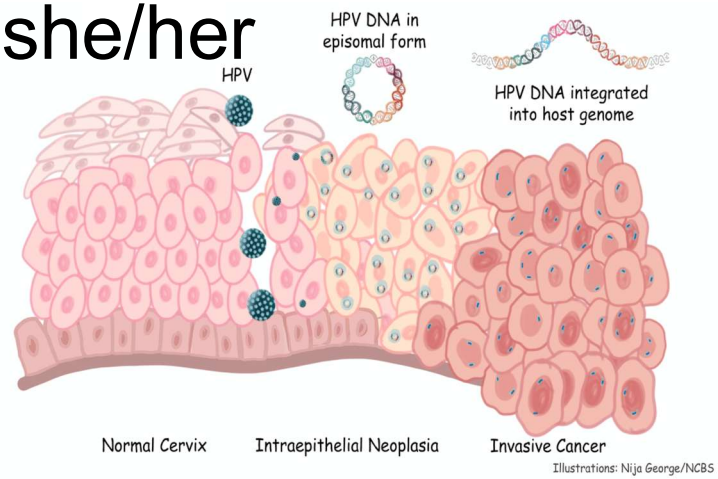
Micro to Macro Perspectives on Vaccine Preventable Cancers

Kaitlin Sundling, MD, PhD she/her
Pathologist



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I have no financial conflicts of interest to disclose.

The discussion of cancer vaccines includes vaccines that are not yet FDA-approved—citations are provided on each slide.

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Objectives

- Low magnification:
  - Recognize vaccination as an essential part of a multilayered approach to cancer prevention and public health
- Intermediate magnification:
  - Evaluate the impact of vaccination on cancer risk
- High magnification:
  - Appreciate the role of pathology in cancer diagnosis and public health

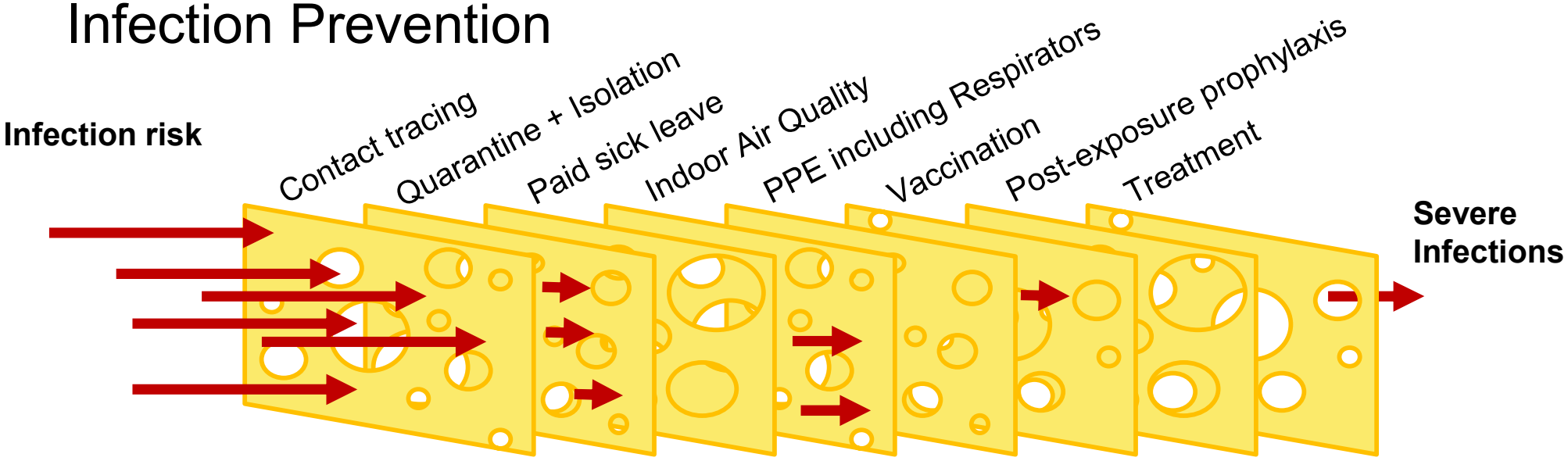
About me

- MD-PhD Physician-Scientist
- Pathologist – specialist in laboratory testing of all kinds
- Subspecialty in cytopathology – small samples with a focus on cancer and precancer (dysplasia) diagnosis
- Public health advocate
- Steering committee member, Wisconsin Families for Vaccines

Image: https://www.fox13news.com/news/magic-school-bus-show-from-the-90s-will-be-transformed-into-a-live-action-movie, Fair use, https://en.wikipedia.org/w/index.php?curid=82546324

