

Employment and Activity Limitations Among Adults with Chronic Obstructive Pulmonary Disease — United States, 2013

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Chronic obstructive pulmonary disease (COPD) is a group of progressive respiratory conditions, including emphysema and chronic bronchitis, characterized by airflow obstruction and symptoms such as shortness of breath, chronic cough, and sputum production. COPD is an important contributor to mortality and disability in the United States (1,2). *Healthy People 2020* has several COPD-related objectives,* including to reduce activity limitations among adults with COPD. To assess the state-level prevalence of COPD and the association of COPD with various activity limitations among U.S. adults, CDC analyzed data from the 2013 Behavioral Risk Factor Surveillance System (BRFSS). Among U.S. adults in all 50 states, the District of Columbia (DC), and two U.S. territories, 6.4% (an estimated 15.7 million adults) had been told by a physician or other health professional that they have COPD. Adults who reported having COPD were more likely to report being unable to work (24.3% versus 5.3%), having an activity limitation caused by health problems (49.6% versus 16.9%), having difficulty walking or climbing stairs (38.4% versus 11.3%), or using special equipment to manage health problems (22.1% versus 6.7%), compared with adults without COPD. Smokers who have been diagnosed with COPD are encouraged to quit smoking, which can slow the progression of the disease (3) and reduce mobility impairment (4). In addition, COPD patients should consider participation in a pulmonary rehabilitation program that combines patient education and exercise training to address barriers to physical activity, such as respiratory symptoms and muscle wasting (5).

Each year, the BRFSS survey is administered by state health departments in collaboration with CDC. BRFSS is

a random-digit-dialed telephone survey (landline and cell phone) of noninstitutionalized civilian adults aged ≥18 years that includes various questions about respondents' health and risk behaviors. Response rates for BRFSS are calculated using standards set by the American Association of Public Opinion Research Response Rate Formula #4.† The response rate is the number of respondents who completed the survey as a proportion of all eligible and likely eligible persons. The median survey response rate for all states, territories, and DC in 2013 was 46.4%, and ranged from 29.0% to 60.3%. Additional information is presented in the BRFSS 2013 Summary Data Quality Report.§

† Available at http://www.aapor.org/AAPORKentico/AAPOR_Main/media/MainSiteFiles/StandardDefinitions2011_1.pdf.

§ Available at http://www.cdc.gov/brfss/annual_data/2013/pdf/2013_DQR.pdf.

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*Additional information available at <http://www.healthypeople.gov/2020/topics-objectives/topic/respiratory-diseases/objectives?topicId=36>.



Self-reported, physician-diagnosed COPD was defined as a positive response to the question, “Have you ever been told by a doctor or health professional that you have COPD, emphysema, or chronic bronchitis?” Several questions addressed activity limitations: “Are you limited in any way in any activities because of physical, mental, or emotional problems?”; “Do you have serious difficulty walking or climbing stairs?”; and “Do you now have any health problem that requires you to use special equipment, such as a cane, a wheelchair, a special bed, or a special telephone?” Being unable to work was defined for respondents who reported they were unable to work in response to the question, “Are you currently...? Employed for wages, self-employed, out of work for 1 year or more, out of work for less than 1 year, a homemaker, a student, retired, or unable to work.” Current smokers reported having smoked at least 100 cigarettes in their life and currently smoking cigarettes some days or every day. Former smokers reported having smoked at least 100 cigarettes in their life but were not current smokers. Respondents were categorized as engaging in physical activity if they answered “yes” to the question, “During the past month, other than your regular job, did you participate in any physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise?”

The age-adjusted prevalence of self-reported, physician-diagnosed COPD (with 95% confidence intervals) was calculated by state, selected demographic characteristics, smoking status,

physical activity status, and activity limitation characteristics. Additionally, the age-adjusted prevalence of activity limitation measures was calculated by COPD status, current smoking status, and physical activity status. T-tests were used to compare prevalence between subgroups (significance at $p < 0.05$). All indicated differences between subgroups are statistically significant. Data are weighted to state population estimates, and statistical software that took into account the complex sampling design was used.

Overall, 6.4% of U.S. adults (an estimated 15.7 million) were told by a physician or other health care provider that they have COPD (age-adjusted prevalence = 6.0%) (Table). Prevalence of COPD ranged from 2.6% among those aged 18–34 years to 12.3% among those aged ≥ 75 years. In age-adjusted comparisons by race/ethnicity, Asians were the least likely to report COPD (2.0%), whereas adults who identified themselves as multiracial or American Indian/Alaska Native reported the highest prevalence (10.7% and 10.2%, respectively). Women were more likely to report COPD than men (6.6% compared with 5.4%). COPD prevalence was lower among employed adults (3.6%) compared with other employment categories. COPD prevalence was lower with greater educational level. COPD also varied by marital status, with divorced, widowed, or separated respondents being more likely to report COPD (9.1%) than married respondents (4.7%). COPD was more common among current smokers (14.3%) than former smokers

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TABLE. Age-adjusted* percentage of adults aged ≥18 years reporting having ever been told by a physician that they had chronic obstructive pulmonary disease (COPD)[†], by selected characteristics — Behavioral Risk Factor Surveillance System, United States, 2013

Characteristic	No.	% [§]	(95% CI)	Estimated no. [¶] with COPD
Total respondents (crude)	486,921	6.4	(6.3–6.5)	15,667,000
Total (age-adjusted)	486,921	6.0	(5.9–6.1)	
Age group (yrs) (unadjusted)				
18–34	77,294	2.6	(2.4–2.8)	1,931,000
35–44	59,556	3.6	(3.3–3.9)	1,447,000
45–54	83,324	6.7	(6.4–7.1)	2,976,000
55–64	106,090	9.7	(9.3–10.0)	3,823,000
65–74	89,992	11.8	(11.4–12.2)	3,061,000
≥75	70,665	12.3	(11.8–12.8)	2,429,000
Race/Ethnicity				
White, non-Hispanic	373,527	6.3	(6.2–6.5)	11,237,000
Black, non-Hispanic	38,686	6.5	(6.1–6.9)	1,844,000
American Indian/Alaska Native, non-Hispanic	7,626	10.2	(8.8–11.7)	267,000
Asian, non-Hispanic	9,381	2.0	(1.4–2.9)	181,000
Native Hawaiian/Pacific Islander, non-Hispanic	1,531	6.2	(3.1–12.0)	30,000
Other race, non-Hispanic	2,627	4.8	(3.8–5.9)	44,000
Multiracial, non-Hispanic	9,059	10.7	(9.2–12.4)	321,000
Hispanic	36,826	4.1	(3.7–4.5)	1,414,000
Sex				
Men	199,660	5.4	(5.2–5.6)	6,679,000
Women	287,261	6.6	(6.4–6.8)	8,988,000
Employment status				
Employed	239,796	3.6	(3.5–3.8)	4,352,000
Unemployed	26,081	8.2	(7.6–8.9)	1,351,000
Homemaker	31,367	4.5	(4.1–5.0)	782,000
Student	12,602	7.5	(5.1–10.8)	309,000
Retired	136,906	8.7	(6.6–11.4)	4,714,000
Unable to work	37,170	20.4	(19.3–21.4)	4,067,000
Education level				
Less than high school diploma or GED	41,949	9.8	(9.3–10.3)	3,898,000
High school diploma or GED	141,867	6.8	(6.6–7.0)	5,145,000
At least some college	301,281	4.6	(4.5–4.8)	6,556,000
Marital status				
Married	251,036	4.7	(4.5–4.9)	6,924,000
Divorced/Widowed/Separated	145,601	9.1	(8.7–9.5)	5,822,000
Member of unmarried couple	74,536	6.9	(6.4–7.3)	2,339,000
Never married	13,127	7.0	(6.1–8.1)	511,000

See table footnotes on page 293.

(7.0%) or never smokers (2.8%) and among respondents who reported not exercising in the past month compared with those who had exercised (8.8% versus 4.9%). COPD was also more common among those who reported each of the activity limitation measures: health-related activity limitation (15.1% versus 3.6%), difficulty walking or climbing stairs (18.2% versus 3.9%), use of special equipment (18.7% versus 4.9%), and being unable to work (20.4% versus 4.8%). State-specific prevalence of COPD ranged from 3.6% in Puerto Rico and 4.0% in Minnesota and South Dakota to >9% in West Virginia (9.4%), Alabama (9.6%), and Kentucky (10.3%). COPD prevalence was highest for states along the Ohio and lower Mississippi rivers (Figure 1).

More than one third (38.0%) of adults with COPD were current smokers. Activity limitations were common among adults with COPD. Adults who reported having COPD were more likely to report being unable to work (24.3% versus 5.3% for adults without COPD), having activity limitation because of health problems (49.6% versus 16.9%), having difficulty walking or climbing stairs (38.4% versus 11.3%), and use of special equipment for health problems (22.1% versus 6.7%) compared with adults without COPD. Among adults with COPD, nonsmokers who also reported being physically active were least likely to report all of the activity limitation measures (Figure 2), whereas those not physically active, regardless of smoking status, were most likely to report the activity limitations.

