HPV Vaccination: Trends & Updates

Nita Lee, MD, MPH

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Hello!

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AT THE FOREFRONT
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NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

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Learning Objectives

Understand the burden, trends and disparities of HPV related diseases and cancers.

Review the current data on HPV vaccine uptake efforts in IL and nationally.

Review HPV vaccine indications, gaps, opportunities and best practices of HPV vaccination for normal risk and special populations.

Review data on the effects of HPV vaccine on pre-cancer and cancer.

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Understanding the burden, trends and disparities of HPV related diseases and cancers.

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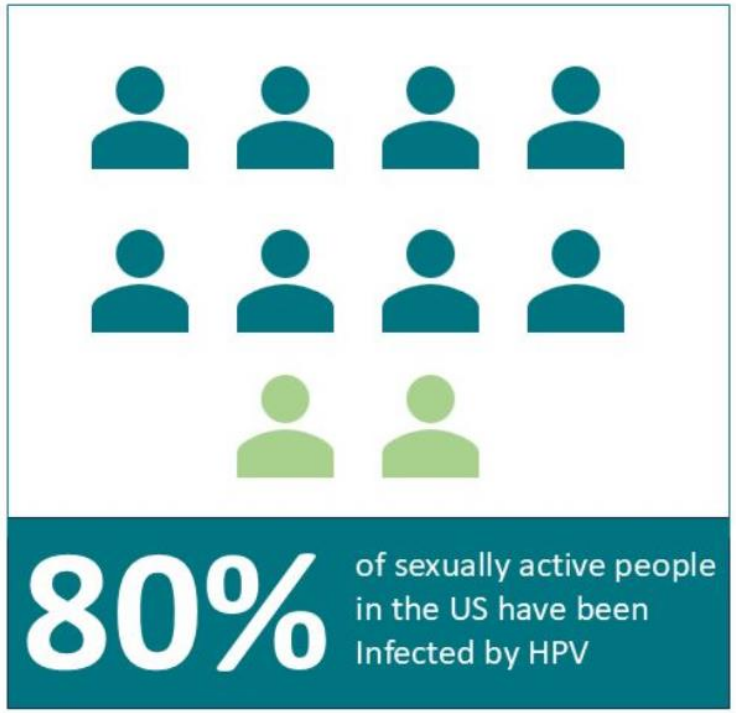
The Why?



Over 37,000 cases in US of HPV related cancers each year can be prevented.

Morbidity and Long term Sequelae of Treatments

Deaths due to HPV Cancers

All Male and Female are at Risk

Pediatrics and Primary Care in Primary Prevention of HPV diseases and cancer

Primary prevention:

HPV Vaccine

Secondary prevention:

Surgical Treatment of pre-cancer

Many diseases with no screen

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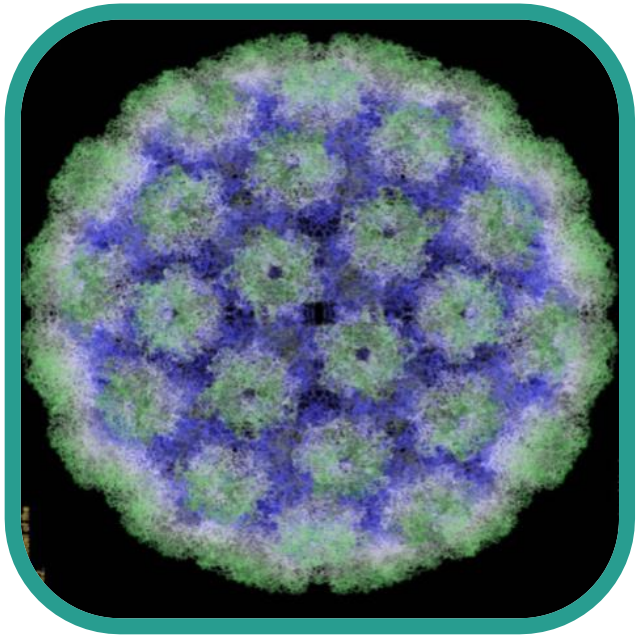
HPV Review

- HPV stands for human papillomavirus.
- There are more than 200 types HPV.
- HPV can be harmless and often goes away by itself, but some types of HPV can lead to genital warts or certain types of cancer.
- Two types of HPV (types 6 and 11) cause most cases of genital warts.
- HPV (types 16 and 18), high-risk HPV, lead to the majority of cancer cases.



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HPV Review

- Currently most common sexually transmitted infection.
- Highest prevalence within 2-5 years of initiation of sexual activity.
- 2nd peak in the 4-5th decade.
- ~10% of infections are not cleared within 2 years.

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How is HPV Transmitted?

- Skin to skin contact.
- HPV types that are specific to genital areas are transmitted by skin to skin contact in the genital area.
- Considered a sexually transmitted disease.
- Mixed feelings about this classification and associated stigma.

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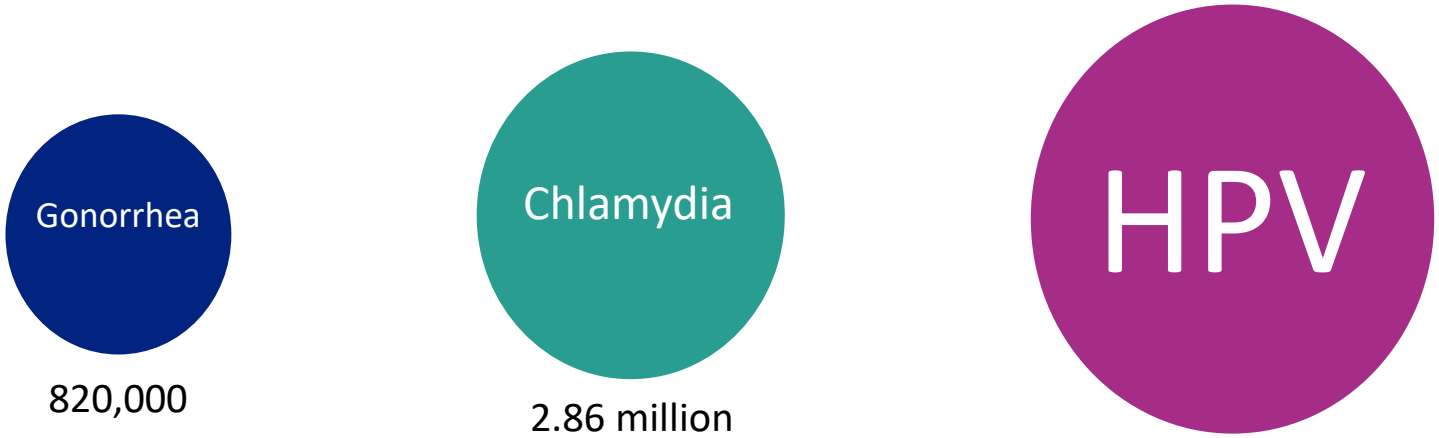
HPV is Common

- HPV is extremely common – nearly 80 million Americans are currently infected (~1 in 4).

New cases per year, as estimated by the CDC.



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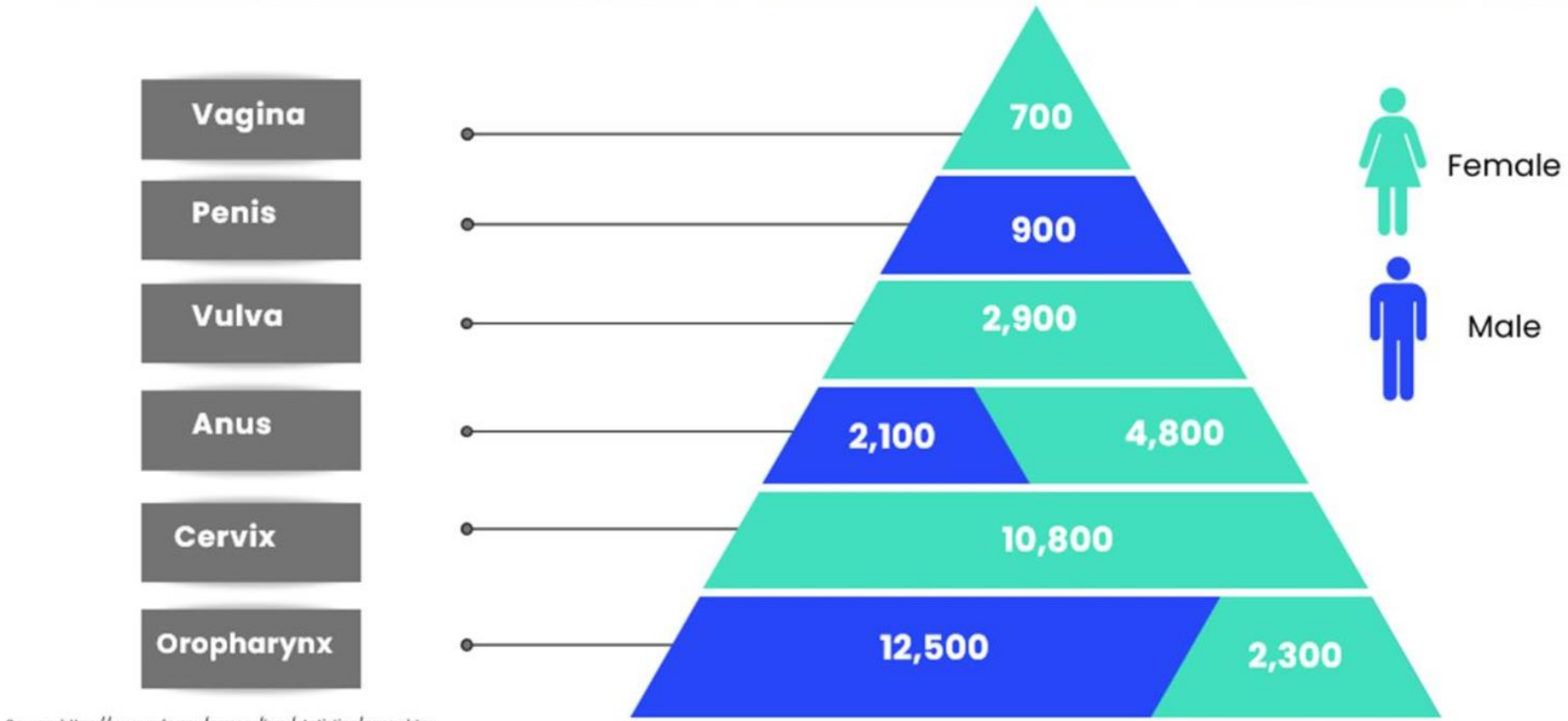
U.S. HPV-Attributable Cancer Cases: 37,000



Source: https://www.cdc.gov/cancer/hpv/statistics/cases.htm

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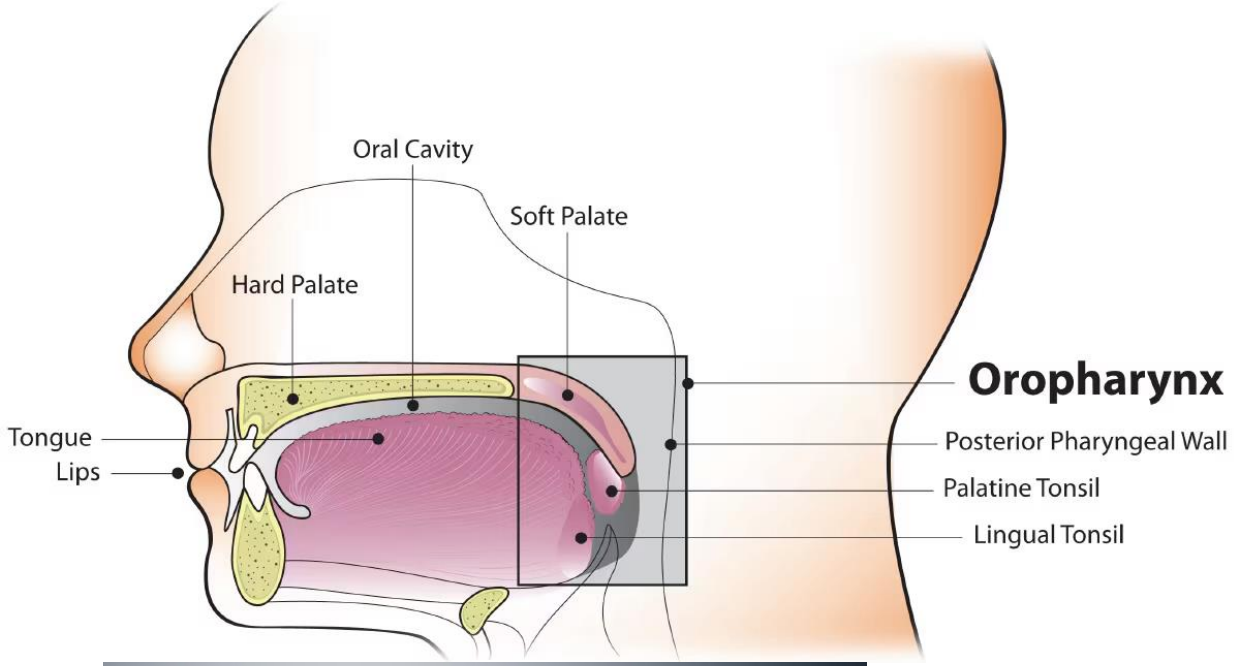
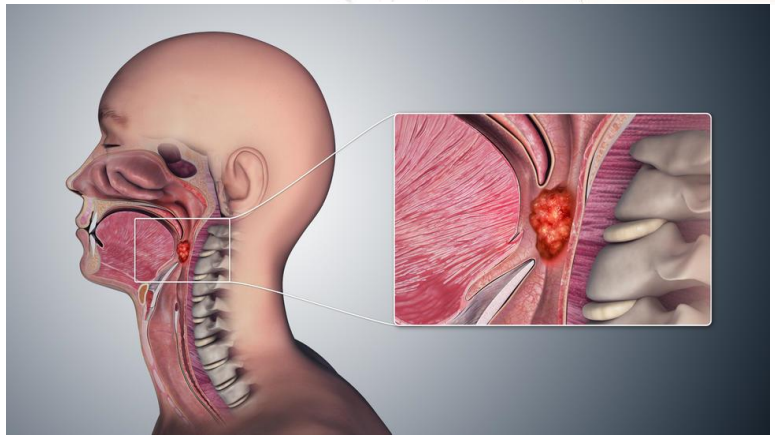
Data are from population-based cancer registries participating in CDC's National Program of Cancer Registries (NPCR) and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program for 2017 to 2021, covering 98% of the United States population.

