Protecting Vulnerable Lives:

The Importance of Improving Vaccine Coverage in Patients with Cancer

Pfizer

Executive Summary

Eighteen million American adults are currently living with a diagnosis of cancer. In addition to the challenges inherent to cancer treatment and survivorship, the disease- and treatment-related immunosuppression experienced by many patients with cancer increases their risk of morbidity and mortality when exposed to viral or bacterial pathogens. For example, patients with cancer who contract influenza are more likely to experience complications, require hospitalization, or die when hospitalized than otherwise healthy individuals.

Vaccination is a cornerstone of helping to prevent infection in patients with cancer and is recommended by national and international organizations such as the National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology (ASCO), and the Spanish Society of Medical Oncology. However, vaccination rates in patients with cancer remain suboptimal, resulting in avoidable healthcare costs, treatment delays, and diminished outcomes. These coverage gaps can be attributed to a range of patient, provider, and health system factors, including:

- Vaccine hesitancy (fueled by misinformation and inadequate provider-patient communication)
- Fragmented care delivery
- Limited awareness of vaccination guidelines
- Complex and inconsistent reimbursement structures

This white paper presents compelling evidence of the toll vaccine-preventable diseases exact on patients with cancer and the importance of closing the gaps in vaccine coverage in this vulnerable population. As the number of cancer survivors continues to grow, improving immunization rates among patients with cancer is likely to become an increasingly urgent priority for payers committed to value-based care.

Payers are uniquely positioned to drive change, reduce the cost of care, improve the quality of care, and protect lives by investing in initiatives that enhance vaccine access and promote vaccine adherence.

Introduction

Adequate immunization against vaccine-preventable diseases remains a significant public health issue,[1-3] particularly for individuals whose immune defenses are compromised.[2,3] A recent analysis of 2021 National Health Interview Survey data indicates that 6.6% of adults in the US—roughly 17 million people—may be immunocompromised.[4,5] Patients with cancer represent a sizeable proportion of this high-risk group.[6-8]

As of January 2022, the American Cancer Society estimated that 18 million American adults were living with a history of cancer, including approximately 5 million individuals who were within 5 years of diagnosis.[9] An analysis of US cancer and mortality statistics from the Surveillance, Epidemiology, and End Results registries projected that more than 690,000 Americans would be living with metastatic breast, prostate, lung, colorectal, melanoma, or bladder cancer by January 2025.[10]

The immune defenses of these individuals can be weakened in a variety of ways—encompassing both the disease process and its treatment—that can persist for months or even years after treatment has been completed.[11,12] The impact of these deficits is evident in the increased morbidity and mortality experienced by cancer patients who contract vaccine-preventable respiratory diseases:

- Individuals living with cancer may be 3 to 10 times more likely to be hospitalized with influenza-related infections (depending on age) and up to 10 times more likely to die while hospitalized than the general population.[13,14]
- In patients with recently diagnosed cancer, SARS-CoV-2 infection was associated with a 7-fold increase in death.[15]
- Compared with the general population of healthy adults, patients with hematological cancers or solid tumors have been found to have a 38-fold and 23-fold higher risk, respectively, of invasive pneumococcal disease (IPD).[16] Patients with multiple myeloma have been reported to have a 62.8 times greater risk.[17]

The disproportionate impact of these conditions on patients with cancer illustrates the unique vulnerability of this group to infectious diseases and the importance of vaccines in protecting this vulnerable population.[11,18] In this white paper, we will explore the potential of vaccinations to help reduce the morbidity, mortality, and healthcare costs associated with vaccine-preventable diseases in patients with cancer and cancer survivors, with a focus on:

- How cancer and its treatment increase the risk of both contracting vaccine-preventable diseases and experiencing adverse outcomes—during and after treatment
- Current vaccine recommendations for patients with cancer from NCCN and ASCO
- Gaps in vaccine coverage of cancer patients and survivors
- Evidence-based strategies to optimize vaccination and minimize infectious disease risk in cancer patients, including vaccination of healthcare providers and household contacts
- Actionable recommendations for key stakeholders and decision makers

It is noteworthy that despite wide recognition that patients with cancer are at high risk of vaccine-preventable diseases, these authors found that limited data are available on vaccine coverage, benefits, and barriers specific to patients with cancer in the United States. This gap underscores both the need for greater awareness of the role of vaccines in the care of patients with cancer and the need for more research on optimizing vaccine coverage in the US.

Infectious Disease in Patients with Cancer: Understanding the Risks

Immunosuppression in patients with cancer is a multifactorial process that involves the effects of the disease process and of the therapies used to treat it. In some cancers (eg, non-small-cell lung, colorectal), tumor progression itself is associated with systemic immune suppression that reduces defenses against viral and bacterial pathogens.[12]

Cancer treatments such as cytotoxic chemotherapy, radiation, and hematopoietic stem cell transplantation (HSCT) damage bone marrow, suppressing the production of immune cells crucial to mounting a defense against infectious agents (**Table 1**).[12,19] In addition, treatment-related adverse effects such oral mucositis can disrupt natural defensive barriers, increasing the risk of infections.[12]

Table 1. Impact of Cancer Treatments on Immune Function and Implications for Vaccination[12,20,21]

Cancer Therapy	Impact on Immune Function and Implications for Vaccination
Radiation	▪ Can cause immunosuppression when radiation fields encompass substantial bone marrow[20] – Immunosuppression is dose-dependent and more likely during curative treatment ▪ Clinically significant immunosuppression can be seen during treatment of prostate, cervical, and anal cancers[20]
Cytotoxic Chemotherapy	▪ Myelotoxicity, especially neutropenia[12] ▪ Reduced seroconversion if vaccines are administered when leukocytes are at their nadir (generally 7 to 14 days post treatment)[20]
Targeted Agents	▪ In addition to influencing immune responses against cancer cells, targeted agents such as small-molecule kinase inhibitors and monoclonal antibodies can alter immune homeostasis in normal cells[21] – Some agents can cause leukopenia or decreased humoral immunity[20]
High-Dose Glucocorticoids*	▪ Suppression of macrophage and neutrophil activity, suppression of inflammatory cell migration to sites of infection[12]

*As cancer therapy or for treatment of immune-related adverse events in patients receiving immune checkpoint inhibitors

Once treatment is complete, cancer survivors remain at risk due to the late effects of cancer and the lingering effects of treatment.[11,22] Long term immune deficits are particularly common in patients who receive HSCT, chimeric antigen receptor T-cell therapy, or monoclonal antibody treatment, and in those whose bone marrow has not recovered after undergoing chemotherapy.[11] As a result of this ongoing immune suppression, the immune response to vaccines may be impaired in cancer survivors.[23]

Impact of vaccine-preventable diseases on patients with cancer

The profound immunosuppression experienced by many patients with cancer increases their risk of poor outcomes when exposed to viral or bacterial pathogens. For example:

- Cancer patients who contract **influenza** are at much higher risk of complications and have longer lengths of stay when hospitalized, with reported mortality rates that range from 5% to as high as 33% (varies by cancer diagnosis).[14,19,24,25]
- Patients with lung cancer and some hematologic cancers (eg, chronic lymphocytic leukemia, lymphoma, multiple myeloma) have a high risk of **IPD**.[24]
- In a retrospective cohort study using administrative healthcare databases in Ontario, Canada, **COVID-19**-associated 14-day hospitalization and 28-day mortality rates were significantly higher in individuals with cancer than individuals without cancer. Patients with hematologic malignant neoplasms were 75% more likely to be hospitalized and twice as likely to die, and those with solid tumors were 11% more likely to be hospitalized and 31% more likely to die.[26]

These risks are not limited to respiratory diseases. In patients receiving chemotherapy, inactivated hepatitis B virus (HBV) can become reactivated, leading to liver damage. In addition, up to 50% of patients with pre-existing immunity to HBV who undergo stem cell transplantation lose that immunity following treatment. The rate of HBV infection-related mortality in patients with cancer has been estimated at up to 5%.[24]

Disease- or treatment-related decreases in T-cell immunity can also allow reactivation of herpes zoster (HZ) in patients with cancer.[27] A meta-analysis of studies on risk factors for HZ found that hematological malignancies such as lymphoma or leukemia more than doubled patients' risk of latent HZ compared to controls.[27] A systemic review found that rates of postherpetic neuralgia were as high as 41% in patients with hematologic cancers or a history of HSCT.[28]

The increased risk of infection in cancer patients is often accompanied by increased costs. In an analysis of cost of HZ infections in immunocompromised patients in the US, costs during the first quarter after HZ diagnosis were $2,500 to $3,100 higher for patients with cancer and HZ infection than for those with cancer without HZ.[29]

Gaps in vaccine coverage

Studies of immunization rates for vaccine-preventable diseases in adults in general and cancer patients in particular have consistently found rates below those recommended by health authorities (**Table 2**).[23,30,31] An analysis of data from the 2016–2017 and 2017–2018 National Health Interview Surveys (NHIS) found that 64% of respondents with self-reported cancer had received the influenza vaccine—a rate that was higher than that for respondents without cancer, but still below the target rate of 70%.[31]

A similar pooled analysis of data on patients with a history of cancer (aka cancer survivors) from the 2008–2018 NHIS datasets found overall patient-reported vaccination rates of 62.9% for influenza, 72.2% for pneumococcal pneumonia, 21.5% for HBV, and 30.8% for HZ, with an increase in vaccination rates over time. Of note, this analysis also found that African American race, lower education levels, lower income, and lack of private insurance were associated with lower adherence to recommended vaccinations, an indicator of the enduring socioeconomic disparities in vaccine coverage in the US.[32]

Table 2. Immunization Rates in Adults and Patients with Cancer

Vaccine	US Target Immunization Rate[33] (National Vaccine Program Office)		Patients Immunized, 2024[34] (McKinsey & Company analysis of CDC data)			Patients with Cancer Immunized [32] (2008-2018 NHIS data sets)
Influenza	Adults ≥18 years		Adults 18–49 years	Adults 50–64 years	Adults ≥65 years	Adults ≥18 years
	70%*		33%	46%	70%	62.9%
Pneumococcal	High-risk adults 18–64 years	Adults >65 years†	Adults ≥65 years			Adults ≥65 years
	60%*	90%*	64%			72.2%
Herpes Zoster	Adults >60 years		Adults 50–64 years	Adults ≥65 years		Adults ≥60 years
	30%*		36%	44%		30.8%

*Per Healthy People 2020; †Noninstitutionalized individuals
CDC, Centers for Disease Control and Prevention; NHIS, National Health Interview Survey

Approach to Vaccination in Cancer Patients and Survivors

US and international guidelines are clear on the importance of vaccination as "a cornerstone of infection prevention" in patients with cancer as well as the importance of vaccinating family members and others in close contact with cancer patients (see **Herd Immunity at Home: The Importance of Vaccinations in Caregivers and Close Contacts of Patients with Cancer** on page 9).[12,19,23,35] Inactivated (inactivated or killed pathogens), subunit/conjugate, and mRNA vaccines are recommended in patients with cancer, as these vaccines will not replicate and cause infections in immunocompromised or weakened patients (**Table 3**).[12,35] Live-attenuated vaccines (eg, measles, mumps, rubella, varicella) are contraindicated due to the potential risk of virus replication and infection.[12,35]

Table 3. Summary of Recommendations for Vaccination of Immunocompromised Adults (Adult Cancer Patients/Survivors)*

Vaccine	Guideline
Influenza (Inactivated)[23,35,36*]	▪ All ages: annually, with IIV3 (inactivated influenza vaccine) or RIV3 (recombinant influenza vaccine) ▪ Adults ≥65 years: use of preferred formulations such as high-dose, adjuvanted, or recombinant vaccines is recommended to enhance effectiveness ▪ Live-attenuated influenza vaccine (LAIV) should be avoided
Pneumococcal[23,35,36*]	▪ Adults 19-49 years: PCV20 or PCV21 or PCV15 + PPSV23 ▪ Adults ≥50 who have not previously received a pneumococcal vaccine: PCV20 or PCV21 or PCV15 + PPSV23 at least 1 year after the PCV15 dose (minimum interval of 8 weeks) ▪ Adults who received an incomplete series (eg, PCV13 only; PCV13 [at any age]+ PPSV23 at <65 years): PCV20 or PCV21 ▪ Adults ≥65 years who have only received PVC13: PCV20 or PCV21 per shared clinical decision making
COVID-19[23,35-37]	▪ All ages, per CDC recommendations for immunocompromised patients,[36] based on shared clinical decision making ▪ Age-appropriate boosters may be administered ≥2 months after patient has received last recommended vaccine dose ▪ Postpone immunization for 2–3 months for individuals who recently had a COVID-19 infection

(continued)

Continuation of Table 3. Summary of Recommendations for Vaccination of Immunocompromised Adults (Adult Cancer Patients/Survivors)*