TABLE. (Continued) Age-adjusted* percentage of adults aged ≥18 years reporting having ever been told by a physician that they had chronic obstructive pulmonary disease (COPD)[†], by selected characteristics — Behavioral Risk Factor Surveillance System, United States, 2013

Characteristic	No.	% [§]	(95% CI)	Estimated no. [¶] with COPD
Smoking status**				
Current smoker	76,266	14.3	(13.8–14.8)	5,754,000
Former smoker	137,125	7.0	(6.7–7.3)	5,653,000
Never smoker	258,811	2.8	(2.7–2.9)	3,752,000
Physical activity^{††}				
Yes	329,512	4.9	(4.8–5.0)	8,327,000
No	124,313	8.8	(8.5–9.1)	6,159,000
Activity limitation due to health problems^{§§}				
Yes	115,869	15.1	(14.6–15.6)	8,430,000
No	361,933	3.6	(3.5–3.7)	6,867,000
Difficulty walking or climbing stairs				
Yes	85,876	18.2	(17.4–19.0)	7,237,000
No	389,975	3.9	(3.8–4.1)	8,019,000
Use of special equipment				
Yes	55,401	18.7	(17.6–19.8)	4,415,000
No	421,944	4.9	(4.8–5.0)	10,874,000
Unable to work				
Yes	37,170	20.4	(19.3–21.4)	4,067,000
No	446,752	4.8	(4.7–4.9)	11,509,000
State/Area				
Kentucky	10,933	10.3	(9.5–11.2)	367,000
Alabama	6,450	9.6	(8.6–10.8)	382,000
West Virginia	5,853	9.4	(8.5–10.3)	155,000
Tennessee	5,750	8.7	(7.8–9.7)	473,000
Mississippi	7,401	8.4	(7.5–9.3)	195,000
Arkansas	5,208	8.2	(7.3–9.3)	200,000
Michigan	12,646	7.9	(7.2–8.5)	661,000
Ohio	11,851	7.6	(7.0–8.3)	737,000
Indiana	10,237	7.5	(6.9–8.1)	394,000
South Carolina	10,601	7.3	(6.7–8.0)	292,000
Oklahoma	8,202	7.3	(6.7–8.0)	227,000
Louisiana	5,207	7.2	(6.3–8.2)	261,000
Missouri	7,056	7.1	(6.3–8.0)	351,000
North Carolina	8,768	6.9	(6.2–7.6)	556,000
Rhode Island	6,455	6.8	(6.0–7.8)	61,000
Arizona	4,205	6.8	(5.3–8.6)	350,000
Wyoming	6,370	6.6	(5.9–7.4)	32,000
Florida	33,776	6.4	(5.9–7.0)	1,139,000
Pennsylvania	11,303	6.4	(5.8–7.0)	712,000
New Hampshire	6,383	6.4	(5.6–7.2)	74,000
Virginia	8,374	6.3	(5.7–7.0)	422,000
Nevada	5,047	6.3	(5.2–7.6)	142,000

See table footnotes on page 293.

Discussion

COPD is an important contributor to both mortality and disability in the United States (1,2). COPD is the primary contributor (>95%) to deaths from chronic lower respiratory diseases, the third leading cause of death in the United States (1). Among diseases and injuries, COPD also is the sixth largest contributor to number of years lived with disability in the United States (2). COPD is costly, with COPD-related medical costs estimated at \$32 billion in the United States in 2010 and an additional \$4 billion in absenteeism costs (6). Persons with COPD are less likely to be employed and more likely to be limited in the type of work they can do compared with persons without COPD (7).

In this study, adults with COPD were more likely to report activity limitations and being unable to work compared with adults without COPD. COPD has been found to be associated with a lower likelihood of employment, comparable with that for stroke and greater than that associated with heart disease or hypertension (8). After accounting for age, U.S. adults with COPD are also more likely to collect Social Security Disability Insurance and Supplemental Security Income than those without the condition (8). Together, these results underscore the substantial economic burden of COPD, which only adds to the impaired quality of life experienced by persons with COPD. Because there is currently no cure for COPD, public health efforts should focus on prevention, such as antismoking

TABLE. (Continued) Age-adjusted* percentage of adults aged ≥18 years reporting having ever been told by a physician that they had chronic obstructive pulmonary disease (COPD)[†], by selected characteristics — Behavioral Risk Factor Surveillance System, United States, 2013

Characteristic	No.	% [§]	(95% CI)	Estimated no. [¶] with COPD
Georgia	8,051	6.2	(5.6–6.9)	485,000
Maine	8,031	6.1	(5.5–6.8)	75,000
District of Columbia	4,841	6.0	(5.1–7.2)	31,000
Oregon	5,908	6.0	(5.3–6.8)	199,000
Guam	1,875	6.0	(4.6–7.9)	6,000
Kansas	23,135	5.8	(5.5–6.2)	135,000
Montana	9,638	5.8	(5.2–6.5)	51,000
Iowa	8,094	5.8	(5.2–6.5)	149,000
Alaska	4,533	5.6	(4.7–6.7)	30,000
New Mexico	9,224	5.5	(4.9–6.2)	93,000
Delaware	5,150	5.5	(4.8–6.3)	43,000
New Jersey	13,179	5.4	(4.9–6.0)	400,000
Texas	10,783	5.3	(4.7–5.9)	1,040,000
Connecticut	7,609	5.3	(4.7–6.0)	163,000
Washington	11,065	5.3	(4.8–5.8)	301,000
New York	8,805	5.2	(4.7–5.9)	856,000
Massachusetts	14,914	5.1	(4.7–5.7)	296,000
Vermont	6,322	5.1	(4.5–5.8)	28,000
Maryland	12,830	5.0	(4.5–5.6)	244,000
Wisconsin	6,521	5.0	(4.2–5.8)	245,000
Nebraska	17,017	4.9	(4.4–5.3)	74,000
Illinois	5,586	4.8	(4.1–5.5)	491,000
California	11,507	4.5	(4.1–5.0)	1,352,000
North Dakota	7,725	4.5	(3.9–5.1)	27,000
Colorado	13,487	4.4	(4.0–4.9)	182,000
Hawaii	7,788	4.4	(3.7–5.1)	51,000
Utah	12,648	4.2	(3.8–4.6)	80,000
Idaho	5,573	4.2	(3.6–4.9)	52,000
South Dakota	6,859	4.0	(3.4–4.7)	28,000
Minnesota	14,180	4.0	(3.4–4.6)	175,000
Puerto Rico	5,967	3.6	(3.1–4.2)	104,000
Median (range)		6.0	(3.6–10.3)	

Abbreviations: CI = confidence interval; GED = General Education Development certificate.

* Age-adjusted to the 2000 U.S. standard population aged ≥18 years.

[†] Includes emphysema and chronic bronchitis.

[§] Weighted percentage.

[¶] Numbers might not add to total because of rounding.

** Current smokers smoked ≥100 cigarettes in their life and currently smoking cigarettes some days or every day. Former smokers smoked ≥100 cigarettes in their life but were not current smokers. Never smokers did not smoke ≥100 cigarettes in their life.

^{††} Respondents were categorized as engaging in physical activity if they answered “yes” to the question, “During the past month, other than your regular job, did you participate in any physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise?”

^{§§} Respondents were categorized as having activity limitations if they answered “yes” to the question, “Are you limited in any way in any activities because of physical, mental, or emotional problems?”

efforts, and treatment to slow the progression of the disease, manage comorbidities, and lessen symptoms (9).

Smoking, the leading cause of COPD in the United States, is also associated with worse symptoms among persons with COPD (10), and smoking cessation has been shown to slow the progression of COPD (3). Among adults with COPD in these analyses, more than one third were current smokers. Current smoking was associated with a greater likelihood of three of the four activity limitations measured among those who reported being physically active. This result reinforces the importance of smoking cessation by COPD patients. Health care providers play a critical role in motivating and assisting their patients, including those with COPD, with smoking

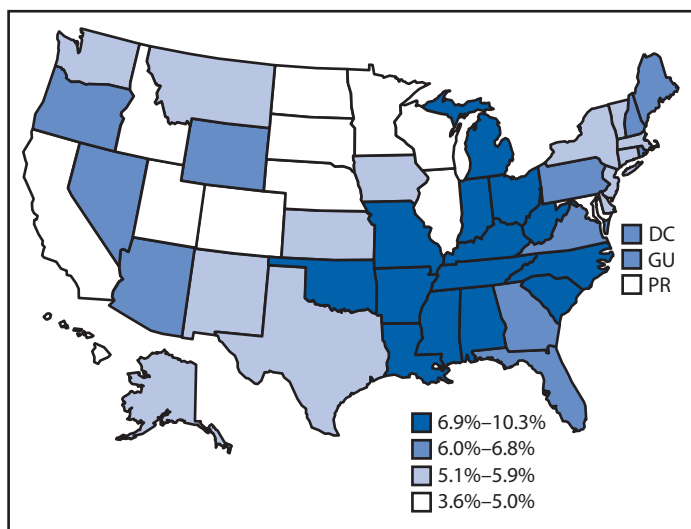
cessation. Information for health care providers on helping patients quit smoking is available online.[¶] Quitting resources for patients also are available.**

Not being physically active was associated with a greater likelihood of all the activity limitation measures among persons with COPD. This association might indicate that COPD affects patients' ability to be physically active, but not being physically active might also reinforce activity limitations. Although respiratory symptoms such as shortness of

[¶] Available at <http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/index.html> and at <http://www.cdc.gov/tobacco/campaign/tips/partners/health/hcp>.

** Available at <http://www.cdc.gov/tobacco/campaign/tips/quit-smoking/quitting-resources.html>.

FIGURE 1. Age-adjusted prevalence* of chronic obstructive pulmonary disease (COPD)[†] among adults aged ≥18 years — Behavioral Risk Factor Surveillance System, United States, 2013



* Age-adjusted to the 2000 U.S. standard population aged ≥18 years.

[†] Based on a positive response to the question, "Have you ever been told by a doctor or health professional that you have COPD, emphysema, or chronic bronchitis?"

breath can cause activity limitations, COPD is also associated with muscle weakness, which can also contribute to limited mobility (5). Although physical activity might be challenging for persons with COPD, exercise training is an essential part of pulmonary rehabilitation (5). Pulmonary rehabilitation is a personalized program that includes both education and exercise components to improve management of breathing problems, increase stamina, and decrease shortness of breath. These programs should incorporate both strength and endurance (or aerobic) training. Patients can learn more about pulmonary rehabilitation online.^{††} Physicians should refer to the latest clinical practice guidelines (5).

The findings in this report are subject to at least three limitations. First, COPD diagnosis relied on self-report and not on evaluation by breathing tests or review of medical records. Second, this was a cross-sectional study; therefore, it is not possible to determine whether the COPD or activity limitations came first. Finally, state response rates ranged from 29.0% to 60.3%; therefore, nonresponse bias might have affected the results.