HPV and Head and Neck Cancers





- HPV is thought to cause 60% to 70% of oropharyngeal cancers in the United States.
- Male > Female
- No screening tests
- Can present late stage with LN involvement
- Morbidity related to treatment

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HPV Head and Neck Cancer Treatment

Chemo-radiation

Surgery

Immunotherapy

HPV Head and Neck Cancer Treatment and Sequelae

PAIN

SWALLOWING DIFFICULTY

SPEECH PROBLEMS

NEUROPATHY

HEARING LOSS

LONG TERM DENTAL ISSUES AND TOOTH LOSS

PSYCHOSOCIAL STRESSORS

HPV infection oral is increasing

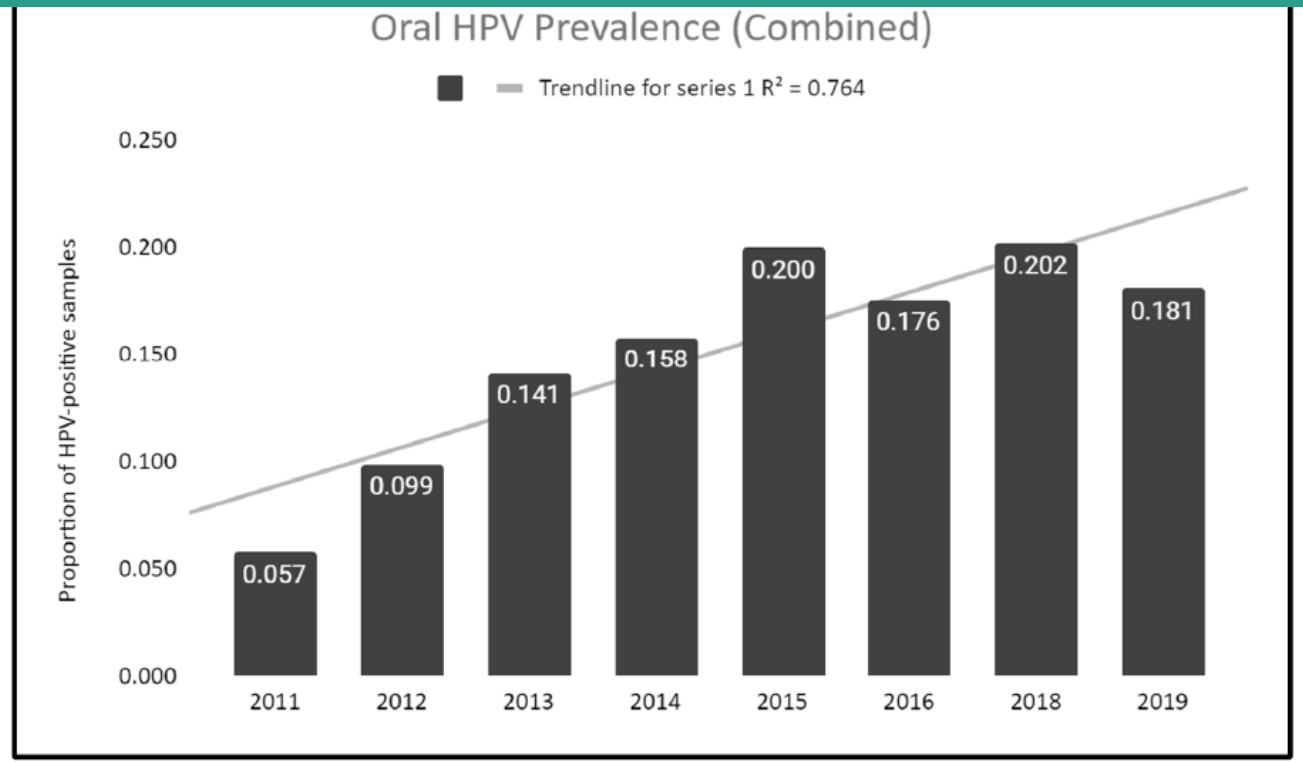


Figure 1. Change in prevalence of high-risk oral HPV over time. Analysis of both pediatric and adult patients revealed an increase in high-risk HPV of 3.17-fold from 5.7% in 2011 to 18.1% in 2019, with the coefficient of determination or $R^2 = 0.764$, suggesting a strong, positive correlation between more recent sample years and HPV-positive results.

Assessment of Oral Human Papillomavirus Prevalence in Pediatric and Adult Patients within a Multi-Ethnic Clinic Population

Melissa Solomon Kornhaber [1], Taylor Florence [2], Trexton Davis [2] and Karl Kingsley [3,*]

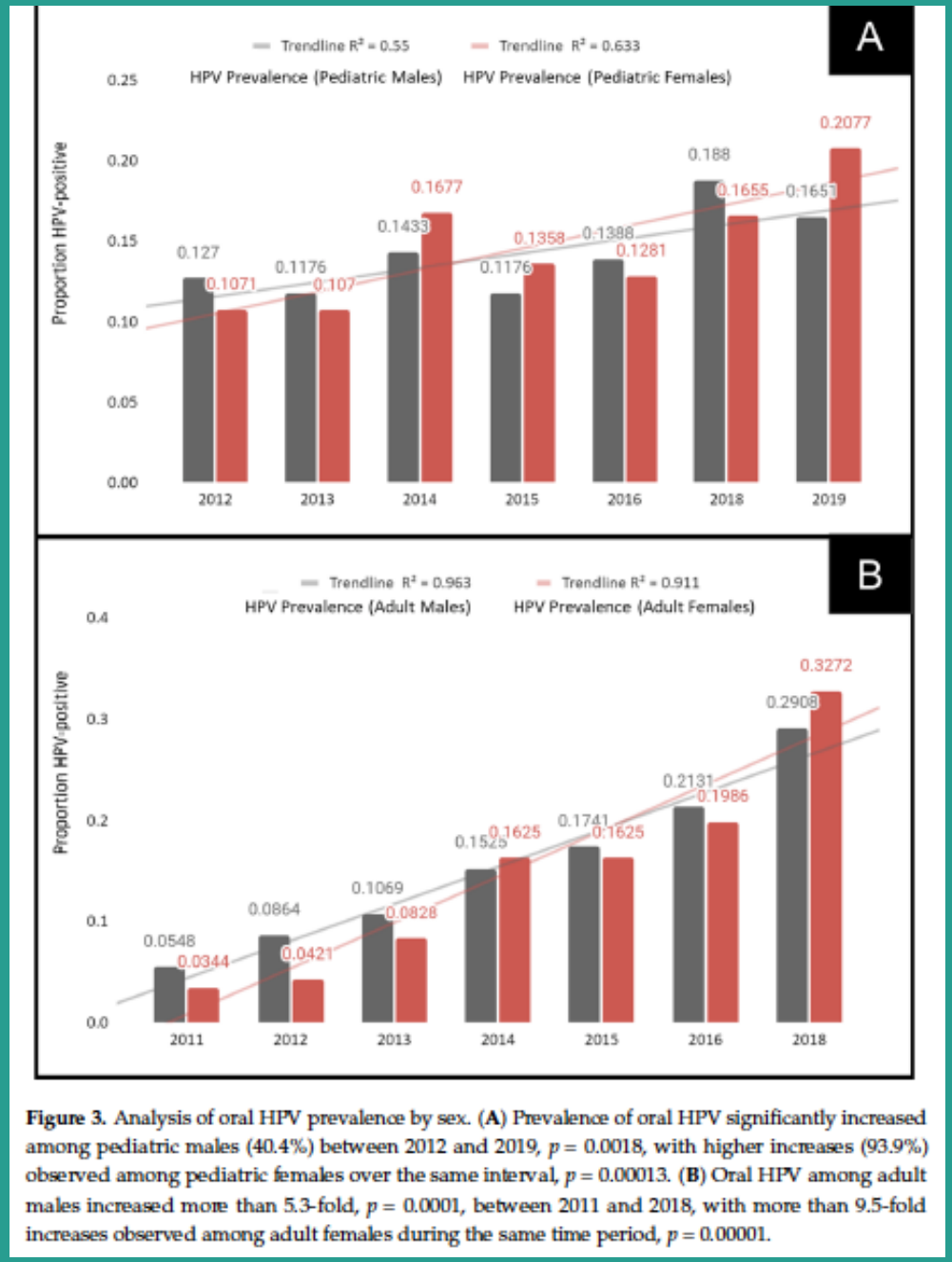
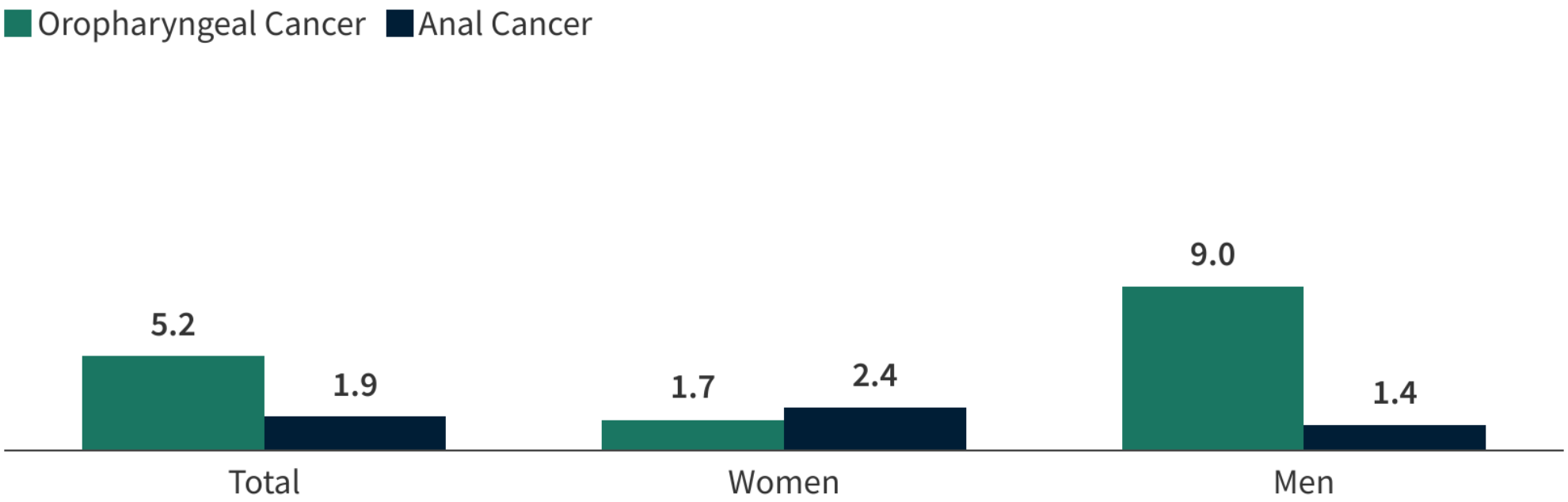


Figure 3. Analysis of oral HPV prevalence by sex. (**A**) Prevalence of oral HPV significantly increased among pediatric males (40.4%) between 2012 and 2019, $p = 0.0018$, with higher increases (93.9%) observed among pediatric females over the same interval, $p = 0.00013$. (**B**) Oral HPV among adult males increased more than 5.3-fold, $p = 0.0001$, between 2011 and 2018, with more than 9.5-fold increases observed among adult females during the same time period, $p = 0.00001$.

Figure 2

Rates of HPV-Associated Oropharyngeal and Anal Cancers Among Men and Women, 2015-2019

Age-adjusted Rates per 100,000 People



Source: CDC, United States Cancer Statistics, October 2022

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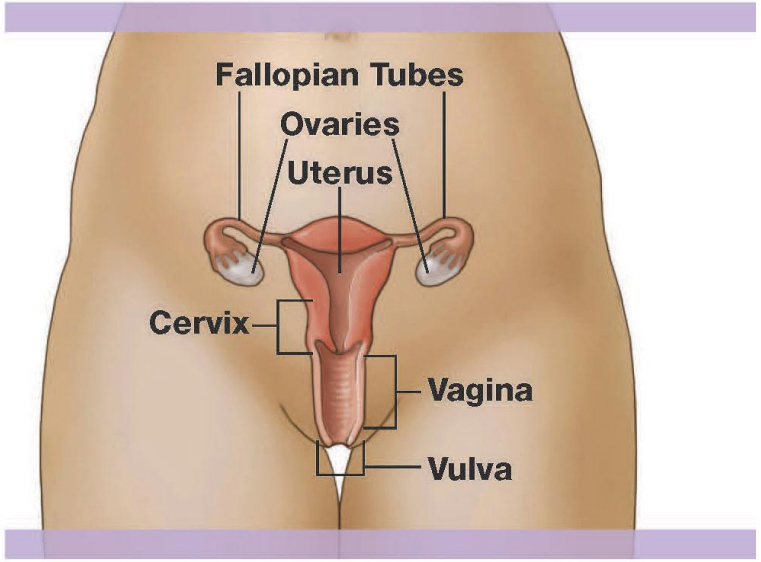
Facts: Cervical Cancer

- Cervix is the opening to the uterus or womb.
- Anyone with a cervix is at risk.
- 4th most common cancer among women globally.
- Most frequently diagnosed in women: 35 and 44.
  - Average age being 50.
- Most at risk if no pap or no pap in 5 years.
- ~11500+ new cases in US, 4000 die each year.
- Due to HPV infection with a high-risk type.
- Precancer can be caught/treated early.