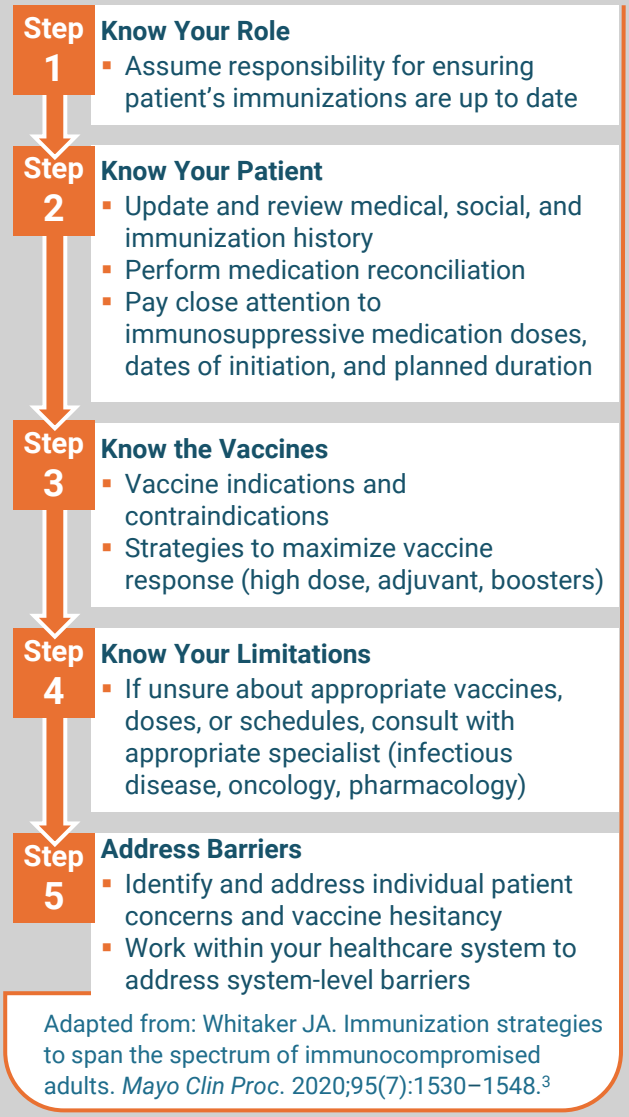
Vaccine	Guideline
Hepatitis B[23,35,36,38]	▪ Recommended for adults 19–59 years and adults ≥60 years with risk factors (eg, history of IV drug use or STDs) ▪ Adults ≥20 years: 2-, 3-, or 4-dose series (see CDC guidelines[36] for details) – Screening is essential to ensure patient is not currently infected, as the vaccine is ineffective for those who are already infected – Vaccine series should be given ≥2 weeks before initiating chemotherapy or other immunosuppressive therapies to maximize the immune response – Cancer and its treatments can weaken the immune system, leading to a less effective vaccine response. High-antigen vaccines or additional doses may be used to improve immunity in such patients
Tdap/Td[23,35,36*]	▪ Adults ≥19 years: one dose of Tdap, followed by Td or Tdap booster every 10 years
HPV[23,35,36,39]	▪ Patients 9–26 years: 3-dose series (0, 1–2, and 6 months) ▪ Previously unvaccinated adults 27–45 years: 3-dose series (0, 1–2, and 6 months) based on individual risk and shared decision making
Herpes Zoster (Recombinant, inactivated)[23,35,36,40*]	▪ Adults ≥19 years: 2 doses ≥4 weeks apart
RSV[35,41]	▪ Adults ≥50 years: single dose to prevent serious RSV infection and hospitalization

*Included in HEDIS Adult Immunization Status measure[42]

CDC, Centers for Disease Control and Prevention; HEDIS, Healthcare Effectiveness Data and Information Set; HPV, human papillomavirus; IV, intravenous; PCV, pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; PCV15, 15-valent pneumococcal conjugate vaccine; PCV20, 20-valent pneumococcal conjugate vaccine; PCV21, 21-valent pneumococcal conjugate vaccine; PPSV-23, 23-valent pneumococcal polysaccharide vaccine; RSV, respiratory syncytial virus; STD, sexually transmitted disease; Td, tetanus and diphtheria; Tdap, tetanus, diphtheria, and pertussis.

Optimal timing and adherence to vaccination schedules are crucial to maximizing protection. Prior to initiating anticancer therapy, clinicians should determine patients' vaccination status and ensure that they are up to date on seasonal and age- and risk-based vaccines (**Figure 1**).[3,24,35]

Figure 1. Stepwise approach for network providers to ensure immunization in cancer patients



Adapted from: Whitaker JA. Immunization strategies to span the spectrum of immunocompromised adults. *Mayo Clin Proc.* 2020;95(7):1530–1548.[3]

Herd Immunity at Home: The Importance of Vaccinations in Caregivers and Close Contacts of Patients with Cancer

Family members and household-based caregivers in close proximity to patients with cancer can potentially transmit vaccine-preventable diseases to these vulnerable patients. To fully protect immunocompromised patients with cancer, it is important to leverage the concept of herd immunity at the level of the home environment, by ensuring close contacts are fully vaccinated in accordance with current recommendations.[43,44] This approach is analogous to the well-established practice of "cocooning" newborns from pertussis by vaccinating parents, siblings, and other close contacts for Tdap.[45]

Guidelines from ASCO, the Infectious Diseases Society of America (IDSA) and the NCCN all stress that immunocompetent adults and children who live with or come in close contact with immunocompromised patients should receive all recommended vaccines.[23,35,43] Vaccines containing recombinant viral antigens (eg, HPV or HBV) or inactivated or purified antigens or bacterial components (eg, influenza, Tdap) are considered safe for close contacts of cancer patients and survivors[23]; however, live attenuated vaccines such as the oral polio vaccine may be contraindicated due to the risk of viable virus transmission to immunocompromised patients.[23]

Despite broad recognition of the need for vaccine coverage in family, caregivers, and other close contacts of patients with cancer, messaging around this issue has been limited. An analysis of National Cancer Institute cancer center websites recently found that although 53 of the 70 sites included information on preventative health for caregivers and patients, only 1 had information on vaccination for caregivers or family contacts.[46]

Promoting routine vaccinations for close contacts is critical to ensuring individual- and community-level protection from vaccine-preventable diseases for patients with cancer. The potential impact of this approach can be inferred from the shift in the incidence of IPD among cancer patients at a major urban cancer center following the introduction of routine childhood immunization with the first pneumococcal conjugate vaccine. A retrospective analysis of IPD rates in patients treated at Memorial Sloan Kettering Cancer Center in the decade prior to the introduction of the vaccine and those treated in the ensuing 10 years (2001–2010) revealed dramatic drops in the rates of IPD in adults (≥15 years) with a wide range of cancer diagnoses.[47] Overall, the incidence of IPD decreased by 64% in patients with hematologic cancers and 49% in those with solid tumors. Of note, the impact was most pronounced in high-risk patients such as those with multiple myeloma, in whom the rate of IPD declined by 74%.[47]

Ideally, vaccination should occur before the start of systemic therapy: at least 2 weeks before for inactivated vaccines and at least 4 weeks before for live vaccines.[23,43] Patients who have completed chemotherapy can generally receive both inactivated and live virus vaccines 3 months after the end of treatment, but consultation with a specialist familiar with vaccination in survivors or patients with cancer is recommended.[23] In patients receiving targeted therapy that causes immunosuppression, timing of vaccination should be adjusted accordingly. Patients treated with anti–B-cell therapy should be vaccinated at least 4 weeks before therapy or at least 6 months after cessation of treatment.[20]