COPD is strongly associated with activity limitations and an inability to work. Current smoking and lack of physical activity were both associated with greater percentages reporting activity limitation and inability to work among those with COPD. COPD patients who smoke should be encouraged

^{††} Available at <http://www.thoracic.org/patients/patient-resources/resources/pulmonary-rehab.pdf>.

What is already known on this topic?

Chronic obstructive pulmonary disease (COPD) is a group of progressive respiratory conditions, including emphysema and chronic bronchitis, characterized by airflow obstruction and symptoms such as shortness of breath, chronic cough, and sputum production. COPD is an important contributor to mortality and disability in the United States.

What is added by this report?

Adults who reported having COPD were more likely to report being unable to work (24.3% versus 5.3%), activity limitation resulting from a health problem (49.6% versus 16.9%), difficulty walking or climbing stairs (38.4% versus 11.3%), and use of special equipment for health problems (22.1% versus 6.7%) compared with adults without COPD. Among adults with COPD, nonsmokers who also reported being physically active were least likely to report all of the activity limitation measures, whereas those who were inactive, regardless of smoking status, were most likely to report the activity limitations.

What are the implications for public health practice?

COPD patients who smoke should be encouraged to quit and provided with the support they need to achieve this objective, whereas all COPD patients might benefit from pulmonary rehabilitation and a personalized exercise regimen.

to quit and provided with the support they need to achieve this objective, whereas all COPD patients might benefit from pulmonary rehabilitation and a personalized exercise regimen. Outside the clinical setting, the development of state and community environmental and policy efforts to address smoking and physical inactivity could improve outcomes for persons with COPD as well as for the general population. CDC's *Best Practices for Comprehensive Tobacco Control Programs—2014* is an evidence-based guide to help states develop and implement tobacco control programs.^{§§} CDC also has compiled a guide to community-based strategies to increase physical activity: *The CDC Guide to Strategies to Increase Physical Activity in the Community*.^{¶¶}

^{§§} Available at http://www.cdc.gov/tobacco/stateandcommunity/best_practices/index.htm.

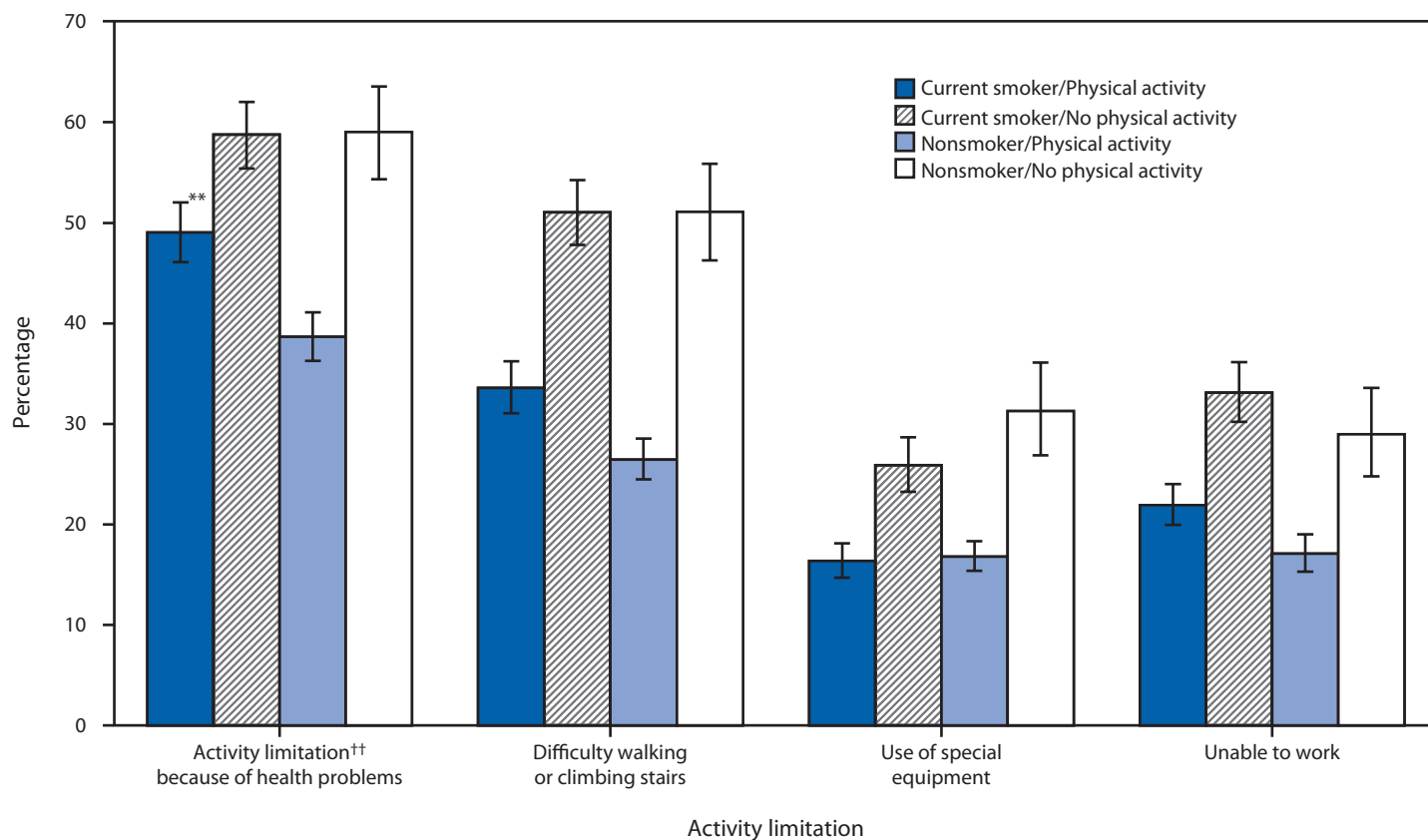
^{¶¶} Available at http://www.cdc.gov/obesity/downloads/PA_2011_WEB.pdf.

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FIGURE 2. Age-adjusted percentage* of adults with chronic obstructive pulmonary disease (COPD)[†] aged ≥18 years with activity limitations, by smoking[§] and physical activity[¶] status — Behavioral Risk Factor Surveillance System, United States, 2013



* Age-adjusted to the 2000 U.S. standard population aged ≥18 years.

[†] Based on a positive response to the question, "Have you ever been told by a doctor or health professional that you have COPD, emphysema, or chronic bronchitis?"

[§] Current smokers reported smoking ≥100 cigarettes in their life and currently smoking cigarettes some days or every day. Nonsmokers include former smokers and never smokers.

[¶] Respondents were categorized as engaging in physical activity if they answered "yes" to the question, "During the past month, other than your regular job, did you participate in any physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise?"

** 95% confidence interval.

^{††} Respondents were categorized as having activity limitations if they answered "yes" to the question, "Are you limited in any way in any activities because of physical, mental, or emotional problems?"

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Mycoplasma pneumoniae Outbreak in a Long-Term Care Facility — Nebraska, 2014

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On June 20, 2014, a Nebraska long-term care facility notified the East Central District Health Department (ECDHD) and Nebraska Department of Health and Human Services (NDHHS) of an outbreak of respiratory illness characterized by cough and fever in 22 residents and resulting in four deaths during the preceding 2 weeks. To determine the etiologic agent, identify additional cases, and implement control measures, Nebraska and CDC investigators evaluated the facility's infection prevention measures and collected nasopharyngeal (NP) and oropharyngeal (OP) swabs or autopsy specimens from patients for real-time polymerase chain reaction (PCR) testing at CDC. The facility was closed to new admissions until 1 month after the last case, droplet precautions were implemented, ill residents were isolated, and group activities were canceled. During the outbreak, a total of 55 persons experienced illnesses that met the case definition; 12 were hospitalized, and seven died. PCR detected *Mycoplasma pneumoniae* DNA in 40% of specimens. *M. pneumoniae* should be considered a possible cause of respiratory illness outbreaks in long-term care facilities. Morbidity and mortality from respiratory disease outbreaks at long-term care facilities might be minimized if facilities monitor for respiratory disease clusters, report outbreaks promptly, prioritize diagnostic testing in outbreak situations, and implement timely and strict infection control measures to halt transmission.

Epidemiologic Investigation

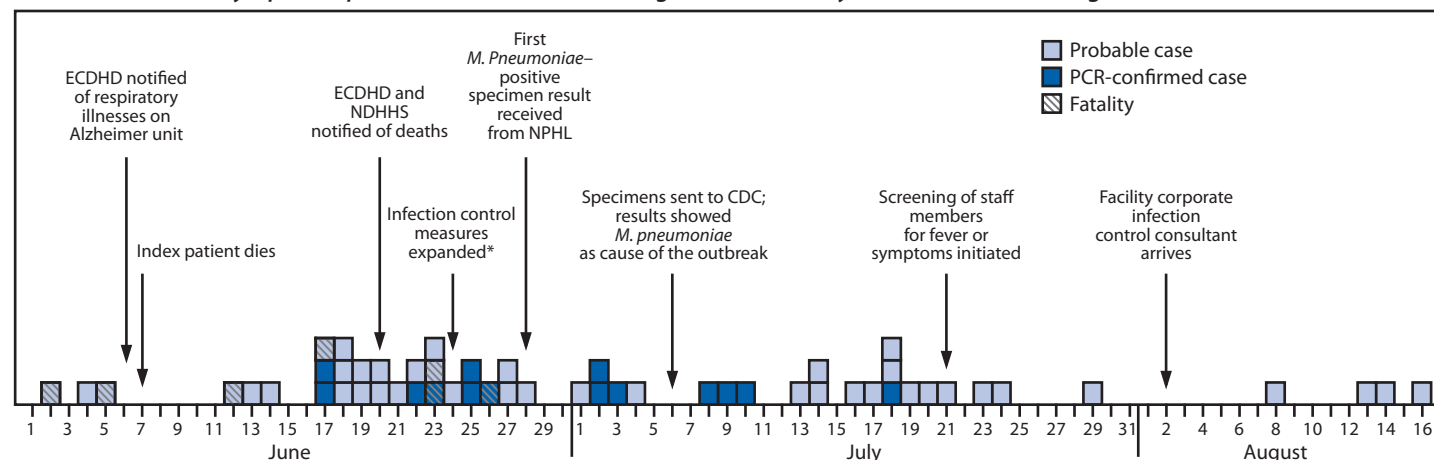
The facility has 152 beds and includes an Alzheimer disease locked unit, a skilled nursing facility, and assisted living wings. A medical director and private physicians provide residents with medical care. At the time of the outbreak, the facility had 143 residents and 132 staff members. On June 20, the facility alerted ECDHD, which then alerted NDHHS, that they had 22 residents ill with a respiratory illness of unknown etiology. The outbreak had started in the Alzheimer unit, where, on June 2, the index patient experienced fever and cough. He was examined in his primary care provider's office on June 4, and on June 5 was started on amoxicillin. He was not hospitalized and died on June 7.

