Evidence to Recommendations Framework

Wording of the age for routine HPV vaccination

Ruth Stefanos, MD, MPH

Advisory Committee on Immunization Practices

April 15, 2025

Current recommendation

- **HPV vaccination is routinely recommended at age 11 or 12 years**
- **Vaccination can be given starting at age 9 years**
- **Since 2006 (first ACIP recommendation), the wording of age at HPV vaccination initiation has not substantially changed**

https://www.cdc.gov/acip-recs/hcp/vaccine-specific/hpv.html

Adolescent platform

1996 **The adolescent platform at 11-12 years was established as "a new strategy to improve the delivery of vaccination services to adolescents and to integrate recommendations for vaccination with other preventive services provided to adolescents."**

Immunization of adolescents. MMWR Recomm Rep. 1996;45(RR-13):1-16.

2006 **Society for Adolescent Health and Medicine endorsed "three distinct adolescent vaccination visits/platforms for adolescents (11–12-year visit, 14–15-year visit, and a 17–18-year visit) to integrate and emphasize the role of vaccination in already recommended comprehensive health care screening and provision visits."**

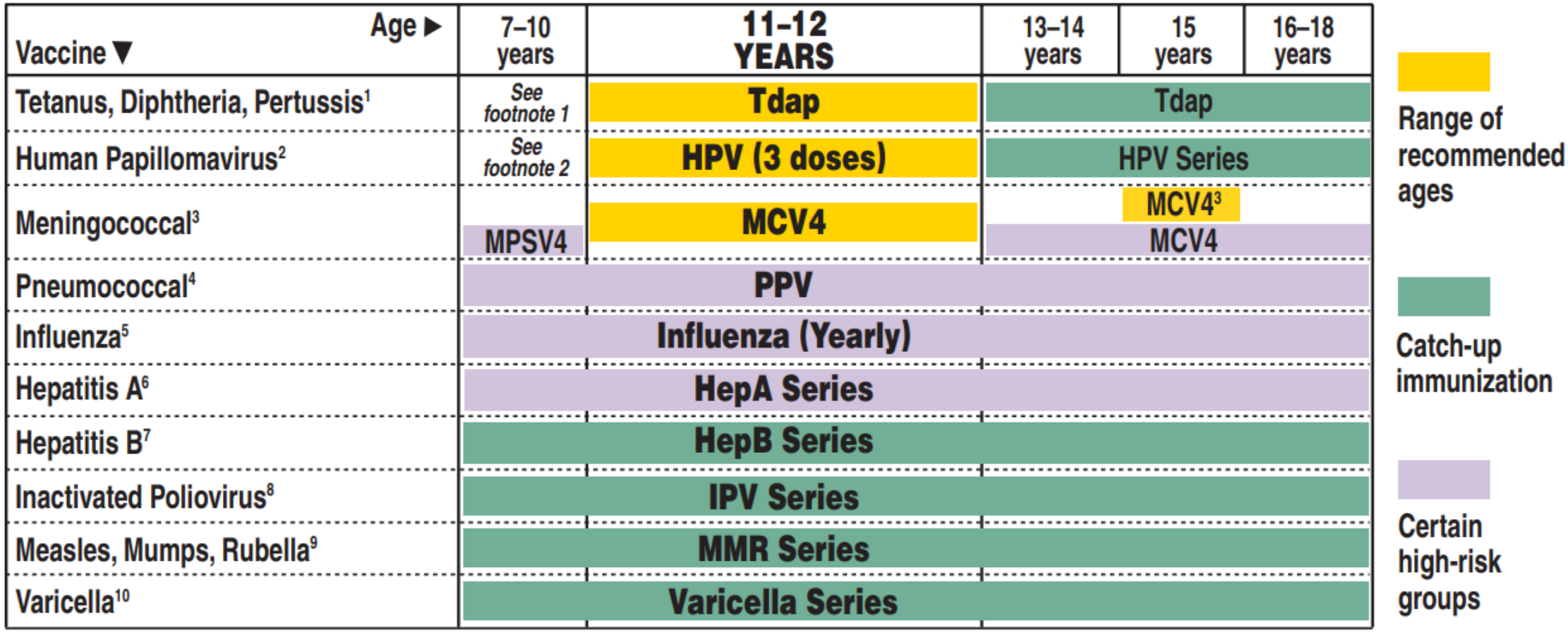
Middleman AB, Rosenthal SL, Rickert VI, et al. J Adolesc Health. 2006;38(3):321-327.

Adolescent vaccination recommendations

Year of Recommendation	Vaccine	Recommended Age
1995	Td	11–12 yrs
2005	Tdap, MenACWY	11–12 yrs
2006	HPV	11–12 yrs
2010	MenACWY booster	16 yrs
2015	MenB*	16–18 yrs preferred

*shared clinical decision-making and individuals who are at increased risk

Representation of HPV vaccination recommendations on child and adolescent immunization schedule, 2007



https://www.cdc.gov/mmwr/PDF/wk/mm5551-Immunization.pdf

Representation of HPV vaccination recommendations on child and adolescent immunization schedule, 2017

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	
HPV														See footnote 13			