Benefits of ensuring adequate vaccine coverage for cancer patients and survivors

Vaccination of cancer patients has been associated with reduced hospitalizations and intensive care admissions, faster recovery times, fewer treatment delays, and improved survival.[26,48] One large-scale retrospective analysis found that a history of just one COVID-19 vaccination reduced patients' risk of 14-day hospitalization by 32%, of 21-day Intensive Care Unit admission by 24%, and of 28-day mortality by 43%. Risks for each outcome in patients with ≥2 vaccinations dropped by 58%, 26%, and 50%, respectively.[26]

These benefits can also yield cost savings. For example, a 2008 analysis of the cost-effectiveness of influenza vaccination in adults with cancer in Taiwan found that influenza vaccination had the potential to prevent 42% of influenza infections and 45% of serious cases—saving up to $2107 (US) in medical costs and $6338 in medical and non-medical costs per case averted.[49]

Barriers to Vaccination in Cancer Patients

Patient level

Vaccine hesitancy is an enduring challenge when trying to improve vaccine coverage in adults and takes on a particular urgency when dealing with immunocompromised patients.[1,19,50,51] Researchers at the University of Texas Health Science Center in Houston recently surveyed 60 patients with cancer on their perceptions of vaccination.[52] Although 73% agreed that it is important to get up to date with vaccines, just 58% were willing to take a vaccine if it was offered to them, and only 43% indicated they received a yearly influenza vaccine. Qualitative analysis revealed that most patients were unaware of the importance of vaccination at the time of their cancer diagnosis, a knowledge gap that typically was not addressed by oncologists. In fact, 32% of patients indicated they were never told of the importance of vaccination.[52]

An earlier survey, conducted as part of a doctoral thesis at a cancer center in Arizona, evaluated influenza vaccination status, knowledge about the flu vaccine, and general attitudes toward vaccination in 84 patients enrolled in phase 1 clinical oncology trials at the center.[49] Influenza vaccination rates were lower than recommended—58% of respondents indicated they had received an influenza vaccination since their cancer diagnosis and only 48% had been vaccinated while on cancer treatment.[53] Of note, although 52% of all respondents indicated that a doctor had recommended flu vaccination, only 37% of unvaccinated patients had been advised by a physician to be vaccinated against influenza. In this group, the most common reasons for not being vaccinated were a belief that they were not at risk for the flu, a belief that the flu vaccine is not effective, and concern that the vaccine can cause the flu.[53]

"Vaccination in patients with cancer is an often-overlooked component of management by clinicians as well as patients, who tend to prioritize the treatment of the primary malignancy."

Sarkar L, et al. *Cancer Res Stat Treat.* 2021;4(3):505-515

Provider level

A common theme in both patient surveys summarized above is a lack of communication from providers on the importance of vaccination. This gap is particularly unfortunate given that a strong vaccine recommendation from a physician increases the likelihood a patient will get vaccinated.[1,54]

Although data on provider barriers specific to vaccination of patients with cancer are limited, ASCO guidelines and a recent multidisciplinary position paper both cite lack of awareness of guideline recommendations as a key gap among physicians caring for these patients.[19,35] Of note, both groups call out the importance of increasing medical education and awareness among "front-line" and general practitioners, who play a significant role in promoting and providing vaccinations.[19,35] The IDSA guidelines on vaccinating immunocompromised patients state that specialists should "share responsibility with the primary care provider" for ensuring that immunocompromised patients are appropriately immunized.[43] However, inadequate communication between oncologists and primary care providers—coupled with a lack of clarity on which discipline is responsible for monitoring and administering vaccines—is a prime contributor to gaps in vaccine coverage.[19] Although US-specific data are limited, a study conducted in the Netherlands found that 46% of general practitioners caring for patients with cancer (breast or colorectal) were unaware that yearly influenza vaccination is recommended in these patients and 48% stated that the responsibility for such vaccinations rested with the oncologist.[55]

Despite the dearth of oncology-specific research on barriers to vaccine coverage, valuable insights can be drawn from data that have been gathered on barriers to adult vaccination and vaccination of other immunocompromised groups. A 3-year (2016–2018) series of surveys of US-based clinicians (physicians, nurse practitioners, and physician assistants [N=4911]) and pharmacists (N=793) assessed implementation of the National Vaccine Advisory Committee's (NVAC) Standards for Adult Immunization Practices (**Table 4**), as well as barriers to implementation of the standards.[56,57]

The NVAC standards include components focused on **assessment of vaccine status**; **recommending needed vaccines to patients**; **administration of (or referral for) recommended vaccines**; **documentation of vaccinations in an Immunization Information System (IIS);** and a **composite measure of complete implementation of the standards**. Although more than 80% of clinicians and pharmacists reported implementing the assessment, recommendation, and administration components of the standards, full implementation was uniformly low, particularly among specialty care clinicians.[53] The component with the lowest reported adherence was documentation of adult vaccinations in an IIS among immunizing clinicians, ranging from 28.4% among non-ob/gyn specialists to 46.5% among family medicine clinicians. In addition, only 46% of clinicians and 42% of pharmacists had a patient reminder-recall system in place.[57]

Table 4. National Vaccine Advisory Committee's Standards for Adult Immunization Practices Applicable to Cancer Patients and Survivors[54]

Target Audience	Summary of Standards
All Providers	▪ Incorporate **immunization needs assessment** into every clinical encounter. ▪ Strongly **recommend needed vaccine(s)** and either **administer vaccine(s) or refer** patient to a provider who can immunize. ▪ Stay up to date on, and educate patients about, vaccine recommendations. ▪ Implement systems to incorporate vaccine assessment into routine clinical care. ▪ Understand how to **access immunization information systems** (ie, immunization registries).
Nonimmunizing Providers	▪ Routinely assess the immunization status of patients, recommend needed vaccine(s), and refer patient to an immunizing provider. ▪ **Establish referral relationships** with immunizing providers. ▪ **Follow up** to confirm patient receipt of recommended vaccine(s).
Immunizing Providers	▪ Ensure professional competencies in immunizations. ▪ Assess immunization status in every patient care and counseling encounter and strongly recommend needed vaccine(s). ▪ **Document receipt of vaccination in patient medical record and immunization registry.**
Professional Healthcare-Related Organizations/ Associations/ Healthcare Systems	▪ Provide immunization education and training of members, including trainees. ▪ Provide resources and assistance to **implement protocols and other systems** to incorporate vaccine needs assessment and vaccination or referral into routine practice. ▪ Encourage members to be up to date on their own immunizations. ▪ Assist members in staying up to date on immunization information and recommendations. ▪ **Partner with other immunization stakeholders** to educate the public. ▪ Seek out collaboration opportunities with other immunization stakeholders. ▪ Collect and share best practices for immunization. ▪ Advocate policies that support adult immunization standards. ▪ Insurers/payers/entities that cover adult immunization services should **ensure that the network is adequate to provide timely immunization** access and augment with additional vaccine providers if necessary.