Three other Alzheimer unit residents became ill, and by the time ECDHD and NDHHS were notified, the illness had spread to other units. No diagnostic specimens had been

collected. On June 22, NDHHS established a working case definition and instructed the facility to ask the attending physician to collect NP and OP swabs from a hospitalized resident and asked the facility to collect specimens from any other residents or staff members with fever $\geq 100.4^{\circ}\text{F}$ ($\geq 38.0^{\circ}\text{C}$) and cough, or a diagnosis of pneumonia. However, specimen collection was delayed 2 days until trained ECDHD staff members visited the facility. ECDHD informed community physicians of the outbreak and requested notification of any unexplained pneumonia cases.

On June 28, NDHHS received the first laboratory report of a specimen found to test positive for *M. pneumoniae*. On July 1, NDHHS distributed a health alert to primary care providers, infectious disease personnel, urgent care centers, and public health departments in eight affected and adjacent counties to facilitate case finding, advise the medical community of the outbreak and suspected etiology, and provide guidance regarding treatment of suspected cases. Fluoroquinolones, tetracyclines, and macrolides were recommended by NDHHS as treatment options, with levofloxacin (a fluoroquinolone) preferred based on early reports of treatment failure with macrolides (Figure). Under a new surveillance case definition, health care providers were asked to notify ECDHD of patients who had a fever $\geq 100.4^{\circ}\text{F}$ ($\geq 38.0^{\circ}\text{C}$), a diagnosis of pneumonia by clinical examination or chest radiograph, and an epidemiologic link to the facility. ECDHD collected NP and OP specimens from these persons if they agreed to testing. Autopsy specimens were obtained from one decedent. At the time of specimen collection, clinical and demographic information was gathered about each affected patient (Table). Specimens were sent to the Nebraska Public Health Laboratory (NPHL) initially, and then to CDC. At CDC, multiplex, real-time PCR testing was performed for *M. pneumoniae*, *Chlamydomphila pneumoniae*, *Legionella* species, and human nucleic acid (as a control) (1).

After the likely etiologic agent was identified as *M. pneumoniae*, the case definition was modified. A probable case was defined as an acute respiratory illness and either a fever $\geq 100.4^{\circ}\text{F}$ ($\geq 38.0^{\circ}\text{C}$) or a pneumonia diagnosed by radiograph in a person with an epidemiologic link (i.e., resident, staff member, staff family member, or visitor). A confirmed case was defined as illness meeting the probable case definition plus a PCR test

FIGURE. Timeline of *Mycoplasma pneumoniae* outbreak in a long-term care facility — Nebraska, June–August 2014

Abbreviations: PCR = polymerase chain reaction; ECDHD = East Central District Health Department; NDHHS = Nebraska Department of Health and Human Services; NPHL = Nebraska Public Health Laboratory.

* Specimens collected from all ill residents. Strict droplet precautions implemented, and facility closed to new admissions.

result positive for *M. pneumoniae* on an NP or OP swab or autopsy specimen during June 2–August 18. Thirty-five of 55 (64%) persons whose illness met the probable case definition were sampled; 14 of the 35 (40%) sampled patients were positive for *M. pneumoniae* by PCR. Because of community concern, 37 patients whose illness did not meet the case definition also were sampled; five (14%) had test results positive for *M. pneumoniae*. However, three of the five did not meet the clinical criteria, and two had no epidemiologic link to the facility; the five were excluded from analysis.

Of the 55 probable and confirmed cases of *M. pneumoniae*, 20 (36%) were in facility residents; 22 (40%) were in staff members; and 13 (24%) were in community members. Ten (50%) of the residents were hospitalized, and seven (35%) died (one of the patients who died was not hospitalized); two (15%) community members with an epidemiologic link to the facility were hospitalized, and one (8%) died. No staff member was hospitalized or died. Among the 55, the overall median age was 46 years (range = 2–96 years); among residents, 89 years (range = 62–96); staff members, 36 years (range = 16–56); and community members, 26 years (range = 2–82). Median age of those who died was 82 years (range = 70–92), compared with 43 years (range = 2–96) for those who survived (chi-square, $p = 0.02$). Forty-two (76%) patients were female. Twenty-three (42%) patients had a chest radiograph, 16 (70%) of whom had findings consistent with pneumonia (Table).

Public Health Response

On June 24, ECDHD closed the facility to new admissions and suspended group activities. The facility had confined ill residents to their rooms, isolated affected hallways, posted signs requesting no visitors, and implemented droplet precautions

(i.e., use of gowns, gloves, and surgical masks). Family members who insisted on visiting were required to abide by droplet precautions. ECDHD monitored compliance with infection control measures. It was recommended that ill residents be moved to one area with the same staff members assigned to that area every day, avoiding movement of staff members between units (i.e., cohorting). However, the facility was unable to fully implement this measure because of staff coverage concerns.

On July 21, on the basis of reports that ill staff members were working, the facility began screening the staff for fever and symptoms of illness when members arrived at work; those who were ill were discharged from duty until afebrile for ≥ 24 hours. The facility's national corporate medical director and infection control nurse worked with ECDHD and NDHHS, and on August 2, the facility's infection prevention consultant performed a site visit. Facility admissions resumed September 14, one month after the last patient's illness onset date.

Discussion

Pneumonia is well-documented as a major cause of morbidity and mortality among persons aged >65 years, particularly those residing in nursing homes (2–6); the patients who died during this outbreak were considerably older than those who survived. Risk factors associated with pneumonia among persons living in nursing homes include older age, difficulty in swallowing because of comorbidities (e.g., Parkinson disease or Alzheimer disease), and being bedridden (4,5). This outbreak was caused by *M. pneumoniae*, an atypical bacterial organism. Although atypical organisms account for $\leq 40\%$ of community-acquired pneumonias (7), previous studies of nursing home-acquired pneumonias have not reported *M. pneumoniae* as a major cause (5,8,9); fatalities from *M. pneumoniae* are uncommon (10).

TABLE. Number of patients with confirmed or probable *Mycoplasma pneumoniae* respiratory illness at a long-term care facility, by selected characteristics — Nebraska, 2014

Characteristic	Confirmed* (n = 14)		Probable† (n = 41)		Total (N = 55)	
	No.	(%)	No.	(%)	No.	(%)
Link to facility						
Resident	6	(43)	14	(34)	20	(36)
Staff member	5	(36)	17	(41)	22	(40)
Community member	3	(21)	10	(24)	13	(24)
Sex						
Women	11	(79)	31	(76)	42	(76)
Men	3	(21)	10	(24)	13	(24)
Symptom						
Fever	10	(71)	39	(95)	49	(89)
Cough	14	(100)	41	(100)	55	(100)
Chest congestion	10	(71)	21	(51)	31	(56)
Sore Throat	8	(57)	15	(37)	23	(42)
Chest radiograph						
No. of patients administered	9	(64)	14	(34)	23	(42)
No. of findings consistent with pneumonia	8	(89)	8	(57)	16	(70)
Outcome[§]						
Hospitalized	4	(29)	8	(20)	12	(22)
Died	2	(14)	5	(12)	7	(13)
Antibiotic treatment[¶]						
Levofloxacin	11	(79)	15	(37)	26	(47)
Azithromycin	1	(7)	7	(17)	8	(15)
Doxycycline	0	—	3	(7)	3	(5)
Vancomycin	2	(14)	2	(5)	4	(7)
Beta-lactams**	2	(14)	13	(32)	15	(27)
Multiple antibiotics	2	(14)	7	(17)	9	(16)

* Respiratory illness in a patient with an epidemiologic link to the long-term care facility, a fever >100.4°F (>38.0°C) or a positive chest radiograph finding, and a positive *Mycoplasma pneumoniae* polymerase chain reaction test result from a nasopharyngeal, oropharyngeal, or autopsy specimen.

† Respiratory illness in a patient with an epidemiologic link to the long-term care facility, a fever >100.4°F (>38.0°C) or a positive chest radiograph finding, with no laboratory testing done.

§ One death and two hospitalizations were among visitors; all other deaths and hospitalizations were among residents. There were no hospitalizations or deaths among staff members.

¶ The list of antibiotics is not mutually exclusive.

** Included ceftriaxone, piperacillin/tazobactam, amoxicillin clavulanate, amoxicillin, and ampicillin.

This outbreak was unusual because of the type of facility and the number of fatalities.

Older patients with pneumonia might have falls, confusion, dizziness, or fatigue, without a fever or other classic pneumonia symptom, or they might have serious comorbidities (e.g., underlying lung disease), making case ascertainment difficult (2,3,5). This outbreak began in the Alzheimer unit, where accurate illness histories could not be obtained and where certain patients were receiving nonaggressive care (e.g., patients might not be tested to determine the cause of an illness or receive

What is already known on this topic?

