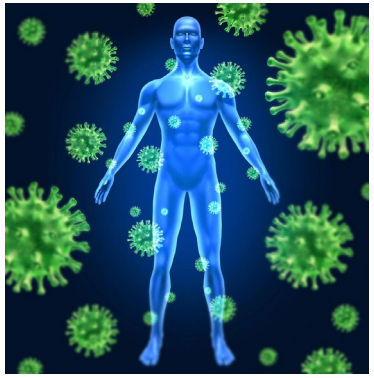

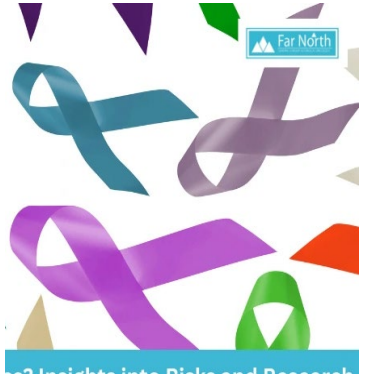

Infection and Cancer
From Oncogenesis to Outcomes

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CARTI

8/21/2026

Conflict of Interest

- No financial interest to declare

At the end of this presentation, the attendees will be able to

I. Identify infections that can cause cancer
II. Understand the seriousness of infections in cancer patients
III. Appreciate the role of vaccines in protecting cancer patients and the importance of implementing vaccines in oncology practices
IV. Learn about the emerging role of vaccination against viral infections in enhancing anticancer treatments

Take Aways

- Many infections, especially viruses, can cause cancer
  - Available vaccines for some of them can prevent the establishment of chronic infections and therefore the development of cancer
- Infections are more severe in cancer patients leading to higher morbidity and mortality than the general population
  - Vaccines for respiratory infections reduce severe infections, hospitalization and death and may decrease the activation of dormant cancer cells
  - All adult cancer patients are eligible for vaccination starting at age 19 (for most vaccines)
  - **Call to Action: Specialty practices can implement adult vaccination for their patients**
- Vaccines for viral respiratory infections may enhance the effect of anticancer therapy, especially immune checkpoint inhibitors
  - Vaccines are being investigated as adjunct anticancer therapy

Some Infections Can Cause Cancer

The International Agency for Research on Cancer (IARC) Classification

- The IARC has classified 13 infectious agents as carcinogenic to humans
- They account for approximately 12% of all cancers worldwide (~2.3 million cases annually)
- These span viruses, bacteria, and parasites
- They are divided into two groups
  - Definite Carcinogens
  - Probable Carcinogens

IARC Group 1 Carcinogens (Definite)

Pathogens -viruses	Cancers	Cases Globally /year
Human papillomavirus (HPV)	Cervical, oropharyngeal, anal, vulvar, vaginal, and penile cancers	~730,000
Hepatitis B virus (HBV)	Hepatocellular carcinoma (HCC)	~380,000
Hepatitis C virus (HCV)	HCC, non-Hodgkin lymphoma	~160,000
Epstein-Barr virus (EBV)	Nasopharyngeal carcinoma, Burkitt lymphoma, Hodgkin lymphoma, gastric carcinoma, post-transplant lymphoproliferative disorder	~240,000
Human T-cell lymphotropic virus type 1 (HTLV-1)	Adult T-cell leukemia/lymphoma	
Kaposi sarcoma-associated herpesvirus (KSHV/HHV-8)	Kaposi sarcoma, primary effusion lymphoma	
Human immunodeficiency virus type 1 (HIV-1)	Acts primarily through immunosuppression, increasing risk of Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer	

IARC Group 1 Carcinogens (Definite)

Pathogens -Bacterium	Cancers	Cases Globally /year
Helicobacter pylori	Gastric adenocarcinoma (non-cardia), gastric MALT lymphoma	~850,000

Pathogens -Parasites	Cancers	Cases Globally /year
Schistosoma haematobium	Bladder cancer (squamous cell carcinoma)	
Opisthorchis viverrini	cholangiocarcinoma (bile duct cancer)	
Clonorchis sinensis	cholangiocarcinoma	

IARC Group 2A (Probable Carcinogens)

Pathogens	**Cancers**	**Cases Globally** /year
Merkel cell polyomavirus (MCPyV)	Merkel cell carcinoma	
Plasmodium falciparum	Burkitt lymphoma (in endemic malaria regions, acting as a cofactor with EBV)	

In The U.S.

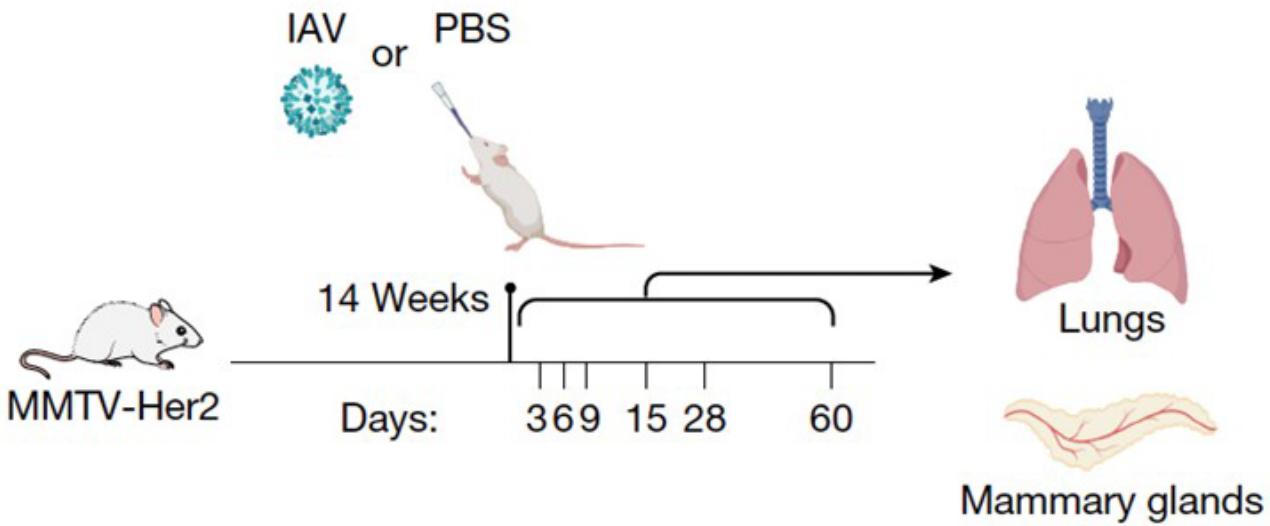
- Approximately 4.3% of adult cancers are infection-attributable
  - HPV is responsible for the largest share (38,230 cases in 2017)
  - H. pylori (10,624)
  - HCV (9,006)
  - EBV (7,581)
  - HBV
  - HIV
  - EBC
  - HTLV
  - MCPyV

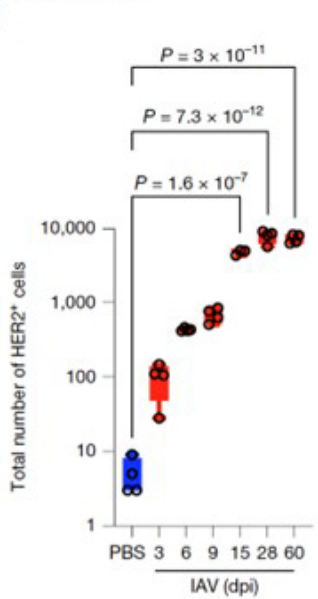
Infection May Awaken Dormant Cancer Cells