PREVENTABLE and TREATABLE

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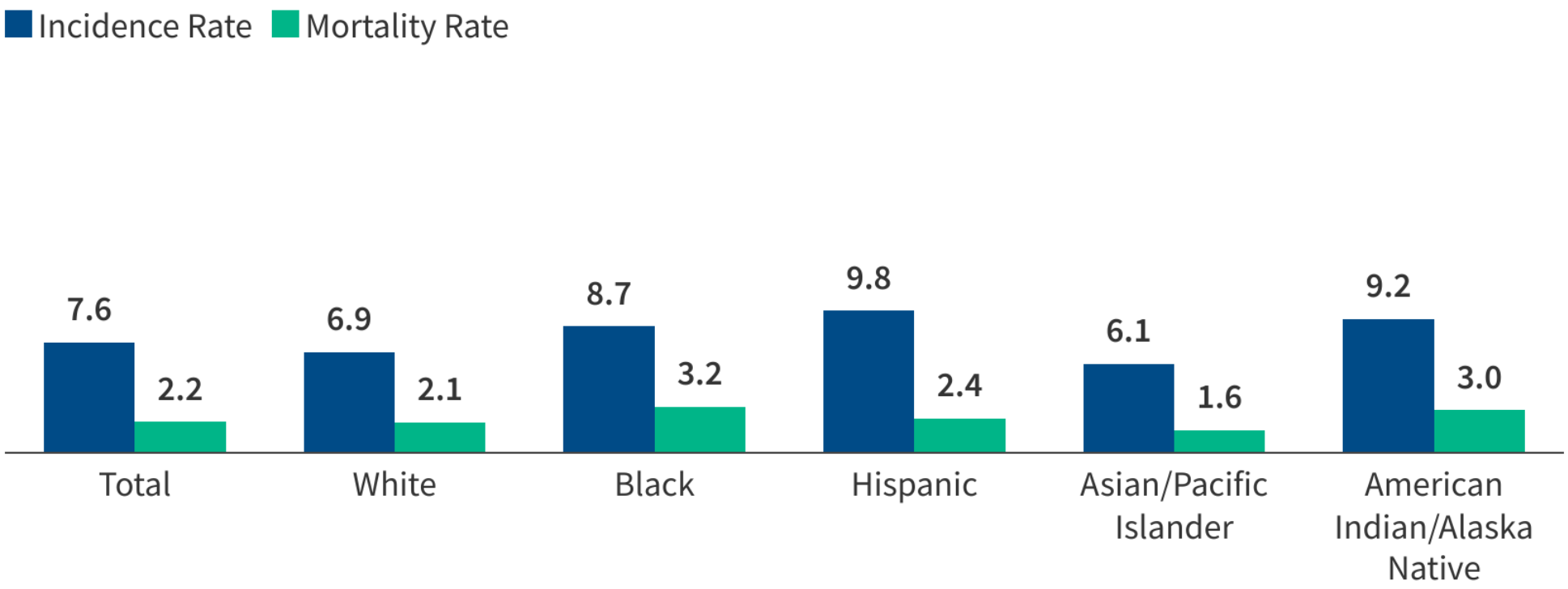
https://www.who.int/news-room/fact-sheets/detail/cervical-cancer

https://www.cancer.org/cancer/cervical-cancer/about/key-statistics.html#:~:text=The%20American%20Cancer%20Society's%20estimates,will%20die%20from%20cervical%20cancer.

Figure 1

Cervical Cancer Incidence and Mortality Rates by Race/Ethnicity, 2018-2022

Age-adjusted Rates per 100,000 People



Source: National Cancer Institute, SEER Cancer Stat Facts: Cervix Uteri Cancer.

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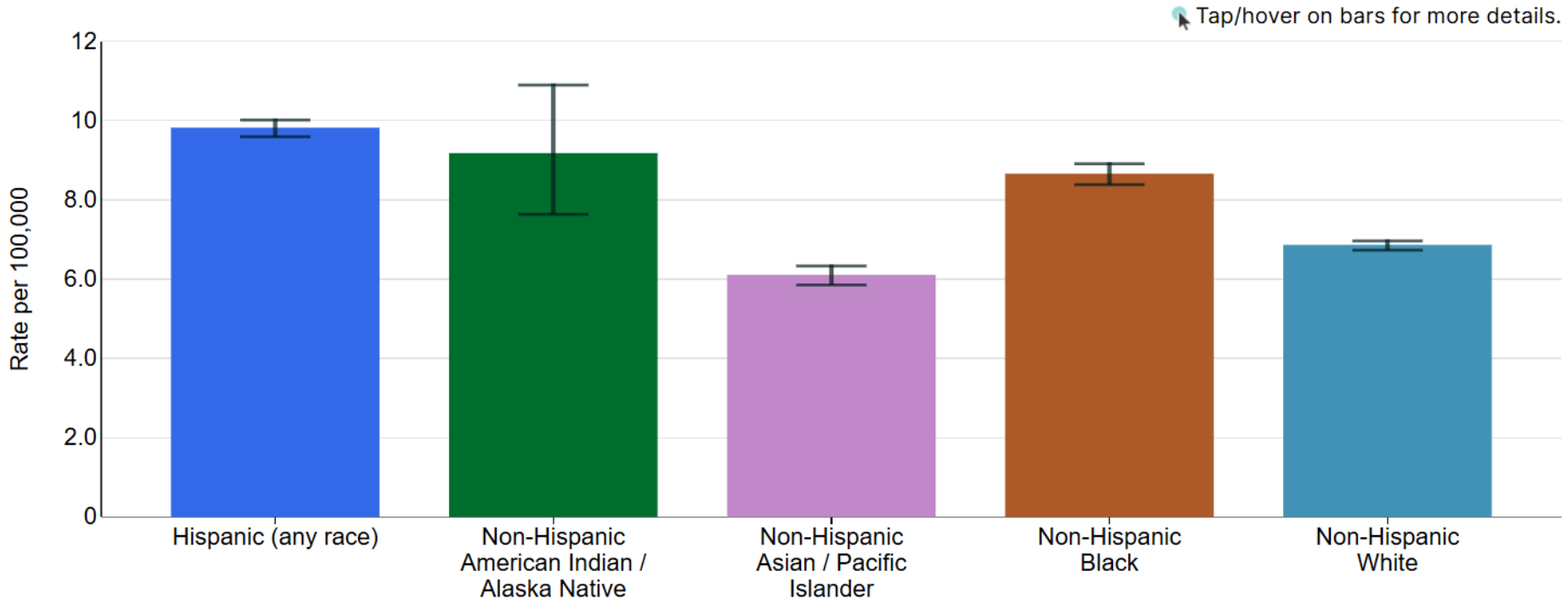
Cervix Uteri, SEER 5-Yr Age-Adjusted Incidence Rates, 2017-2021

Females by Race / Ethnicity



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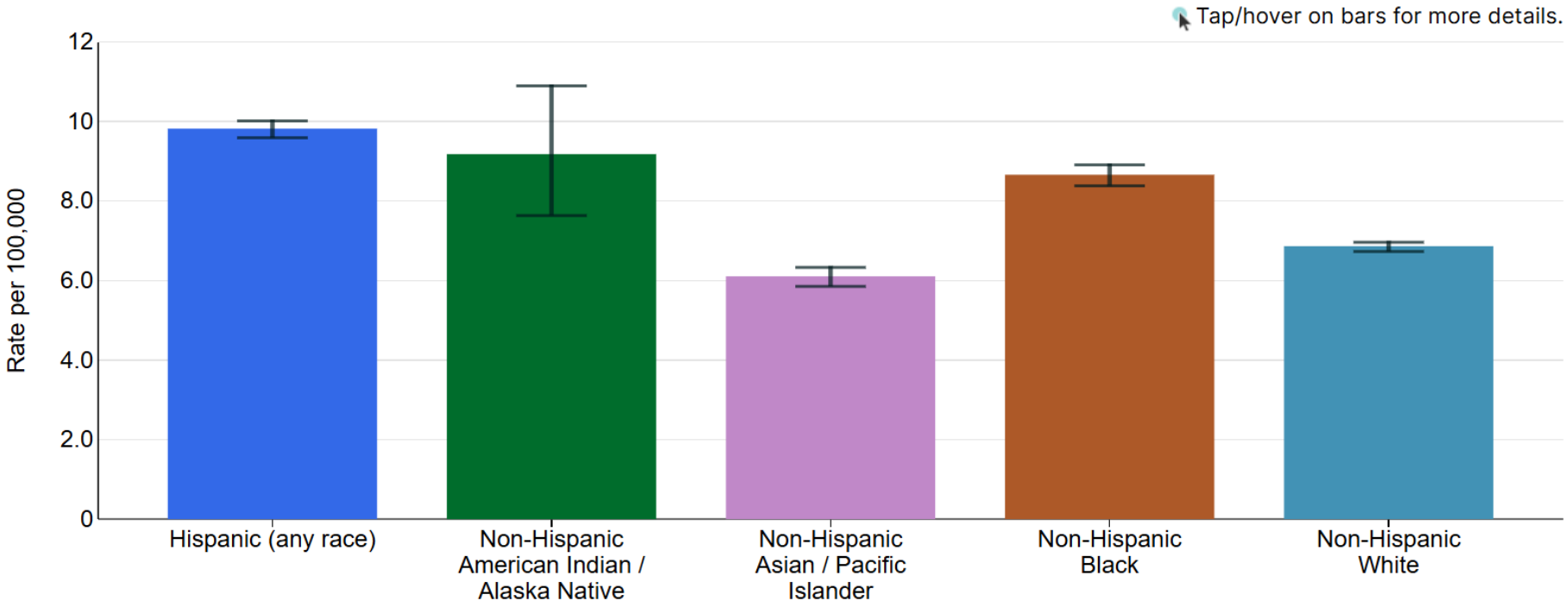
Source: https://seer.cancer.gov/statistics-network/explorer/application.html?site=57&data_type=1&graph_type=10&compareBy=race&chk_race_6=6&chk_race_5=5&chk_race_4=4&chk_race_9=9&chk_race_8=8&series=9&hdn_sex=3&age_range=1&stage=101&advopt_precision=1&advopt_show_ci=on&hdn_view=0#resultsRegion0

Cervix Uteri, SEER 5-Yr Age-Adjusted Mortality Rates, 2017-2021

Females by Race / Ethnicity



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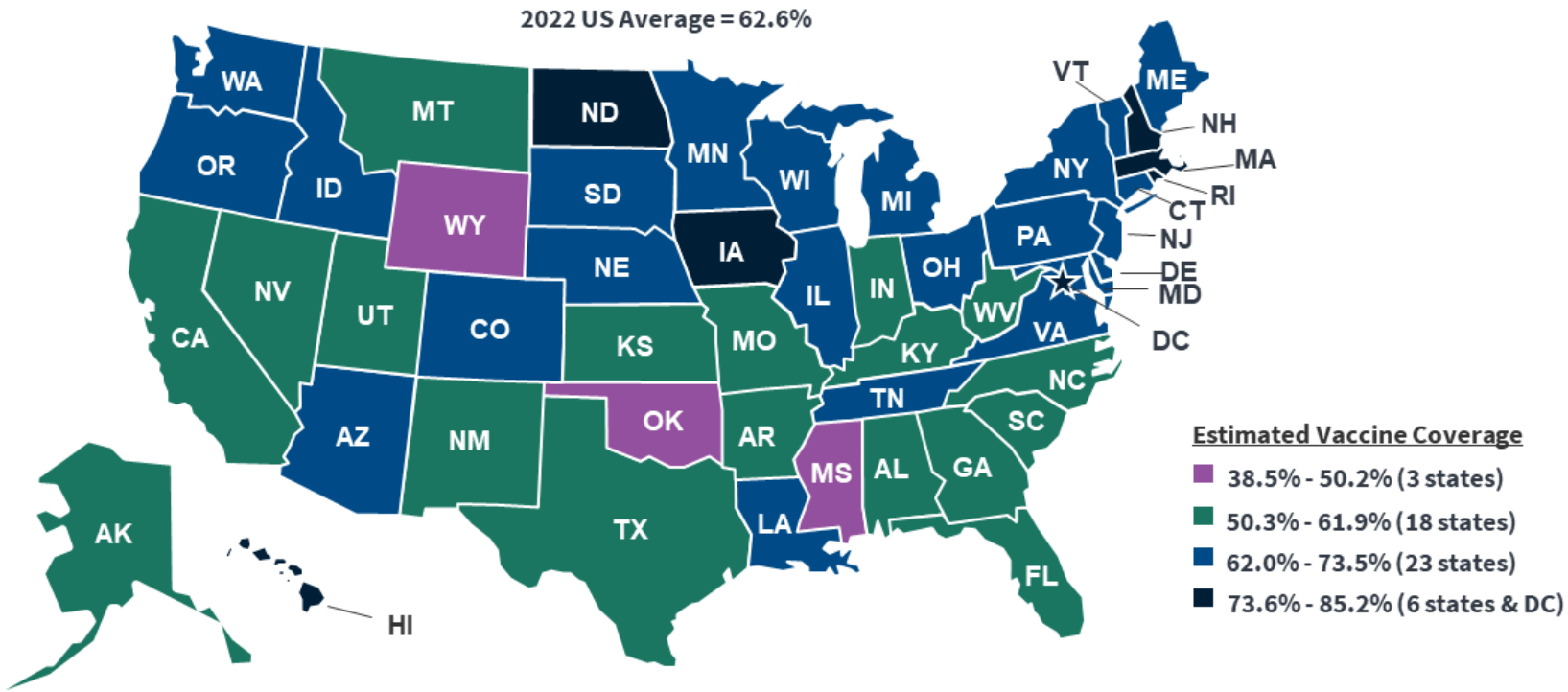
Source: https://seer.cancer.gov/statistics-network/explorer/application.html?site=57&data_type=1&graph_type=10&compareBy=race&chk_race_6=6&chk_race_5=5&chk_race_4=4&chk_race_9=9&chk_race_8=8&series=9&hdn_sex=3&age_range=1&stage=101&advopt_precision=1&advopt_show_ci=on&hdn_view=0#resultsRegion0