Adapted from: National Vaccine Advisory Committee. Recommendations from the National Vaccine Advisory Committee: Standards for adult immunization practice. *Public Health Rep*. 2014;129(2):115–123.

Based on results from the 2017 survey, researchers grouped barriers to full implementation of the NVAC standards into three broad categories:[56]

- ***Assessment barriers:*** Many providers believe that vaccinating adults is not within their scope of practice and/or feel that the time and resources required for vaccine assessment would not be adequately reimbursed by payers. Forty percent of clinicians reported that their practices "cannot afford" to assess vaccination status of adults because the time required to counsel patients would not be sufficiently reimbursed.
- ***Administration barriers:*** Insufficient staff to administer vaccines and/or follow-up on vaccine status and insufficient space for vaccine storage were commonly cited by clinicians and pharmacists, including nearly 21% of pharmacists who said that they would lose money by stocking and administering adult vaccines.
- ***Documentation barriers:*** Most clinicians and pharmacists who did not document vaccinations in IIS reported they were unaware their region had an IIS that included adults and/or were unsure their electronic records system could link to IIS.

The potential scope and impact of these issues can be seen in a study of immunization costs and barriers in another high-risk immunocompromised group: patients with HIV. A 2015 study estimated the costs of providing immunizations against HPV, pneumococcal pneumonia, and HZ to 2887 patients at an urban HIV clinic in Alabama.[58] Although reimbursement for each vaccine and its administration varied depending on insurer type, overall, administration of all 3 vaccines to all eligible patients would result in a net loss to the clinic of more than $97,000 per year.[58]

System level

For vaccine providers, vaccination costs include labor and vaccine storage, as well as costs associated with vaccine wastage and inventory shrinkage.[59] Due to wide variations in coverage, securing reimbursement for vaccine services can be complex and difficult to navigate, as not all healthcare providers who vaccinate adults are considered "providers" by third party payers. For example, of the 16 vaccines currently recommended for adults in the US,[36] for Medicare recipients, only influenza, pneumococcal, HBV; and COVID-19 are covered as medical benefits under Medicare part B; all others are considered Part D pharmacy benefits.[60] As most medical providers are not enrolled as pharmacy providers, receiving reimbursement for administration of these vaccines can be challenging.[59] As a result, patient access to needed vaccines can be blocked by the limited number of clinicians available to provide them.[1]

These barriers are in addition to the well-documented disparities in vaccine access that have always stood in the way of optimal immunization, notably;[1,35]

- Racial/ethnic (lower uptake in marginalized communities/groups)
- Socioeconomic (lack of insurance, lower uptake in poor communities)
- Geographic (infrastructure/logistical barriers to distribution of vaccines)

Solutions and Best Practices

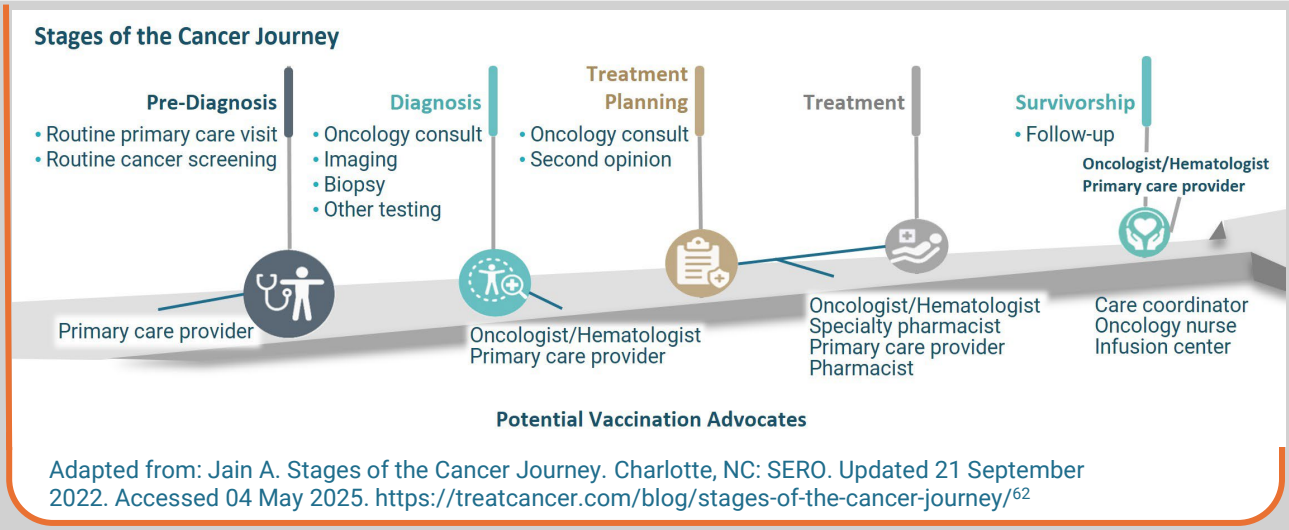
As noted in ASCO's guidelines for vaccination of adults with cancer, improving the availability, accessibility, and use of vaccines among patients with cancer requires a multifaceted approach, particularly for patients in areas with limited resources or infrastructure.[37] Incorporation of vaccination programs into oncology care settings—including integration of vaccination within the oncology care pathway (**Figure 2**)—is crucial to ensuring adequate coverage of this uniquely vulnerable group.[19]

Collaboration between oncologists, infectious disease specialists, and primary care providers is key to preventing patients from falling between the cracks during cancer treatment and survivorship.[19] Digital tools such as standing orders, enhanced reminders, and recall messages can help ensure that vaccines are delivered on a timely basis,[1,19,35] whereas participation in an IIS can provide consolidated immunization histories for use by vaccination providers and patients to track vaccination history and gaps.[1] To expand access and facilitate "vaccinating in the moment," healthcare systems should consider providing vaccination at locations other than medical offices and hospitals (eg, infusion centers, pharmacies, health fairs, workplaces, schools) and incorporating nonphysician healthcare providers to counsel patients and assess/administer vaccines (see **Case Studies: Leveraging Electronic Health Records and Nonphysician Care Extenders** on the next page).[1,61]

Inclusion of assessment and support for recommended adult vaccinations into payer-provided oncology care management programs may also enhance vaccine awareness and uptake.

> **"To protect people, both primary care providers and specialists must work together and not miss opportunities to vaccinate patients whenever and wherever they connect with the health care system."**
>
> Whitaker JA. *Mayo Clin Proc.* 2020;95(7):1530-1548

Figure 2. Potential inflection points for vaccination along cancer journey



Adapted from: Jain A. Stages of the Cancer Journey. Charlotte, NC: SERO. Updated 21 September 2022. Accessed 04 May 2025. https://treatcancer.com/blog/stages-of-the-cancer-journey/[62]

The National Foundation for Infectious Diseases has stated that awareness and understanding of adult vaccine recommendations by "all healthcare professionals" is key to improving rates of adult immunization in the US.[1] This is particularly true for cancer patients and survivors, who come in contact with a wide range of providers, each of whom can be a touchpoint for identifying vaccine needs and encouraging appropriate immunization (see **Figure 2** on previous page). Information campaigns, educational initiatives, and educational materials that address vaccine hesitancy and knowledge gaps in specific communities and high-risk groups—including providers, patients, and caregivers—can expand the safety net for patients with cancer and increase vaccine coverage.[1,46]

At the policy level, despite changes in Medicare/Medicaid policies that have reduced or eliminated copays and out-of-pocket expenses for recommended adult vaccines, there are still coverage gaps for uninsured adults.[1] Efforts are needed to address these gaps and ensure that uninsured and underinsured individuals have access to all recommended vaccines.[1] Stakeholders can be further incentivized by incorporating vaccination assessment and coverage into performance measures.[1]

Case Studies: Leveraging Electronic Health Records and Nonphysician Care Extenders

Two recent programs implemented at cancer centers in Baltimore and Philadelphia offer potentially valuable insights into how vaccination status can be monitored and improved at the level of the oncology practice.

At the Sidney Kimmel Cancer Center in Philadelphia, only 49% of patients had a documented vaccination against influenza during the 2022–2023 flu season, leaving most patients at risk. Aiming to improve vaccination rates, the center instituted a quality improvement initiative consisting of 4 cycles:[63]

- During Cycle 1, baseline data on vaccination status were collected via electronic health records (EHRs), and gaps in vaccine knowledge and vaccine hesitancy were identified
- In Cycle 2, medical assistants were trained in reconciliation of vaccination records in EHRs and in how to engage patients in effective conversations on vaccination
- In Cycle 3, patient education materials on vaccination were integrated into the clinical encounter
- Cycle 4 scaled the updated workflows to the entire clinic

At the end of the 2023–2024 flu season, 68% of oncology patients had a documented influenza vaccination. Integration of vaccine assessment and reconciliation into the medical assistants' workflows were found to have the biggest impact on vaccination rates.[63]

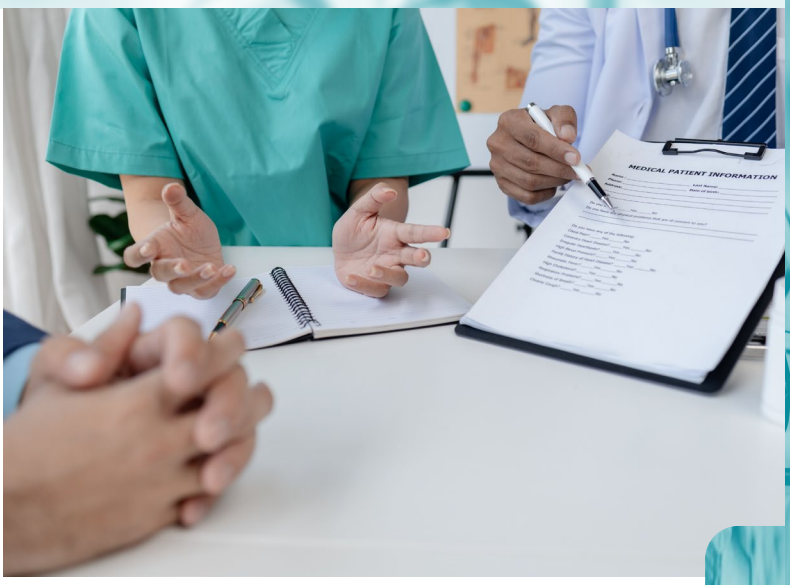
A similar project at a breast cancer center in Baltimore—conducted as part of a doctoral thesis—sought to increase rates of pneumococcal, HZ, and influenza vaccination in breast cancer patients at an academic, multidisciplinary breast clinic.[64] The intervention was conducted by an oncology nurse navigator who was an integral part of the care team and regularly coordinated health services for patients at the center, and consisted of[64]

- Reconciliation of patient's vaccine records in the EHRs and from outside facilities
- Review of patient's required vaccinations with medical oncologist, based on age, vaccination history, and risk factors
- Counseling and education of patient on the importance of vaccinations (including recommending concurrent vaccinations when appropriate)
- Follow-up within 2 weeks to confirm patient received vaccinations, with additional follow-up as needed
- Documentation of reconciliation, assessment, recommendation, and follow-up in EMR

Prior to the quality improvement initiative, none of the breast center patients had appropriate pneumococcal, HZ, or influenza vaccinations documented. Sixteen weeks after starting the initiative, vaccine documentation had increased to 88.5% for influenza, 70.8% for pneumococcal, and 58.3% for HZ.[64]

Conclusion/Call to Action

The human and economic burdens of vaccine-preventable diseases in patients with cancer underscore the urgency of implementing robust vaccination programs for these patients. Payers and other healthcare stakeholders can play a central role in facilitating change by working to improve coverage and distribution of recommended vaccines; supporting educational initiatives targeting patients, providers, and families/close contacts; and collaborating with healthcare systems to integrate vaccination services into the oncology care pathway.



References

1. National Foundation for Infectious Diseases. *Call to Action: Strategies to Improve Adult Immunization in the US*. National Foundation for Infectious Diseases. Updated 09 September 2024. Accessed 25 January 2025. https://www.nfid.org/resource/call-to-action-strategies-to-improve-adult-immunization-in-the-us/
2. Ison MG. Vaccines for use in special populations: Immunocompromised hosts. *J Infect Dis*. 2025;231(3):552–555.
3. Whitaker JA. Immunization strategies to span the spectrum of immunocompromised adults. *Mayo Clin Proc*. 2020;95(7):1530–1548.
4. Martinson ML, Lapham J. Prevalence of immunosuppression among US adults. *JAMA*. 2024;331(10):880–882.
5. Ogunwole S, Rabe M, Roberts A, Caplan Z. *Population Under Age 18 Declined Last Decade*. United States Census Bureau. Updated 06 November 2024. Accessed 02 May 2025. https://www.census.gov/library/stories/2021/08/united-states-adult-population-grew-faster-than-nations-total-population-from-2010-to-2020.html
6. Singson J, Kirley P, Pham H, et al. Factors associated with severe outcomes among immunocompromised adults hospitalized for COVID-19—COVID-NET, 10 states, March 2020–February 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(27):878–884.
7. Wallace BI, Kenney B, Malani PN, Clauw DJ, Nallamothu BK, Waljee AK. Prevalence of immunosuppressive drug use among commercially insured US adults, 2018–2019. *JAMA Netw Open*. 2021;4(5):e214920. doi:10.1001/jamanetworkopen.2021.4920

References (continued)

8. Zhang D, Petigara T, Yang X. Clinical and economic burden of pneumococcal disease in US adults aged 19–64 years with chronic or immunocompromising diseases: an observational database study. *BMC Infect Dis*. 2018;18(1):436. doi:10.1186/s12879-018-3326-z
9. American Cancer Society. *Cancer Treatment & Survivorship Facts & Figures (2022–2024)*. 2022. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/cancer-treatment-and-survivorship-facts-and-figures/2022-cancer-treatment-and-survivorship-fandf-acs.pdf
10. Gallicchio L, Devasia TP, Tonorezos E, Mollica MA, Mariotto A. Estimation of the number of individuals living with metastatic cancer in the United States. *J Natl Cancer Inst*. 2022;114(11):1476–1483.
11. Rodriguez MA. Vaccinations for patients with cancer and cancer survivors. *J Natl Compr Canc Netw*. 2022;20(5.5):607–610.
12. Echavarria I, Carrion Galindo JR, Corral J, et al. SEOM clinical guidelines for the prophylaxis of infectious diseases in cancer patients (2021). *Clin Transl Oncol*. 2022;24(4):724–732.
13. American Public Health Association. *Annual Influenza Vaccination Requirements for Health Workers*. 2010. November 9. https://www.apha.org/Policies-and-Advocacy/Public-Health-Policy-Statements/Policy-Database/2014/07/11/14/36/Annual-Influenza-Vaccination-Requirements-for-Health-Workers
14. Cooksley CD, Avritscher EB, Bekele BN, Rolston KV, Geraci JM, Elting LS. Epidemiology and outcomes of serious influenza-related infections in the cancer population. *Cancer*. 2005;104(3):618–628.
15. Valvi N, Patel H, Bakoyannis G, Haggstrom DA, Mohanty S, Dixon BE. COVID-19 diagnosis and risk of death among adults with cancer in Indiana: Retrospective cohort study. *JMIR Cancer*. 2022;8(4):e35310. doi:10.2196/35310
16. Kyaw MH, Rose CE, Jr., Fry AM, et al. The influence of chronic illnesses on the incidence of invasive pneumococcal disease in adults. *J Infect Dis*. 2005;192(3):377–386.
17. Wong A, Marrie TJ, Garg S, Kellner JD, Tyrrell GJ. Increased risk of invasive pneumococcal disease in haematological and solid-organ malignancies. *Epidemiol Infect*. 2010;138(12):1804–1810.
18. Boire A, Burke K, Cox TR, et al. Why do patients with cancer die? *Nat Rev Cancer*. 2024;24(8):578–589.
19. Bonanni P, Maio M, Beretta GD, Icardi G, Rossi A, Cinieri S. Improving influenza vaccination coverage in patients with cancer: A position paper from a multidisciplinary expert group. *Vaccines*. 2024;12(4). doi:10.3390/vaccines12040420
20. Einarsson J, Wilkinson AN. Vaccination considerations for patients receiving cancer therapy. *Can Fam Physician*. 2022;68(10):751–752.
21. Kersh AE, Ng S, Chang YM, et al. Targeted therapies: Immunologic effects and potential applications outside of cancer. *J Clin Pharmacol*. 2018;58(1):7–24.
22. Tonorezos E, Devasia T, Mariotto AB, et al. Prevalence of cancer survivors in the United States. *Natl Cancer Inst*. 2024;116(11):1784–1790.
23. Denlinger CS, Ligibel JA, Are M, et al. Survivorship: Immunizations and prevention of infections, version 2.2014. *J Natl Compr Canc Netw*. 2014;12(8):1098-111.
24. Ariza-Heredia EJ, Chemaly RF. Practical review of immunizations in adult patients with cancer. *Hum Vaccin Immunother*. 2015;11(11):2606–2614.
25. Li J, Zhang D, Sun Z, Bai C, Zhao L. Influenza in hospitalised patients with malignancy: a propensity score matching analysis. *ESMO Open*. 2020;5(5):e000968. doi:10.1136/esmoopen-2020-000968
26. Hosseini-Moghaddam SM, Shepherd FA, Swayze S, Kwong JC, Chan KKW. SARS-CoV-2 infection, hospitalization, and mortality in adults with and without cancer. *JAMA Netw Open*. 2023;6(8):e2331617. doi:10.1001/jamanetworkopen.2023.31617
27. Marra F, Parhar K, Huang B, Vadlamudi N. Risk factors for herpes zoster infection: A meta-analysis. *Open Forum Infect Dis*. 2020;7(1):ofaa005. doi:10.1093/ofid/ofaa005
28. McKay SL, Guo A, Pergam SA, Dooling K. Herpes zoster risk in immunocompromised adults in the United States: A systematic review. *Clin Infect Dis*. 2020;71(7):e125–e134.

References (continued)