Range of recommended ages for all children

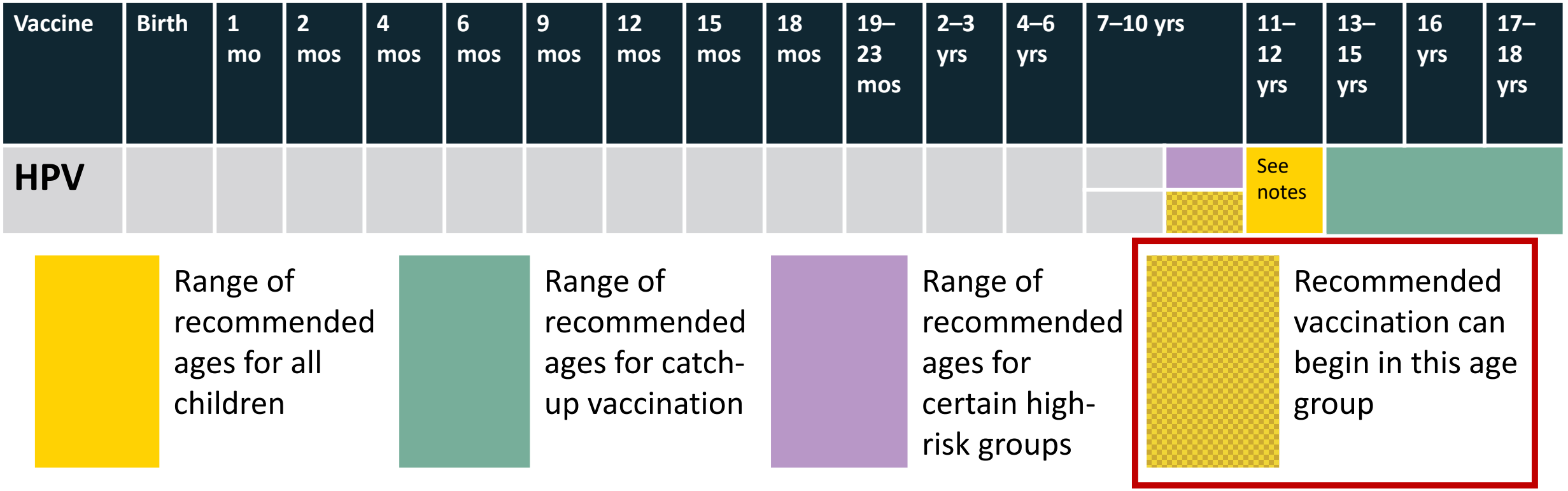
Range of recommended ages for catch-up immunization

Range of recommended ages for certain high-risk groups

Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical decision making

https://www.cdc.gov/vaccines/hcp/imz-schedules/downloads/past/2017-child.pdf

Representation of HPV vaccination recommendations on Table 1 of the child and adolescent immunization schedule, 2022–2025



Notes and full schedule available at: https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-age.html

Policy question

Should the ACIP recommendations state:

HPV vaccination is routinely recommended at age 9–12 years

instead of

HPV vaccination is routinely recommended at age 11 or 12 years; vaccination can be given starting at age 9 years

Evidence to Recommendations (EtR) Framework

EtR Domain	Question
Public Health Problem	Is the problem of public health importance?
Benefits and Harms	How substantial are the desirable anticipated effects? How substantial are the undesirable anticipated effects? Do the desirable effects outweigh the undesirable effects? What is the overall certainty of this evidence for the critical outcomes?
Values	Does the target population feel that the desirable effects are large relative to undesirable effects? Is there important uncertainty about or variability in how much people value the main outcomes?
Acceptability	Is the intervention acceptable to key stakeholders?
Resource Use	Is the intervention a reasonable and efficient allocation of resources?
Equity	What would be the impact on health equity?
Feasibility	Is the intervention feasible to implement?

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Public Health Problem

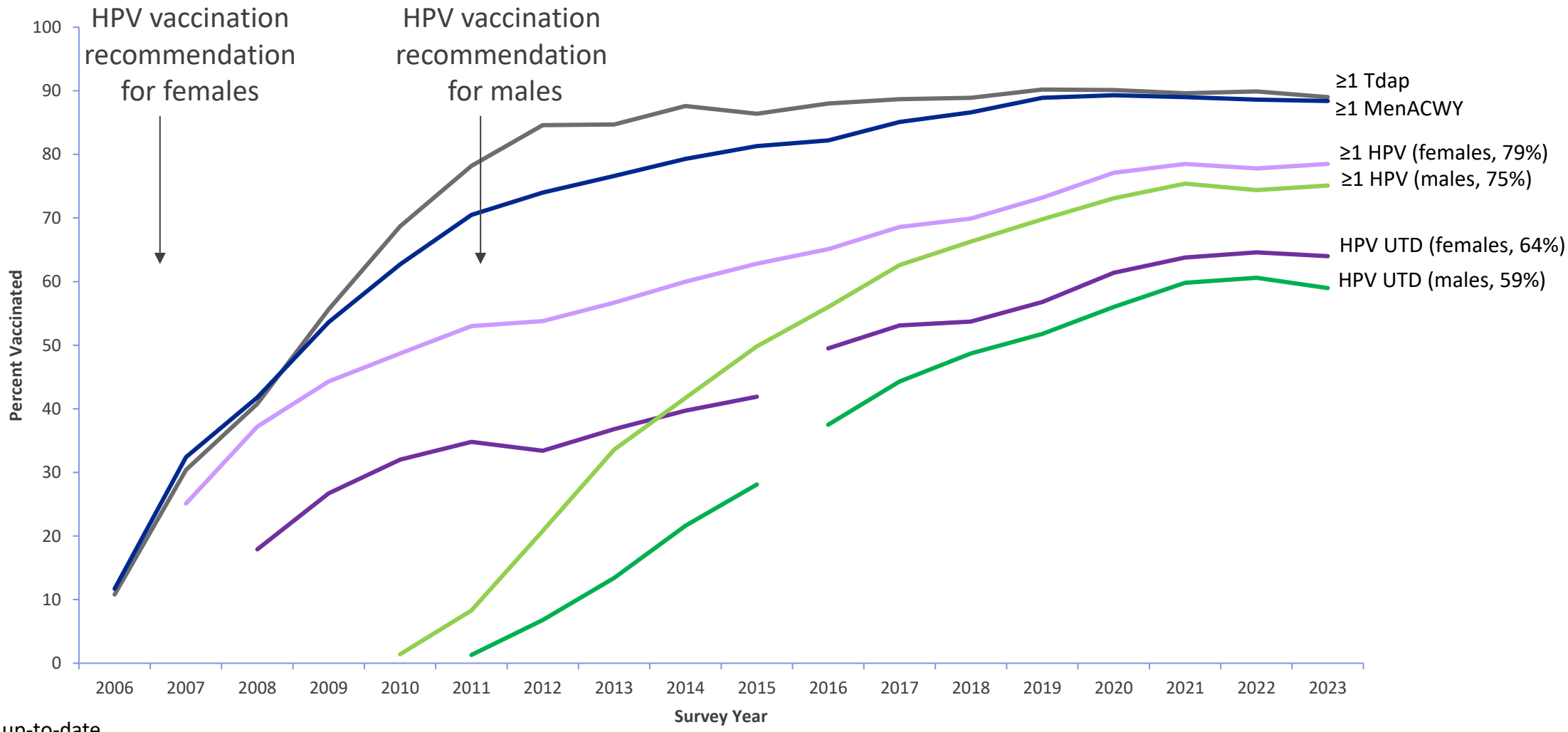
Is HPV-related disease of public health importance?