Figure 3

HPV Vaccination Rates of Adolescents by State

Adolescents Ages 13-17 with Up-to-Date (UTD) HPV Vaccination Series, 2022



NOTE: HPV UTD includes those with ≥3 doses, and those with 2 doses when the first HPV vaccine dose was initiated before age 15 years and there was at least 5 months minus 4 days between the first and second dose.
SOURCE: CDC, Vaccination Coverage Among Adolescents Aged 13-17 Years – National Immunization Survey – Teen, United States, 2022. *MMRW* 72(34).

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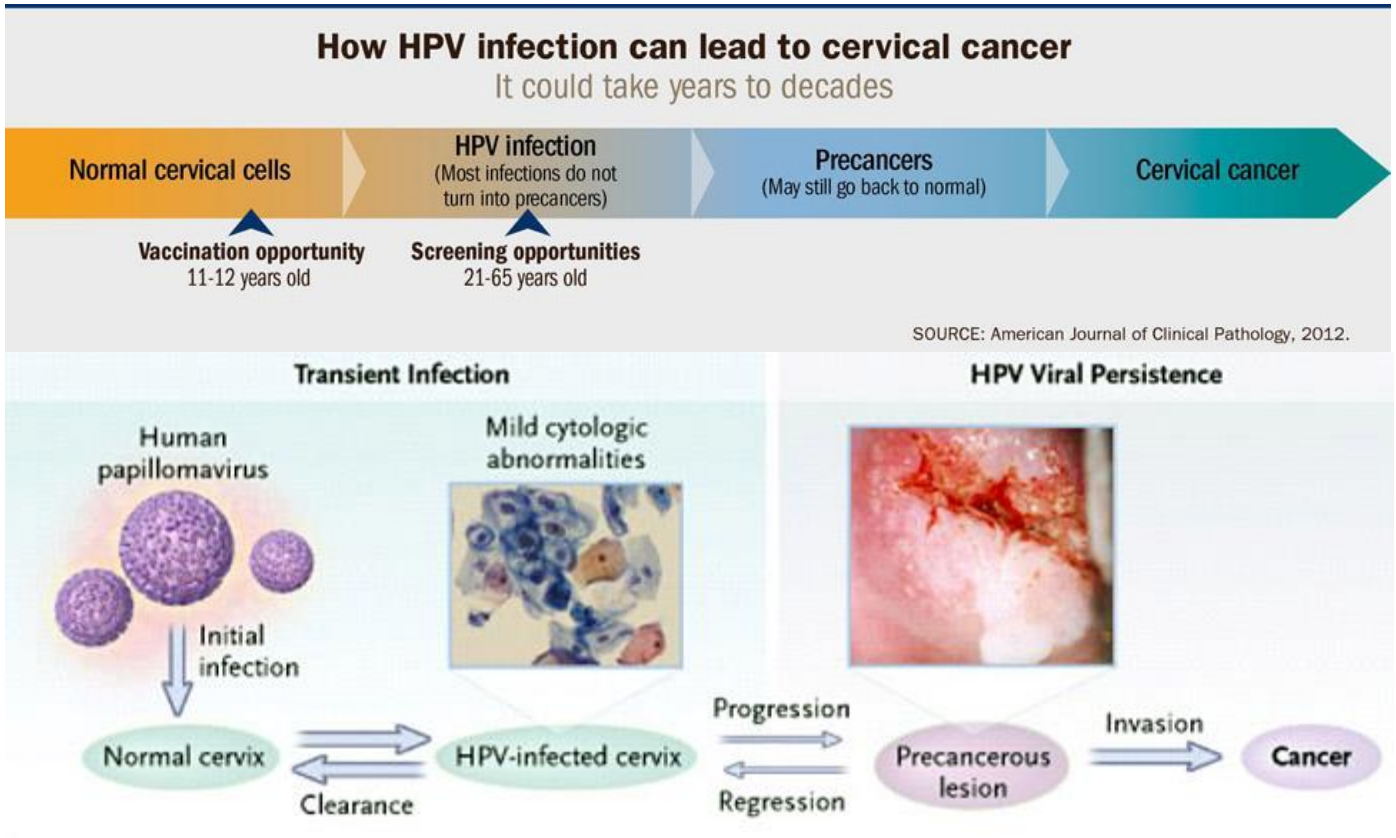
HPV>Cancer

- Increased Risks If:
  - Smoking.
  - Immune system issues.
  - HIV.
  - Transplant.



- Slow progression from persistent hrHPV infection to CIN to cancer.
- Clinically significant persistent infections = last at least 2 years.

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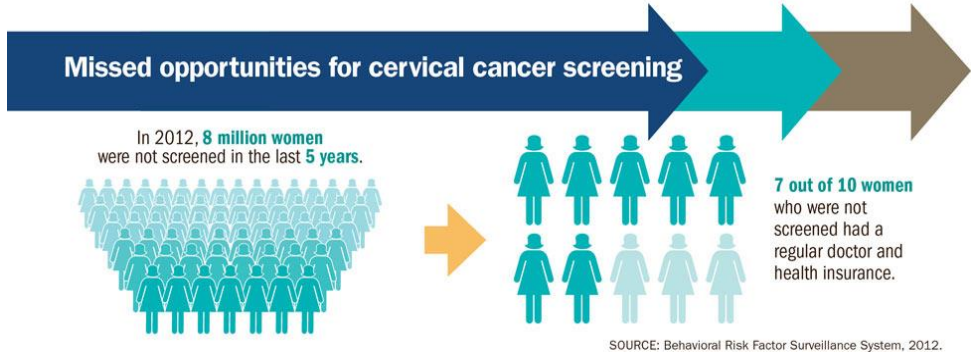
The Problem with Screening

- Stigma.
- Other health issues.
- Lack of time.
- Discomfort with exams.
- Lack of knowledge (“Does not apply to me”).
- Lack of navigation.
- Fear, embarrassment, shame.
- Prior abuse or trauma.



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Eradication of Cervical Cancer

- Primary Prevention: HPV Vaccine.
- Screening and Secondary Prevention:
  - Pap test and HPV test.
- Early Detection.
- Improved Diagnostics:
  - Better follow up and navigation; Better access.
- Equitable treatment.
- Novel treatments.

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The World Health Assembly adopted the global strategy to accelerate the elimination of cervical cancer as a public health problem by 2030.

WHO'S ELIMINATION STRATEGY 3 PILLARS*

1. **Prevention through vaccination**
   HPV vaccination offers long-term protection against cervical cancer.

2. **Screening and treatment of precancerous lesions**
   can prevent pre-cancer from developing into cancer.

3. **Timely treatment and palliative care for invasive cervical cancer**
   can save lives and palliative care can greatly reduce pain and suffering.

***To eliminate cervical cancer, all countries must reach and maintain an incidence rate below four per 100 000 women.**

90-70-90 To Eliminate Cervical Cancer

90%
of women identified with cervical disease receive treatment (90% of women with precancer treated, and 90% of women with invasive cancer managed).

90%
of girls fully vaccinated with HPV vaccine by age 15 years.

70%
of women are screened with a high-performance test by 35 years of age and again by 45 years of age.

#GlowTeal

GET INFORMED. GET SCREENED. GET VACCINATED.
LEARN MORE AT WWW.WHO.INT

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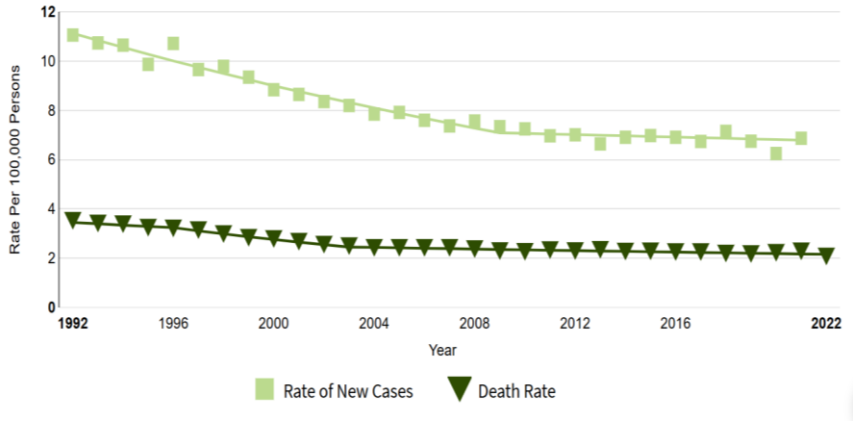
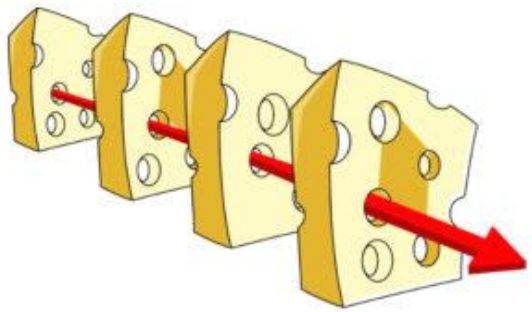
Screening Saves Lives: 1992-2022

- Who is still getting cervical cancer in the US?
- People who miss screening completely.
- Get screening but no follow up.
- Uninsured or underinsured.
- Disabled women.
- Immigrant communities.
- Rural communities.
- Hispanic women have higher rates of diagnosis.
- Black women have cervical cancer mortality.





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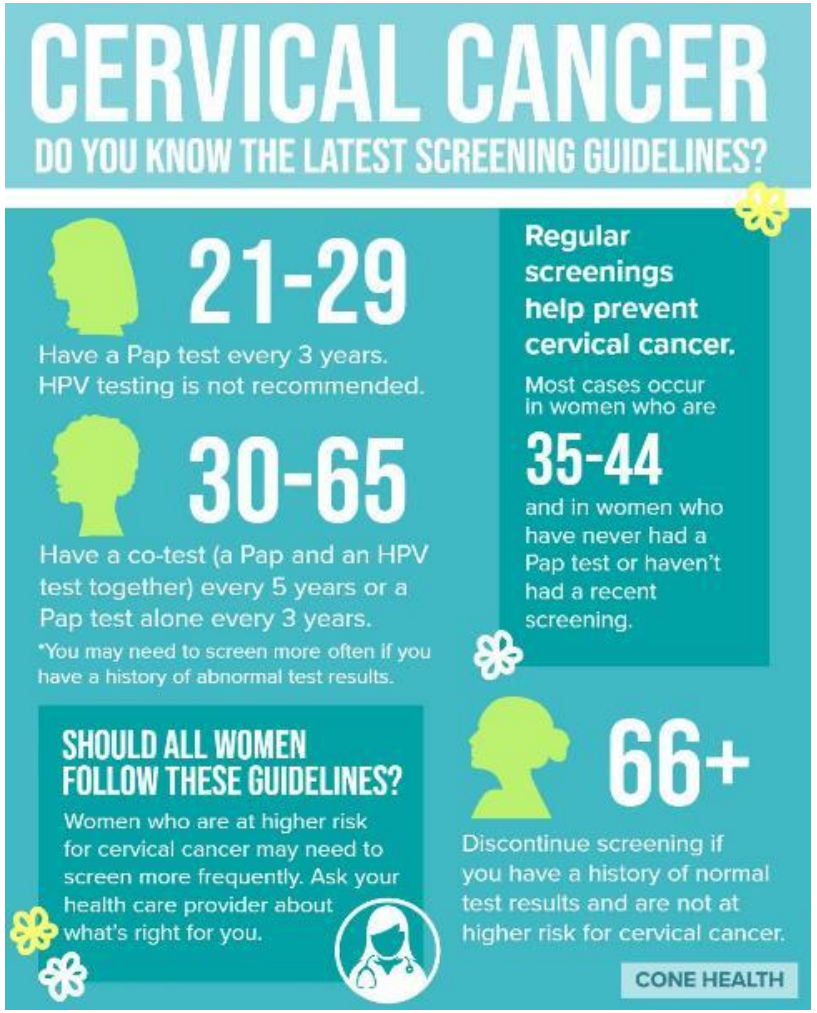
https://seer.cancer.gov/statfacts/html/cervix.html

Cervical Cancer Screening

- When to start? When to stop?
- After age 21 years old.
- Start at age 21 until age 65 years old.
- Some can start at age 25 years old with special HPV test.
- May test if older than 65 years old if symptoms of bleeding or abnormal discharge.
- Have not had regular testing.
- History of abnormal pap smears.