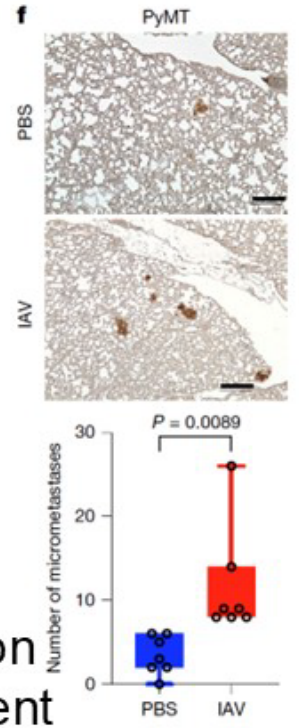
Respiratory viral infections awaken metastatic breast cancer cells in lungs

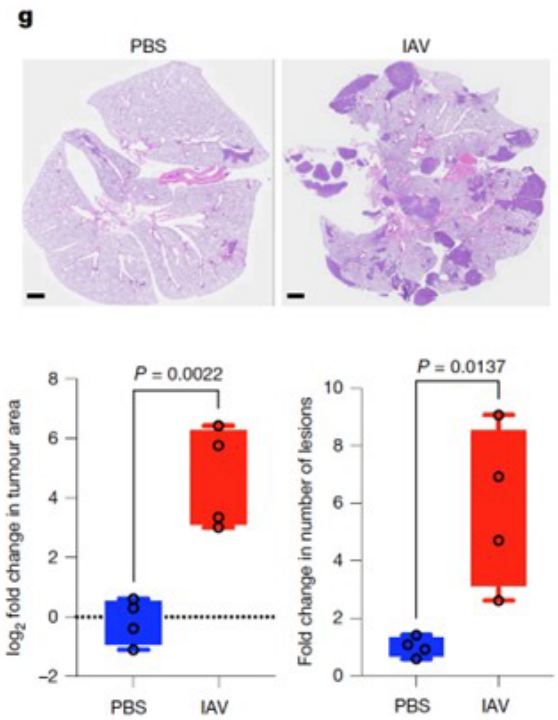
Hypothesis: pulmonary viral infections increase cancer deaths by triggering the development of metastases from dormant DCCs

Approach: Effects of viral respiratory infections (influenza virus and SARS-CoV-2) on breast cancer dormancy (DCC) in mouse models and correlate with humans





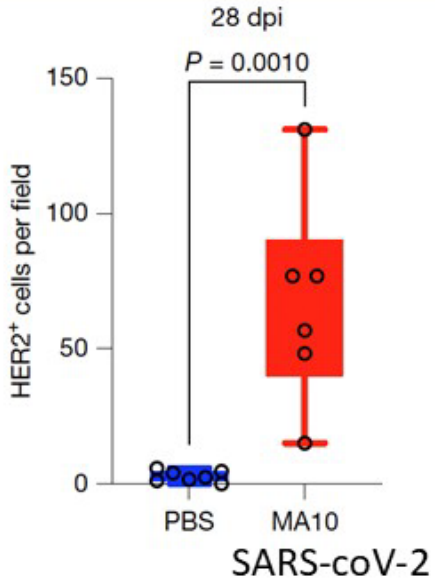


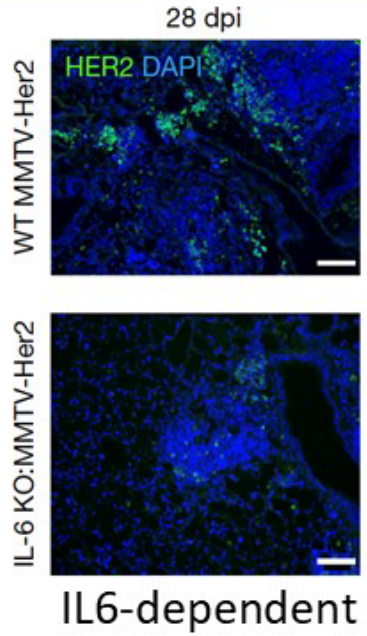


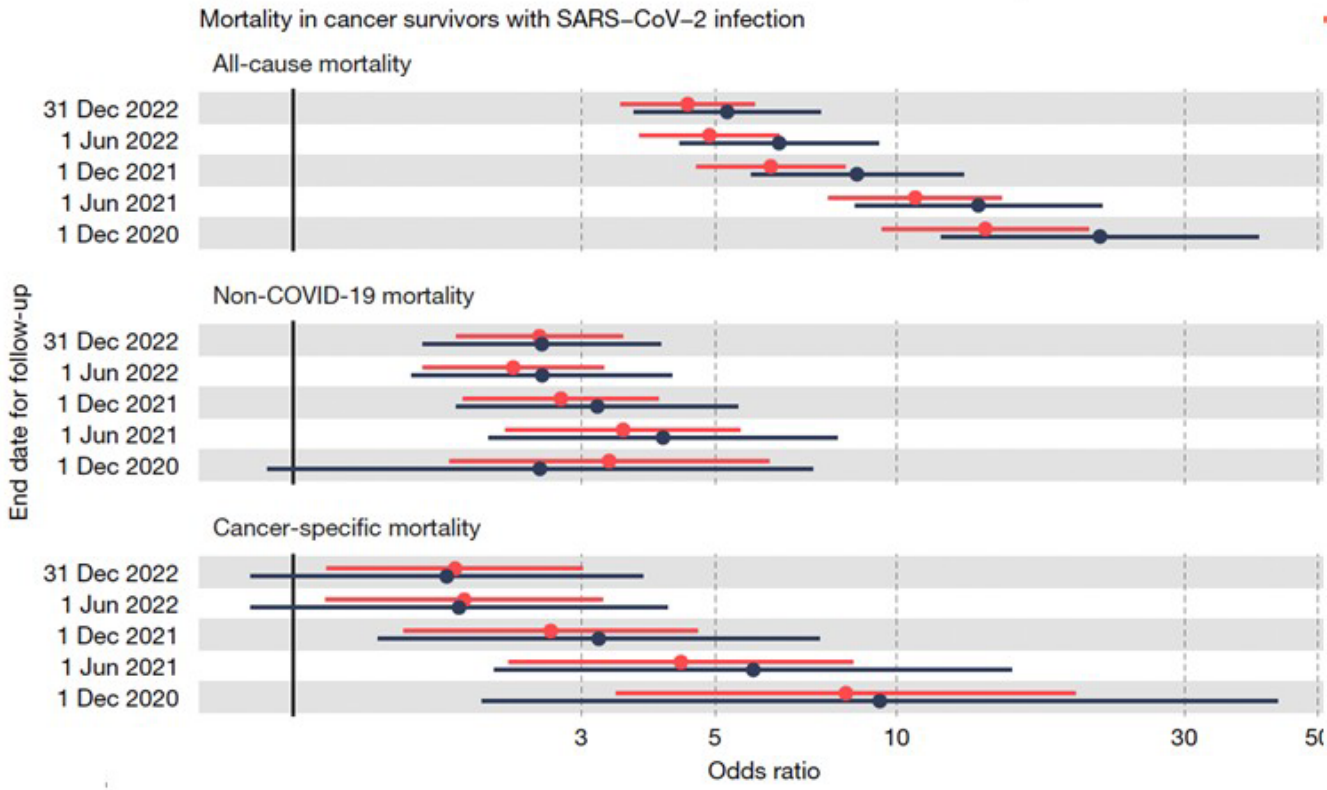
- Influenza and SARS-CoV-2 infection trigger local and systemic inflammation
- Activate DCC proliferation in the lung within days of infection. IL-6 dependent with DCCs impairing lung T cell activation