Estimated HPV-associated and HPV-attributable cancer cases per year, United States, 2017–2021

Cancer site	Number of HPV-associated cancers	Percentage probably caused by any HPV type	Estimated number probably caused by any HPV type*		
			Female	Male	Both sexes
Cervix	11,959	91%	10,800	0	10,800
Vagina	898	75%	700	0	700
Vulva	4,418	69%	3,000	0	3,000
Penis	1,381	63%	0	900	900
Anus**	7,854	91%	5,000	2,200	7,200
Oropharynx	21,474	70%	2,300	12,900	15,200
TOTAL	**47,984**	**79%**	**21,800**	**16,000**	**37,800**

*Estimates were rounded to the nearest 100. Estimated counts might not sum to total because of rounding.
**Includes anal and rectal squamous cell carcinomas
Sources: https://www.cdc.gov/cancer/hpv/cases.html and http://www.cdc.gov/cancer/dataviz

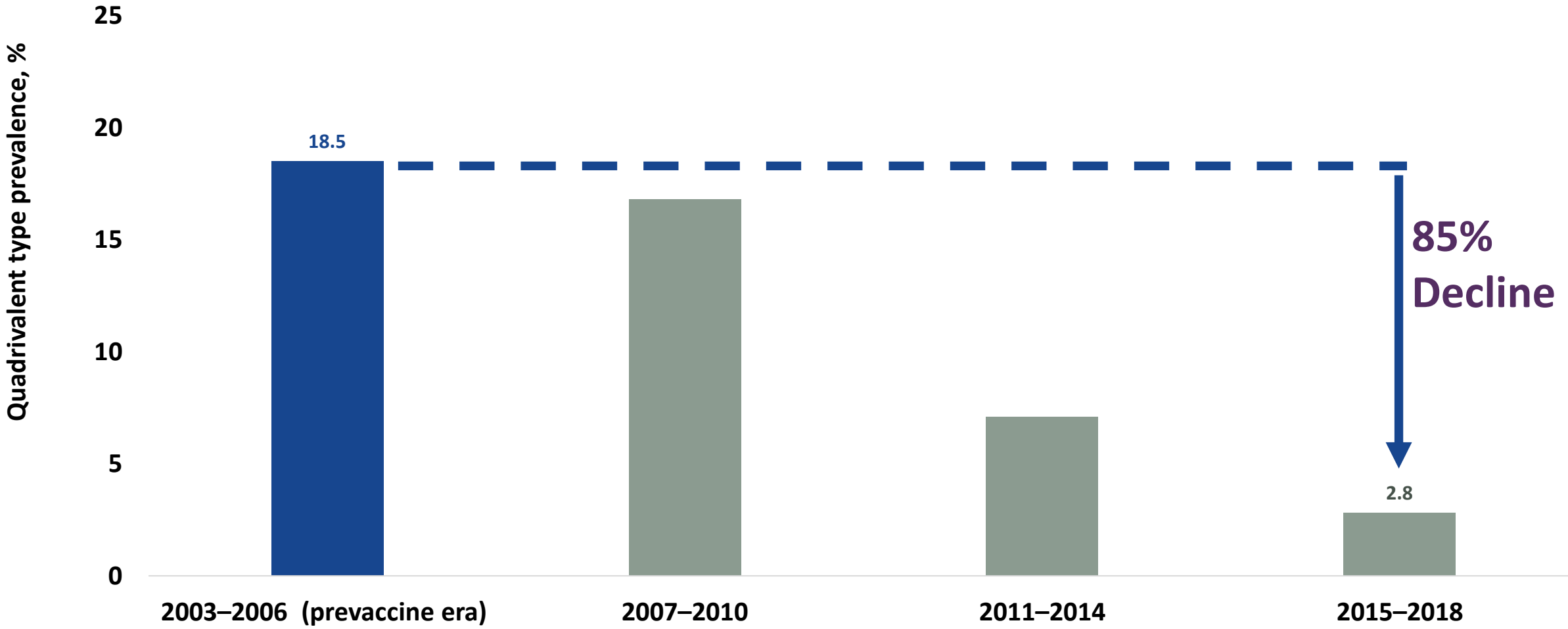
Estimated vaccination coverage, adolescents aged 13–17 years, National Immunization Survey-Teen, United States, 2006–2023