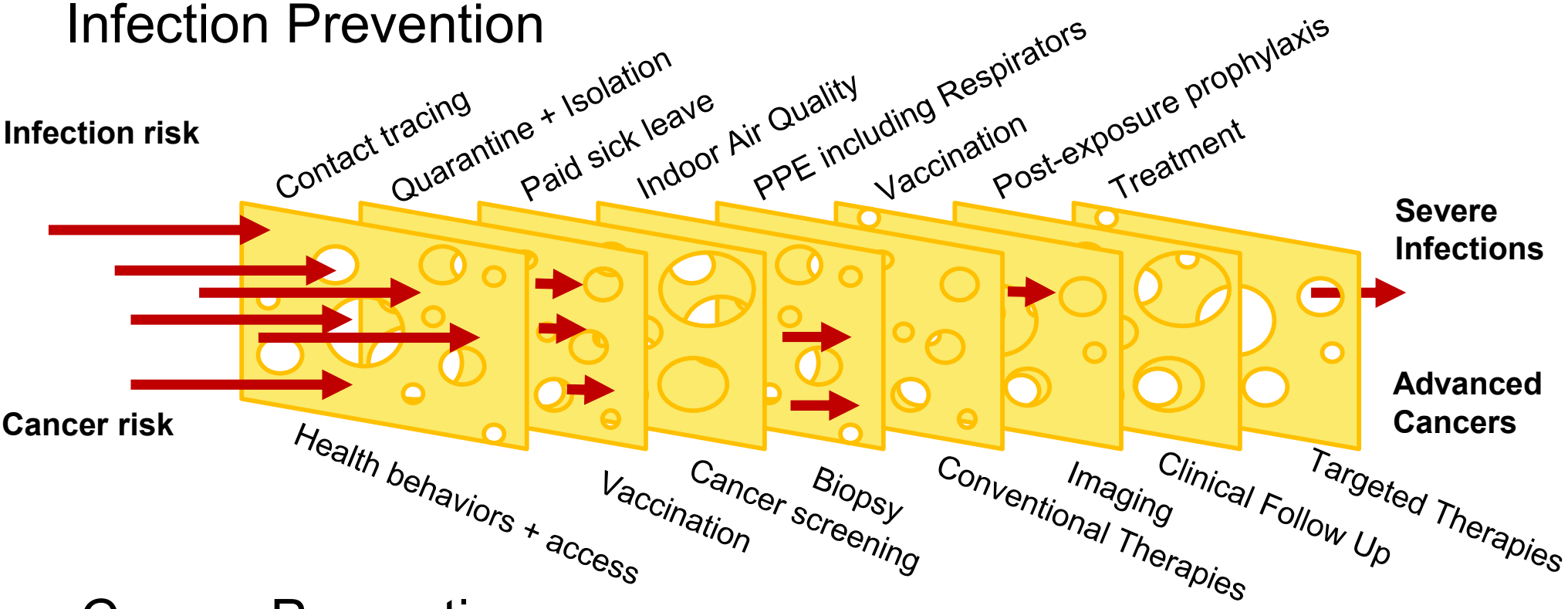
Swiss Cheese (multilayered) approach

Infection Prevention



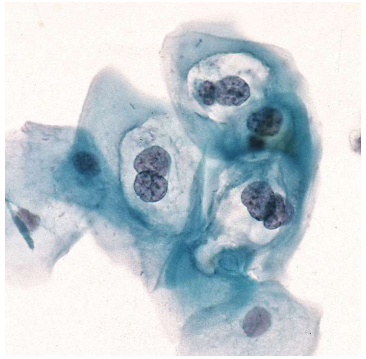
Swiss Cheese (multilayered) approach

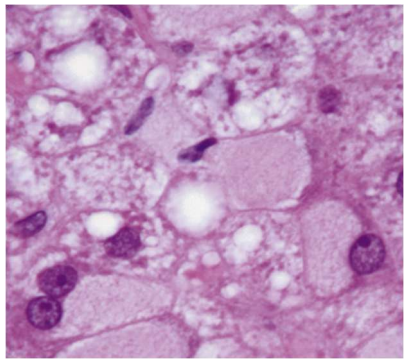
Infection Prevention



Cancer Prevention

Cancer-associated viruses



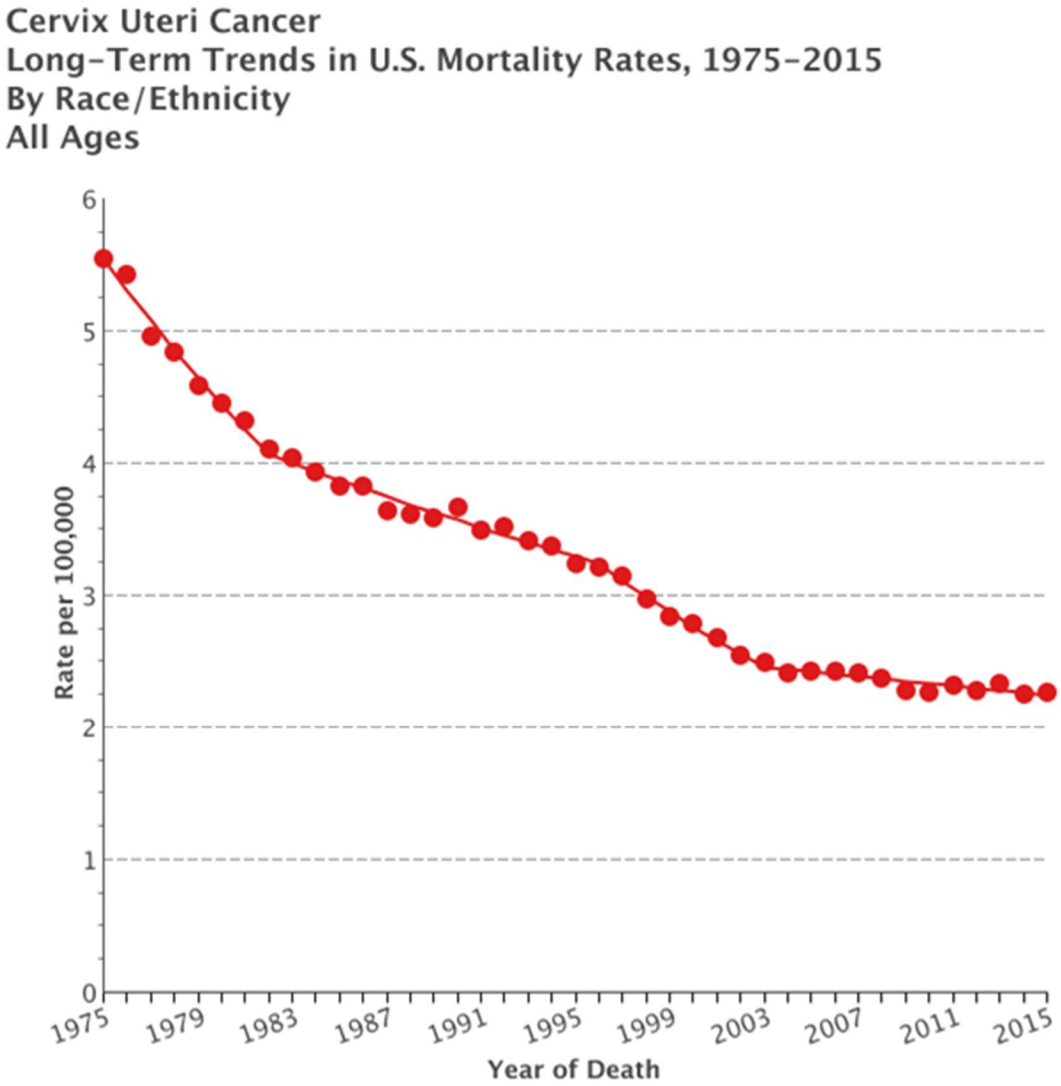


- Human papillomavirus - HPV
- Hepatitis B virus - HBV
- Epstein-Barr Virus EBV
- Human Herpesvirus 8 or Kaposi's Sarcoma Virus - HHV-8
- Human T-Lymphotropic Virus 1 - HTLV-1
- Merkel cell polyomavirus
- Human Immunodeficiency Virus - HIV

- Vaccines available

- 10-15% of cancers worldwide are caused by viruses

White MK, Pagano JS, Khalili K. Viruses and Human Cancers: a Long Road of Discovery of Molecular Paradigms. *Clin Microbiol Rev*. 2014. doi:10.1128/CMR.00124-13
Moore PS, Chang Y. Why do viruses cause cancer? Highlights of the first century of human tumour virology. *Nat Rev Cancer*. 2010. doi:10.1038/nrc2961
Images: https://bethesda.soc.wisc.edu/ViewItem.aspx?id=136; Practical Hepatic Pathology, 2nd edition

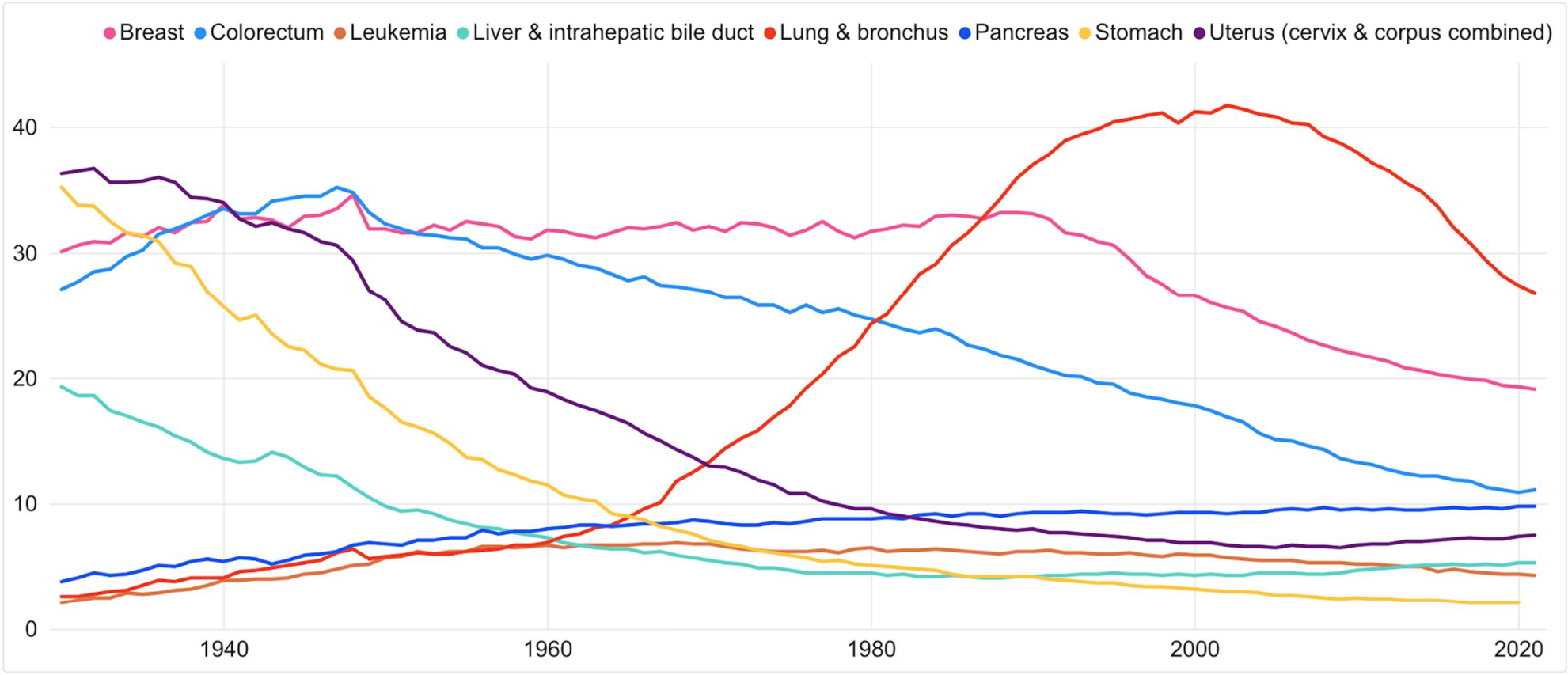


https://seer.cancer.gov/explorer/application.php

HPV and the Pap Test: A Public Health Success Story

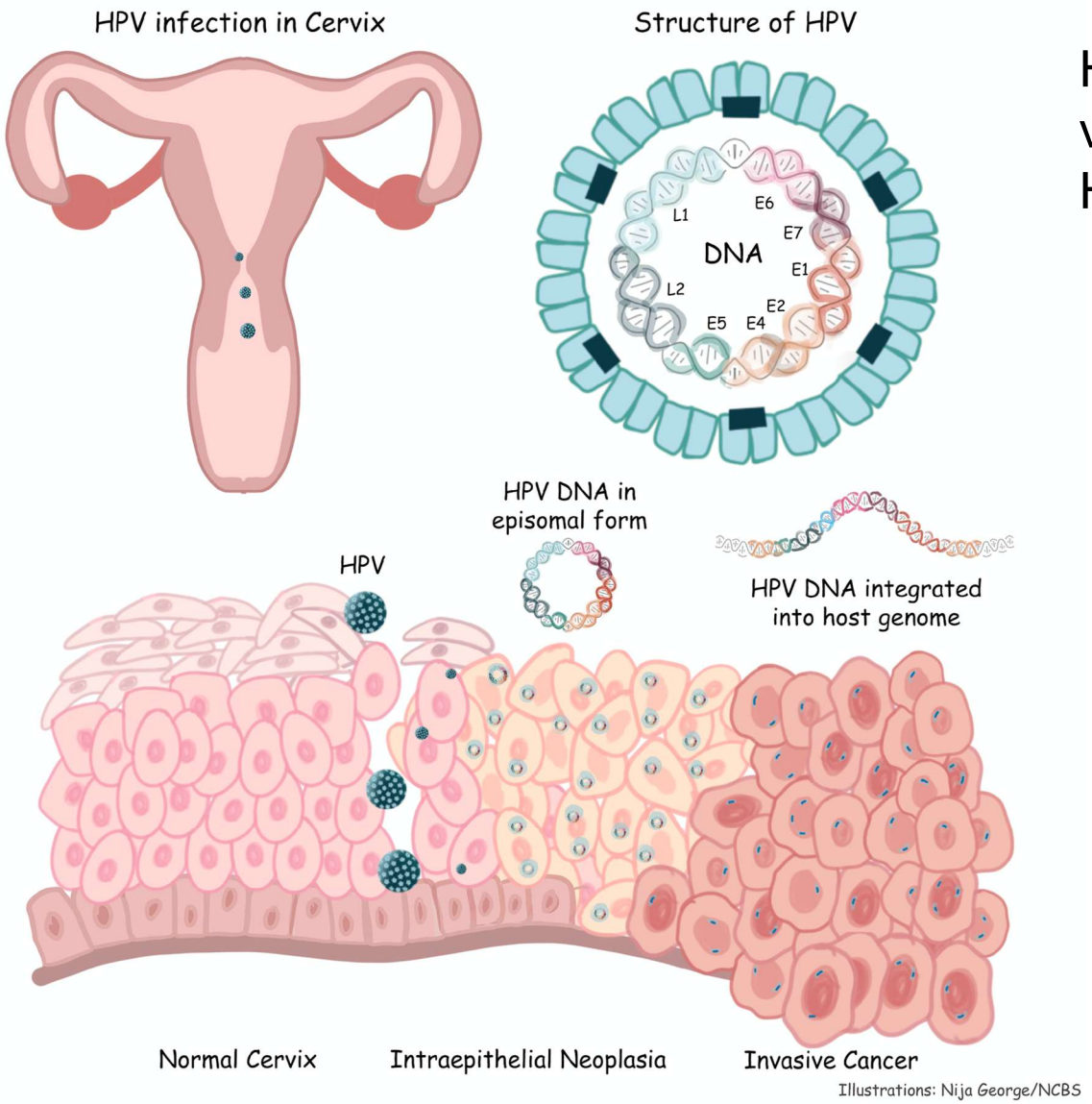
Documentary: The Cancer Detectives on PBS's American Experience https://www.pbs.org/wgbh/americanexperience/films/cancer-detectives/