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Screening Recommendations for Average Risk

2020 Guidelines Update some differences with 2018 USPSTF Guidelines.

	2020 ACS	2012 ACS	2018 USPSTF
Age 21–24	No screening	Pap test every 3 years	Pap test every 3 years
Age 25–29	HPV test every 5 years (preferred) HPV/Pap cotest every 5 years (acceptable) Pap test every 3 years (acceptable)	Pap test every 3 years	Pap test every 3 years
Age 30–65	HPV test every 5 years (preferred) HPV/Pap cotest every 5 years (acceptable) Pap test every 3 years (acceptable)	HPV/Pap cotest every 3 years (preferred) Pap test every 3 years (acceptable)	Pap test every 3 years, HPV test every 5 years, or HPV/Pap cotest every 5 years
Age 65 and older	No screening if a series of prior tests were normal	No screening if a series of prior tests were normal	No screening if a series of prior tests were normal and not at high risk for cervical cancer

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https://www.cancer.gov/news-events/cancer-currents-blog/2020/cervical-cancer-screening-hpv-test-guideline#:~:text=ACS%20recommends%20cervical%20cancer%20screening,Pap%20test%20every%203%20years.

Chor J, Davis AM, Rusiecki JM. Cervical Cancer Screening Guideline for Individuals at Average Risk. JAMA. 2021 Dec 7;326(21):2193-2194. doi: 10.1001/jama.2021.13448. PMID: 34766970.

Who is average risk? Who is still getting cervical cancer?

- Average risk.
- Not immunocompromised.
- No prior abnormal paps or HR HPV present.
- Does not include structural risks of lack of insurance, follow up, etc.
- Does not include other barriers to care.

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TABLE 2. Comparison of Current and Previous American Cancer Society (ACS) Guidelines for Cervical Cancer Screening

RECOMMENDATIONS FOR CERVICAL CANCER SCREENING		
POPULATION	**ACS 2020[a]**	**ACS 2012[b]**
Aged <25 y	No screening	Cytology alone every 3 y starting at age 21 y
Aged 25-65 y	Starting at age 25 y, primary HPV test alone every 5 y (preferred)	Cytology alone every 3 y until age 29 y
	Use an FDA-approved HPV test for primary screening	Aged 30-65 y, switch to cotesting (preferred), cytology alone every 3 y (acceptable)[a]
	Cotesting every 5 y or cytology alone every 3 y are acceptable options[b]	*Screening by primary HPV testing alone not recommended for most clinical settings*
	Cotesting or cytology testing alone are acceptable where access to primary HPV testing is limited or not available; as the United States makes the transition to primary HPV testing, the use of cotesting or cytology alone for cervical cancer screening will not be included in future guidelines[b]	
	For management of positive results and subsequent surveillance, refer to ASCCP 2020 Risk-Based Management Consensus Guideline (Perkins, 2020[21])	
Aged >65 y	Discontinue screening if adequate negative prior screening	No screening after adequate negative prior screening
	Individuals aged >65 y without documentation of prior screening should continue screening until criteria for cessation are met	
	Adequate negative prior screening is currently defined as 2 consecutive, negative primary HPV tests, or 2 negative cotests, or 3 negative cytology tests within the past 10 y, with the most recent test occurring within the past 3-5 y, depending on the test used	
After hysterectomy	Individuals without a cervix and without a history of CIN2 or a more severe diagnosis in the past 25 y or cervical cancer ever should not be screened	No screening after hysterectomy (with removal of the cervix) for reasons not related to cervical cancer and no history of cervical cancer or serious precancer
HPV vaccinated	Follow age-specific screening recommendations (same as unvaccinated individuals)	Follow age-specific screening recommendations

Review and understand current data on HPV vaccine uptake efforts in IL and nationally

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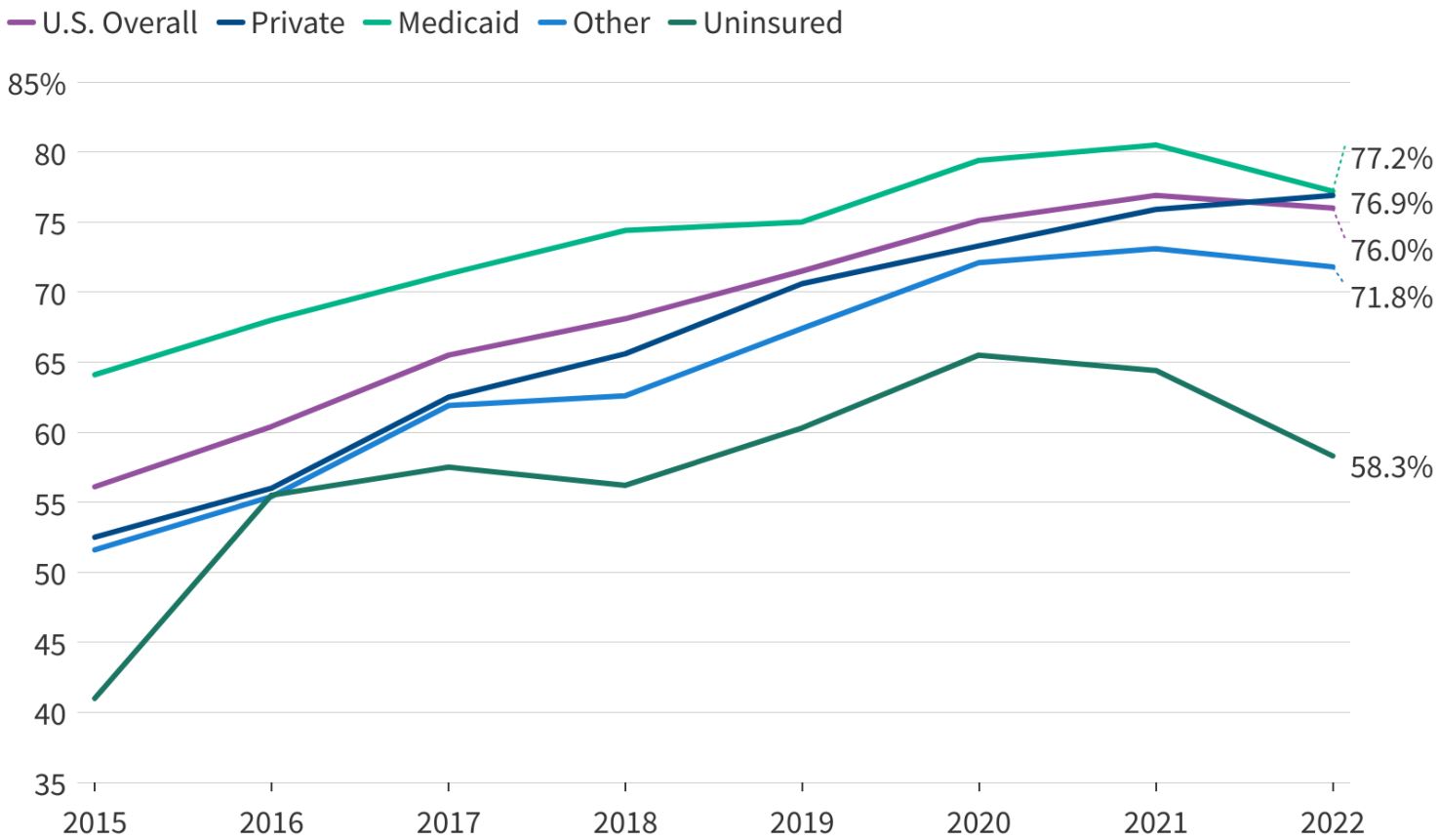
Figure 4

Rates of HPV Vaccine Initiation Among Adolescents Ages 13-17 in the U.S., by Insurance Status

Share of adolescents who have had at least one HPV vaccine, by insurance status, 2015-2022



Note: "Other" insurance includes the Children's Health Insurance Program, military insurance, Indian Health Service, and any other type of health insurance not mentioned elsewhere

Source: SUPPLEMENTARY FIGURE 1. Vaccination Coverage Among Adolescents Aged 13–17 Years — National Immunization Survey–Teen, United States, 2022. MMRW 72(34);
SUPPLEMENTARY FIGURE 2. Vaccination Coverage Among Adolescents Aged 13-17 Years - National Immunization Survey - Teen, United States, 2022. *MMRW* 72(34)

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National Trends

- 2023 National Immunization Survey - Teen
  - 61.4% of adolescents in the United States between the ages of 13 and 17 received all recommended doses of the HPV vaccine (2nd year that HPV vaccine rates have not increased).
  - The percentage of VFC-eligible adolescents who were up to date with HPV vaccination was 10.3 percentage points lower among adolescents born in 2010 compared with those born in 2007.

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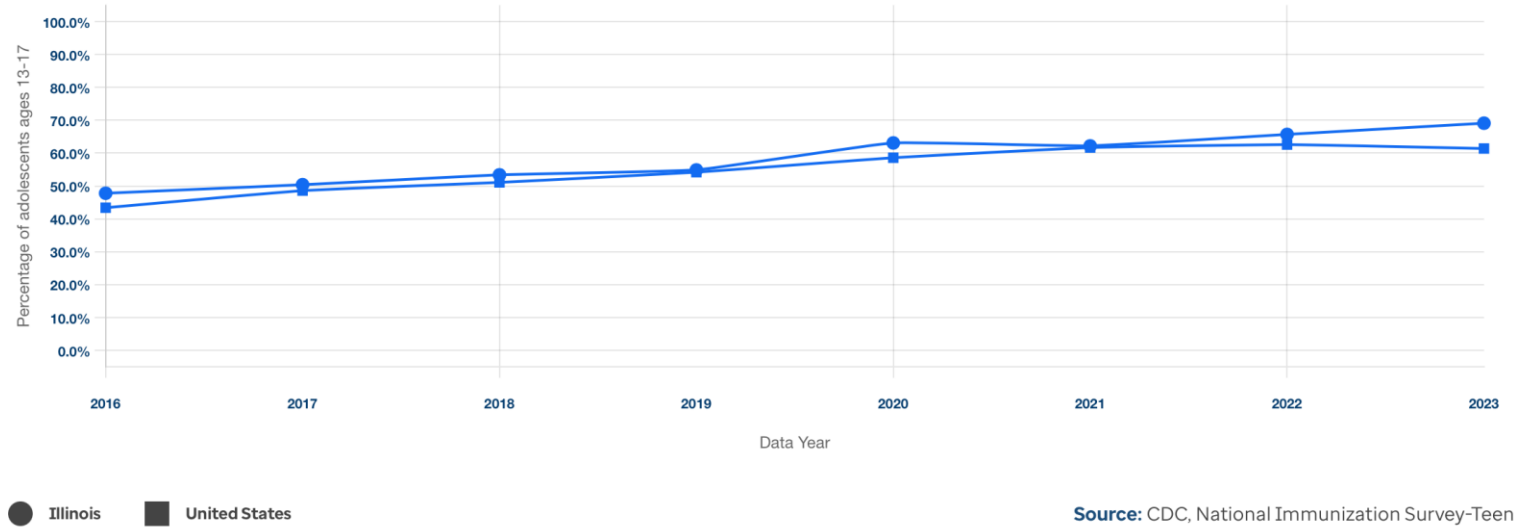
Walker B, Anderson A, Stoecker C, Shao Y, LaVeist TA, Callison K. COVID-19 and Routine Childhood and Adolescent Immunizations: Evidence from Louisiana Medicaid. Vaccine. 2021 Dec 24:S0264-410X(21)01630-3. doi: 10.1016/j.vaccine.2021.12.022. Epub ahead of print. PMID: 35033386; PMCID: PMC8702432

Lei et al. NEJM 2020;383:1340-1348

State Trends

- Statewide vaccination rate: 69.1% completely up to date (UTD).
- 81% 13-17 year olds have at least one dose.
- 17% increase for at least one dose, 15% (UTD) since 2016.