Shi B. Chia…James DeGregori: Respiratory viral infections awaken metastatic breast cancer cells in lungs. Nature Vol 645 11 September 2025

Respiratory viral infections awaken metastatic breast cancer cells in lungs

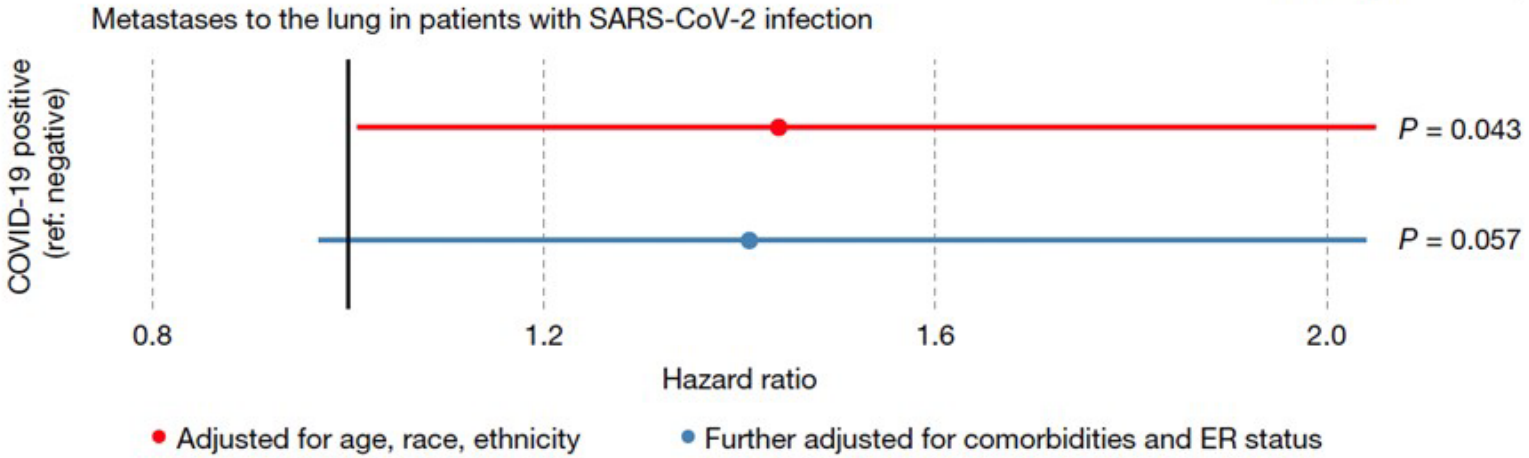






UK Biobank

Flatiron Health



Shi B. Chia…James DeGregori: Respiratory viral infections awaken metastatic breast cancer cells in lungs. Nature Vol 645 11 September 2025

Cancer Increases the risk of Severe Infections and Death

Cancer Patients Suffer from high Morbidity and Mortality from Infections

- Compared to the general population, overall **Standardized Mortality Ratio (SMR)** is 1.5, higher across all cancer types
- The risk is most pronounced in the first two months after cancer diagnosis (SMR 7.37), and in
  - Hematological malignancies: severe sepsis is 15 times more common than in the general population
  - SMR in brain/CNS cancers ----5.74
  - SMR in respiratory cancers --- 3.52
  - SMR in myeloma ----------3.25

Cancer Patients are at Increased Risk for Severe Respiratory Infections Leading to Hospitalization and Death

Disease	General Population	
	Mortality – unvaccinated	**Mortality – vaccinated**
Flu	10/10,000	5/10,000
Pneumo/Non-invasive **IPD**	1.8% 10-20%	0.6% 5%
COVID	0.3 - 1%	0.003 – 0.3%

IPD: Invasive Pneumococcal Disease requiring hospitalization

Cancer Patients are at Increased Risk for Severe Respiratory Infections Leading to Hospitalization and Death

Disease	General Population		Cancer patients (Hospitalization 3-5x)		
	Mortality – unvaccinated	Mortality – vaccinated		**Mortality – unvaccinated**	Mortality – vaccinated
Flu	10/10,000	5/10,000	All patients (Pts) Hospitalized Pts Hosp. Pts on ICI	60-120/10,000 19% 4.3%	30-60/10,000 11.2% 10%
Pneumo/Non-invasive IPD	1.8% 10-20%	0.6% 5%	 Hem/Solid tumors	5% 35%/25%	2.7% 11%
COVID	0.3 - 1%	0.005 – 0.3%	2-3x	22-25%	1.3 – 6.7%

IPD: Invasive Pneumococcal Disease requiring hospitalization

Why Cancer Patients Are More Vulnerable?

- Neutropenia
  - The depth and duration of neutropenia are the strongest determinants of infection risk
  - Post-chemotherapy neutropenia (<500 cells/μL) carries a mortality rate of 5-13%, and febrile neutropenia has a major complication rate of 25–30% with mortality up to 50% in septic shock
- Disease-related immune defects
- Treatment-related immunosuppression
- Barrier disruption
- Antimicrobial resistance

ANTIMICROBIAL PROPHYLAXIS BASED ON OVERALL INFECTION RISK IN PATIENTS WITH CANCER

See Antibacterial Agents (FEV-A) for dosing, spectrum, and specific comments/cautions

Overall Infection Risk in Patients with Cancer[a]	Disease/Therapy Examples	Antimicrobial Prophylaxis
Low <10% 10-20% >20%	• Standard chemotherapy regimens for most solid tumors • Anticipated neutropenia* <7 days	• Bacterial - None • Fungal - None • Viral - None unless prior herpes simplex virus (HSV) episode
Intermediate	• Autologous hematopoietic cell transplant (HCT) • Lymphoma[c] • Multiple myeloma[c] • Chronic lymphocytic leukemia (CLL)[c] • Purine analog therapy (ie, fludarabine, clofarabine, nelarabine, cladribine) • Anticipated neutropenia* 7–10 days • Chimeric antigen receptor (CAR) T-cell therapy	• Bacterial - Consider fluoroquinolone prophylaxis during neutropenia[d] • Fungal - Consider prophylaxis during neutropenia and for anticipated mucositis (INF-2); consider *Pneumocystis jirovecii* pneumonia (PJP) prophylaxis (INF-6) • Viral - During neutropenia and longer depending on risk (INF-3, INF-4, INF-5) • See Immune and Targeted Treatments (INF-A 11 of 13)
High[b]	• Allogeneic HCT including cord blood • Acute leukemia ▸ Induction ▸ Consolidation/maintenance • Alemtuzumab therapy • Moderate to severe graft-versus-host disease (GVHD) • Anticipated neutropenia* >10 days	• Bacterial - Consider fluoroquinolone prophylaxis during neutropenia[d] • Fungal - Consider prophylaxis during neutropenia (INF-2); consider PJP prophylaxis (INF-6) • Viral - During neutropenia and longer depending on risk (INF-3, INF-4, INF-5) • Length of prophylaxis depends on immune reconstitution.

*Neutropenia: ≤500 neutrophils/mcL or ≤1000 neutrophils/mcL and a predicted decline to ≤500/mcL over the next 48 hours.