Prior to the Pap test, cervical cancer was a leading cause of cancer death in women (and people with a cervix)



Data Souce: National Center for Health Statistics, Centers for Disease Contol and Prevention, 2022
Average annual rate per 100,000, age-adjusted to the 2000 US standard population.

https://cancerstatisticscenter.cancer.org/?_ga=2.204471254.757885087.1550850240-643476592.153254151(

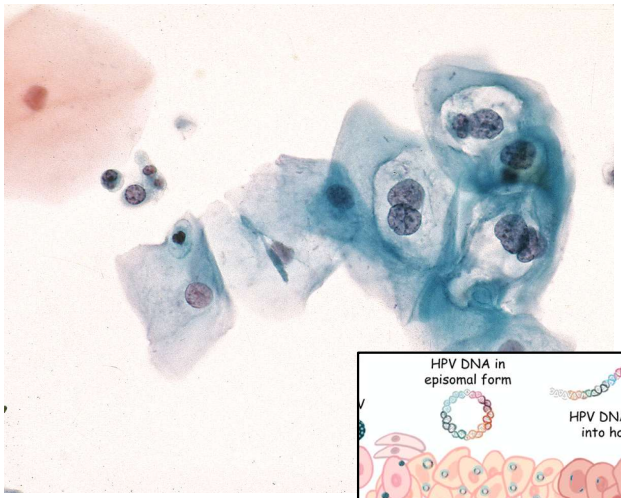


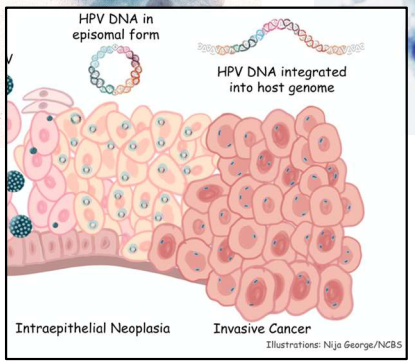
Human papillomavirus (HPV) vaccine prevents about 97% of HPV infections

Kreimer AR, Porras C, Liu D, et al. Noninferiority of One HPV Vaccine Dose to Two Doses. *New England Journal of Medicine*. 2025;393(24):2421-2433. doi:10.1056/NEJMoa2506765

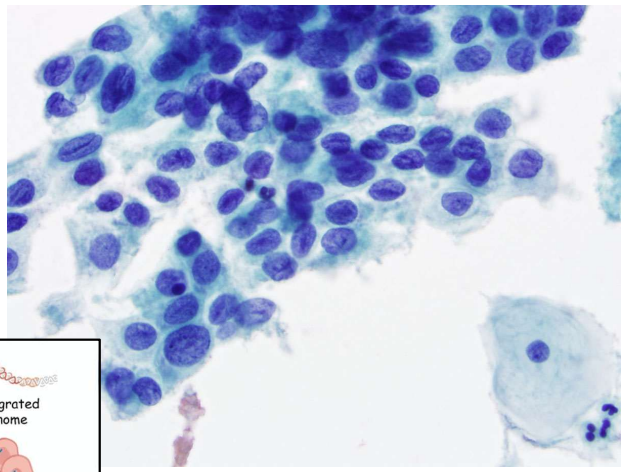
Diagram: Nija George, National Centre for Biological Sciences,
Tata Institute of Fundamental Research

Low Grade Squamous Intraepithelial Lesion
Productive HPV infection

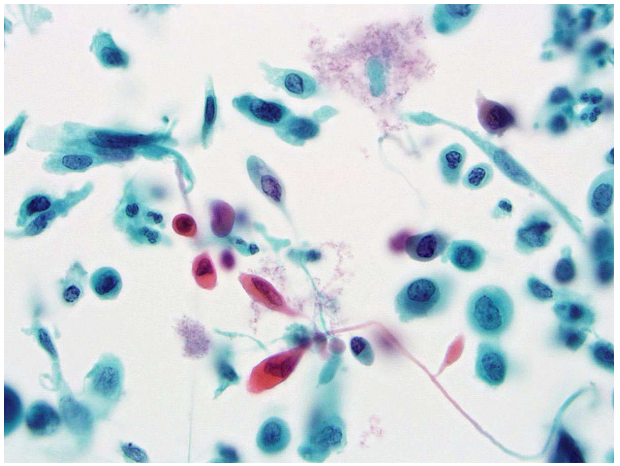




High Grade Squamous Intraepithelial Lesion
Oncogenic viral integration

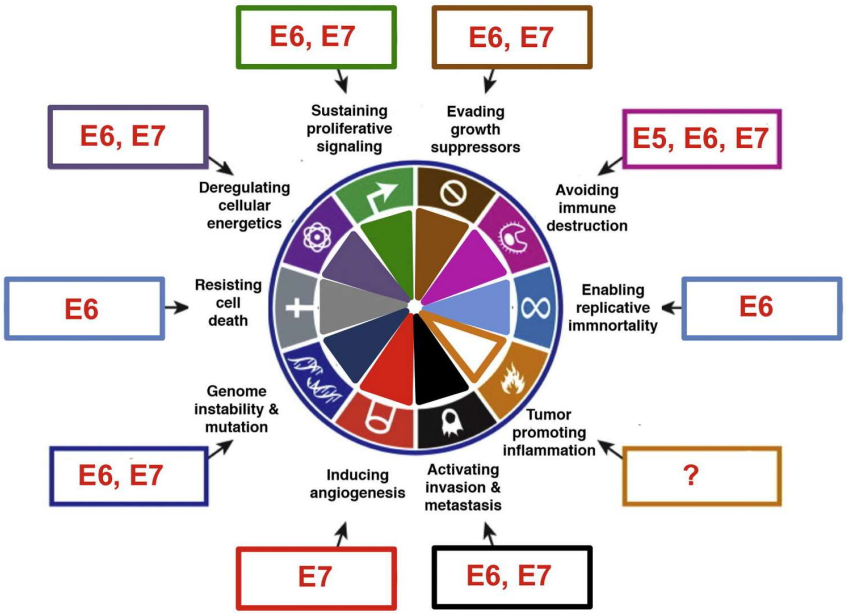


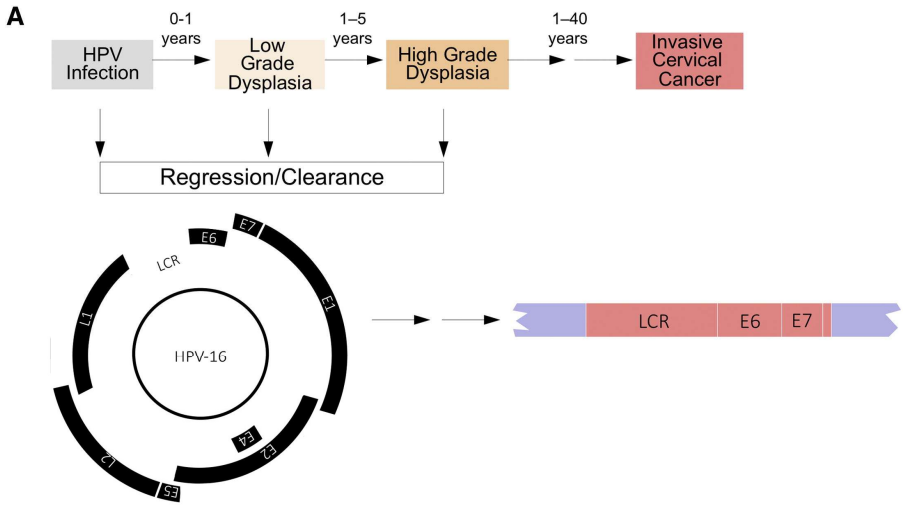
Squamous Cell Carcinoma
Cellular transformation



https://bethesda.soc.wisc.edu/ViewItem.aspx?id=136;
https://bethesda.soc.wisc.edu/ViewItem.aspx?id=156;
https://bethesda.soc.wisc.edu/ViewItem.aspx?id=188