Source: CDC, National Immunization Survey-Teen

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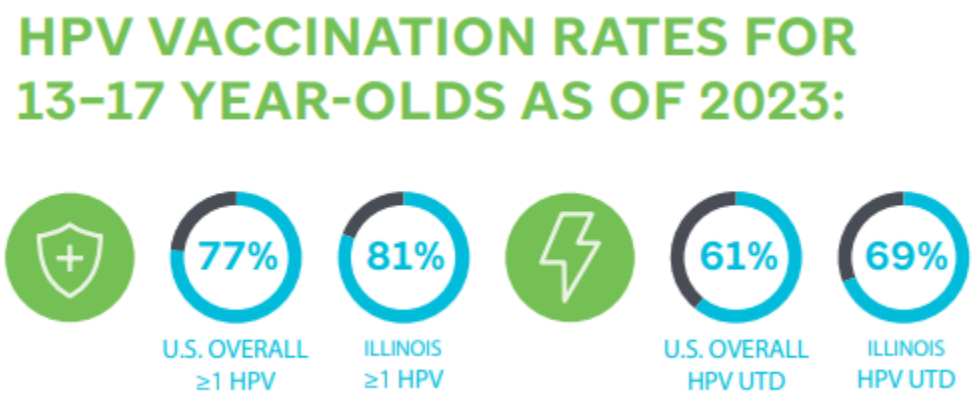
St. Jude Children's Research Hospital | HPV Cancer Prevention Program



- Illinois has increased HPV vaccination coverage of ≥1 dose by 17% and up-to-date (UTD) by 15% since 2016.
- Coverage in Illinois is higher than the U.S. average but still falls below the Healthy People 2030 goal of 80% UTD

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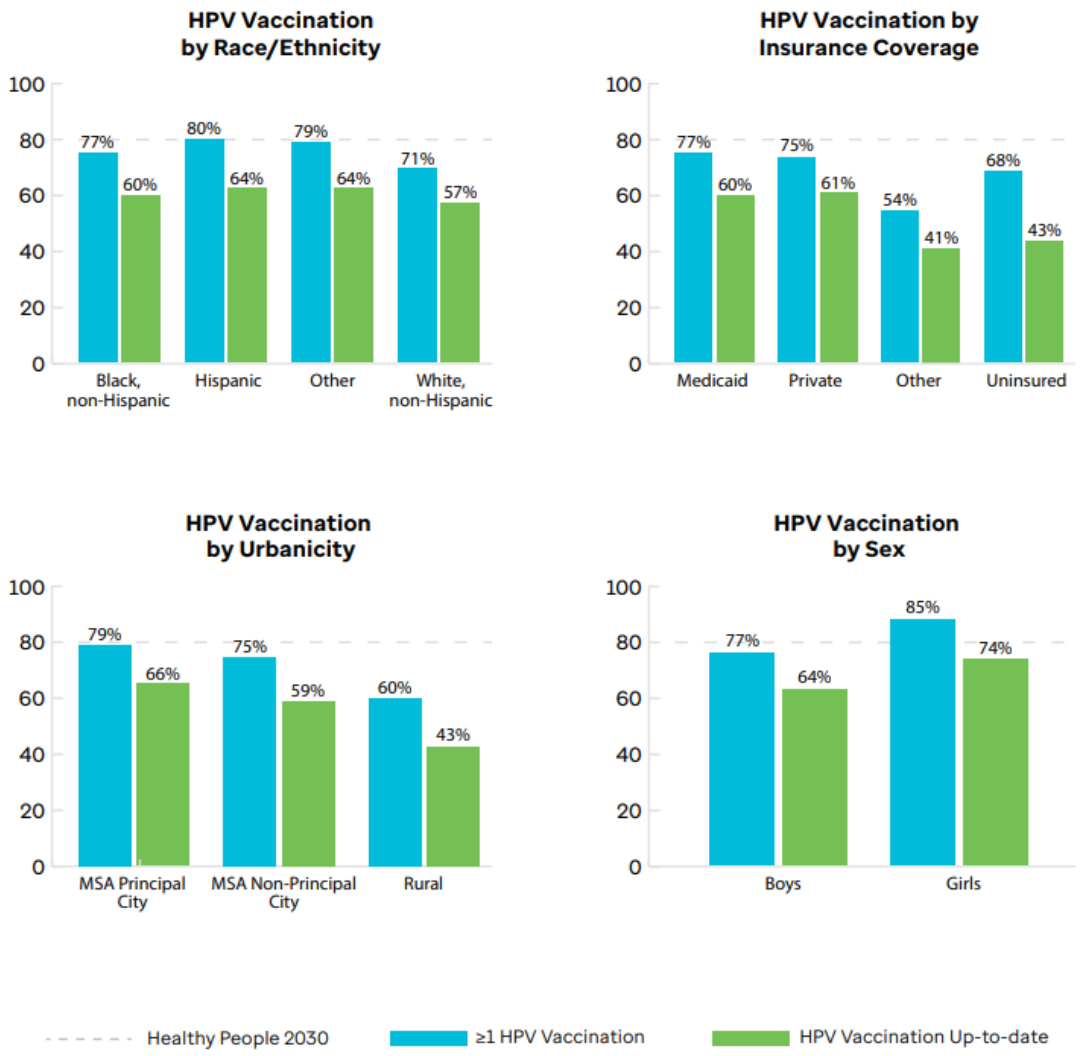
IL Rates HPV Vaccine



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Review HPV and indications and recommendations for HPV Vaccine

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Prophylactic HPV Vaccines

- DNA-free virus-like proteins (VLPs).
- Major capsid antigens L1 and L2.
- Serve as immunogens.
- Induce a strong humoral response – neutralizing antibodies.
- Some cellular response.
- Non-infectious and non-oncogenic.

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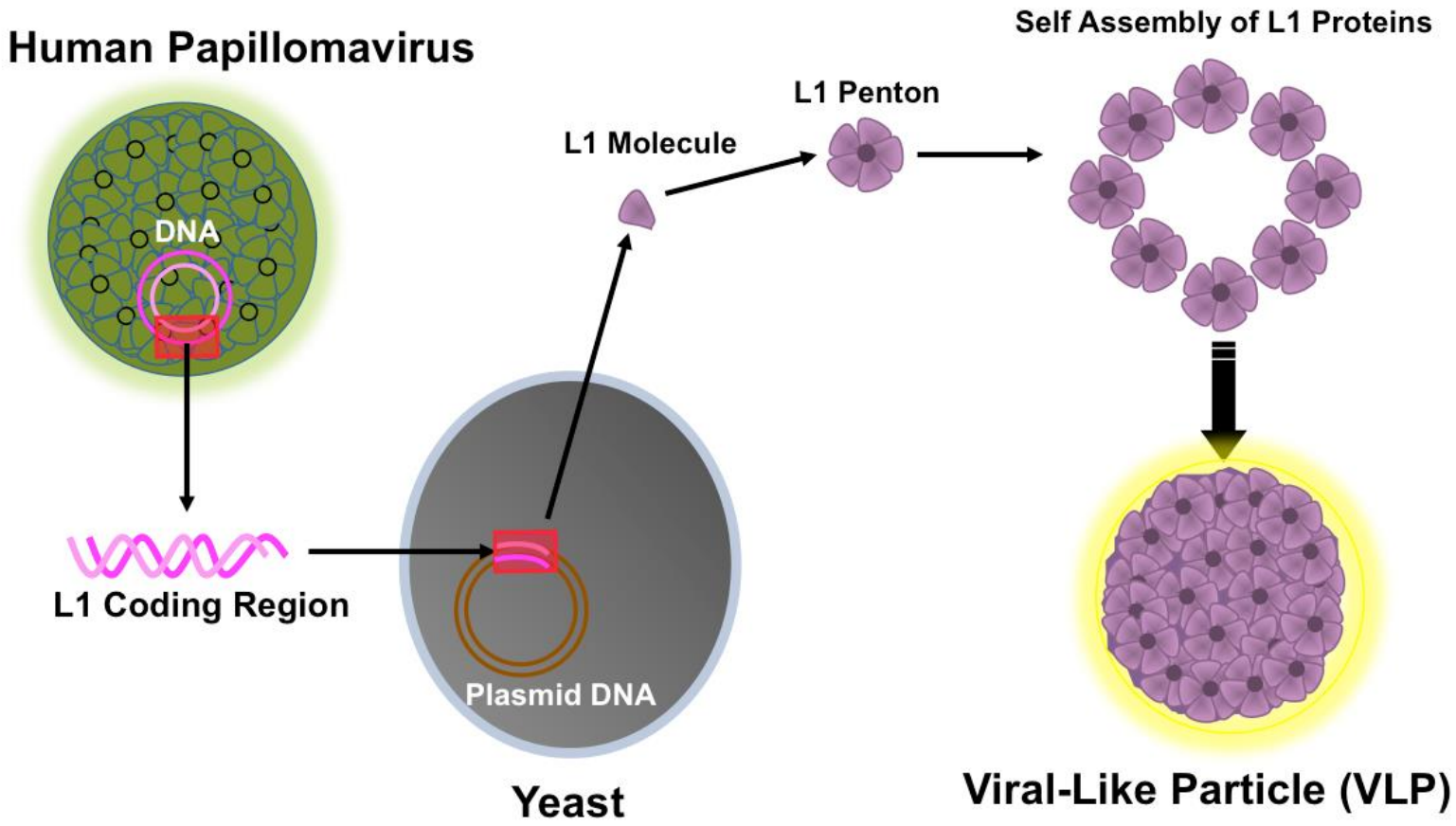
Virus-like Particle



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Serological Response to HPV

Natural Infection

- Local cell mediated immunity.
- Seroconversion ~60%.
- Time to seroconversion: 12 months.
- Delayed and low-titer Ab.

Vaccination

- Strong humoral immunity.
- Seroconversion ~100%.
- Higher titers.
- Significant cross protection.

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Efficacy of HPV Vaccine

- Australia was the first country to implement a national HPV vaccination program in 2007.
- Other European countries have also reached 10-year post HPV vaccination program implementation period.
- Data on the efficacy of vaccination published.

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Efficacy of HPV Vaccine

Estimates of genital HPV prevalence among sexually active women aged 18–24 years, by HPV type, Australia, 2005–2012 (n = 1,260)

HPV type	Pre-vaccination era (2005–07) (n = 202)	Post-vaccination era (2010–12) (n = 1,058)		
	Overall population prevalence	Overall population prevalence	Prevalence in vaccinated	Prevalence in unvaccinated
HPV 6	5.5%	0.9%	0.2%	2.7%
HPV 11	1.5%	0.4%	0%	1.3%
HPV 16	21.3%	4.2%	1.5%	12.1%
HPV 18	8.4%	1.9%	0.6%	7.4%
HPV 31	5.0%	4.0%	2.7%	8.1%
HPV 33	4.0%	1.5%	1.4%	2.0%
HPV 45	1.0%	2.6%	1.7%	6.0%
HPV 52	7.4%	8.2%	6.9%	9.4%
HPV 58	5.5%	3.4%	3.9%	2.7%
HPV 6/11	6.9%	1.3%	0.2%	4.0%
HPV 16/18	26.2%	5.4%	2.1%	16.1%
HPV 31/33/45	9.4%	7.8%	5.6%	14.8%
4vHPV types[a]	28.7%	6.5%	2.3%	18.8%
High-risk HPV types[b]	47.0%	34.9%	34.4%	44.3%
All HPV types	59.9%	48.8%	49.4%	55.7%

REVIEW

The impact of 10 years of human papillomavirus (HPV) vaccination in Australia: what additional disease burden will a nonavalent vaccine prevent?

Cyra Patel[1], Julia ML Brotherton[2,3], Alexis Pillsbury[1], Sanjay Jayasinghe[1,4], Basil Donovan[5,6], Kristine Macartney[1,4], Helen Marshall[7,8]

1. National Centre for Immunisation Research and Surveillance, Westmead, Australia
2. VCS Population Health, VCS Foundation, East Melbourne, Australia
3. School of Population and Global Health, University of Melbourne, Parkville, Australia
4. Discipline of Child and Adolescent Health, Faculty of Medicine and Health, University of Sydney, Sydney, Australia
5. The Kirby Institute, University of New South Wales, Sydney, Australia
6. Sydney Sexual Health Centre, Sydney Hospital, Sydney, Australia
7. Vaccinology and Immunology Research Trials Unit, Women's and Children's Hospital, North Adelaide, Australia
8. Robinson Research Institute and Adelaide Medical School, University of Adelaide, North Adelaide, Australia

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Euro Surveill. 2018;23(41)

Efficacy of HPV Vaccine

- Additional findings -
  - Substantial decrease in genital condylomas.
  - Decrease in HPV prevalence among heterosexual men.
    - *Herd immunity effect.*
- Mathematical models -
  - Reduction in other HPV-associated cancers (anal, vulvar, vaginal, oral, oropharyngeal).

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HPV Vaccination Guidelines

Who Gets Two Doses?

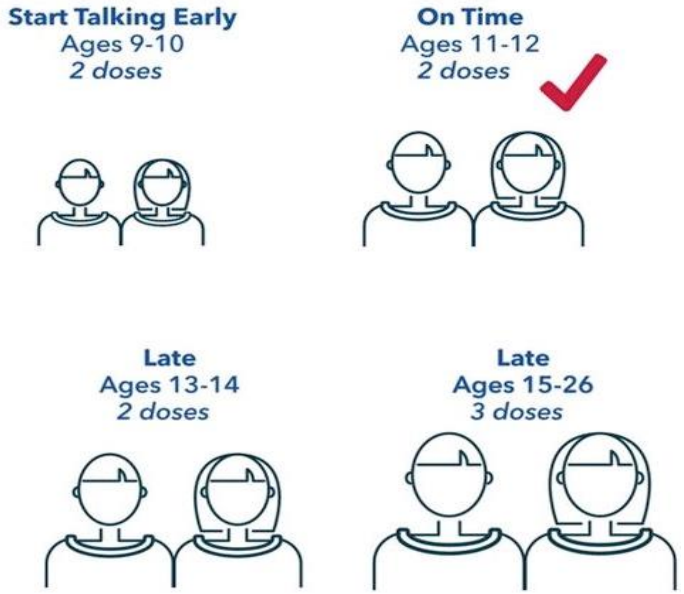
9-14 YEAR OLDS

- A 2-dose schedule is recommended for **people who get the first dose before their 15th birthday**. In a 2-dose series, the second dose should be given 6–12 months after the first dose (0, 6–12-month schedule).
- The minimum interval is 5 months between the first and second dose. If the second dose is administered after a shorter interval, a third dose should be administered a minimum of 5 months after the first dose and a minimum of 12 weeks after the second dose.
- If the vaccination schedule is interrupted, vaccine doses do not need to be repeated (no maximum interval).
- Immunogenicity studies have shown that two doses of HPV vaccine given to 9–14-year-olds at least 6 months apart provided as good or better protection than three doses given to older adolescents or young adults.