Vaccines Protect Cancer Patients From Death From Infection

Vaccine	Recommended Age	Schedule
Influenza	19 years and older	Annually
RSV	60 years and older	Once
COVID-19	19 years and older	As per the latest CDC schedule for immunocompromised
Tdap or Td	19 years and older	One dose of Tdap, followed by Td or Tdap booster every 10 years
Hepatitis B	19-59 years: eligible 60 years and older: immunize those with other risk factors	For adults 20 years and older, use high antigen (40 µg) and administer as a three-dose Recombivax HB series (0, 1, 6 months) or four-dose Engerix-B series (0, 1, 2, 6 months)
Recombinant zoster vaccine	19 years and older	Two doses at least 4 weeks apart
Pneumococcal vaccine	19 years and older	One dose PCV15 followed by PPSV23 8 weeks later OR One dose PCV20
HPV	19-26 years: eligible 27-45 years: *shared decision making*	Three doses, 0, 1–2, 6-months

Optimal Timing and Practical Considerations

- Pre-treatment vaccination is ideal
  - 2–4 weeks before cancer treatment initiation when possible
  - Non-live vaccines (influenza, COVID-19) , can be administered during treatment
- **Live attenuated vaccines are contraindicated** during chemotherapy or significant immunosuppression
- After anti-B-cell antibody therapy (e.g., rituximab)
  - Vaccination should be delayed ≥6 months
- After HSCT
  - Systematic revaccination begins at 3–6 months for inactivated vaccines and ≥24 months for live vaccines
- Household contacts and caregivers should be fully vaccinated to provide indirect protection (“**Cocooning**")

Vaccination of Cancer Patients Against Respiratory Infections Prevents Hospitalization and Death

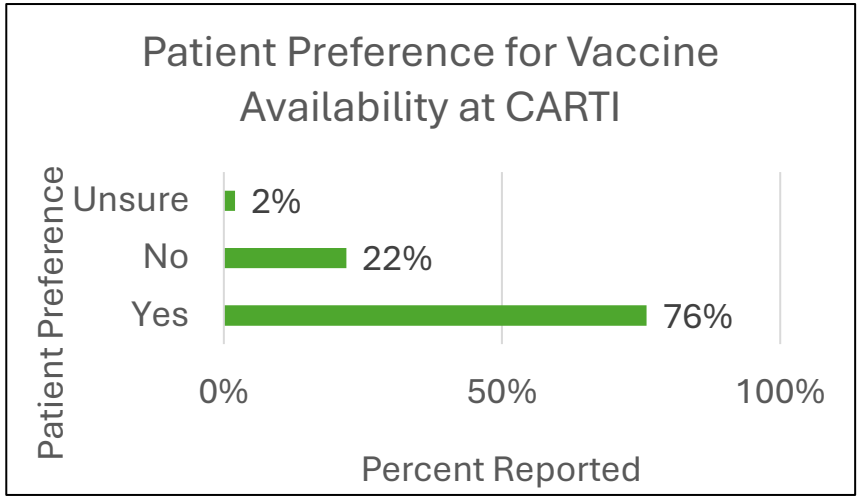
Disease	General Population		Cancer patients (Hospitalization 3-5x)		
	Mortality – unvaccinated	**Mortality – vaccinated**		**Mortality – unvaccinated**	**Mortality – vaccinated**
Flu	10/10,000	5/10,000	All patients (Pts) Hospitalized Pts Hosp. Pts on ICI	60-120/10,000 19% 4.3%	30-60/10,000 11.9% 0%
Pneumo/Non-invasive IPD	1.8% 10-20%	0.6% 5%	Hem/Solid tumors	5% 35%/25%	2% (?) 7-10%/10%
COVID	0.3 - 1%	0.006 – 0.3%	Hops. 2-3x	22-25%	1.3 - 6.7%

IPD: Invasive Pneumococcal Disease requiring hospitalization

Can Cancer-Focused Programs Provide Vaccines to Cancer Patients?

Launch of On-Site Immunizations for CARTI Patients (October 1st, 2024)

- **On site Immunization was launched in All CARTI Cancer Centers and Satellite Clinics for**
  - Influenza
  - COVID-19
  - Pneumococcal
  - Shingles &
  - Tdap



Community-Based Learning Collaborative for Vaccination of Cancer Patients

- In February 2026, we started a learning collaborative with Genesis cancer and blood institute (Dr. Chen) and Mercy Oncology and Hematology (Dr. Reddy)
- All three programs
  - Collected baseline data
  - Mapped workflow in our respective organizations
  - Conducted a survey with staff and physicians to assess knowledge, readiness and barriers to implementation
  - Evaluated EHR capabilities and identified areas for improvement
  - Are still working on vaccination workflow
- The three organizations decided to offer vaccination to cancer patients