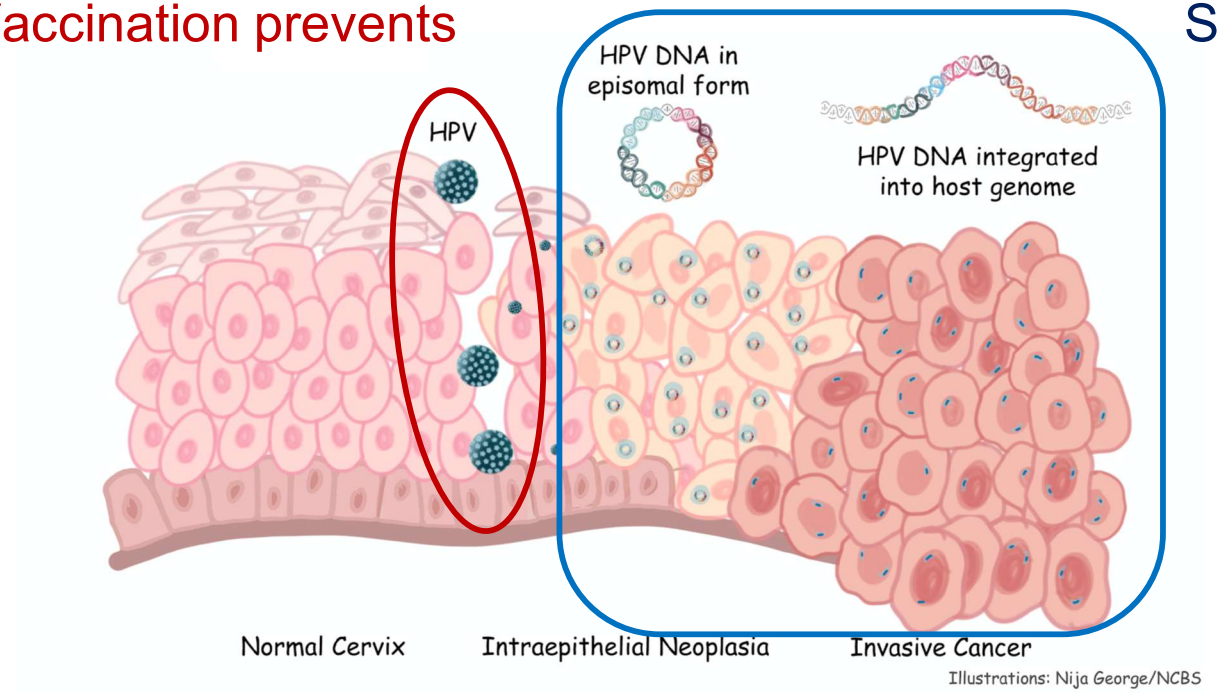
Viral oncoproteins target multiple cancer mechanisms (hallmarks)





Mesri EA, Feitelson MA, Munger K. Human Viral Oncogenesis: A Cancer Hallmarks Analysis. *Cell Host & Microbe*. 2014. doi:10.1016/j.chom.2014.02.011

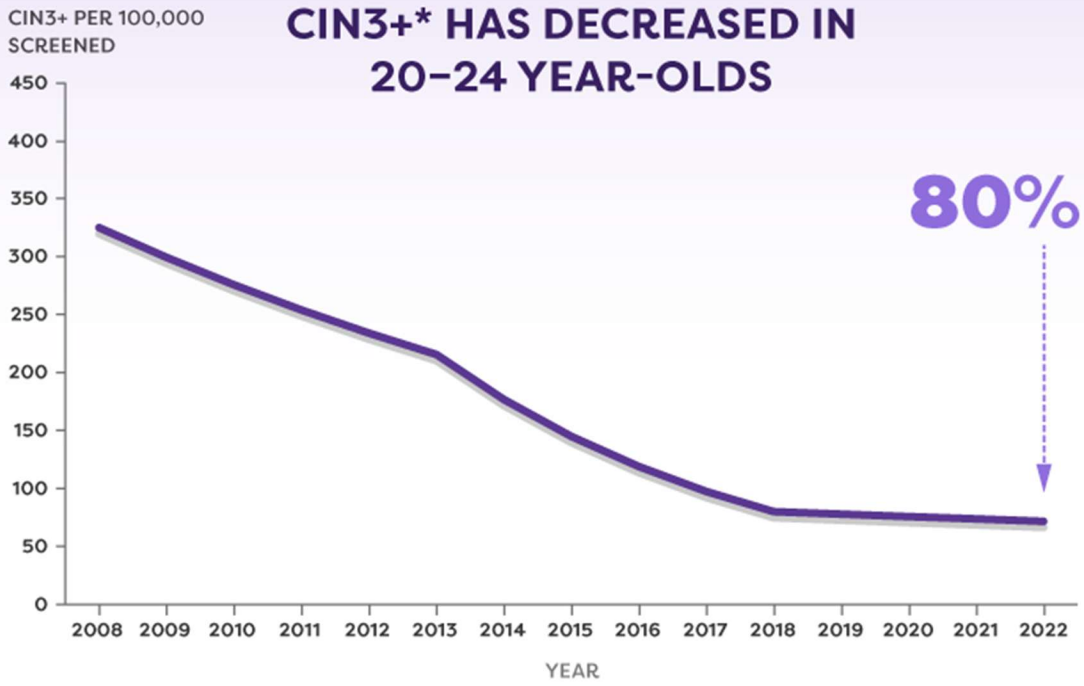
Vaccination prevents



Screening/diagnosis detects

Diagram: Nija George, National Centre for Biological Sciences,
Tata Institute of Fundamental Research

Cervical precancers decreased after HPV vaccine was introduced in the United States in 2006



Health care providers should recommend HPV vaccination for girls and boys ages 11-12. Vaccination can be started at age 9, and catch-up is recommended through age 26.

CDC.GOV

tinyurl.com/mm7406a4

FEBRUARY 27, 2025

*CIN3+ cervical precancers are most likely to progress to invasive cancer

MMWR

https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a4.htm

HPV vaccination rates by state

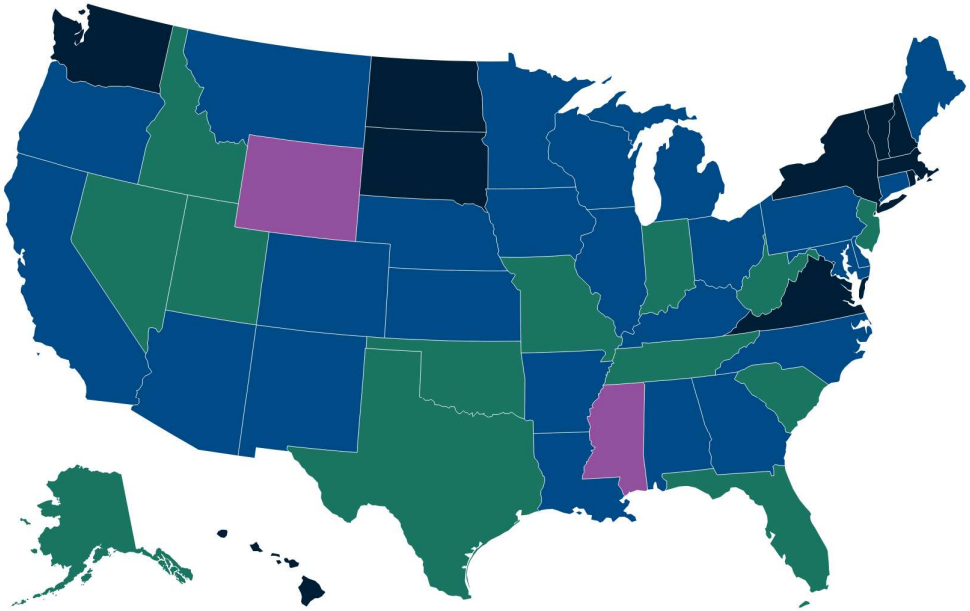
Figure 3

HPV Vaccination Rates of Adolescents by State, 2024

Share of adolescents ages 13-17 with up-to-date (UTD) HPV vaccine series

U.S. Overall = 62.9%

- 39%-49.3% (2 states)
- 49.3%-59.5% (13 states)
- 59.5%-69.6% (25 states)
- 69.6%-80% (10 states and D.C.)