Mycoplasma pneumoniae is an atypical bacterial organism that can be treated with fluoroquinolones, tetracyclines, or macrolides. *M. pneumoniae* usually is not associated with fatalities, and outbreaks are not commonly reported among geriatric populations. However, older persons are at increased risk for death, and diagnosis of *M. pneumoniae* infection can be delayed because older patients, who might have dementia and other comorbidities, often do not have fever or classic pneumonia symptoms.

What is added by this report?

During June–August 2014, 41 probable and 14 laboratory-confirmed cases of *M. pneumoniae* were associated with a single long-term care facility. Seven patients died, and the facility was closed to new admissions for a prolonged period. Delayed recognition of the outbreak and of the etiologic agent prolonged the transmission period and delayed effective interventions.

What are the implications for public health practice?

Long-term care facilities should consider *M. pneumoniae* during respiratory illness outbreaks. These facilities need to be alert to outbreaks and plan for prompt diagnostic testing, isolation or cohorting of ill residents, and screening of staff members for illness. Facilities can protect their staff members and residents with education regarding monitoring for outbreaks and infection prevention measures. Delayed recognition of an outbreak and determination of the etiologic agent might prolong the transmission period and delay effective interventions.

interventions beyond those needed for comfort). Additionally, certain patients at the facility were in hospice care for other diseases. These factors are common to outbreaks among older persons (3) and resulted in clinicians deferring diagnostic testing early in the outbreak. Certain patients, including the index patient, were treated with antibiotics ineffective against *M. pneumoniae* infection. After the outbreak's etiology was confirmed, clinicians frequently prescribed antibiotics on the basis of nursing reports of a fever or cough rather than on patient evaluation or diagnostic test results. As a result, some probable cases might not have been *M. pneumoniae* infection, and certain cases might not have been identified because they did not meet the case definition, particularly those in persons who did not have fever.

Negative PCR results in some probable cases might be attributable to the timing of sampling, the difficulty in obtaining NP samples from certain patients, and the circulation at the time of the outbreak of other respiratory viruses that cause similar symptoms. *M. pneumoniae* was not suspected early in this outbreak, which highlights the need at extended care facilities for prompt recognition and reporting of outbreaks, diagnostic evaluation and testing, and implementation of timely and strict infection control measures to prevent morbidity and mortality.

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Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV Vaccination Recommendations of the Advisory Committee on Immunization Practices

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During its February 2015 meeting, the Advisory Committee on Immunization Practices (ACIP) recommended 9-valent human papillomavirus (HPV) vaccine (9vHPV) (Gardasil 9, Merck and Co., Inc.) as one of three HPV vaccines that can be used for routine vaccination (Table 1). HPV vaccine is recommended for routine vaccination at age 11 or 12 years (1). ACIP also recommends vaccination for females aged 13 through 26 years and males aged 13 through 21 years not vaccinated previously. Vaccination is also recommended through age 26 years for men who have sex with men and for immunocompromised persons (including those with HIV infection) if not vaccinated previously (1). 9vHPV is a noninfectious, virus-like particle (VLP) vaccine. Similar to quadrivalent HPV vaccine (4vHPV), 9vHPV contains HPV 6, 11, 16, and 18 VLPs. In addition, 9vHPV contains HPV 31, 33, 45, 52, and 58 VLPs (2). 9vHPV was approved by the Food and Drug Administration (FDA) on December 10, 2014, for use in females aged 9 through 26 years and males aged 9 through 15 years (3). For these recommendations, ACIP reviewed additional data on 9vHPV in males aged 16 through 26 years (4). 9vHPV and 4vHPV are licensed for use in females and males. Bivalent HPV vaccine

(2vHPV), which contains HPV 16, 18 VLPs, is licensed for use in females (1). This report summarizes evidence considered by ACIP in recommending 9vHPV as one of three HPV vaccines that can be used for vaccination and provides recommendations for vaccine use.

Methods

From October 2013 to February 2015, the ACIP HPV Vaccine Work Group reviewed clinical trial data assessing the efficacy, immunogenicity, and safety of 9vHPV, modeling data on cost-effectiveness of 9vHPV, and data on burden of type-specific HPV-associated disease in the United States. Summaries of reviewed evidence and Work Group discussions were presented to ACIP before recommendations were proposed. Recommendations were approved by ACIP in February 2015. Evidence supporting 9vHPV use was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework (5) and determined to be type 2 (moderate level of evidence) among females and 3 (low level of evidence) among males; the recommendation was categorized as a Category A recommendation (for all persons in an age- or risk-factor-based group) (6).

HPV-Associated Disease

HPV is associated with cervical, vulvar, and vaginal cancer in females, penile cancer in males, and anal cancer and oropharyngeal cancer in both females and males (7–10). The burden of HPV infection also includes cervical precancers, including cervical intraepithelial neoplasia grade 2 or 3 and adenocarcinoma in situ (\geq CIN2). The majority of all HPV-associated cancers are caused by HPV 16 or 18, types targeted by 2vHPV, 4vHPV and 9vHPV (2,11,12). In the United States, approximately 64% of invasive HPV-associated cancers are attributable to HPV 16 or 18 (65% for females; 63% for males; approximately 21,300 cases annually) and 10% are attributable to the five additional types in 9vHPV: HPV 31, 33, 45, 52, and 58 (14% for females; 4% for males; approximately 3,400 cases annually) (1,12,13). HPV 16 or 18 account for 66% and the five additional types for about 15% of cervical cancers (12). Approximately 50% of \geq CIN2 are caused by HPV 16 or 18

Recommendations for routine use of vaccines in children, adolescents and adults are developed by the Advisory Committee on Immunization Practices (ACIP). ACIP is chartered as a federal advisory committee to provide expert external advice and guidance to the Director of the Centers for Disease Control and Prevention (CDC) on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for routine use of vaccines in children and adolescents are harmonized to the greatest extent possible with recommendations made by the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG). Recommendations for routine use of vaccines in adults are harmonized with recommendations of AAFP, ACOG, and the American College of Physicians (ACP). ACIP recommendations approved by the CDC Director become agency guidelines on the date published in the Morbidity and Mortality Weekly Report (MMWR). Additional information about ACIP is available at <http://www.cdc.gov/vaccines/acip/>.

TABLE 1. Characteristics of the three human papillomavirus (HPV) vaccines licensed for use in the United States

Characteristic	Bivalent (2vHPV)*	Quadrivalent (4vHPV)†	9-valent (9vHPV)‡
Brand name	Cervarix	Gardasil	Gardasil 9
VLPs	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58
Manufacturer	GlaxoSmithKline	Merck and Co., Inc.	Merck and Co., Inc.
Manufacturing	<i>Trichoplusia ni</i> insect cell line infected with L1 encoding recombinant baculovirus	<i>Saccharomyces cerevisiae</i> (Baker's yeast), expressing L1	<i>Saccharomyces cerevisiae</i> (Baker's yeast), expressing L1
Adjuvant	500 µg aluminum hydroxide, 50 µg 3-O-desacyl-4' monophosphoryl lipid A	225 µg amorphous aluminum hydroxyphosphate sulfate	500 µg amorphous aluminum hydroxyphosphate sulfate
Volume per dose	0.5 ml	0.5 ml	0.5 ml
Administration	Intramuscular	Intramuscular	Intramuscular

Abbreviation: L1 = the HPV major capsid protein; VLPs = virus-like particles.

* Only licensed for use in females in the United States. Package insert available at <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM186981.pdf>.

† Package insert available at <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf>.

‡ Package insert available at <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM426457.pdf>.

and 25% by HPV 31, 33, 45, 52, or 58 (14). HPV 6 or 11 cause 90% of anogenital warts (condylomata) and most cases of recurrent respiratory papillomatosis (15).

9vHPV Efficacy, Immunogenicity, and Safety

In a phase III efficacy trial comparing 9vHPV with 4vHPV among approximately 14,000 females aged 16 through 26 years, 9vHPV efficacy for prevention of \geq CIN2, vulvar intraepithelial neoplasia grade 2 or 3, and vaginal intraepithelial neoplasia grade 2 or 3 caused by HPV 31, 33, 45, 52, or 58 was 96.7% in the per protocol population* (Table 2) (2,16). Efficacy for prevention of \geq CIN2 caused by HPV 31, 33, 45, 52, or 58 was 96.3% and for 6-month persistent infection was 96.0% (16). Few cases were caused by HPV 6, 11, 16, or 18 in either vaccine group. Noninferior immunogenicity of 9vHPV compared with 4vHPV was used to infer efficacy for HPV 6, 11, 16, and 18. Geometric mean antibody titers (GMTs) 1 month after the third dose were noninferior for HPV 6, 11, 16, and 18; in the 9vHPV group, >99% seroconverted to all nine HPV vaccine types (Table 3).

Two immunobridging trials were conducted. One compared 9vHPV in approximately 2,400 females and males aged 9 through 15 years with approximately 400 females aged 16 through 26 years. Over 99% seroconverted to all nine HPV vaccine types; GMTs were significantly higher in adolescents aged 9 through 15 years compared with females aged 16 through 26 years. In a comparison of 4vHPV with 9vHPV in approximately 600 adolescent females aged 9 through 15 years, 100% seroconverted to HPV 6, 11, 16, and 18 in both

groups, and GMTs were noninferior in the 9vHPV group compared with the 4vHPV group.

Immunogenicity in males aged 16 through 26 years was compared with females of the same age group in a separate study. In both females and males, >99% seroconverted to all nine HPV vaccine types, and GMTs in males were noninferior to those in females (4).

The immunogenicity of concomitant and nonconcomitant administration of 9vHPV with quadrivalent meningococcal conjugate vaccine (Menactra, MenACWY-D) and tetanus, diphtheria, acellular pertussis vaccine (Adacel, Tdap) was evaluated. The GMTs were noninferior for all nine HPV vaccine types in the co-administered group (all $p < 0.001$). For Menactra, the noninferiority criterion was met for all four serogroups, and for Adacel, for diphtheria, tetanus, and all four pertussis antigens.

Safety has been evaluated in approximately 15,000 subjects in the 9vHPV clinical development program; approximately 13,000 subjects in six studies were included in the initial application submitted to FDA (2). The vaccine was well-tolerated, and most adverse events were injection site-related pain, swelling, and erythema that were mild to moderate in intensity. The safety profiles were similar in 4vHPV and 9vHPV vaccinees. Among females aged 9 through 26 years, 9vHPV recipients had more injection-site adverse events, including swelling (40.3% in the 9vHPV group compared with 29.1% in the 4vHPV group) and erythema (34.0% in the 9vHPV group compared with 25.8% in the 4vHPV group). Males had fewer injection site adverse events. In males aged 9 through 15 years, injection site swelling and erythema in 9vHPV recipients occurred in 26.9% and 24.9%, respectively. Rates of injection-site swelling and erythema both increased following each successive dose of 9vHPV.

* Females who received all 3 vaccinations within 1 year of enrollment, did not have major deviations from the study protocol, were naïve (polymerase chain reaction [PCR] negative and seronegative) to the relevant HPV type(s) before dose 1, and who remained PCR negative to the relevant HPV type(s) through 1 month after dose 3 (month 7).

TABLE 2. Results of a Phase III efficacy trial comparing 9-valent human papillomavirus (HPV) vaccine (9vHPV) with quadrivalent HPV vaccine (4vHPV), per protocol population* in females aged 16 through 26 years†

Endpoint-related types	Endpoint	9vHPV		4vHPV		Vaccine efficacy	
		No. participants	Cases	No. participants	Cases	%	(95% CI)
HPV 31, 33, 45, 52, 58	≥CIN2, VIN2/3, ValN2/3	6,016	1	6,017	30	96.7	(80.9–99.8)
	≥CIN2	5,948	1	5,943	27	96.3	(79.5–99.8)
	6-month persistent infection	5,939	35	5,953	810	96.0	(94.4–97.2)
HPV 6, 11, 16, 18	≥CIN2 [§]	5,823	1	5,832	1	—	—
	Anogenital warts	5,876	5	5,893	1	—	—

Abbreviations: CI = confidence interval; ≥CIN2 = cervical intraepithelial neoplasia grade 2 or 3 or adenocarcinoma in situ; ValN2/3 = vaginal intraepithelial neoplasia grade 2 or 3; VIN2/3 = vulvar intraepithelial neoplasia grade 2 or 3.

Sources: Package insert available at <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM426457.pdf>.

Joura EA, Giuliano AR, Iversen OE, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *N Engl J Med* 2015;372:711–23.

* Females who received all 3 vaccinations within 1 year of enrollment, did not have major deviations from the study protocol, were naïve (polymerase chain reaction [PCR] negative and seronegative) to the relevant HPV type(s) before dose 1, and who remained PCR negative to the relevant HPV type(s) through 1 month after dose 3 (month 7).

† Participants were enrolled from sites in 18 countries; median duration of follow-up was 40 months.

TABLE 3. Human papillomavirus (HPV) 6, 11, 16, and 18 seroconversion and geometric mean titers (GMTs*) after 3 doses of 9-valent HPV vaccine (9vHPV) compared with quadrivalent HPV vaccine (4vHPV), per protocol population† in females aged 16 through 26 years[§]

Assay (cLIA)	9vHPV			4vHPV		
	No. participants	Seropositivity (%)	GMT (mMU/mL)	No. participants	Seropositivity (%)	GMT (mMU/mL)
Anti-HPV 6	3,993	(99.8)	893	3,975	(99.8)	875
Anti-HPV 11	3,995	(100)	666	3,982	(99.9)	830
Anti-HPV 16	4,032	(100)	3,131	4,062	(100)	3,157
Anti-HPV 18	4,539	(99.8)	805	4,541	(99.7)	679

Abbreviations: cLIA = competitive Luminex immunoassay; mMU = milli-Merck units.

Source: Joura EA, Giuliano AR, Iversen OE, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women, and supplementary appendix. *N Engl J Med* 2015;372:711–23.

* The noninferiority criterion for GMTs was met for all four HPV types ($p < 0.001$).

† Females who received all 3 vaccinations within 1 year of enrollment, did not have major deviations from the study protocol, were naïve (polymerase chain reaction [PCR] negative and seronegative) to the relevant HPV type(s) before dose 1, and who remained PCR-negative to the relevant HPV type(s) through 1 month after dose 3 (month 7).

[§] Participants were enrolled from sites in 18 countries; median duration of follow-up was 40 months.

Health Impact and Cost Effectiveness

Introduction of 9vHPV in both males and females was cost-saving when compared with 4vHPV for both sexes in a cost-effectiveness model that assumed 9vHPV cost \$13 more per dose than 4vHPV. Cost-effectiveness ratios for 9vHPV remained favorable compared with 4vHPV (9vHPV was cost-saving in most scenarios, and the cost per quality-adjusted life year gained did not exceed \$25,000 in any scenario) when varying assumptions about HPV natural history, cervical cancer screening, vaccine coverage, vaccine duration of protection, and health care costs, but were sensitive to 9vHPV cost assumptions (17). Because the additional five types in 9vHPV account for a higher proportion of HPV-associated cancers in females compared with males and cause cervical precancers, the additional protection from 9vHPV will mostly benefit females.

Recommendations for Use of HPV Vaccines

ACIP recommends that routine HPV vaccination be initiated at age 11 or 12 years. The vaccination series can be started

beginning at age 9 years. Vaccination is also recommended for females aged 13 through 26 years and for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series (1). Males aged 22 through 26 years may be vaccinated.† Vaccination of females is recommended with 2vHPV, 4vHPV (as long as this formulation is available), or 9vHPV. Vaccination of males is recommended with 4vHPV (as long as this formulation is available) or 9vHPV.

2vHPV, 4vHPV, and 9vHPV all protect against HPV 16 and 18, types that cause about 66% of cervical cancers and the majority of other HPV-attributable cancers in the United States (1,12). 9vHPV targets five additional cancer causing types, which account for about 15% of cervical cancers (12). 4vHPV and 9vHPV also protect against HPV 6 and 11, types that cause anogenital warts.

† Vaccination is also recommended through age 26 years for men who have sex with men and for immunocompromised persons (including those with HIV infection) if not vaccinated previously.

What is currently recommended?

The Advisory Committee on Immunization Practices (ACIP) recommends routine HPV vaccination at age 11 or 12 years. The vaccination series can be started beginning at age 9 years. Vaccination is also recommended for females aged 13 through 26 years and for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series. Males aged 22 through 26 years may be vaccinated. ACIP recommends vaccination of men who have sex with men and immunocompromised persons through age 26 years if not vaccinated previously.

Why are the recommendations being updated now?

9-valent HPV vaccine (9vHPV) was approved by the Food and Drug Administration on December 10, 2014. This vaccine targets HPV types 6, 11, 16, and 18, the types targeted by the quadrivalent HPV vaccine (4vHPV), as well as five additional types, HPV types 31, 33, 45, 52, and 58. ACIP reviewed results of a randomized trial among approximately 14,000 females aged 16 through 26 years that showed noninferior immunogenicity for the types shared by 4vHPV and 9vHPV and high efficacy for the five additional types. Other trials in the 9vHPV clinical development program included studies that compared antibody responses across age groups and females and males and concomitant vaccination studies. The evidence supporting 9vHPV vaccination was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework and determined to be type 2 (moderate level of evidence) among females and 3 (low level of evidence) among males; the recommendation was designated as a Category A recommendation (recommendation for all persons in an age- or risk-factor–based group).

What are the new recommendations?

9vHPV, 4vHPV or 2vHPV can be used for routine vaccination of females aged 11 or 12 years and females through age 26 years who have not been vaccinated previously or who have not completed the 3-dose series. 9vHPV or 4vHPV can be used for routine vaccination of males aged 11 or 12 years and males through age 21 years who have not been vaccinated previously or who have not completed the 3-dose series. ACIP recommends either 9vHPV or 4vHPV vaccination for men who have sex with men and immunocompromised persons (including those with HIV infection) through age 26 years if not vaccinated previously.

Administration. 2vHPV, 4vHPV, and 9vHPV are each administered in a 3-dose schedule. The second dose is administered at least 1 to 2 months after the first dose, and the third dose at least 6 months after the first dose[§] (1). If the vaccine schedule is interrupted, the vaccination series does not need to be restarted.

If vaccination providers do not know or do not have available the HPV vaccine product previously administered, or

are in settings transitioning to 9vHPV, any available HPV vaccine product may be used to continue or complete the series for females for protection against HPV 16 and 18; 9vHPV or 4vHPV may be used to continue or complete the series for males. There are no data on efficacy of fewer than 3 doses of 9vHPV.

Special Populations. HPV vaccination is recommended through age 26 years for men who have sex with men and for immunocompromised persons (including those with HIV infection) who have not been vaccinated previously or have not completed the 3-dose series.

Precautions and Contraindications. HPV vaccines are contraindicated for persons with a history of immediate hypersensitivity to any vaccine component. 4vHPV and 9vHPV are contraindicated for persons with a history of immediate hypersensitivity to yeast. 2vHPV should not be used in persons with anaphylactic latex allergy.

HPV vaccines are not recommended for use in pregnant women (1). If a woman is found to be pregnant after initiating the vaccination series, the remainder of the 3-dose series should be delayed until completion of pregnancy. Pregnancy testing is not needed before vaccination. If a vaccine dose has been administered during pregnancy, no intervention is needed. A new pregnancy registry has been established for 9vHPV (2). Pregnancy registries for 4vHPV and 2vHPV have been closed with concurrence from FDA (1,18). Exposure during pregnancy can be reported to the respective manufacturer.[¶] Patients and health care providers can report an exposure to HPV vaccine during pregnancy to the Vaccine Adverse Event Reporting System (VAERS).

Adverse events occurring after administration of any vaccine should be reported to VAERS. Additional information about VAERS is available by telephone (1-800-822-7967) or online at <http://vaers.hhs.gov>.

Cervical Cancer Screening. Cervical cancer screening is recommended beginning at age 21 years and continuing through age 65 years for both vaccinated and unvaccinated women (19,20). Recommendations will continue to be evaluated as further postlicensure monitoring data become available.

Future Policy Issues

A clinical trial is ongoing to assess alternative dosing schedules of 9vHPV. ACIP will formally review the results as data become available. HPV vaccination should not be delayed pending availability of 9vHPV or of future clinical trial data.

[¶] 9vHPV exposure during pregnancy should be reported to the Merck Pregnancy Registry at telephone 1-800-986-8999; 4vHPV exposure during pregnancy can be reported to Merck at telephone 1-877-888-4231. 2vHPV exposure during pregnancy can be reported to GlaxoSmithKline at telephone 1-888-825-5249.

[§] Minimum intervals are 1 month between the first and second dose, 3 months between the second and third dose, and 6 months between the first and third dose.

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ACIP members (membership roster for July 2014–June 2015 available at <http://www.cdc.gov/vaccines/acip/committee/members-archive.html>). ACIP HPV Work Group.

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Updated Recommendations for the Use of Typhoid Vaccine — Advisory Committee on Immunization Practices, United States, 2015

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These revised recommendations of the Advisory Committee on Immunization Practices update recommendations published in *MMWR* in 1994 (1) and include updated information on the two currently available vaccines and on vaccine safety. They also include an update on the epidemiology of enteric fever in the United States, focusing on increasing drug resistance in *Salmonella enterica* serotype Typhi, the cause of typhoid fever, as well as the emergence of *Salmonella* serotype Paratyphi A, a cause of paratyphoid fever, against which typhoid vaccines offer little or no protection.

Introduction

Salmonella enterica serotypes Typhi and Paratyphi A, Paratyphi B (tartrate negative), and Paratyphi C cause a protracted bacteremic illness referred to respectively as typhoid and paratyphoid fever, and collectively as enteric fever. Enteric fever can be severe and even life-threatening. It is most commonly acquired from water or food contaminated by the feces of an infected person. The incubation period is 6–30 days, and illness onset is insidious, with gradually increasing fatigue and fever. Malaise, headache, and anorexia are nearly universal. A transient macular rash can occur. When serious complications (e.g., intestinal hemorrhage or perforation) occur, it is generally

after 2–3 weeks of illness. Untreated illness can last a month (2). Patients with untreated typhoid fever were reported to have case-fatality rates >10% (3); the overall case-fatality rate with early and appropriate antibiotic treatment is typically <1% (4).

Typhoid fever is uncommon in the United States, with an average of about 400 cases reported annually during 2007–2011 (5). Approximately 90% of U.S. cases occur among persons returning from foreign travel, and >75% of travelers had been in India, Bangladesh, or Pakistan (5). Most travelers (≥55%) reported that their reason for travel was visiting friends or relatives (5). Even short-term travel to high-incidence areas is associated with risk for typhoid fever (6). CDC recommends typhoid vaccination for travelers to many Asian, African, and Latin American countries, but, as of 2010, no longer recommends typhoid vaccine for travelers to certain Eastern European and Asian countries (7); the most recent pre-travel vaccination guidelines are available at <http://wwwnc.cdc.gov/travel>.

The importance of vaccination and other preventive measures for typhoid fever is heightened by increasing resistance of *Salmonella* serotype Typhi to antimicrobial agents, including fluoroquinolones, in many parts of the world (8).

Paratyphoid fever, caused primarily by *Salmonella enterica* serotype Paratyphi A, but also by serotypes Paratyphi B (tartrate negative) and C, is an illness clinically indistinguishable from typhoid fever (9). Serotype Paratyphi A is responsible for a growing proportion of enteric fever cases in many countries, accounting for as much as half of the cases (8). Neither typhoid vaccine available in the United States is licensed by the Food and Drug Administration for prevention of paratyphoid fever, although limited observational data suggest the oral, live-attenuated Ty21a vaccine might offer some protection against Paratyphi B (tartrate negative) (10).

Typhoid Vaccines

Two typhoid vaccines are available for use in the United States: 1) a Vi capsular polysaccharide vaccine for parenteral use (Typhim Vi, manufactured by Sanofi Pasteur) and 2) an oral live-attenuated vaccine (Vivotif, manufactured from the Ty21a strain of *Salmonella* serotype Typhi by PaxVax). A parenteral heat-phenol-inactivated whole-cell vaccine first licensed by Wyeth in 1952 and associated with high rates of fever and systemic reactions was discontinued in 2000 (6).

Recommendations for routine use of vaccines in children, adolescents, and adults are developed by the Advisory Committee on Immunization Practices (ACIP). ACIP is chartered as a federal advisory committee to provide expert external advice and guidance to the Director of the Centers for Disease Control and Prevention (CDC) on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for routine use of vaccines in children and adolescents are harmonized to the greatest extent possible with recommendations made by the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG). Recommendations for routine use of vaccines in adults are harmonized with recommendations of AAFP, ACOG, and the American College of Physicians (ACP). ACIP recommendations approved by the CDC Director become agency guidelines on the date published in the Morbidity and Mortality Weekly Report (MMWR). Additional information is available at <http://www.cdc.gov/vaccines/acip>.

No efficacy studies among travelers from nonendemic areas are available for either vaccine, though a Ty21a vaccine challenge study among North American volunteers demonstrated significant protection from disease (11,12). The two currently available vaccines have moderate efficacy in populations where typhoid is endemic. In a systematic review and meta-analysis, the estimated 2.5–3.0 year cumulative efficacy was 55% (95% confidence interval [CI] = 30%–70%) for the parenteral Vi polysaccharide vaccine and 48% (CI = 34%–58%) for the oral Ty21a vaccine, each based on a single trial (13). A trial in Kolkata, India, of the Vi polysaccharide vaccine found a protective effectiveness of 61% (CI = 41%–75%) among all participants (14). Studies conflict regarding the effectiveness of the Vi vaccine in young children. The trial in Kolkata, which included adults as well as children, found 80% (CI = 53%–91%) effectiveness among those 2–4 years (14), whereas a trial in Karachi, Pakistan, which included only children 2–16 years, showed no protection among children 2–4 years (15). Herd effects might have contributed to the high effectiveness observed among young children in the Kolkata trial. An observational study of the effectiveness of typhoid vaccination in U.S. travelers estimated 80% protection; however, this study addressed typhoid vaccination in general, not specific vaccines (16).

Protein-conjugated Vi polysaccharide vaccines have been shown to have high efficacy in young children (17) and have been licensed in other countries (18), but are not currently licensed or available in the United States.

Vaccine Usage

Routine typhoid vaccination is not recommended in the United States.

Vaccination is recommended for the following groups:

- Travelers to areas where there is a recognized risk for exposure to *Salmonella* serotype Typhi (the most recent guidelines are available at <http://wwwnc.cdc.gov/travel>). Risk is greatest for travelers who have prolonged exposure to possibly contaminated foods and beverages, although short-term travelers are also at risk (6). Most travel-associated typhoid fever cases in the United States occur among travelers who are visiting friends or relatives; many travelers in this group do not seek pre-travel health care (19). Multidrug-resistant strains of *Salmonella* serotype Typhi have become common in many regions (8), and cases of typhoid fever that are treated with drugs to which the organism is resistant can be fatal. Travelers should be cautioned that typhoid vaccination is not a substitute for careful selection of food and beverages. Typhoid vaccines are not 100% effective, and vaccine-induced protection can be overwhelmed by large inocula of *Salmonella* serotype Typhi.

- Persons with intimate exposure (e.g., household contact) to a documented *Salmonella* serotype Typhi chronic carrier (defined as excretion of *Salmonella* serotype Typhi in urine or stool for >1 year).
- Microbiologists and other laboratory workers routinely exposed to cultures of *Salmonella* serotype Typhi or specimens containing this organism or who work in laboratory environments where these cultures or specimens are routinely handled.

Choice of Vaccine

Parenteral Vi polysaccharide and oral Ty21a are both acceptable forms of typhoid vaccine.

The Vi polysaccharide vaccine is administered as a single injection and is approved for adults and children aged ≥ 2 years. The oral Ty21a vaccine is administered in 4 doses on alternating days over 1 week and is approved for adults and children aged ≥ 6 years. Immunocompromised persons should not use Ty21a because it is a live-attenuated vaccine. Because antibacterial drugs might be active against the vaccine strain and reduce immunogenicity, the Ty21a vaccine should not be administered to persons taking these medications.

Vaccine Administration

Vi polysaccharide

Primary vaccination with Vi polysaccharide consists of one 0.5-mL (25- μ g) dose administered intramuscularly. This vaccine should be given at least 2 weeks before potential exposure.

Ty21a

Primary vaccination with live-attenuated Ty21a vaccine consists of one enteric-coated capsule taken on alternate days (day 0, 2, 4, and 6), for a total of four capsules. The capsules must be kept refrigerated (not frozen). Each capsule should be taken with cool water no warmer than 98.6°F (37.0°C), approximately 1 hour before a meal. All doses should be completed at least 1 week before potential exposure.

Repeat Doses

If continued or repeated exposure to *Salmonella* serotype Typhi is expected, repeat doses of typhoid vaccine are needed to maintain immunity (Table). An optimal revaccination schedule for the Vi polysaccharide vaccine has not been established; however, the manufacturer recommends a repeat dose every 2 years after the primary dose if continued or renewed exposure is expected (20). The manufacturer of Ty21a recommends revaccination with the entire 4-dose series every 5 years if continued or renewed exposure to *Salmonella* serotype Typhi is expected (21).

TABLE. Updated dosage and schedules for typhoid fever vaccination — Advisory Committee on Immunization Practices, United States, 2015

Vaccination	Age (yrs)	Dosage			
		Dose/mode of administration	No. of doses	Dosing schedule	Boosting interval
Vi capsular polysaccharide vaccine					
Primary series	≥2	0.50 mL*	1	1 dose	—
Booster	≥2	0.50 mL*	1	1 dose	Every 2 yrs
Oral live-attenuated Ty21a vaccine					
Primary series	≥6	1 capsule†	4	Days 0, 2, 4, 6	—
Booster	≥6	1 capsule†	4	Days 0, 2, 4, 6	Every 5 yrs

* Intramuscularly.

† Each orally administered capsule contains 2.0–10.0 × 10⁹ viable *Salmonella enterica* serotype Typhi Ty21a and 5–50 × 10⁹ nonviable *Salmonella enterica* serotype Typhi Ty21a.

Adverse Reactions

Evidence from trials and postmarketing studies suggest that parenteral Vi vaccines are usually tolerated well (20). In field trials, pain (risk ratio [RR] = 8.0; CI = 3.7–17.2) and swelling at the injection site (RR = 6.0; CI = 1.1–34.2) were more common among vaccinees than placebo recipients, but no significant difference was found in the incidence of fever or erythema (13). In a manufacturer-funded postmarketing safety study conducted in 11 U.S. travel clinics, the most common reactions were injection site pain (77%), tenderness (75%), and muscle aches (39%) (22). In postmarketing surveillance of the Vi vaccine (administered alone or simultaneously with other vaccines) during 1995–2002, an estimated 0.3 serious events* per 100,000 doses distributed were reported to the U.S. Vaccine Adverse Events Reporting System (VAERS) (23). Among the 321 VAERS reports of events occurring after Vi vaccination, the most commonly reported symptoms included injection site reactions, fever, headache, rash, urticaria, abdominal pain, and nausea. It is important to note that adverse events reported to VAERS might not be caused by the vaccine.

In a meta-analysis of Ty21a vaccine placebo-controlled trials, fever was more common among vaccinees (RR = 1.8; CI = 1.0–3.1), but other adverse events occurred with equal frequency among groups receiving vaccine and placebo; risk for any mild adverse event was higher among vaccinees (RR = 1.7; CI = 1.0–2.7) (13). In a combined analysis of data from a pilot study and a field trial, fewer than 10% of vaccinees reported abdominal pain (6.4%), nausea (5.8%), headache (4.8%), fever (3.3%), diarrhea (2.9%), vomiting (1.5%), or skin rash (1.0%) (21,24,25). One nonfatal case of anaphylactic shock, which was considered to be an allergic reaction to the vaccine, was reported to the manufacturer (21). In VAERS postmarketing surveillance of the Ty21a vaccine (administered alone or simultaneously with other vaccines) during 1991–2002, an

estimated 0.6 serious events per 100,000 doses distributed were reported (23). Among the 345 reports of events occurring after Ty21a vaccination, the most commonly reported symptoms included diarrhea, nausea, fever, abdominal pain, headache, rash, vomiting, and urticaria (23).

Precautions and Contraindications

No data have been reported on the use of either typhoid vaccine in pregnant women. In general, live vaccines like Ty21a are contraindicated in pregnancy (26). Vi polysaccharide vaccine should be given to pregnant women only if clearly needed (20).

Because Ty21a is a live-attenuated vaccine, antimicrobial agents might interfere with vaccine activity. To be sure the vaccine is fully effective, the vaccine manufacturer advises that Ty21a should not be given until at least 3 days after the last dose of antimicrobial agent and, if possible, antimicrobial agents should not be started within 3 days of the last dose of Ty21a vaccine (27). A longer interval should be considered for long-acting antimicrobials (e.g., azithromycin). The antimalarial agents mefloquine and chloroquine and the combinations atovaquone/proguanil and pyrimethamine/sulfadoxine can, at doses used for prophylaxis, be administered together with the Ty21a vaccine; however, the manufacturer advises that other antimalarial agents only be administered at least 3 days after the last vaccine dose (27). Ty21a vaccine can be administered simultaneously or at any interval before or after other live vaccines (injectable or intranasal) or immune globulin if indicated (26). Ty21a should not be administered to persons during an acute febrile illness or acute gastroenteritis (21).

Live-attenuated Ty21a vaccine should not be used by immunocompromised persons. The Vi vaccine is theoretically safer for this group. Although the Ty21a strain can be shed in the stool of vaccinees, transmission has not been documented (21). The Ty21a strain has not been isolated from blood cultures after vaccination (21). Both the Vi polysaccharide and Ty21a vaccines are contraindicated in patients with a history of hypersensitivity to any component of the vaccine.

* Serious adverse events were defined as reports of death, hospitalizations, prolongation of hospitalization, permanent disability, life-threatening illness, or congenital anomaly.

What is currently recommended?

In 1994, Advisory Committee on Immunization Practices (ACIP) approved recommendations for typhoid vaccination, stating that typhoid vaccine is indicated for U.S. travelers to certain countries, close contacts of chronic carriers, and certain laboratory workers. Since 1994, the parenteral heat-phenol-inactivated whole-cell vaccine has been discontinued.

Why are the recommendations being modified now?

The updated recommendations contain new data on the epidemiology of typhoid fever and vaccine effectiveness and safety. No substantive changes have been made to ACIP typhoid vaccine recommendations apart from removing the discontinued parenteral whole-cell vaccine from the list of available typhoid vaccines. The two typhoid vaccines available in the United States are parenteral Vi capsular polysaccharide vaccine and oral live-attenuated Ty21a vaccine.

What are the new recommendations?

Typhoid vaccine continues to be recommended for U.S. travelers to certain countries (the most recent guidelines are available at <http://wwwnc.cdc.gov/travel>), close contacts of chronic carriers, and certain laboratory workers.

Acknowledgments

ACIP members (membership roster for July 2014–June 2015 available at <http://www.cdc.gov/vaccines/acip/committee/members.html>).

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Announcement

Autism Awareness Month and World Autism Day — April 2015

April is Autism Awareness Month, and April 2 is World Autism Day. These observances offer the opportunity to highlight the increasing number of children identified with autism spectrum disorder (ASD) and the substantial burden on families and health, educational and other support services, as well as an opportunity to celebrate the unique perspectives of those living with ASD.

ASD is a developmental disability that can cause major social, communication, and behavioral challenges. Signs of ASD begin during early childhood and usually last throughout a person's life (1). The cause of most cases of ASD is unknown, and there is currently no cure. CDC's most recent surveillance data indicate that about one in 68 children has been identified with ASD (2), which represents an almost 30% increase since the previous estimate in 2012. CDC has been active in documenting changes in the number and characteristics of children with ASD over the past decade. However, there remains an urgent need to continue research into causes of and effective interventions for ASD (3) and help children living with ASD to achieve their potential.

CDC, working with its state and academic partners, is committed to tracking the changing number and characteristics of children with ASD, researching what puts children at greater risk for ASD, and promoting early identification of children with ASD.

Information about CDC's data on ASD is available at <http://www.cdc.gov/ADDM>. Information on CDC's study for understanding risk factors and causes of ASD is available at <http://www.cdc.gov/SEED>. Resources to help parents, health care providers, and early childhood care and education providers track each child's development are available for download free of charge at <http://www.cdc.gov/ActEarly>.

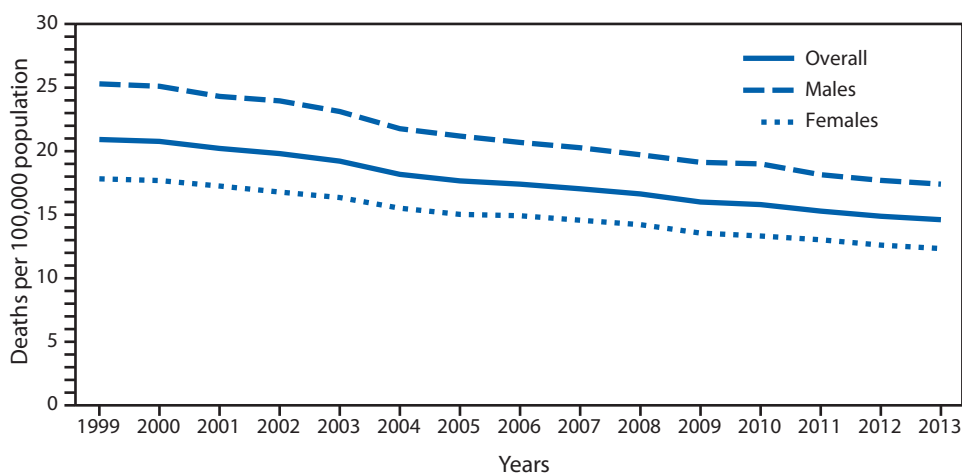
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QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Colorectal Cancer* Death Rates,[†] by Sex — National Vital Statistics System, United States, 1999–2013



* Malignant neoplasms of colon, rectum and anus (C18–C21) as the underlying cause of death includes the following *International Classification of Diseases, 10th Revision* codes: malignant neoplasm of colon (C18), malignant neoplasm of rectosigmoid junction (C19), malignant neoplasm of rectum (C20), and malignant neoplasm of anus and anal canal (C21).

[†] Age-adjusted rates (deaths per 100,000) based on the 2000 U.S. standard population. Populations used for computing death rates for 2011–2013 are postcensal estimates based on the 2010 census, estimated as of July 1, 2013. Rates for census years are based on populations enumerated in the corresponding censuses. Rates for noncensus years before 2010 are revised using updated intercensal population estimates and might differ from rates previously published.

In 2013, the age-adjusted death rate for colorectal cancer was 14.6 per 100,000 population, the lowest rate ever recorded. From 1999 to 2013, colorectal cancer death rates decreased 30.1% (from 20.9 to 14.6 per 100,000 population). For males, the rate decreased 31.2%, and for females the rate decreased 30.9%. In 2013, a total of 52,252 colorectal cancer deaths were reported in the United States.

Source: National Vital Statistics System. Mortality public use data files, 2013. Available at http://www.cdc.gov/nchs/data_access/vitalstatsonline.htm.

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