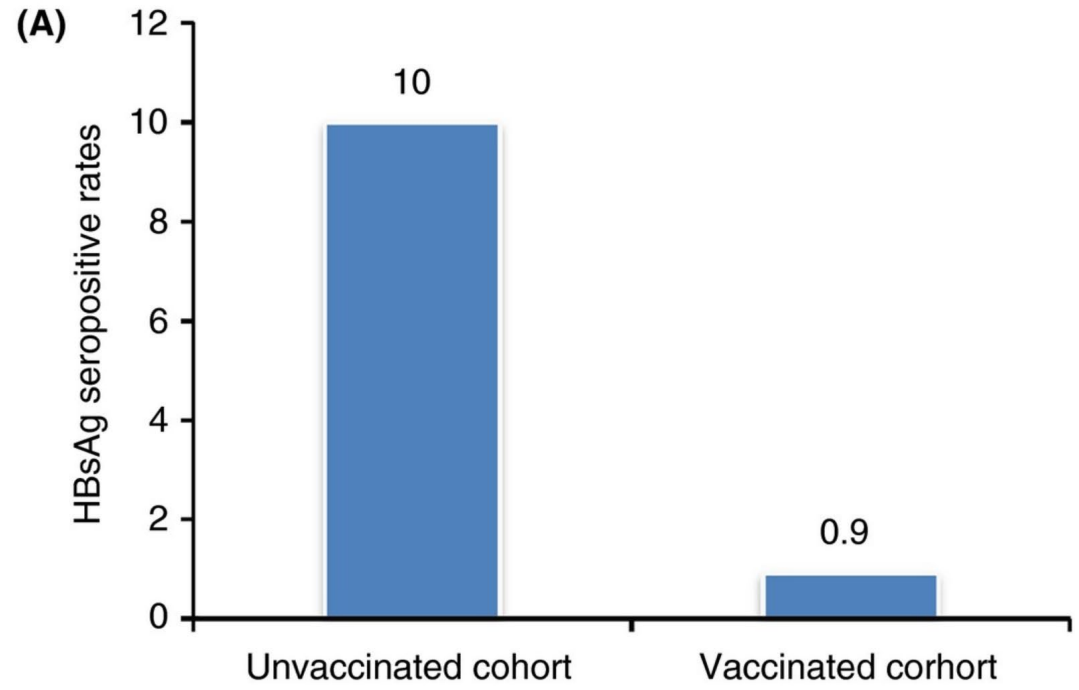
Vaccines as Cancer Prevention

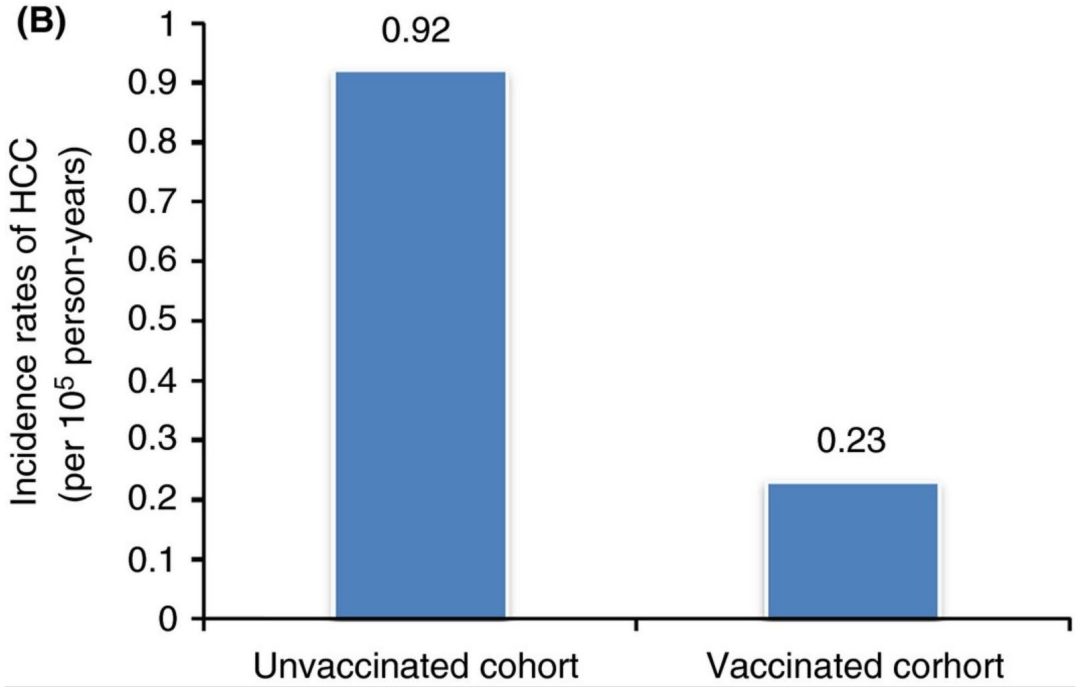
Children born before and after the launch of universal hepatitis B vaccination program in Taiwan

A. The HB sAg seropositive rate incidence

B. Rate of hepatocellular carcinoma

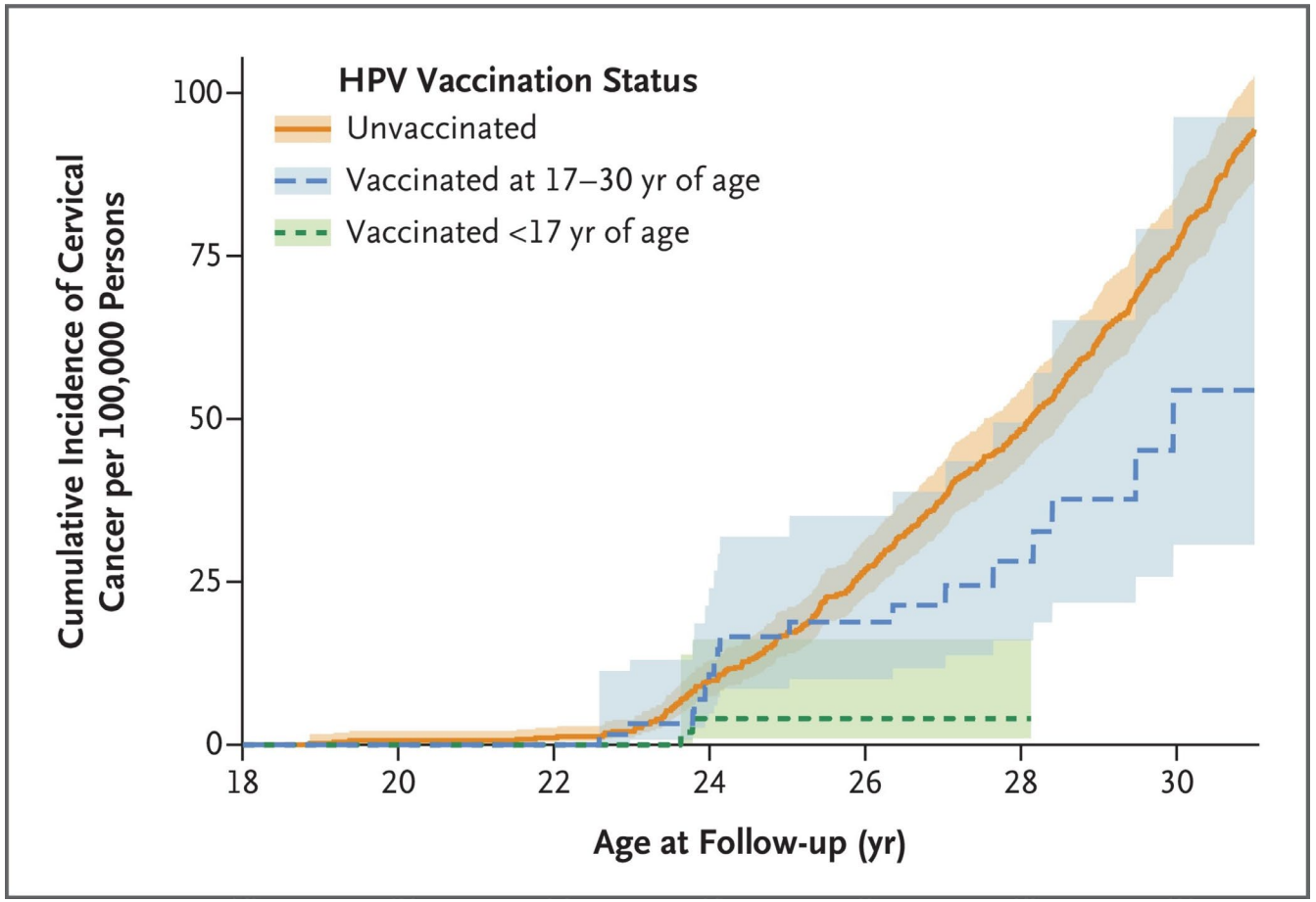
A 74% decrease in HCC





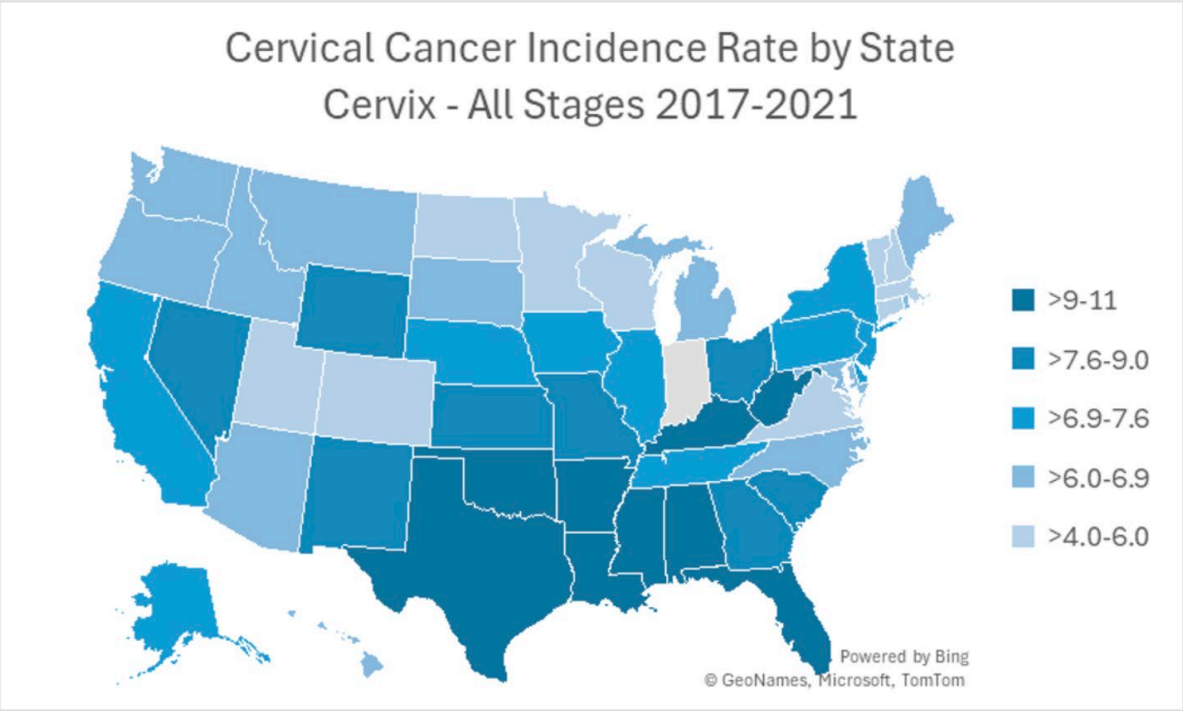
Ni et al and Changet al Pharmacol Ther. June 30, 2018.