UTD: up-to-date

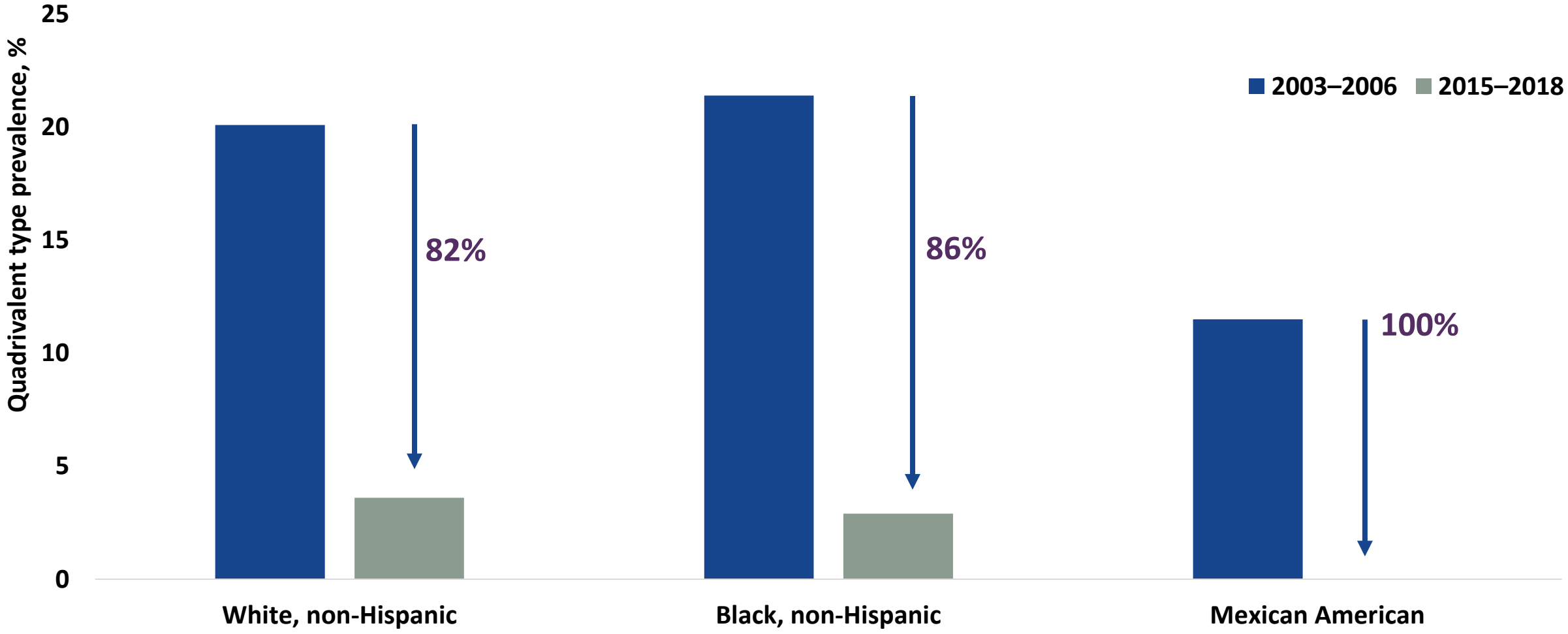
Pingali C, Yankey D, Chen M, et al. MMWR. 2024;73(33):708-714.

Quadrivalent HPV vaccine-type prevalence declined 85% among 14–24-year-old sexually experienced females



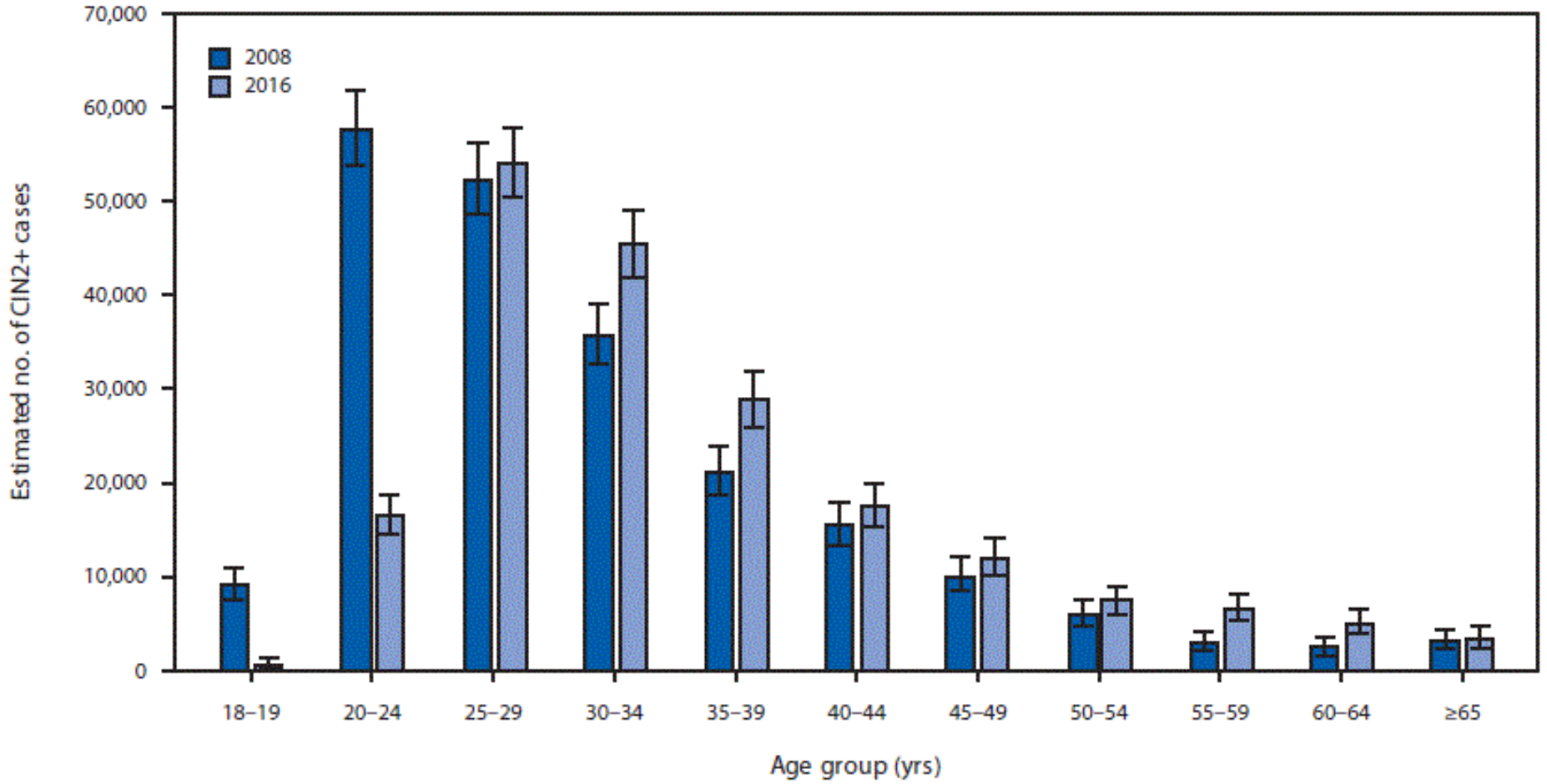
Rosenblum HG, Lewis RM, Gargano JW, Querec TD, Unger ER, Markowitz LE. Ann Intern Med. 2022;175(7):918-926.