Who Gets Three Doses?

A 3-dose schedule is recommended for **people who get the first dose on or after their 15th birthday**, and for people with certain immunocompromising conditions.

- In a 3-dose series, the second dose should be given 1–2 months after the first dose, and the third dose should be given 6 months after the first dose (0, 1–2, 6-month schedule).
- The minimum intervals are 4 weeks between the first and second dose, 12 weeks between the second and third doses, and 5 months between the first and third doses. If a vaccine dose is administered after a shorter interval, it should be re-administered after another minimum interval has elapsed since the most recent dose.
- If the vaccination schedule is interrupted, vaccine doses do not need to be repeated (no maximum interval).



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https://www.cdc.gov/hpv/hcp/clinical-overview/?CDC_AAref_Val=https://www.cdc.gov/hpv/hcp/schedules-recommendations.html

Current Indications

- Females
  - Age 9-45 for prevention of cervix, vulvar, vaginal, anal, oropharyngeal/other head and neck cancers (2020).
  - Cervical, vulvar, vaginal, anal, precancerous/dysplastic lesions.
  - Genital warts.
- Males
  - Age 9-45 for prevention of anal, oropharyngeal/other head and neck cancers (2020).
  - Anal precancerous/dysplastic lesions.
  - Genital warts.

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Current CDC Recommendations

- Any licensed HPV vaccine can be used to complete series on same schedule.
- No maximum interval (no need to repeat dose if schedule interrupted).
- Minimum intervals:
  - 4 weeks b/w 1st and 2nd dose.
  - 12 weeks b/w 2nd and 3rd dose.
  - 5 months b/w 1st and 3rd dose.
  - If 2 dose regimen, 5 months b/w 1st and 2nd dose.
- Extended intervals between the 1st and 2nd dose (anywhere from 12-53 months) have been studied and appear to be effective.

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https://publications.aap.org/pediatrics/article/154/2/e2023064693/197680/Immunogenicity-and-Safety-of-Extended-Interval-2?autologincheck=redirected

Current CDC Recommendations

- Age 27-45: consider for those most likely to benefit.
  - Shared decision-making consideration:
    - *Adults at risk of new infection (new sexual partner).*
    - *Change in life circumstances; people living longer.*
    - *No clinical Ab test to determine immunity.*
    - *Prophylactic; does not treat/prevent progression if already infected.*
    - *Cost.*
- Not recommended in pregnancy (not studied).
- Immunocompromised: 3 doses.

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WHO & CDC Considerations

- WHO updates recommendations on HPV vaccination schedule:
  - “a single-dose schedule, referred to as an alternative, off-label single–dose schedule can provide a comparable efficacy and durability of protection to a two-dose regimen.”
    - *https://www.who.int/news/item/20-12-2022-WHO-updates-recommendations-on-HPV-vaccination-schedule*
- Will the US consider following suit?
  - A CDC HPV Vaccines Workgroup has been established and is reviewing the number of doses in the series and the wording for routine vaccination age.
    - *https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/01-hpv-Brooks-508.pdf*

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Safety

- Most common adverse reactions:
  - Injection site reactions (20-90%).
  - Temp 100F (10-30%).

- Well tracked and monitored.
- >350 million doses worldwide.

Gardasil® 9 was studied in clinical trials with more than 15,000 females and males.

Gardasil® was studied in clinical trials with more than 29,000 females and males.

Cervarix® was studied in clinical trials with more than 30,000 females.

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Contraindications / Precautions

- Anaphylaxis to vaccine component.
- Anaphylactic allergy to latex (bivalent).
- Immediate hypersensitivity to yeast.
- Moderate or severe acute illness (precaution – defer until sxs improve)
- Minor acute illness is NOT a reason to defer vaccination.

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Review data on the effects of HPV vaccine on pre-cancer and cancer

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Early Vaccination is Key

- Population-based cancer registry data from multiple countries support the importance of early vaccination.
- Recent studies suggest that HPV vaccination, especially when given at a younger age, is associated with substantial reductions in the risk of cervical cancer.
- Adult vaccinations (27-45) has the potential to prevent thousands of cancers per year but many clinicians and patients unaware of vaccine is approved for this age group.

Mix JM, et al. Cancer Epidemiol Biomarkers Prev. 2021;30(1):30-37. Liao C-I, et al. JAMA Netw Open. 2022;5(3):e222530.
Falcaro M, et al. Lancet. 2021;398(10316):2084-2092. Lei J, et al. N Engl J Med. 2020;383(14):1340-1348.
King LM et al. Open Forum Infectious Disease. Volume 10, Issue 1, January 2023.

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The Value of Starting HPV Vaccine Conversations at Age 9

- Age of vaccination increases, cancer prevention decreases.
- Increases likelihood of vaccinating prior to first HPV exposure.
- Offers more time for completion of the series by age 13.
- Decreases how many shots are given per visit.

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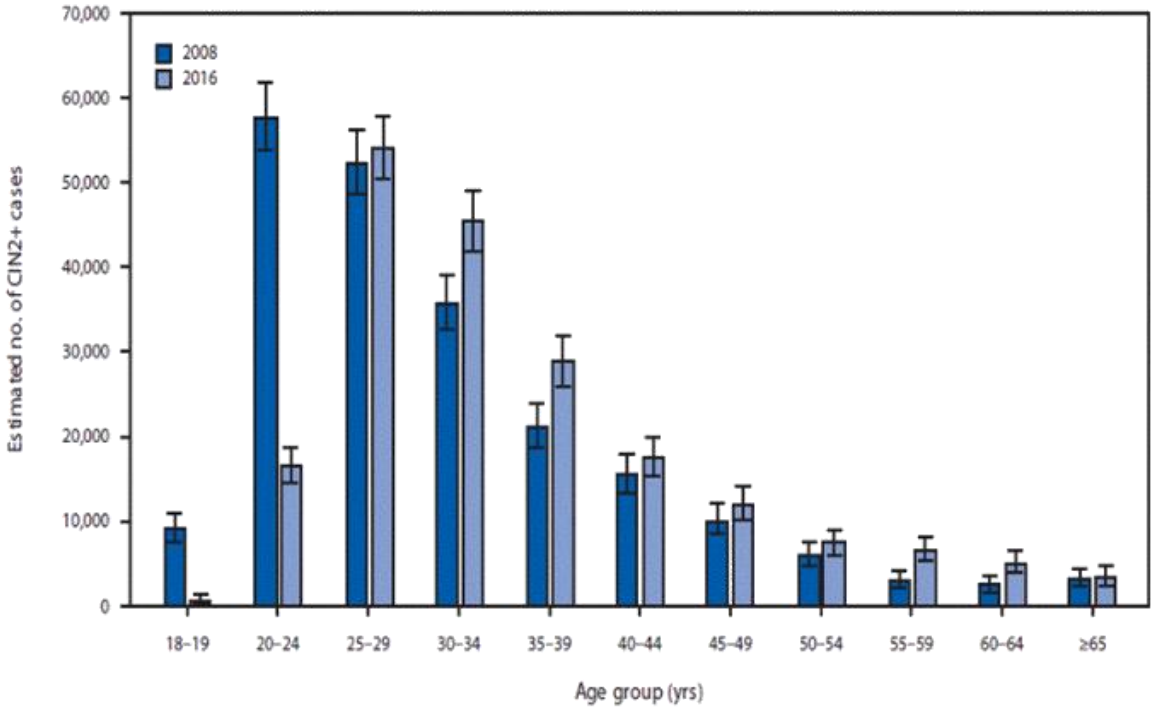
HPV Vaccination Reduces Cervical Pre-Cancers

Women have seen dramatic decreases in high-grade cervical lesions in the U.S.



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Slide from National HPV Roundtable
Source: McClung, et al. MMWR 2019 https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6815-H.pdf

Duration of Protection

- Continued protection against high grade cervical, vaginal, vulvar neoplasia observed through at least 10 years after vaccination.
- Persistent antibody levels and protection against infection also reported up to 10 years after vaccination.
- Additional data as followed over time.
- No current evidence that booster/revaccination is necessary.

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Kjaer et al. Clin Infect Dis 2018;66(3):339; Huh et al. Lancet 2017;390(10108):2143; Ferris et al. Pediatrics 2014;134(3):e657; Donken et al. J Infect Dis 2018;217(10):1579.

Prevention of Cervical Cancer

- Cervical Cancer Incidence in Young U.S. Females After HPV Introduction.
- Cross section SEER Study.
- Compared 4 year average annual incidence of cervix cancer in 2003-2006 and 2011-2014 (pre and post vaccine).
- 4 year average annual incidence rates (age 15-24).
  - 29% lower post vs pre vaccine (6.0 vs 8.4 per 1,000,000 people).
  - No significant decrease for age 25-34.

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Guo et al. Am J Prev Med 2018. 55 (2):197-204

Prevention of Cervical Cancer

- N=1,672,983.
- 527,871 vaccinated; 1,145, 112 unvaccinated.
- Among vaccinated, 83.2% initiated before 17 y/o.
- Cervical cancer cases.
- 19 in vaccinated.
- 2 if vaccinated before 17y/o.
- 17 if vaccinated age 17-30y/o.

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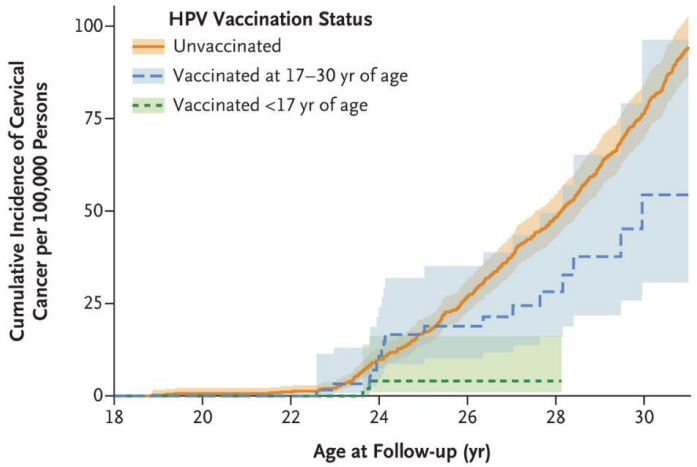
Prevention of Cervical Cancer

HPV Vaccination and Risk of Invasive Cervical Cancer

- Incidence rate ratio vaccinated/unvaccinated adjusted for age at f/u = 0.51.
- Adjusted for other covariates = 0.37.
- Adjusted for all covariates.
- 0.12 if vaccinated <17 y/o.
- 0.47 if vaccinated age 17-30 y/o.



Risk of cervical cancer in those vaccinated before 17 y/o was 88% lower than those never vaccinated

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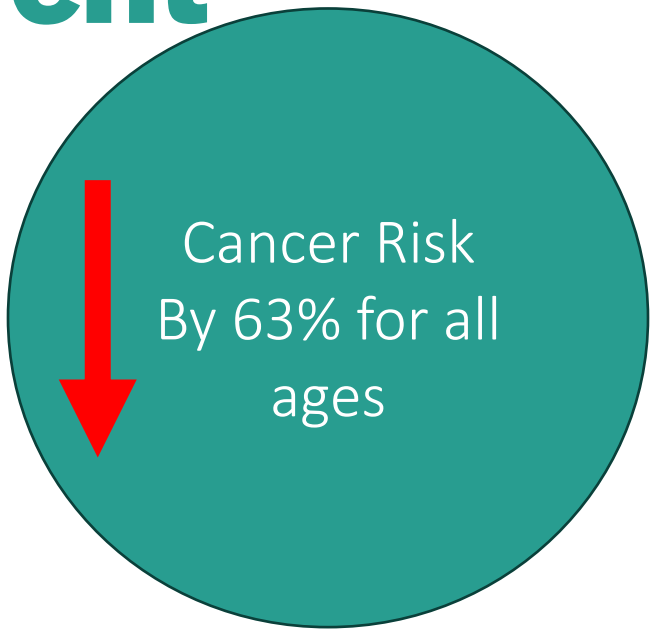
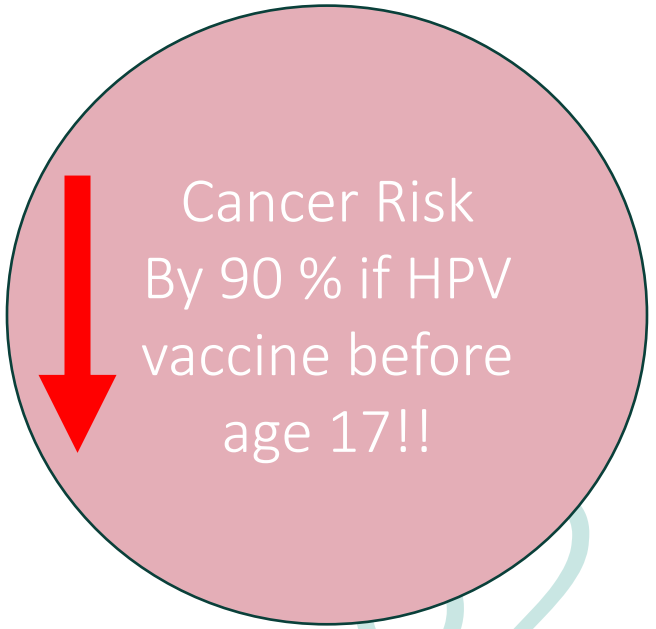
Lei et al. NEJM 2020;383:1340-1348

HPV Vaccine WORKs to prevent cancer

Studies from other countries

- A study of nearly 1.7 million Swedish women found that the HPV vaccine reduced the risk of cervical cancer by 63%.
- The vaccine was especially effective for girls vaccinated before age 17, reducing their risk of cervical cancer by nearly 90%.
- The vaccine was also effective for women vaccinated between ages 17 and 30, reducing their risk of cervical cancer by 53%.