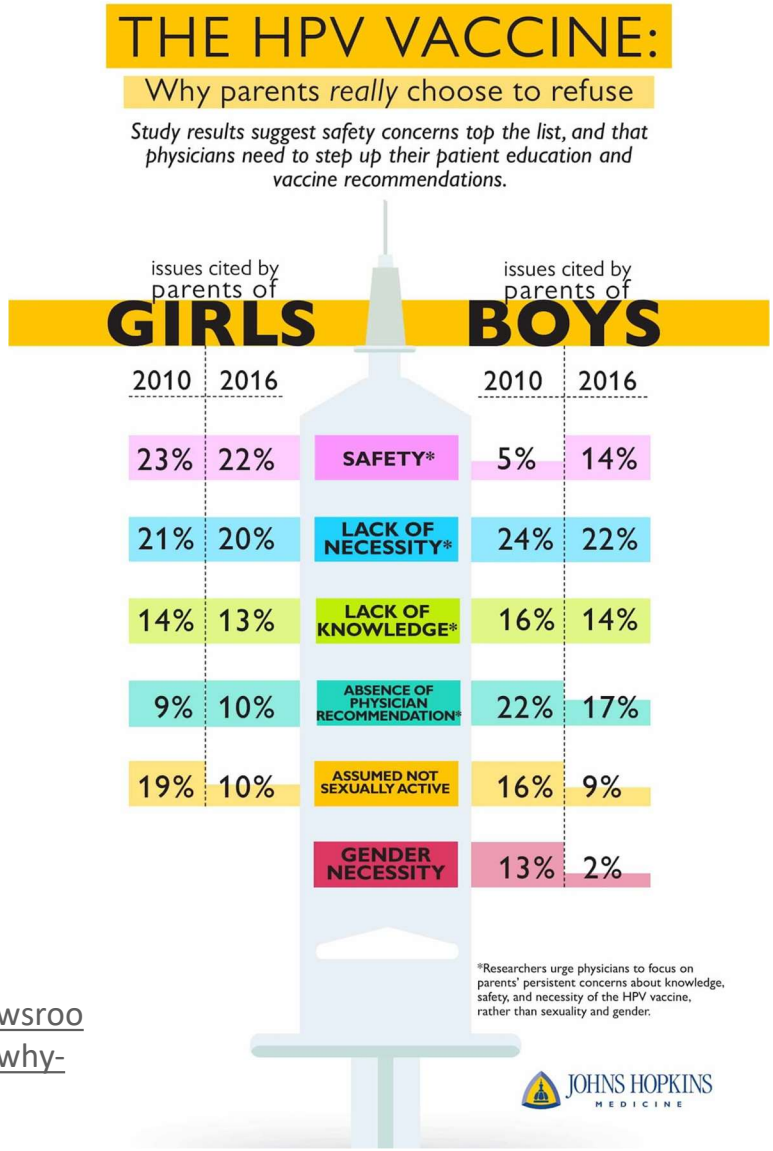


Note: HPV UTD vaccination status includes those with ≥3 doses, and those with 2 doses when HPV vaccine series was initiated before age 15 years and there was at least 5 months minus 4 days between the first and second dose.

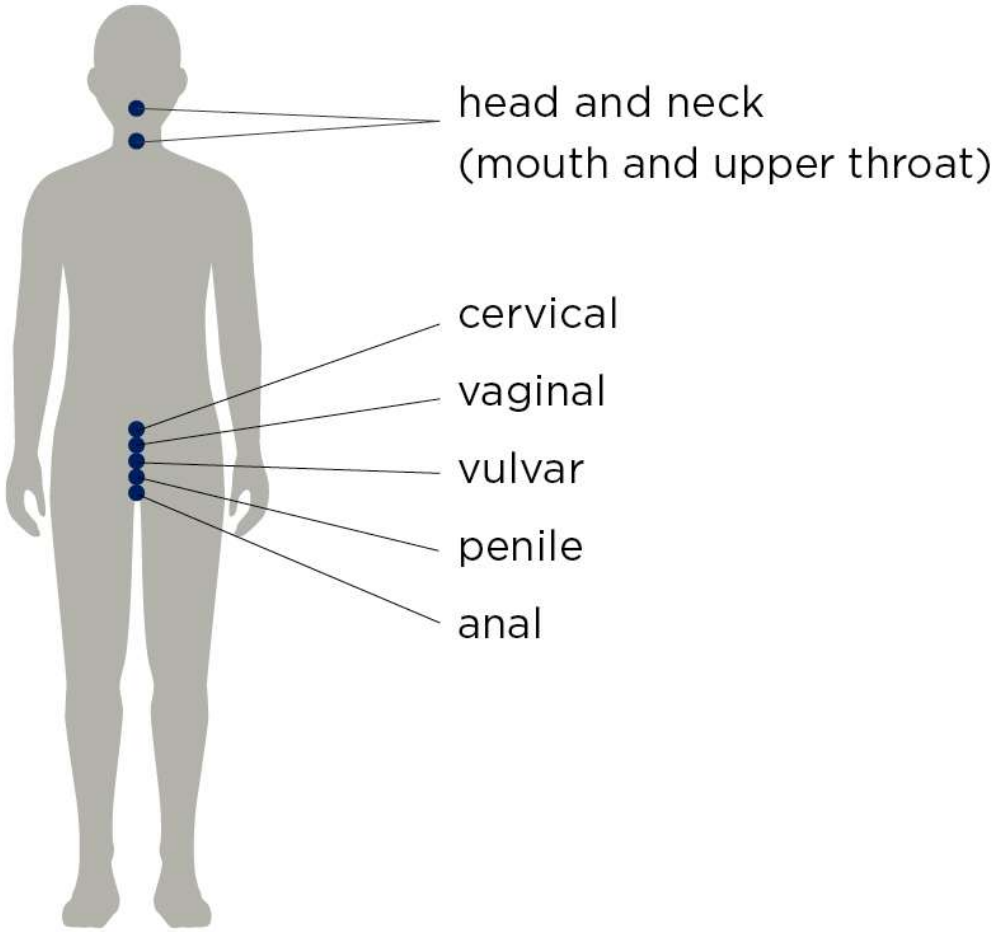
Source: SUPPLEMENTARY TABLE. Vaccination Coverage Among Adolescents Aged 13–17 Years — National Immunization Survey-Teen, United States, 2024. *MMRW* 74(30).

KFF

https://www.kff.org/womens-health-policy/the-hpv-vaccine-access-and-use-in-the-u-s/



https://www.hopkinsmedicine.org/news/newsroom/news-releases/2018/10/the-hpv-vaccine-why-parents-really-choose-to-refuse

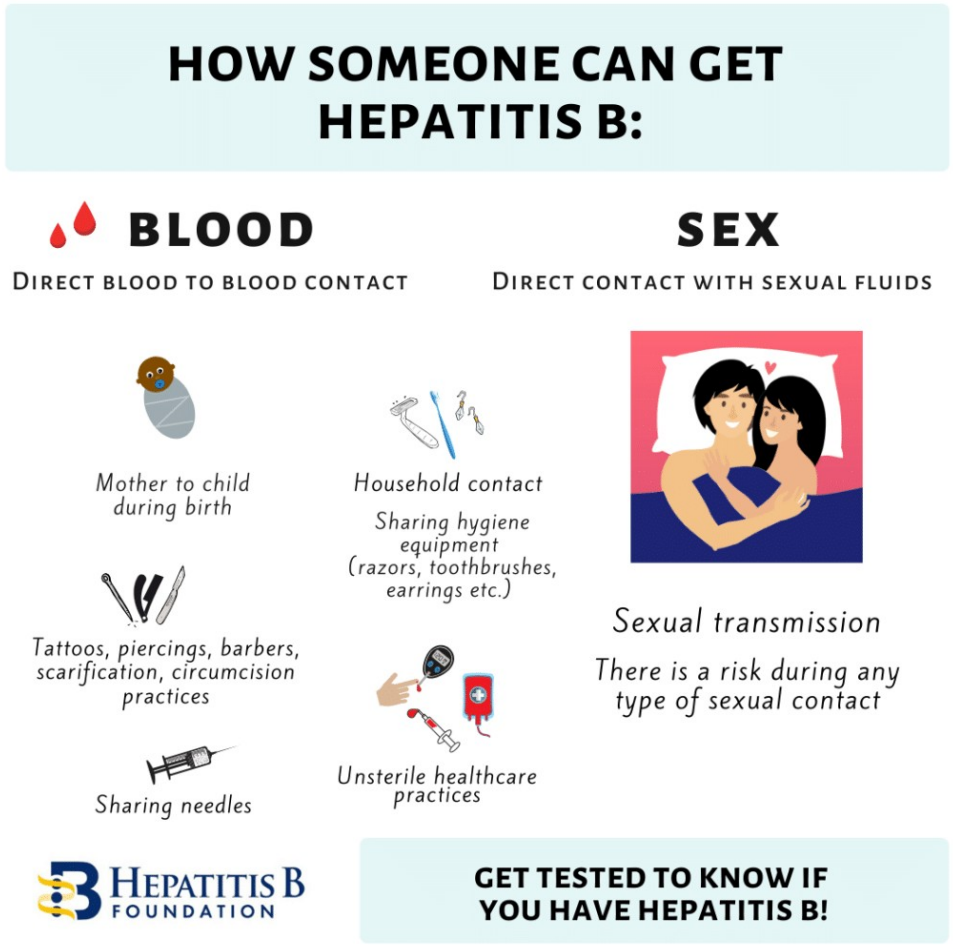


HPV cancers throughout the body

- Screening methods are available for cervical and anal lesions
- Diagnosis of head and neck cancers is more challenging and may occur once the cancer has spread to a lymph node
- HPV vaccination prevents HPV-driven cancers at all body sites