Quadrivalent HPV vaccine-type prevalence declined >80% among 14–24-year-old sexually experienced females in different racial/ethnic groups



Stefanos R, Lewis RM, Querec TD, Gargano JW, Unger ER, Markowitz LE. Hum Vaccin Immunother. 2024;20(1):2308378.

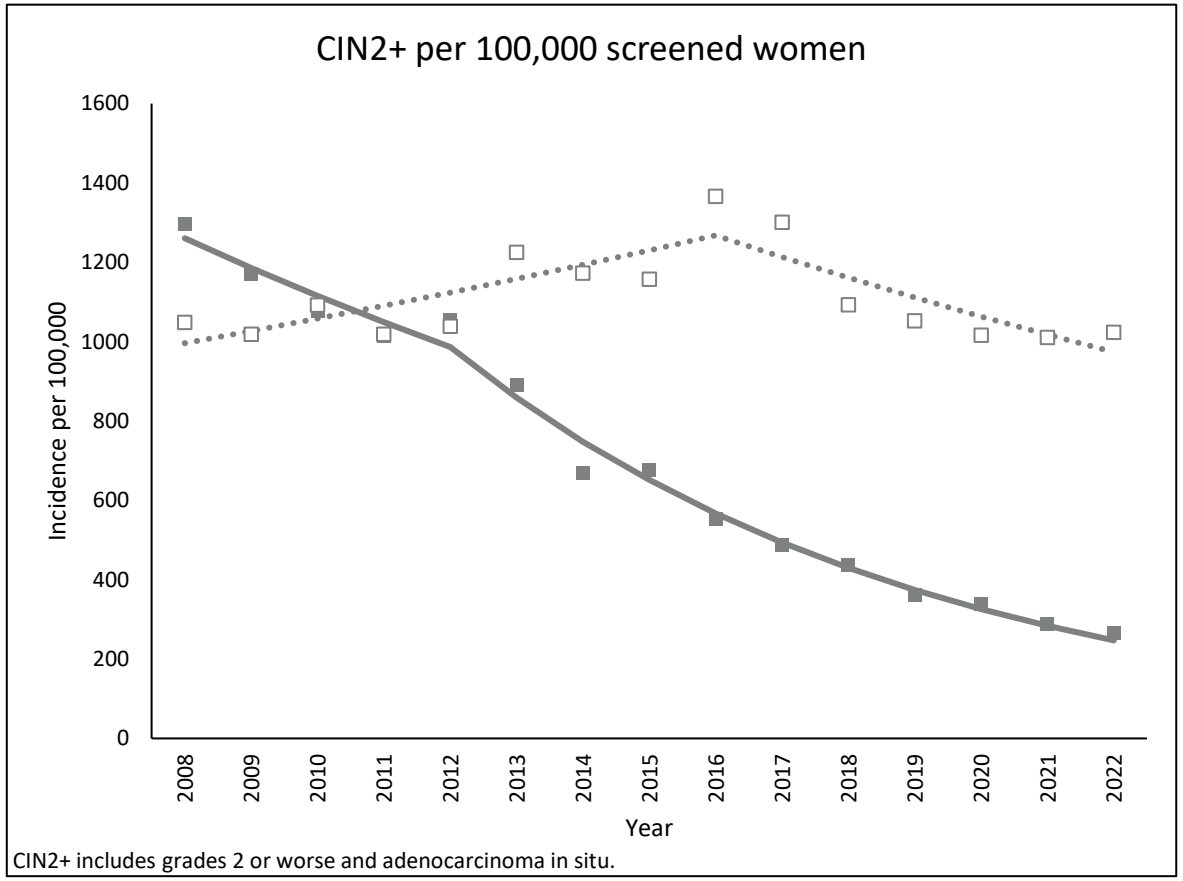
Estimated number of cervical precancer (CIN2+) cases per year, United States, 2008 and 2016