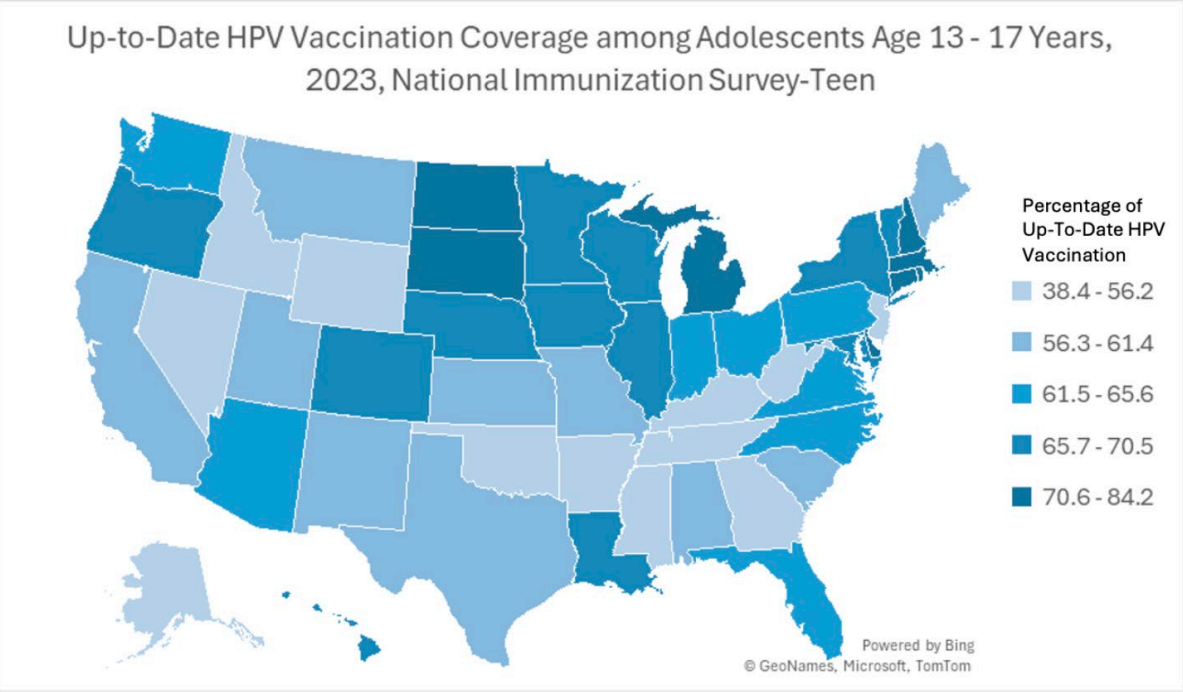
Cumulative Incidence of Invasive Cervical Cancer According to HPV Vaccination Status



…But It is Not Only Cervical Cancer

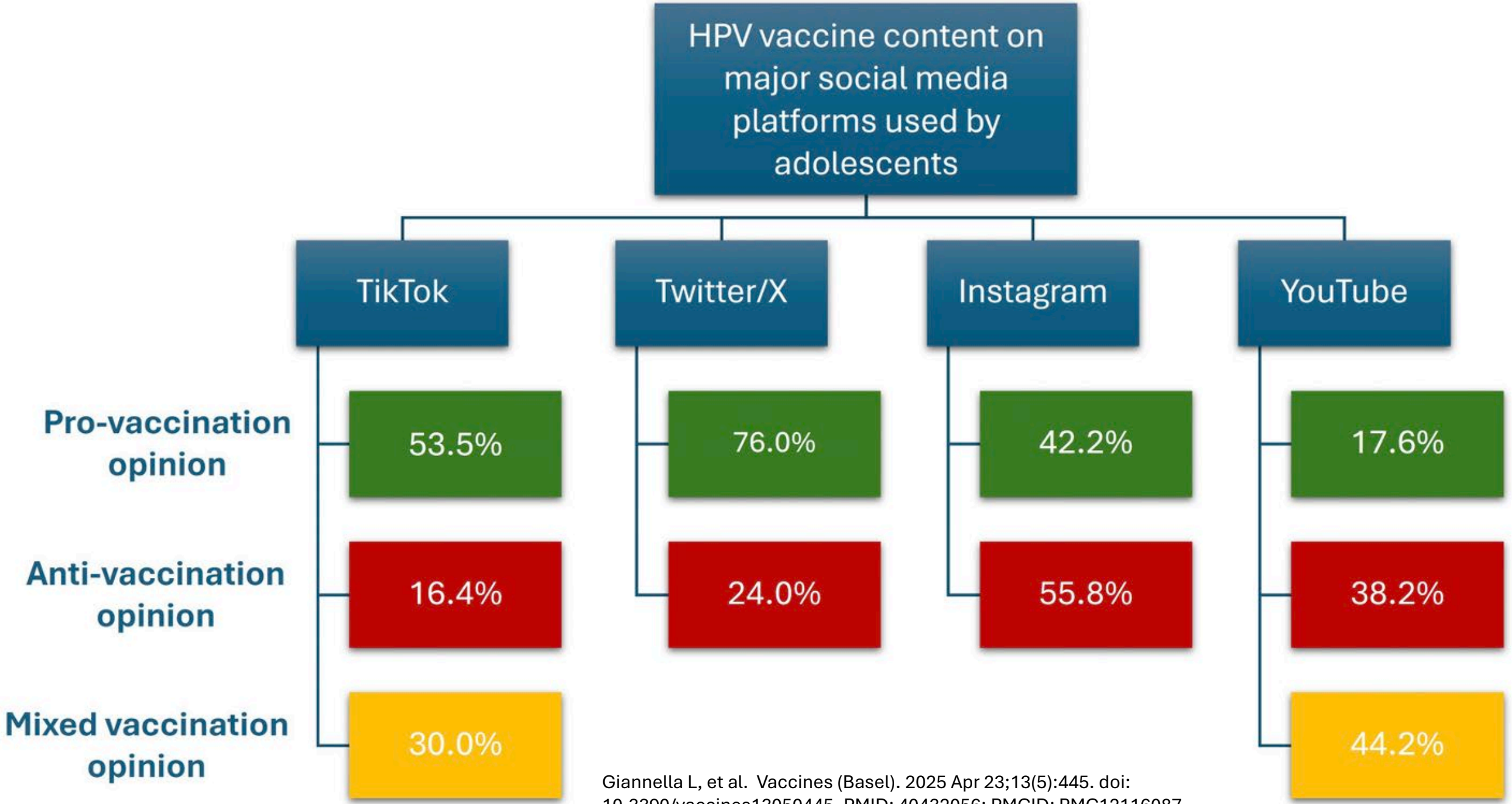
Cancer Site	Key Effect Estimate
Cervical cancer	RR 0.37 (overall); RR 0.20 (vaccinated ≤16 yrs)
CIN2+/CIN3	51–97% reduction depending on age/setting
Vulvar/vaginal (precancer)	RR 0.48 for high-grade VIN/VaIN
Anal HSIL+	HR 0.30 (vaccinated <17 yrs)
Head and neck cancer	HR 0.19 (laryngeal)
HPV-related cancers in males (composite)	HR 0.54 (9v-HPV vaccine)