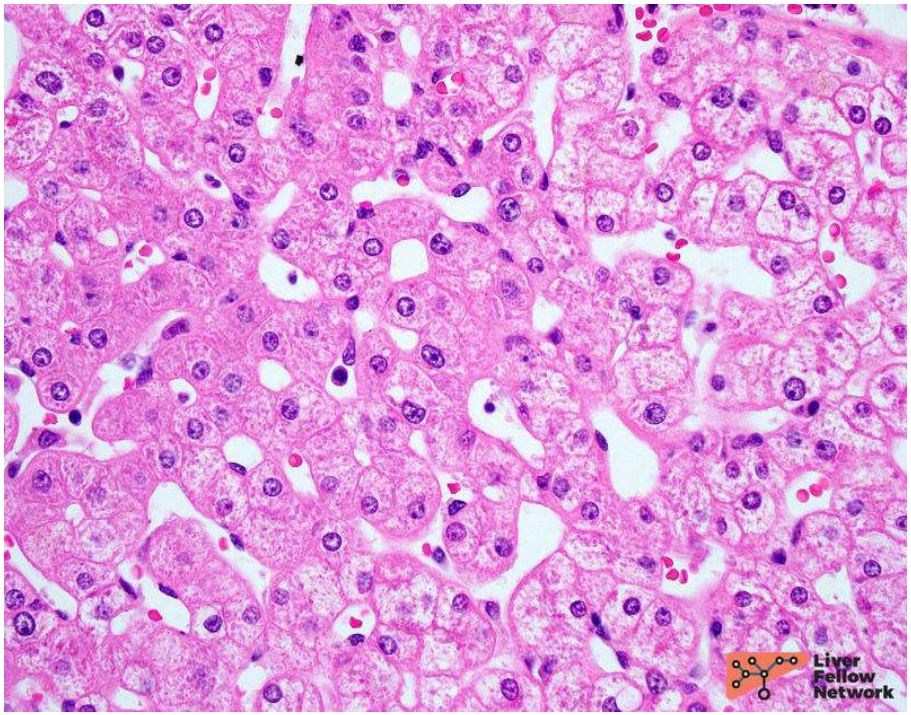
https://www.mskcc.org/cancer-care/patient-education/preventing-hpv-related-cancers

Hepatitis B transmission



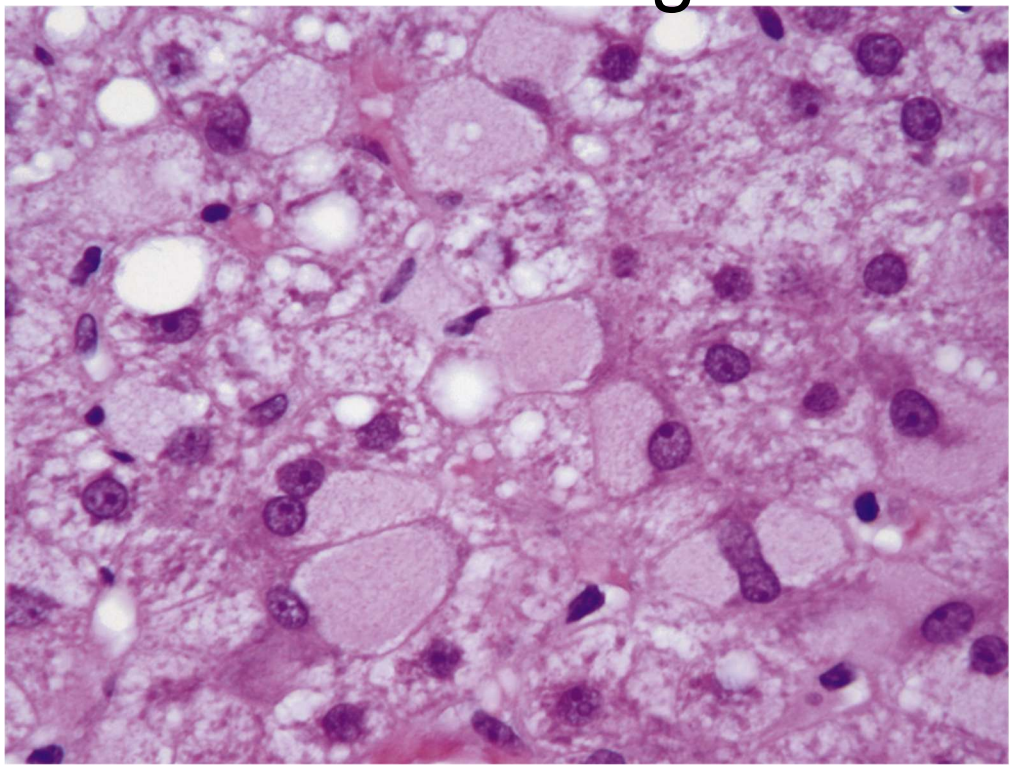
https://www.hepb.org/blog/transmission-graphic-asian-and-african-social-media-1/

Normal Liver



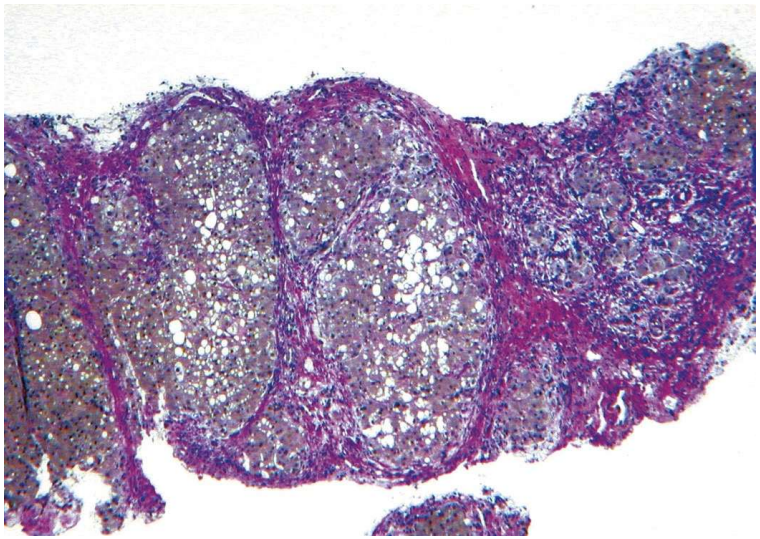
https://www.aasld.org/liver-fellow-network/core-series/pathology-pearls/liver-biopsy-interpretation-special-stains

Liver with Hepatitis B viral change



Practical Hepatic Pathology, 2nd edition

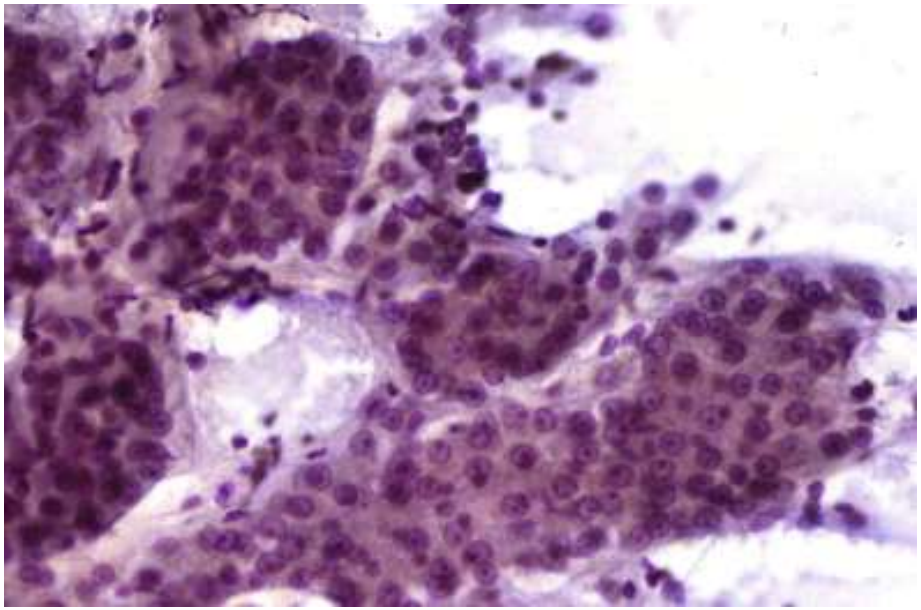
Cirrhosis – not always seen with Hepatitis B infection



Practical Hepatic Pathology, 2nd edition

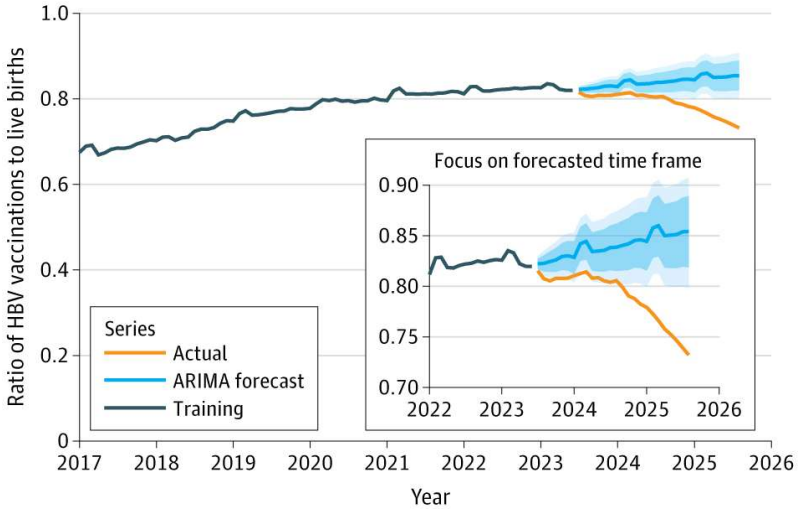
Hepatocellular carcinoma

- In patients with chronic Hepatitis B, may occur with or without a background of cirrhosis
- Potential treatment options:
  - Surgery
  - Liver transplant
  - Ablation therapy
  - Embolization therapy
  - Targeted therapy
  - Radiation therapy



Robbins Pathologic Basis of Disease
Bibbo Comprehensive Cytopathology, Liver Chapter