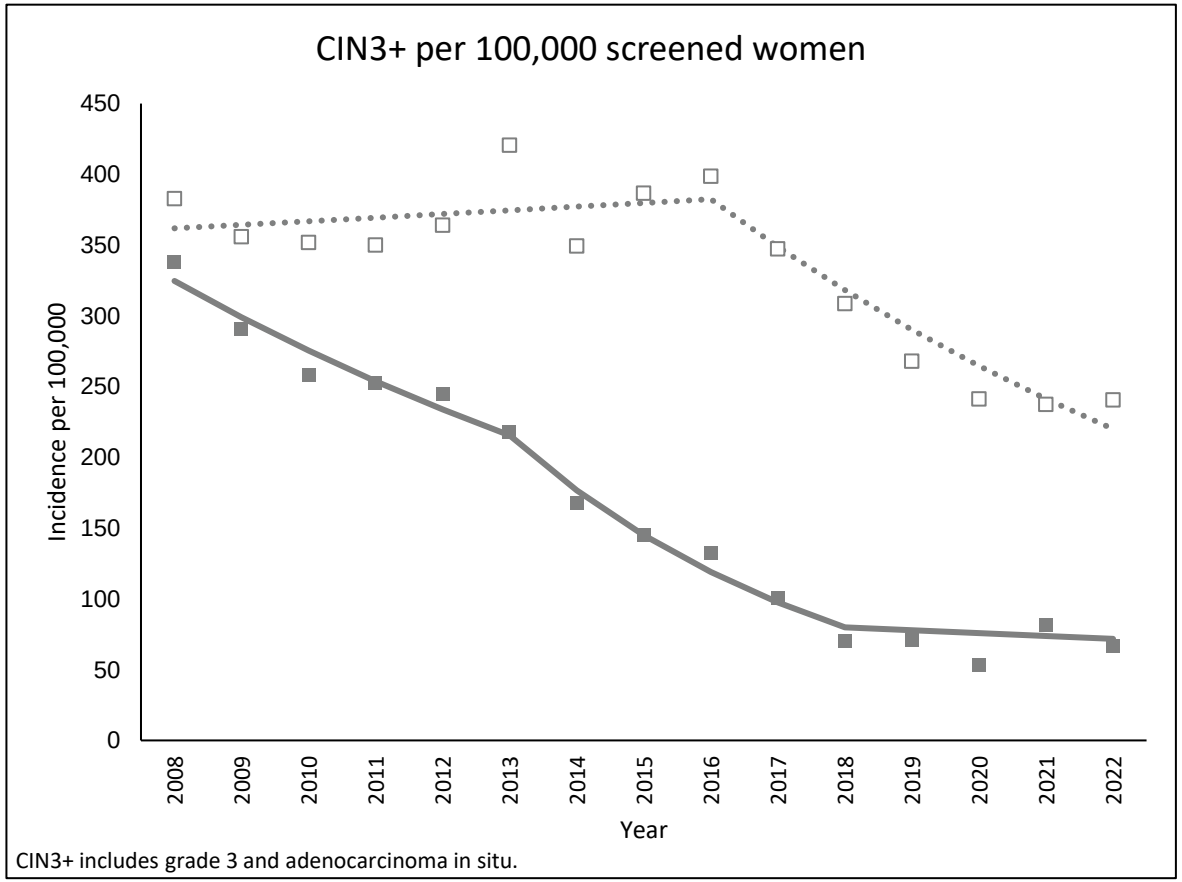


Error bars indicate range of low and high estimates based on lower-incidence and higher-incidence sites.

McClung NM, Gargano JW, Park IU, et al. MMWR. 2019;68(15):337-343.

CIN2+ and CIN3+ declined in young women, HPV-IMPACT,* 2008–2022



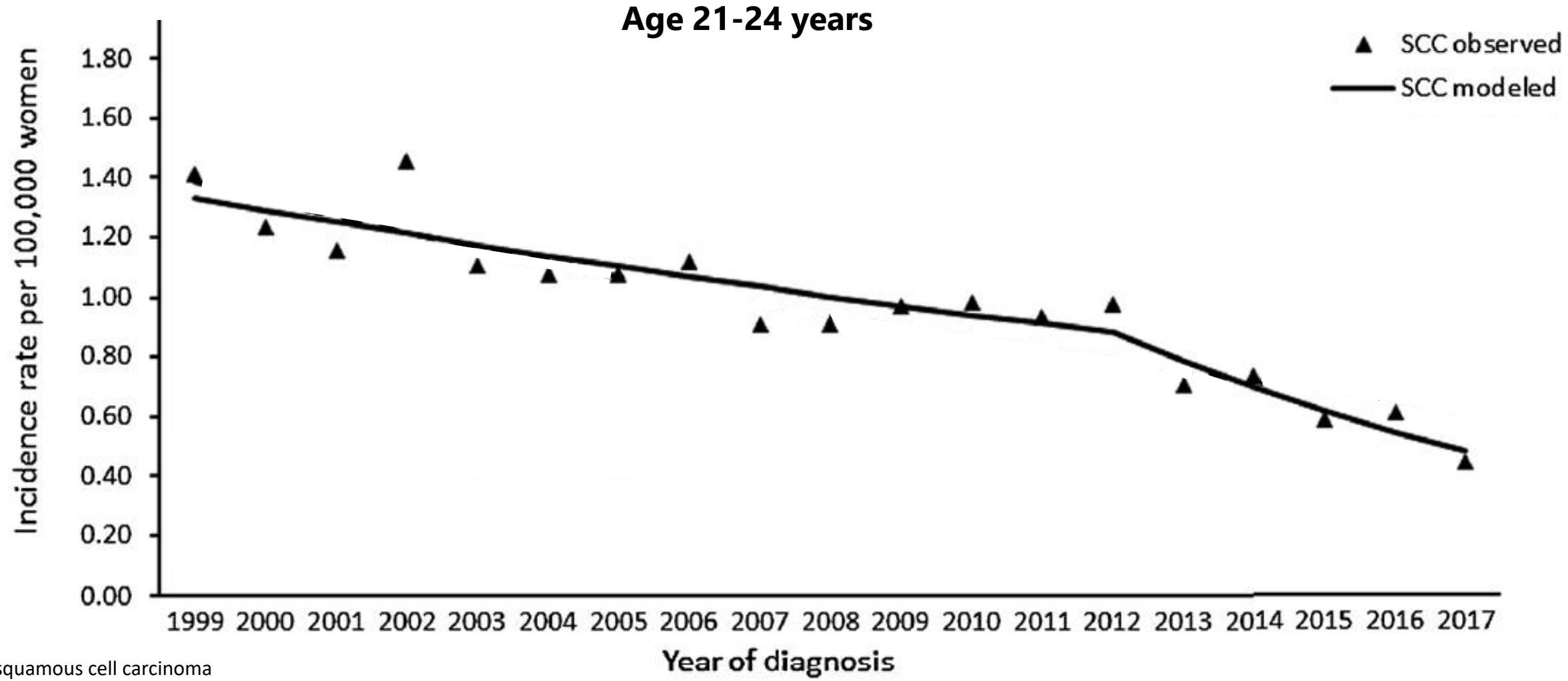


20–24-year-olds observed 25–29-year-olds observed 20–24-year-olds modeled 25–29-year-olds modeled

*HPV-IMPACT: Human Papillomavirus Vaccine Impact Monitoring Project https://www.cdc.gov/hpv-impact/about/index.html

Gargano JW, Stefanos R, Dahl RM, et al. MMWR. 2025;74(6):96-101.

Cervical cancer declined in young women, United States Cancer Statistics, 1999–2017



SCC: squamous cell carcinoma

Mix JM, Van Dyne EA, Saraiya M, Hallowell BD, Thomas CC. Cancer Epidemiol Biomarkers Prev. 2021;30(1):30-37.

Estimated costs of HPV-attributable disease

- **CDC estimated annual direct medical costs of HPV-attributable disease in 2020 US dollars, published in 2023.**
- **Annual total cost of HPV-attributable disease is $9.01 billion.**
- **Annual total cost due to treatment is $4.05 billion.**

Clay PA, Thompson TD, Markowitz LE, Ekwueme DU, Saraiya M, Chesson HW. Vaccine. 2023;41(14):2376-2381.