29. Li Q, Chen S-Y, Burstin SJ, Levin MJ, Suaya JA. Cost of herpes zoster in patients with selected immune-compromised conditions in the United States. *Open Forum Infect Dis*. 2016;3(2):ofw067. doi:10.1093/ofid/ofw067
30. Loulergue P, Mir O, Alexandre J, Ropert S, Goldwasser F, Launay O. Low influenza vaccination rate among patients receiving chemotherapy for cancer. *Ann Oncol*. 2008;19(9):1658. doi:10.1093/annonc/mdn531
31. Chang A, Ellingson MK, Flowers CR, Bednarczyk RA. Influenza vaccination rates among patients with a history of cancer: Analysis of the National Health Interview Survey. *Open Forum Infect Dis*. 2021;8(7):ofab198. doi:10.1093/ofid/ofab198
32. Abdel-Rahman O. Patterns and association of vaccination among adults with a history of cancer in the USA: a population-based study. *J Comp Eff Res*. 2021;10(11):899–907.
33. National Vaccine Program Office. *National Adult Immunization Plan*. US Dept of Health and Human Services; 2015. https://www.hhs.gov/sites/default/files/nvpo/national-adult-immunization-plan/naip.pdf
34. Sabow H, Heller J, Conway M, Benefield J. *The Potential of Adult Vaccination in the United States*. 2025. April. https://www.mckinsey.com/industries/life-sciences/our-insights/the-potential-of-adult-vaccination-in-the-united-states
35. Kamboj M, Bohlke K, Baptiste DM, et al. Vaccination of adults with cancer: ASCO guideline. *J Clin Oncol*. 2024;42(14):1699–1721.
36. US Centers for Disease Control & Prevention. *Recommended Adult Immunization Schedule for Ages 19 Years or Older*. Updated 07 July 2025. Accessed 27 September 2025. https://www.cdc.gov/vaccines/hcp/imz-schedules/downloads/adult/adult-combined-schedule.pdf
37. US Centers for Disease Control & Prevention. *Shared Clinical Decision-Making: Additional Doses of COVID-19 Vaccine for People Who Are Moderately or Severely Immunocompromised*. Updated 01 January 2025. Accessed 27 September 2025. https://www.cdc.gov/vaccines/covid-19/downloads/FS-COVID-Dose-Decision-Making.pdf
38. US Centers for Disease Control & Prevention. *Hepatitis B Vaccine Administration*. Updated 18 September 2025. Accessed 27 September 2025. https://www.cdc.gov/hepatitis-b/hcp/vaccine-administration/index.html
39. US Centers for Disease Control & Prevention. *HPV Vaccine Recommendations*. Updated 09 July 2024. Accessed 27 September 2025. https://www.cdc.gov/hpv/hcp/vaccination-considerations/
40. US Centers for Disease Control & Prevention. *Clinical Considerations for Shingrix Use in Immunocompromised Adults Aged ≥19 Years*. Updated 09 July 2024. Accessed 27 September 2025. https://www.cdc.gov/shingles/hcp/vaccine-considerations/immunocompromised-adults.html
41. US Centers for Disease Control & Prevention. *RSV Vaccine Guidance for Adults*. Updated 08 July 2025. Accessed 27 September 2025. https://www.cdc.gov/rsv/hcp/vaccine-clinical-guidance/adults.html
42. National Committee for Quality Assurance. *Special Report: Results for Measures Leveraging Electronic Clinical Data for HEDIS®*. 2024. November. https://wpcdn.ncqa.org/www-prod/wp-content/uploads/Special-Report-Nov-2024-Results-for-Measures-Leveraging-Electronic-Clinical-Data-for-HEDIS.pdf
43. Rubin LG, Levin MJ, Ljungman P, et al. Executive Summary: 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dise*. 2014;58(3):309–318.
44. Woodfield MC, Pergam SA, Shah PD. Cocooning against COVID-19: The argument for vaccinating caregivers of patients with cancer. *Cancer*. 2021;127(16):2861–2863.
45. Liang J. *"Cocooning" and Tdap Vaccination*. June 25, 2015. https://stacks.cdc.gov/view/cdc/60983
46. Marellapudi A, King AR, Bednarczyk RA. Presentation of caregiver-specific vaccine-related information on National Cancer Institute designated cancer center websites. *Vaccine*. 2020;38(40):6248–6253.
47. Lee YJ, Huang YT, Kim SJ, et al. Trends in invasive pneumococcal disease in cancer patients after the introduction of 7-valent pneumococcal conjugate vaccine: A 20-year longitudinal study at a major urban cancer center. *Clin Infect Dis*. 2018;66(2):244–253.

References (continued)

48. Pedrazzoli P, Lasagna A, Cassaniti I, et al. Vaccination for seasonal influenza, pneumococcal infection and SARS-CoV-2 in patients with solid tumors: Recommendations of the Associazione Italiana Di Oncologia Medica (AIOM). *ESMO Open*. 2023;8(3):101215. doi:https://doi.org/10.1016/j.esmoop.2023.101215
49. Lin HH, Hsu KL, Ko WWC, et al. Cost-effectiveness of influenza immunization in adult cancer patients in Taiwan. *Clin Microbiol Infect*. 2010;16(6):663–670.
50. Stoeklé HC, Sekkate S, Vallée A, Beuzeboc P, Hervé C. Refusal of vaccination against influenza and COVID-19 in patients with solid cancers: From bio-ethical issues to solutions. *Eur J Cancer*. 2023;183:139–141.
51. Sarkar L, Goli VB, Menon N, Patil VM, Noronha V, Prabhash K. Vaccination practices, efficacy, and safety in adults with cancer: A narrative review. *Cancer Res Stat Treat*. 2021;4(3):505-515.
52. Lin J, Chan KH, Farmer A, et al. V CAN intervention: Quality improvement initiative to increase and sustain vaccination rates among adult patients with cancer. *JCO Oncol Pract*. 2023;19(11_suppl):400. doi:10.1200/OP.2023.19.11_suppl.400
53. Dulude A. *Cancer Patient Attitudes Towards Influenza Vaccination and the Prevalence of Vaccination in Cancer Patients* [Submitted in Partial Fulfillment of the Requirements for the Degree of Doctor of Medicine]. University of Arizona; 2015. Accessed May 2, 2025. http://hdl.handle.net/10150/528169
54. National Vaccine Advisory Committee. Recommendations from the National Vaccine Advisory committee: standards for adult immunization practice. *Public Health Rep*. 2014;129(2):115–123.
55. Wumkes ML, van der Velden AM, van der Velden AW, et al. Influenza vaccination coverage in patients treated with chemotherapy: current clinical practice. *Neth J Med*. 2013;71(9):472–477.
56. Srivastav A, Black CL, Lutz CS, et al. U.S. clinicians' and pharmacists' reported barriers to implementation of the Standards for Adult Immunization Practice. *Vaccine*. 2018;36(45):6772–6781.
57. Granade CJ, Parker Fiebelkorn A, Black CL, et al. Implementation of the standards for adult immunization practice: A survey of U.S. health care providers. *Vaccine*. 2020;38(33):5305-5312.
58. Eaton EF, Kulczycki A, Saag M, Mugavero M, Raper JL. Immunization costs and programmatic barriers at an urban HIV clinic. *Clin Infect Dis*. 2015;61(11):1726–1731.
59. Tsai Y, Zhou F, Lindley MC. Insurance reimbursements for routinely recommended adult vaccines in the private sector. *Am J Prev Med*. 2019;57(2):180-190.
60. US Centers for Disease Control and Prevention. *How to Pay for Vaccine*s. US Centers for Disease Control and Prevention. Updated 10 July 2024. Accessed 17 June 2025. https://www.cdc.gov/vaccines-adults/recommended-vaccines/how-to-pay-adult-vaccines.html
61. Eiden AL, Cagle C, Esselman K, et al. Exploring perspectives on vaccinations delivered in complementary nonclinical settings and by nonphysician health professionals: A qualitative interview study. *J Am Pharm Assoc*. 2024;64(6):102193. doi:10.1016/j.japh.2024.102193
62. Jain A. *Stages of the Cancer Journey*. *SERO*. Updated 21 September 2022. Accessed May 4, 2025. https://treatcancer.com/blog/stages-of-the-cancer-journey/
63. Hannan E, Leader A, Worster B, Csik VP, Thomas-Nembhard C, Sylla A. Optimizing influenza vaccination among oncology patients through quality improvement cycles. *JCO Oncol Pract*. 2024;20(10_suppl):285.
64. Russell S. *Improving Vaccination Rates Among Breast Cancer Patients Through Patient Outreach* [Submitted in Partial Fulfillment of the Requirements for the Doctor of Nursing Practice Degree]. University of Maryland at Baltimore 2023. Accessed 02 May 2025. http://hdl.handle.net/10713/20887