HPV VACCINATION AND CERVICAL CANCER RATES – HOW UTAH IS DOING COMPARED TO THE REST OF THE US | Categories Physical Health **|**

DOI: 10.26055/d-g813-rkcs



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Vaccines Enhance the Effect of Anticancer Therapy and Act as Anticancer Therapy

Article

SARS-CoV-2 mRNA vaccines sensitize tumours to immune checkpoint blockade

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Immune checkpoint inhibitors (ICIs) extend survival in many patients with cancer but are ineffective in patients without pre-existing immunity[1–9]. Although personalized mRNA cancer vaccines sensitize tumours to ICIs by directing immune attacks against preselected antigens, personalized vaccines are limited by complex and time-intensive manufacturing processes[10–14]. Here we show that mRNA vaccines targeting SARS-CoV-2 also sensitize tumours to ICIs. In preclinical models, SARS-CoV-2 mRNA vaccines led to a substantial increase in type I interferon, enabling innate immune cells to prime $CD8^+$ T cells that target tumour-associated antigens. Concomitant ICI treatment is required for maximal efficacy in immunologically cold tumours, which respond by increasing PD-L1 expression. Similar correlates of vaccination response are found in humans, including increases in type I interferon, myeloid–lymphoid activation in healthy volunteers and PD-L1 expression on tumours. Moreover, receipt of SARS-CoV-2 mRNA vaccines within 100 days of initiating ICI is associated with significantly improved median and three-year overall survival in multiple large retrospective cohorts. This benefit is similar among patients with immunologically cold tumours. Together, these results demonstrate that clinically available mRNA vaccines targeting non-tumour-related antigens are potent immune modulators capable of sensitizing tumours to ICIs.

Although ICIs substantially improve survival in some patients, most patients do not benefit from these therapies[1–9]. These poor responses are attributed to immunosuppressive tumour microenvironments (TMEs) characterized by tolerogenic dendritic cells (DCs), myeloid suppressor cells and regulatory T cells, and may be predicted in some histologies by low intratumoural PD-L1 before immunotherapy initiation. However, there are currently no clinically available methods to improve responses to ICI by modifying the TME. We recently reported that systemic administration of highly immunogenic mRNA nanoparticles induces a viraemia-like cytokine/chemokine response that resets the systemic and intratumoural immune milieu, sensitizing resistant tumours to ICIs[10–12,14]. Although the personalized mRNA vaccines that we and others are developing remain in clinical evaluation (NCT04573140)[12], COVID-19 mRNA vaccines also induce robust stimulation of cytokine secretion[15], and there are now multiple case reports of patients whose tumours spontaneously resolved after COVID-19 mRNA vaccines[16,17]. However, the impact of COVID-19 mRNA vaccines on immune therapy is unknown.

Here we report that the innate immune response to SARS-CoV-2 spike mRNA vaccination resets the cancer immunotherapy cycle and primes adaptive immunity for synergy with ICIs. We found that receipt of a SARS-CoV-2 mRNA vaccine within 100 days of ICI initiation was associated with substantial improvements in overall survival (OS) in patients with non-small cell lung cancer (NSCLC) and melanoma. In preclinical models, we found that this effect required a surge in type-I interferon (IFN) that enhanced antigen-presenting cell (APC) priming of T cells in lymphoid organs. Although tumour cells subvert these primed responses by increasing PD-L1 expression, co-administration of ICIs sustains T cell responses and elicits epitope spreading against tumour-associated antigens. We revealed analogous response correlates for humans receiving COVID-19 mRNA vaccines, including heightened IFNα production, innate/adaptive immune activation and

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Grippin, Adam J., et al. "SARS-CoV-2 mRNA vaccines sensitize tumours to immune checkpoint blockade." *Nature* (2025): 1-10.

The Study Population

Stage III/IV NSCLC

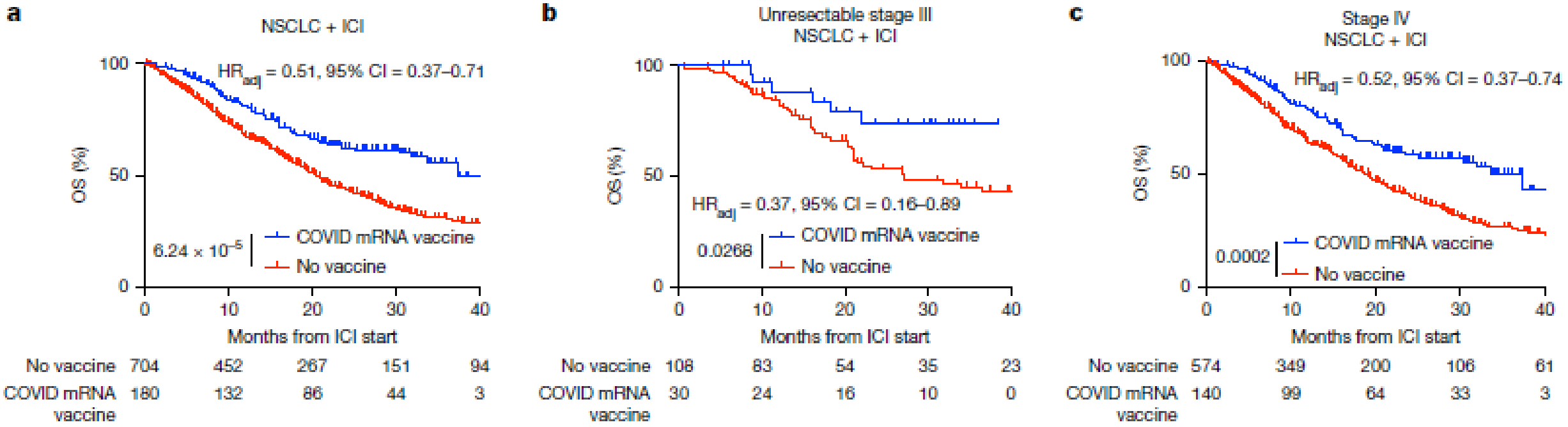
- 180 patients received a COVID mRNA vaccine within 100 days of ICI initiation
- 704 patients who were treated with ICI and did not receive a COVID vaccine

Stage IV Melanoma

- 43 patients received a COVID-19 mRNA vaccine within 100 days of initiating ICI
- 167 did not receive a COVID-19 vaccine

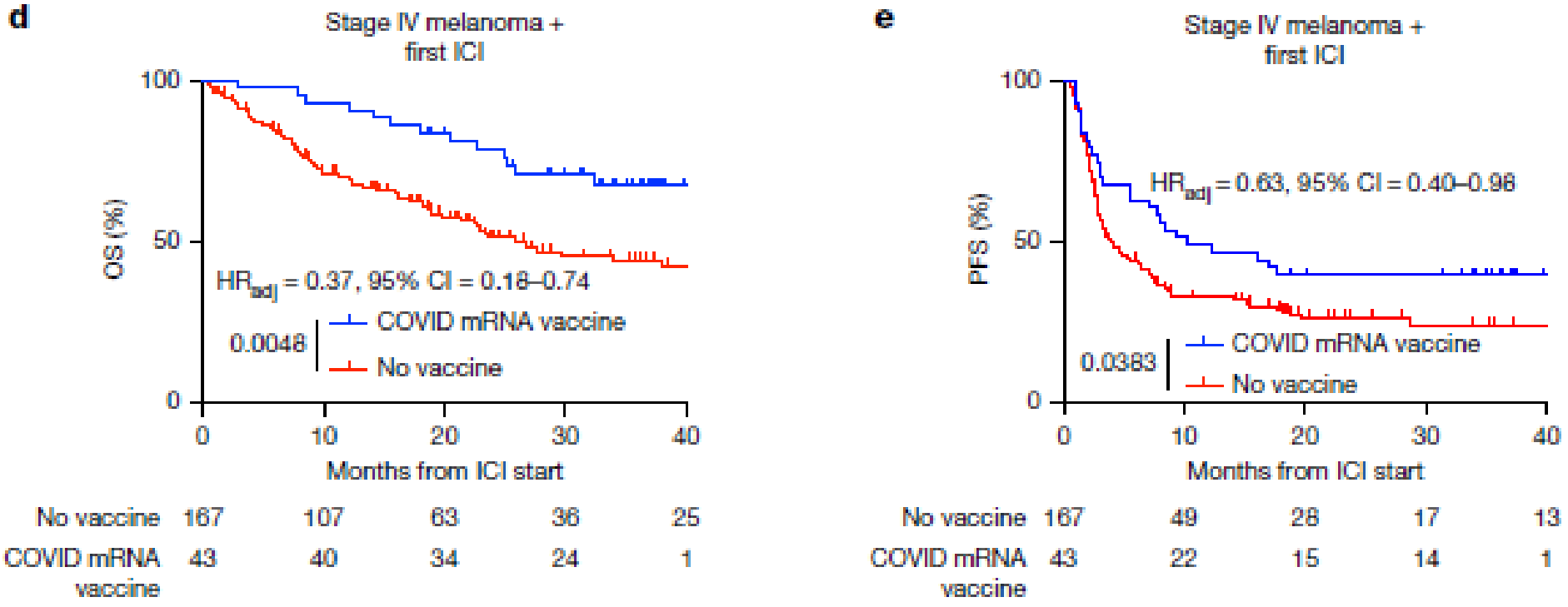
Grippin, Adam J., et al. "SARS-CoV-2 mRNA vaccines sensitize tumours to immune checkpoint blockade." *Nature* (2025): 1-10.

COVID Vaccination Before Starting ICI Decreased Mortality of Stage III/IV NSCLC by 50%



Grippin, Adam J., et al. "SARS-CoV-2 mRNA vaccines sensitize tumours to immune checkpoint blockade." *Nature* (2025): 1-10.

COVID Vaccination Before Starting ICI Decreased Mortality of Stage IV Melanoma by 63%



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How Does mRNA Vaccine Decrease Cancer Mortality?

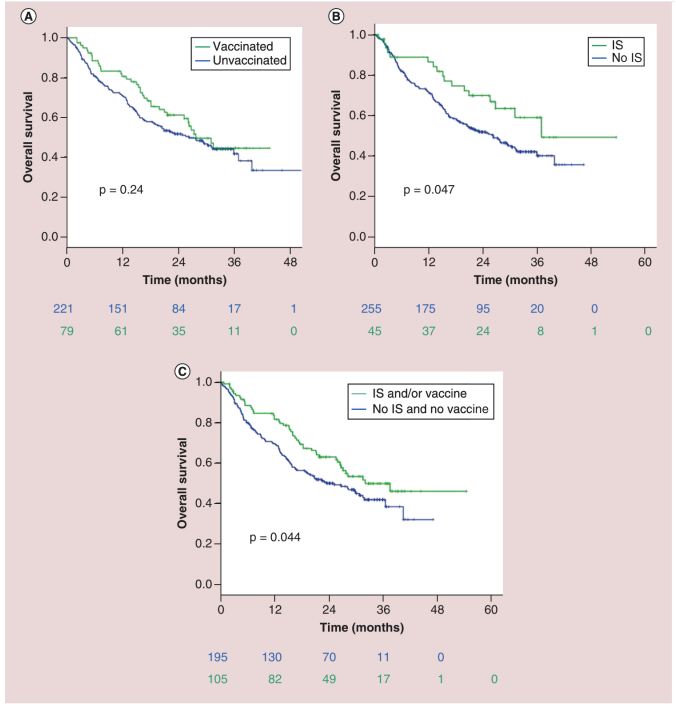
- COVID-19 vaccines shape immunity in humans
  - By stimulating innate immunity
  - By reprograming adaptive immunity

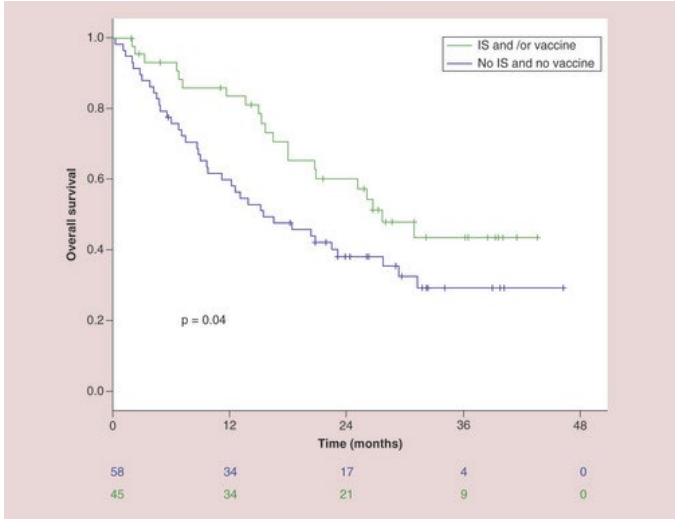
- RNA vaccines amplify PD-L1 in NSCLC and Melanoma

- RNA vaccines boost ICIs in cold tumors by increasing tumor infiltrating lymphocytes (TILs)

Influenza Vaccination and Immune Checkpoint Inhibitor Synergy

- NVIDIa-2 study
  - A prospective multicenter observational study of 1,188 patients with advanced solid tumors receiving ICIs across 82 Italian centers
  - 502 vaccinated matched with 502 unvaccinated
- Influenza vaccination was associated with significantly improved outcomes:
  - Median OS: 27.0 months (vaccinated) vs. 20.9 months (unvaccinated), p = 0.003
  - Median PFS: 12.5 vs. 9.6 months, p = 0.049
  - Disease control rate: 74.7% vs. 66.5%, p = 0.005
  - Multivariable OS HR: 0.75 (95% CI 0.62–0.92, p = 0.005)
- Critically, this survival benefit was independent of infection-related mortality





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Take Aways

- Many infections, especially viruses, can cause cancer
  - Available vaccines for some of them can prevent the establishment of chronic infections and therefore the development of cancer
- Infections are more severe in cancer patients leading to higher morbidity and mortality than the general population
  - Vaccines for respiratory infections reduce severe infections, hospitalization and death and may decrease the activation of dormant cancer cells
  - All adult cancer patients are eligible for vaccination starting at age 19 (for most vaccines)
  - **Call to Action: Specialty practices can implement adult vaccination for their patients**
- Vaccines for viral respiratory infections may enhance the effect of anticancer therapy, especially immune checkpoint inhibitors
  - Vaccines are being investigated as adjunct anticancer therapy

Questions?