Summary: Public Health Problem

- **37,800 HPV-attributable cancers are diagnosed in the US annually.**
- **HPV vaccination coverage lags behind other adolescent vaccinations.**
- **HPV vaccination has led to decreases in infection prevalence and cervical precancer incidence, and there are early signs that vaccination has decreased cervical cancer incidence in young women.**
- **Total cost of HPV-related disease is $9.01 billion.**

Public Health Problem: Work Group Interpretation

Is HPV-related disease of public health importance?

○ No ○ Probably No ○ Probably Yes **○ Yes** ○ Varies ○ Don't Know

Benefits and Harms

How substantial are the desirable anticipated effects of changing the wording of the age for routine vaccination to 9–12 years?

How substantial are the undesirable anticipated effects of changing the wording of the age for routine vaccination to 9–12 years?

Do the desirable effects outweigh the undesirable effects of changing the wording of the age for routine vaccination to 9–12 years?

Potential benefits and harms

Benefits

- Clarity
- Flexibility

Harms

- Separation from adolescent platform
- Prompts at age 9 may not be acceptable to some providers

Benefit: Wording change would increase clarity

HPV vaccination is routinely recommended at age 9–12 years

instead of

HPV vaccination is routinely recommended at age 11 or 12 years; vaccination can be given starting at age 9 years

Benefit: Wording change may increase flexibility for providers who would like to vaccinate at age 9

- **Some partners are interested in vaccination at age 9**
- **9–12 wording would change Clinical Decision Support for Immunization (CDSi) resources and may increase flexibility for providers who are interested in vaccination at age 9**

CDSi implications

- **Current:**
  - Minimum age: 9 years
  - Earliest recommended age: 11 years

Prompt for HPV vaccination occurs at earliest recommended age (11 years)

- **If change adopted:**
  - Minimum age: 9 years
  - Earliest recommended age: 9 years

Prompt for HPV vaccination occurs at earliest recommended age (9 years)

https://www.cdc.gov/iis/cdsi/index.html

Representation of HPV vaccination recommendations on Table 1 of the child and adolescent immunization schedule

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	17–18 yrs
HPV														See notes			

Range of recommended ages for all children

Range of recommended ages for catch-up vaccination

Range of recommended ages for certain high-risk groups

Recommended vaccination can begin in this age group

Notes and full schedule available at: https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-age.html

Potential representation of HPV vaccination recommendations on Table 1 of the child and adolescent immunization schedule

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	17–18 yrs
HPV													See notes				

Range of recommended ages for all children

Range of recommended ages for catch-up vaccination

Policy question is changing the wording of recommended age to 9–12 and not changing the recommended age to 9–10

- **Age 9 Systematic Review*:**
  - Higher vaccination series completion by age 13** when initiating at age 9–10 vs. 11–12, but study limitations preclude a cause-and-effect interpretation.
  - A small percentage of vaccinated adolescents had initiated at age 9–10 in most studies (2–8%).
  - There may be differences between families/providers vaccinating at age 9–10 and those vaccinating at age 11–12.
  - Due to multi-pronged interventions in QI studies, it is unclear if the component focused on initiation at ages 9–10 was responsible for increases in coverage.

*https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/04-hpv-Brewer-508.pdf
**Some studies evaluated completion, but not by age 13 years

Harm: Wording change may affect adolescent platform

- Adolescent platform was established in 1996
- HPV was licensed and recommended in 2006 as part of the adolescent platform
- Adolescent platform (11–12 years): HPV, Tdap, and MCV

Simultaneous administration of HPV vaccine with other recommended vaccines among adolescents aged 13–17 years who initiated HPV vaccine (N=12,995) — NIS-Teen, United States, 2023

Vaccinations in a single visit	n	Weighted %* (95% CI)
Received **HPV vaccine only**	3,874	30.5 (29.0-32.1)
Received **HPV vaccine and one or more vaccine**(s) (Tdap, MenACWY, and/or flu vaccine)	9,121	69.5 (67.9-71.0)
Received **Tdap and MenACWY and HPV vaccines**	6,579	47.8 (46.0-49.5)

NIS-Teen: National Immunization Survey-Teen
*Percentages were calculated among only those adolescents who initiated the HPV vaccine (12,995)

Harm: Wording change may lead to system changes that are not acceptable to some providers

- **1,047 primary care professionals surveyed on perceived advantages and disadvantages of recommending HPV vaccine at age 9:**
  - Most commonly perceived disadvantage of recommending vaccination at age 9 was parents' lack of readiness (73%).
- **2,527 primary care providers and clinical staff randomly assigned to consider the perceived benefits of HPV vaccination at age 9 versus age 12:**
  - Providers were less likely to identify "parents ready to talk about HPV vaccine" as a perceived benefit for vaccination at age 9 vs. age 12.

Kong WY, Huang Q, Thompson P, Grabert BK, Brewer NT, Gilkey MB. Acad Pediatr. 2022;22(4):573-580.
Kahn BZ, Reiter PL, Kritikos KI, Gilkey MB, Queen TL, Brewer NT. Hum Vaccin Immunother. 2023;19(1):2172276.

Summary: Benefits and Harms

- **Changing the wording of the age for routine vaccination to 9–12 may provide clarity and flexibility to support those providers who are interested in vaccination at age 9.**
  - Vaccination at ages 9–10 years is associated with increases in completion by age 13* but due to limitations in studies, it is unclear if this association is causal.
  - QI/Intervention studies have found increases in initiation at all ages and increased completion but unclear contribution of vaccination at ages 9–10 due to multiple interventions implemented simultaneously.
- **48% of adolescents receive the HPV vaccine as part of the adolescent platform and 70% receive it with one or more vaccines; changing the wording of the age for routine vaccination may negatively affect the adolescent platform.**
- **Changing the wording to 9–12 may lead to system changes or prompts to providers for vaccination at age 9 which some may not find acceptable.**

*Some studies evaluated completion, but not by age 13 years

Benefits and Harms: Work Group Interpretation

How substantial are the *desirable* anticipated effects of changing the wording of the age for routine vaccination to 9–12 years?

○ Minimal ○ Small **○ Moderate** ○ Large ○ Varies ○ Don't Know

How substantial are the *undesirable* anticipated effects of changing the wording of the age for routine vaccination to 9–12 years?