Effects of HPV vaccination on the development of HPV-related cancers: A retrospective analysis of a United States-based cohort.

Jefferson DeKloe, Zachary David Urdang, Ubaldo E. Martinez Outschoorn, Joseph M. Curry; Department of Otolaryngology, Thomas Jefferson University, Philadelphia, PA; Departments of Otolaryngology and Clinical/Experimental Pharmacology - Thomas Jefferson University, Philadelphia, PA; Jefferson Kimmel Cancer Center, Philadelphia, PA

	Outcome	HPV Vaccinated: Patients with Outcome	HPV Vaccinated:Total Patients	No HPV Vaccine: Patients with Outcome	No HPV Vaccine: Total Patients	Odds Ratio (Vaccinated vs. Unvaccinated)	P-value
Male Patients							
	Head and Neck Cancers	21	760,467	48	760,054	0.44 (0.26-0.73)	0.0016
	Anal Cancer	Suppressed (n≤10)	760,540	Suppressed (n≤10)	760,539	-	-
	Penile Cancer	Suppressed (n≤10)	760,540	Suppressed (n≤10)	760,539	-	-
	All HPV-related Cancers	26	760,435	57	760,036	0.46 (0.29-0.72)	0.0010
Female Patients							
	Head and Neck Cancers	29	945,953	43	945,580	0.67 (0.42-1.1)	0.10
	Cervical Cancer	70	945,690	99	945,900	0.71 (0.52-0.96)	0.027
	Anal Cancer	Suppressed (n≤10)	896,586	Suppressed (n≤10)	896,589	-	-
	Vulvar Cancer or Vaginal Cancer	20	945,963	12	945,999	1.66 (0.81-3.41)	0.16
	All HPV-related Cancers	109	945,584	149	945,441	0.73 (0.57-0.94)	0.013

Males vaccinated for HPV (n = 760,540) were at decreased odds for HPV-related cancers (odds ratio (OR) = 0.46, 95 % confidence interval (CI) = 0.29-0.72, p-value = 0.001). T

his finding was primarily driven by a significant reduction in HNC (OR = 0.44, CI = 0.26-0.73, p = 0.0016). Females vaccinated for HPV (n = 945,999) had lower odds for cervical (OR = 0.71, CI = 0.52-0.96, p-value = 0.027) cancers and HPV-related cancers overall (OR = 0.73, CI = 0.57-0.94, p = 0.013)

Myths and Facts about HPV Vaccine

Myths and fake messages about human papillomavirus (HPV) vaccination: answers from the ESGO Prevention Committee

Nadja Taumberger [1], Elmar A Joura,[2] Marc Arbyn,[3,4] Maria Kyrgiou,[5,6] Jalid Sehouli,[7] Murat Gultekin [4,8]

	MYTH	FACT
1	PAP smears are also effective: no need for vaccination	• The only screening available is for cervical cancer, not other ✓ cancers • Five other cancers (affecting both women and men) are caused by HPV • Screening is a secondary prevention method to detect pre-cancerous lesions or cancer early • HPV vaccination is effective in the primary prevention of disease
2	HPV vaccines are new so there are no safety and efficacy data on long-term side effects	• We have 25 years of experience with the vaccines • We have 15 years of real-life experience with several hundred million doses distributed worldwide • The possible side effects are well documented • Vaccine safety has been confirmed by WHO, CDC, and many other authorities
3	HPV vaccination can cause ovarian failure or infertility	• No connection between HPV vaccination and ovarian failure has been observed, following observation of 1 million females • HPV infection and treatment for cancer or precancer can lead to infertility

Myths and Facts about HPV Vaccine

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Nadja Taumberger [1], Elmar A Joura,[2] Marc Arbyn,[3,4] Maria Kyrgiou,[5,6] Jalid Sehouli,[7] Murat Gultekin [4,8]

	MYTH	FACT
4	Vaccines cause autoimmune diseases, neurological disease, and death	• The incidence of autoimmune or neurological conditions and death is the same in HPV-vaccinated and unvaccinated populations
5	Children are not sexually active so there is no need to vaccinate them early	• The earlier you vaccinate, the better the immune response ✓ • Fewer doses are needed when individuals are vaccinated under the age of 15 years • The earlier you vaccinate, the better the strength of the prevention
6	Boys and men do not get cervical cancer so they do not need a vaccine	• HPV is linked to at least five malignancies other than cervical cancer: vulvar, vaginal, anal, penile, and oropharyngeal cancers • OP cancer in men in US > # than cervical cancer in US* • Gender-neutral vaccination provides the best protection for all individuals regardless

Myths and Facts about HPV Vaccine

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Nadja Taumberger [1], Elmar A Joura,[2] Marc Arbyn,[3,4] Maria Kyrgiou,[5,6] Jalid Sehouli,[7] Murat Gultekin [4,8]

	MYTH	FACT
7	After the first sexual intercourse the vaccine does not work any longer	• In clinical trials most young women were sexually active and ✓ the level of protection was >90% • Efficacy data up to the age of 45 years are available • Even after treatment for HPV-related disease, the vaccine potentially reduces the risk of subsequent disease
8	Natural HPV infection already creates a protective antibody response so there is no need for vaccination	• Antibody response after natural HPV infection is low ✓ HPV vaccination provides a strong immune response and gives robust protection against disease
9	HPV vaccination increases risky sexual behavior and promiscuity	• There is no evidence that HPV vaccination increases • Studies suggest there is not earlier onset of sexual activity among those getting HPV vaccine *

HPV Vaccine Limitations

- Perception issues regarding efficacy and safety.
- Incomplete protection against all oncogenic HPV types.
- Effect on cervical cancer screening:
  - 96% patients aware of pap need after vaccination.
- Vaccine cost -
  - 9-valent full schedule $360-$580.
- Low provider recommendation (72.6%) -
  - Safety concerns, personal attitudes and beliefs, limited knowledge of HPV, carcinogenesis and vaccine benefits, concerns about reimbursement.

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HPV Vaccine: Opportunities for Childhood Cancer Survivors

- Higher disease burden of HPV related diseases and cancer.
- Lower HPV vaccine rates.

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Ramsay JM, Kaddas HK, Ou JY, Kepka D, Kirchhoff AC. Missed opportunities for concomitant HPV vaccination among childhood cancer survivors. Cancer Med. 2022 Jan 14. doi: 10.1002/cam4.4492. Epub ahead of print. PMID: 35032104.

Engaging Communities and Tailoring Messaging

- Immigrant community education and outreach.
- Language and literacy choices.
- Lay leader engagement.

Cofie LE, Tailor HD, Lee MH, Xu L. HPV vaccination uptake among foreign-born Blacks in the US: insights from the National Health Interview Survey 2013-2017. Cancer Causes Control. 2022 Jan 16. doi: 10.1007/s10552-021-01550-x. Epub ahead of print. PMID: 35034260

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Things That Can Provoke Doubt in Patients

- Follow invalid contraindications to immunization.
  - Low-grade fevers.
  - Mild illness.
  - Clinical team providing different recommendations.
  - Not giving a strong and clear recommendation.

American Academy of Pediatrics: Addressing Common Concerns of Vaccine-Hesitant Parents. Available at: https://www.aap.org/en-us/Documents/immunization_vaccine-hesitant%20parent_final.pdf.

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How Can We Ensure Vaccination?:

- Bundle for recommendation
- Presumptive communication
- Ensure a consistent message across office
- Use every opportunity to vaccinate.
- Provider person examples
- Effectively answer questions.

Presumptive communication assumes people are ready to vaccinate (“We’re going to be …”), whereas participatory communication asks people if they want to vaccinate or seeks their views on vaccination (“Did you want to …”).

Studies have suggested a presumptive approach is associated with higher uptake of childhood vaccines (observational studies) or adolescent HPV vaccines (randomized controlled trial

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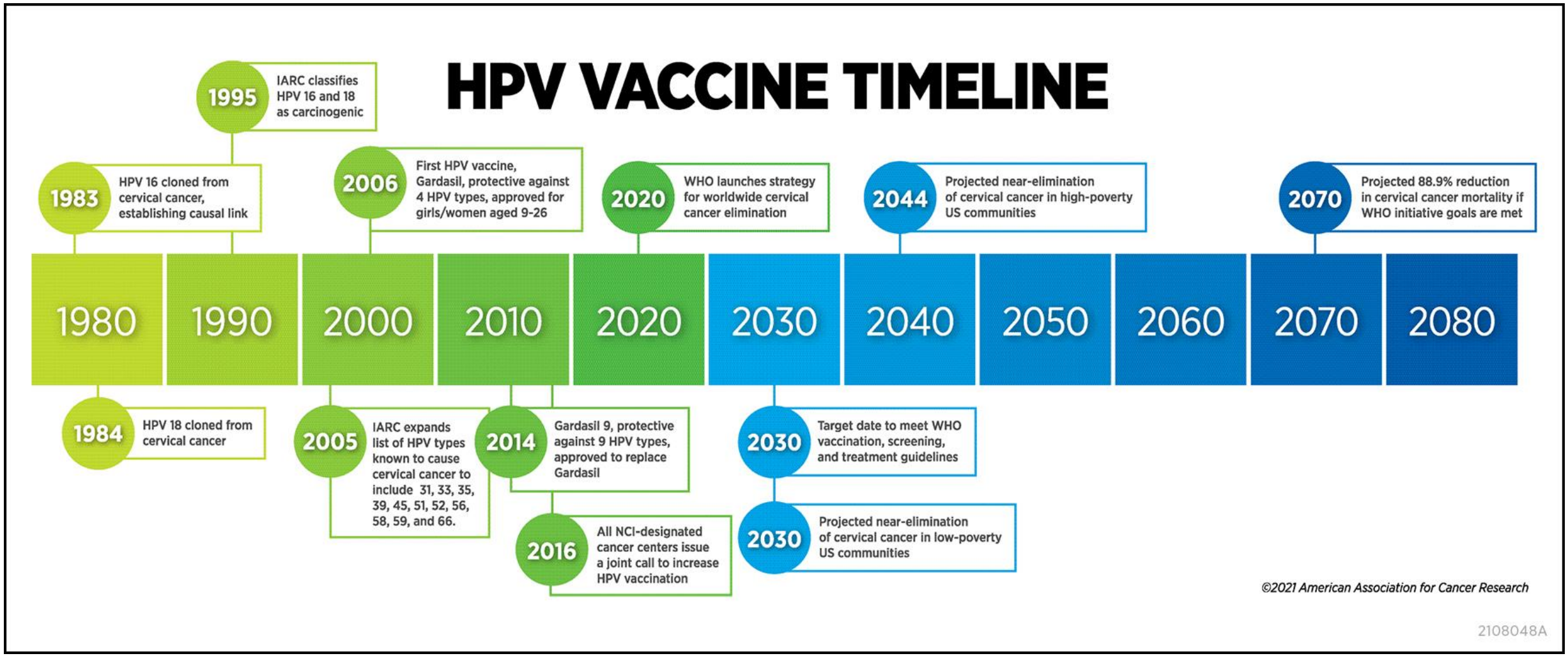

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Summary

- HPV vaccine is safe, effective, and durable.
- Recent evidence for cervical cancer prevention in addition to dysplasia is maturing.
- Vaccination rates are improving but still not at goal.
- Implementation of strategies to ensure routine vaccination coverage urgently needed.

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Lei et al. NEJM 2020;383:1340-1348

Other Resources

- Hpvroundtable.org
- ACS: Cancer.org
- HPV VACs (Vaccinate Against Cancers) Program
- Mission: HPV Cancer Free
- CDC.gov

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Lei et al. NEJM 2020;383:1340-1348

AT THE FOREFRONT
UChicagoMedicine
Comprehensive Cancer Center

NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

Please feel free to reach out for collaborations or more information

THANKS!

nlee@bsd.uchicago.edu

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Questions?

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Check Out Our Social Media Toolkits!

- ICAAP has a number of immunization social media toolkits that allow you to download images, copy and paste pre-written captions, and share on your own social media pages.
- Find the toolkits on our respiratory virus, VFC, and school resources webpages.
- We recommend you check out the Respiratory Virus Vaccine Toolkit now!
  - Share quick and helpful information about the benefits of the flu vaccine, co-administration, signs and symptoms of RSV, ways to limit the spread of germs, tips for taking care of sick children, info on nirsevimab, and more! Simply post the graphic or personalize it by writing your own caption.

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Upcoming ICAAP Immunization Events

- CDPH & IDPH In-Person VFC Trainings
  - March - September
- Immunizations Webinar: The History of Vaccines, Lessons Learned, and a Look Back in Time (Celebrating Adolescent Immunization Action Week)
  - Wednesday March 19, 12-1PM
- Immunizations Webinar: Back to Basics: A Roadmap for Vaccine Advocacy and Policy
  - Wednesday, April 16th from 12-1PM

Scan Here

illinoisaap.org/events

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