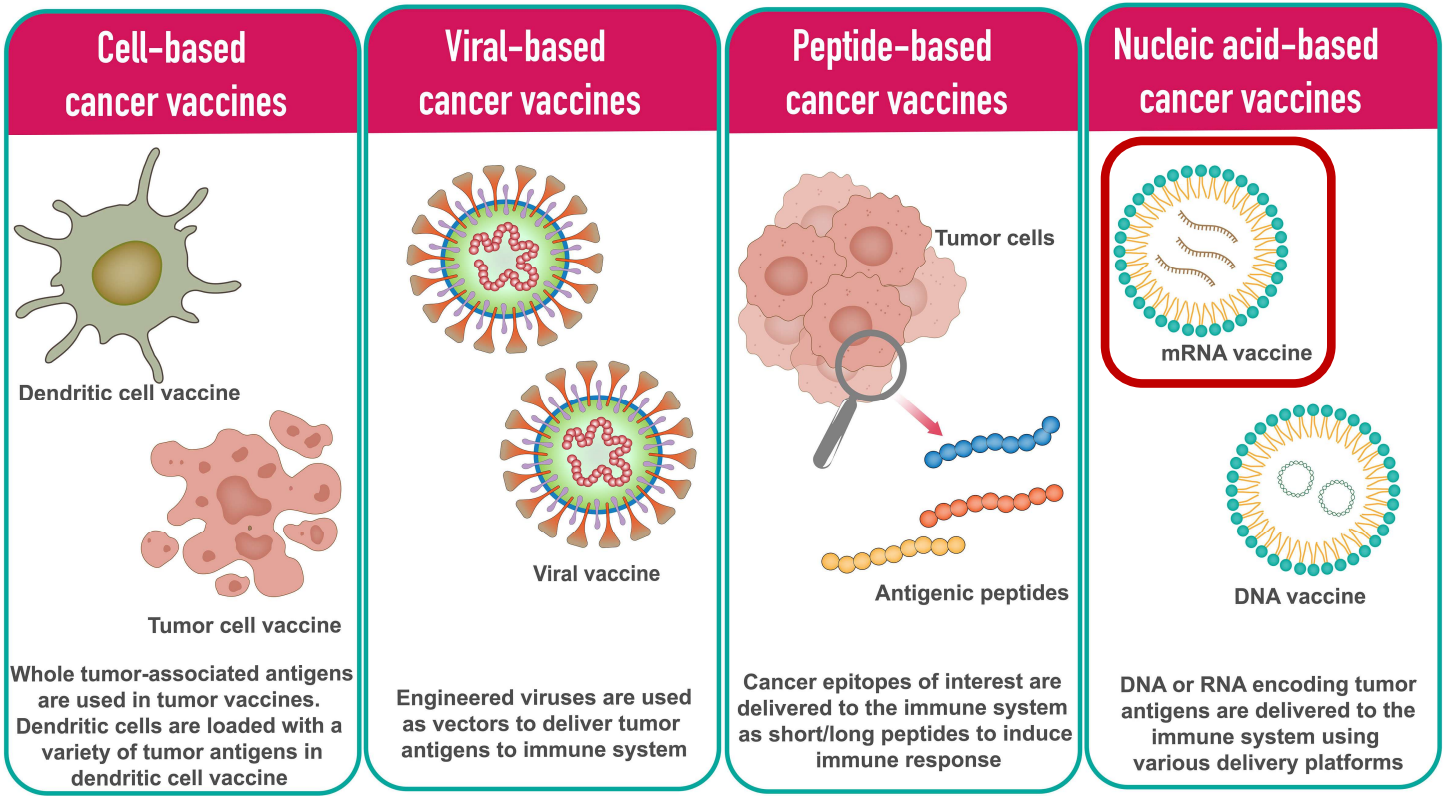
Hepatitis B vaccination prevents chronic infection



- Hepatitis B virus (HBV) vaccine is about 98% effective after a 3-dose series
- Since implementing the universal birth dose of HBV vaccine in 1991, child and adolescent HBV infections in the US dropped by about 99%
- Recent newborn HBV vaccination rates have declined
  - 2025 CDC ACIP vote to end universal HBV vaccination at birth

Image: Rothman JM, Kwan B, Longhurst CA, Jena AB. US Newborn Hepatitis B Virus Vaccination Rates. *JAMA*. 2026;335(12):1086-1087. doi:10.1001/jama.2026.0866
https://publichealth.jhu.edu/2025/why-hepatitis-b-vaccination-begins-at-birth

Cancer vaccines show additional promise



Vishweshwaraiah YL, Dokholyan NV. mRNA vaccines for cancer immunotherapy. *Front Immunol*. 2022;13. doi:10.3389/fimmu.2022.1029069

Comparison of routine vaccines vs. cancer vaccines

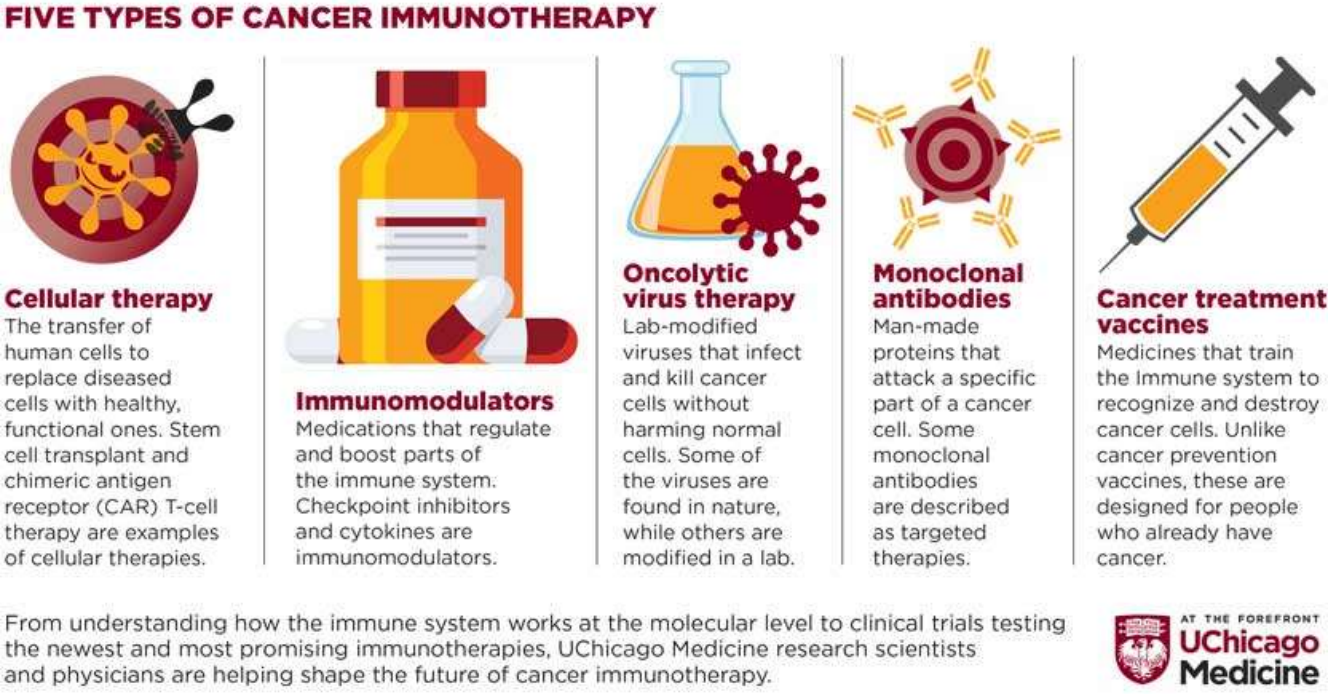
Similarities

- mRNA platform allows more rapid and cost-effective changes to the vaccine target than other platforms
  - Frequent updates
  - Personalized vaccines
- Training immune system to identify and break down the target
- Rigorously tested

Differences

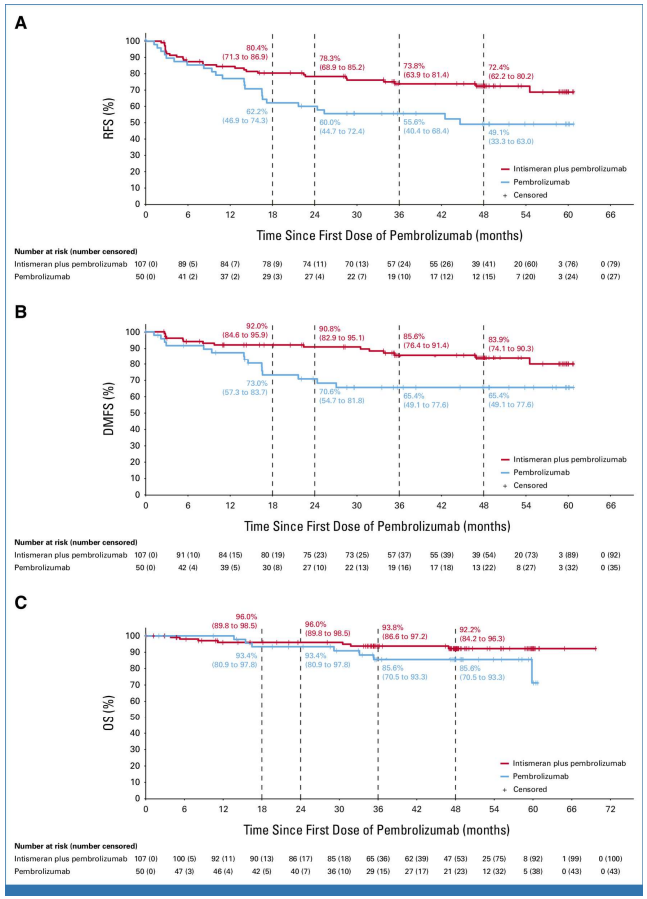
- Often personalized to an individual and requiring a sample of their tumor
- Most routine vaccines prevent infection – cancer vaccines are typically used after the cancer has developed
- Cancer vaccines may not yet be FDA approved in the US
- Routine vaccines are used in a healthy population, expect side effects of cancer vaccines to differ

What is immunotherapy?