○ Minimal ○ Small ○ Moderate ○ Large ○ Varies ○ Don't Know

Benefits and Harms: Work Group Interpretation

Do the *desirable* *effects outweigh the* *undesirable* *effects* of changing the wording of the age for routine vaccination to 9–12 years?

- ○ **Favors change in wording**
- ○ Favors current wording
- ○ Favors both wording options equally
- ○ Varies
- ○ Don't Know

Acceptability/Values

Is changing the wording of the age for routine vaccination to 9–12 years acceptable to key stakeholders (e.g., providers, professional societies, or advocacy groups)?

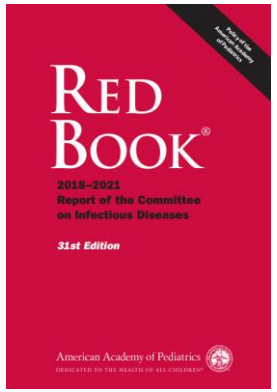
Do parents feel that the desirable effects of changing the wording to 9–12 are large relative to the undesirable effects of changing the wording?

Is there important uncertainty about, or variability in, how much parents value changing the wording to 9–12?

American Academy of Pediatrics Recommendations

Beginning in the 2018–2021 *Red Book*, HPV vaccination recommendation language was modified.

“The AAP recommends starting the series between the ages of 9 and 12 years, at an age that the pediatric health care professional deems optimal for acceptance and completion of the vaccination series.”



American Academy of Pediatrics. Red Book: 2024-2027 Report of the Committee on Infectious Diseases (33rd Edition)

HPV Vaccination Roundtable and American Cancer Society

- The National HPV Vaccination Roundtable is a coalition of about 90 organizations.
- The National HPV Vaccination Roundtable has encouraged providers to vaccinate at age 9 years.

https://hpvroundtable.org/
https://hpvroundtable.org/wp-content/uploads/2023/05/2021-HPV-VACs-Impact-Report.pdf
Foley S, Nkonga J, Fisher-Borne M. Hum Vaccin Immunother. 2023;19(1):2167906.

Adolescent medicine stakeholder comments

Adolescent Immunizations: A Position Paper of the Society for Adolescent Medicine:

"The development of three distinct adolescent vaccination visits/platforms for adolescents (11–12-year visit, 14–15-year visit, and a 17–18-year visit) to integrate and emphasize the role of vaccination in already recommended comprehensive health care screening and provision visits. The 11–12-year platform is the primary immunization platform promulgated by ACIP."

Potential Changes to the Adolescent Immunization Schedule: Implications for the Stability of Adolescent Immunization Platform Visits:

"Moving HPV vaccination to ages 9–10 years weakens the established platform…which could unintentionally result in lower adolescent vaccination rates overall."

Middleman AB, Rosenthal SL, Rickert VI, et al. J Adolesc Health. 2006;38(3):321-327.
Middleman AB, Zimet GD. J Adolesc Health. 2024;75(4):538-542.

Summary: provider behavior/perspective studies (N=5)

2 Clinician Interviews:

- 1 intervention study: providers/nurses reported a positive experience with recommending vaccination at age 9–10
- 1 qualitative study: providers/staff had mixed opinions on initiating at age 9

3 Clinician Surveys:

- 1 survey: among those not currently recommending at age 9, 61% willing to do so
- 1 survey: strong provider recommendations differed by age group of patient and specialty of provider
- 1 survey: provider recommendation at age 9 depended on recommendation framing

Biancarelli DL, Drainoni ML, Perkins RB. J Pediatr. 2020;217:92-97.
Vielot NA, Lane RM, Loefstedt K, et al. Pilot Feasibility Stud. 2023;9(1):153.
Kong WY, Huang Q, Thompson P, Grabert BK, Brewer NT, Gilkey MB. Acad Pediatr. 2022;22(4):573-580.
Lake P, Fuzzell L, Brownstein NC, et al. Hum Vaccin Immunother. 2023;19(1):2181610.
Kahn BZ, Reiter PL, Kritikos KI, Gilkey MB, Queen TL, Brewer NT. Hum Vaccin Immunother. 2023;19(1):2172276.

Summary: caregiver behavior/perspective studies (N=2)

2 Caregiver Studies:

- Few caregivers reported receiving information or recommendations to vaccinate children before age 11.
- Most reported willingness to vaccinate at ages 9–10.

Aragones A, Gany F, Kaplan A, Bruno D. Hum Vaccin Immunother. 2022;18(6):2136444.
Kohler RE, Wagner RB, Careaga K, Btoush R, Greene K, Kantor L. Hum Vaccin Immunother. 2023;19(3):2270842.

Summary: Acceptability/Values

- AAP recommendation language uses ages 9–12.
- Some stakeholders/advocacy groups are interested in vaccination at age 9 and changing the wording will clarify that vaccination at age 9 is consistent with ACIP recommendations.
- Some stakeholders have raised concerns that changing the wording will erode the adolescent platform.
- In limited number of studies, vaccination at ages 9–10 years was acceptable to providers and parents.

Acceptability: Work Group Interpretation

Is changing the wording of the age for routine vaccination to 9–12 years acceptable to key stakeholders (e.g., providers, professional societies, or advocacy groups)?

○ No ○ Probably No ○ **Probably Yes** ○ **Yes** ○ Varies ○ Don't Know

Values: Work Group Interpretation

Do parents feel that the desirable effects of changing the wording to 9–12 are large relative to the undesirable effects of changing the wording?

- ○ No
- ○ Probably No
- ○ Probably Yes
- ○ Yes
- ○ Varies
- ○ **Don't Know**

Is there important uncertainty about, or variability in, how much parents value changing the wording to 9–12?

- ○ Important uncertainty or variability
- ○ **Probably important uncertainty or variability**
- ○ **Probably not important uncertainty or variability**
- ○ No important uncertainty or variability
- ○ No known undesirable outcomes

Minority opinion

Plurality opinion

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Feasibility	Is the intervention feasible to implement?

Acknowledgements

Sarah Brewer, PhD, MPH
Carla DeSisto, PhD, MPH
Julia Gargano, PhD
Lauri Markowitz, MD

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov