥65 years - proposed clarification to revaccination recommendation language

- "*All persons should be vaccinated with PPV23 at age 65 years. Those who received PPV23 before age 65 years should be administered another dose of the vaccine if at least 5 years have passed since their previous dose*."

Pneumococcal Vaccines Workgroup Membership 2007-2008

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