- Using the body's own immune defenses to fight cancer
- Some cancers are more amenable than others
- Microscopic appearance can be a clue

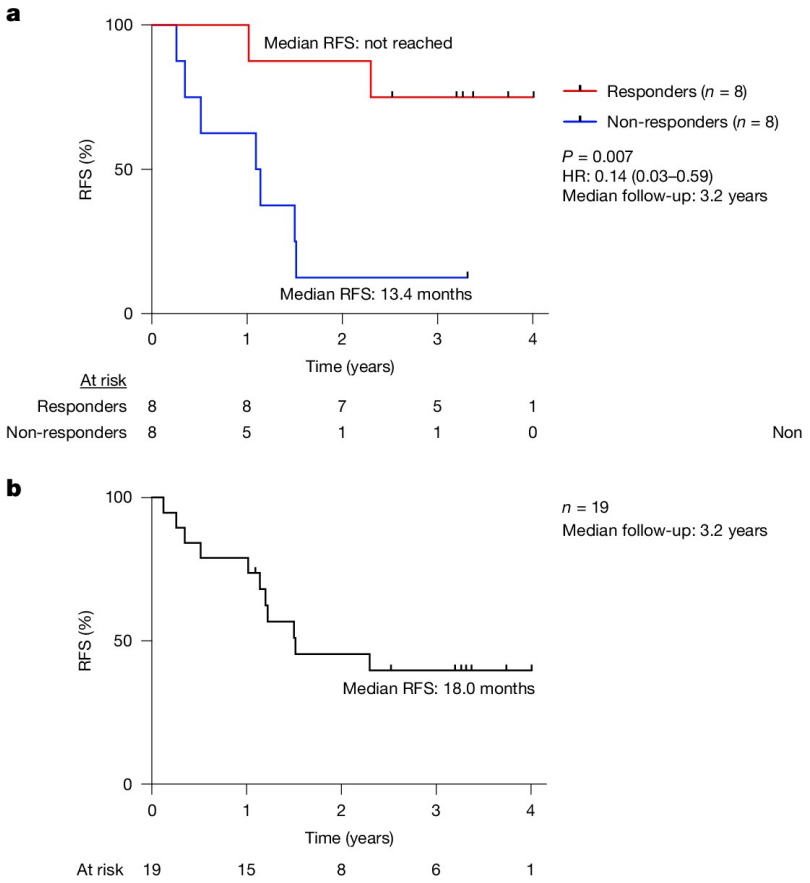
https://www.uchicagomedicine.org/-/media/images/ucmc/adult-images/conditions-and-services/cancer/immunotherapy-infographic.jpg



Cancer Vaccines in the News: Melanoma

- Recent melanoma Phase IIb trial results from Moderna/Merck
- Intismeran autogene mRNA vaccine contains up to 34 personalized cancer antigen targets
- Higher survival and lower rate of recurrence/distant metastasis in patients who received a personalized cancer vaccine

Khattak A, Carlino MS, Meniawy T, et al. Intismeran Autogene Plus Pembrolizumab Versus Pembrolizumab Alone in High-Risk Resected Melanoma. *J Clin Oncol*. 2026;0(0):JCO-26-00835. doi:10.1200/JCO-26-00835
https://www.cnbc.com/2026/08/19/moderna-merck-cancer-vaccine-shows-initial-late-stage-melanoma-data.html



Cancer Vaccines in the News: Pancreatic Cancer

- Pancreatic cancer clinical trial with autogene cevumeran mRNA vaccine
- Up to 20 personalized cancer antigen targets
- Also showed favorable immune responses

Sethna Z, Guasp P, Reiche C, et al. RNA neoantigen vaccines prime long-lived CD8+ T cells in pancreatic cancer. *Nature*. 2025;639(8056):1042-1051. doi:10.1038/s41586-024-08508-4

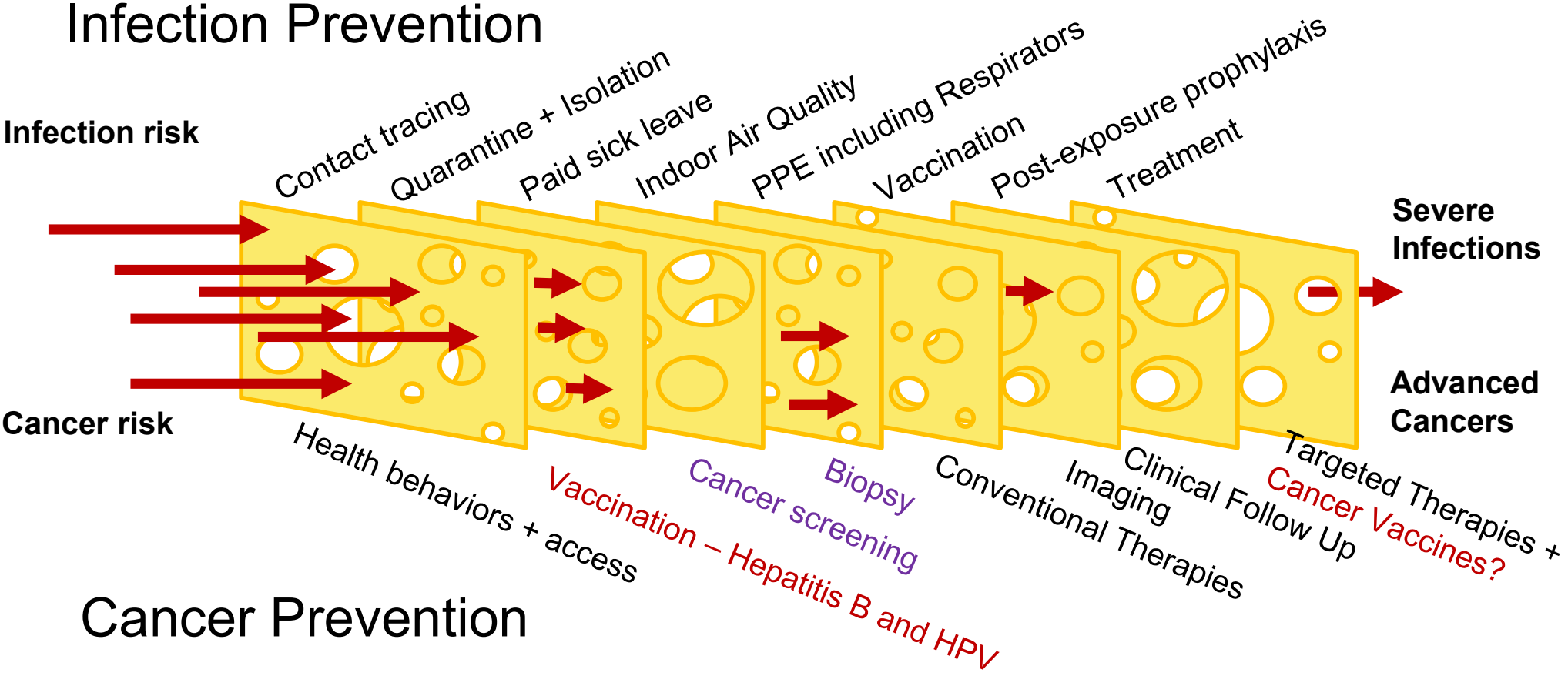
https://www.sciencefriday.com/segments/pancreatic-cancer-mrna-vaccine-aug-2025/

Vaccination and infection prevention for cancer patients

- Patients going through cancer therapy and cancer survivors participate in all areas of public life and visit all parts of the healthcare system, not just designated “high-risk” locations
- Maintaining up-to-date vaccinations is important
- Some patients may not have adequate immune responses and may rely on community protection, including high vaccination rates, masking, and other precautions

Swiss Cheese (multilayered) approach

Infection Prevention



Cancer Prevention

Dolly Parton once gave $1 million to help develop the Moderna COVID vaccine at Vanderbilt

JOHN LAMPARSKI/GETTY IMAGES
https://fortune.com/2026/08/26/dolly-parton-rags-to-riches-philanthropy-one-million-dollars-to-moderna-covid-vaccine-development/

What's next?

- Promote vaccination and science-based, multilayered protections in your role professionally and in your communities
- Support vaccine access, vaccine campaigns, and science-based policies locally, statewide, and nationally
- Advocate for public health and health science funding

@Dollyparton, via Reuters
https://www.nytimes.com/2021/03/02/world/dolly-parton-moderna-vaccine-covid.html

Recommended Resources

- Wisconsin Families for Vaccines: https://www.wifamiliesforvaccines.org/
- Documentary: The Cancer Detectives on PBS's American Experience https://www.pbs.org/wgbh/americanexperience/films/cancer-detectives/
- Book: The Song of the Cell by Siddhartha Mukherjee https://www.simonandschuster.com/books/The-Song-of-the-Cell/Siddhartha-Mukherjee/9781982117368
- https://precaution.substack.com/ - for further reading on my public health advocacy
- https://wcha.substack.com/ - Local public health advocacy group in Wisconsin

Questions?

- Feel free to reach out – kaitlinsundling@gmail.com