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CONSENSUS STATEMENT

Vaccination of people with solid tumors and diabetes: existing evidence and recommendations. A position statement from a multidisciplinary panel of scientific societies

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Abstract

Diabetes and cancer are two of the most common public health concerns worldwide. The complex interplay of these two conditions is a growing area of research, as patients with diabetes are at increased risk for developing cancer, and vice versa. Furthermore, both patient populations show increased risk of many communicable infectious diseases and their adverse consequences, while vaccination can play a crucial role in their prevention, improving patient outcomes. Vaccination should represent a standard part of care for patients with cancer, diabetes, and both the diseases simultaneously, including people undergoing cancer treatment or in remission. Several international guidelines provide recommendations for vaccinating people with cancer or diabetes, but the two conditions have not been specifically evaluated together. Here we present a multidisciplinary consensus position paper on vaccination in patients with cancer and diabetes. The position paper is the result of a collaborative effort between experts from the Italian Association of Medical Oncology (AIOM), Italian Association of Medical Diabetologists (AMD), Italian Society of Diabetology (SID), Italian Society of Endocrinology (SIE), and Italian Society of Pharmacology (SIF). The paper provides a comprehensive overview of the current state-of-the-art knowledge on vaccination in patients with cancer and diabetes. It discusses the importance of vaccination in preventing infections, focuses attention on the need to consider the unique challenges faced by patients with cancer and diabetes when it comes to vaccine administration, and highlights the need for coordinated care to optimize treatment outcomes. Overall, the consensus position paper provides healthcare professionals caring for patients with cancer and diabetes recommendations on the use of various vaccines, including influenza, COVID-19, HZV, and HPV vaccines, as well as guidance on how to address common concerns and challenges related to vaccine administration.

Keywords Diabetes · Cancer · Vaccines · Immunocompromised · COVID-19 · Influenza · Pneumonitis · Vaccine hesitancy · Vaccine-preventable diseases (VPDs)

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Introduction

The very recent COVID-19 pandemic, together with the strategies implemented for tackling its spread, have highlighted the importance of vaccination strategies for immunization from communicable diseases. Immunization from vaccines has always been considered a very effective and safe tool for the prevention of infectious diseases and for prolonging lifespan: to date, some communicable diseases have been completely eradicated thanks to vaccines, while others no longer represent a public health issue, at least in the developed world [1].

Compared to the general population, several groups of individuals present a specific risk of contracting infections or developing more serious consequences. Definitively, cancer patients and people with diabetes are at increased risk from these complications, due to their overall frailty and their state of relative immunosuppression (Fig. 1).

Oncological patients are particularly susceptible to infections and vulnerable to their consequences: this is due to the direct effects of the tumour (e.g., immune system compromission, bone marrow invasion, surgical or functional asplenia) and/or as a result of anti-tumour treatments (effects of cytotoxic chemotherapy or radiotherapy, use of glucocorticoids, or other immunosuppressants) [2, 3]. The most relevant oncologic scientific societies have published recommendations on vaccination against vaccine-preventable diseases in cancer patients beyond those for cancer-causing viruses [4–6].

Subjects with diabetes are also more vulnerable to infectious diseases (e.g., skin and soft tissue infections, pneumonia, urinary tract infections, and sepsis) compared to the general population, with a higher risk of hospitalization, longer hospital stay, and severe complications [7–10]. From a pathophysiological standpoint, chronic hyperglycaemia is thought to promote dysfunction of the immune response primarily through a deficit in neutrophil and macrophage function, reduced release of inflammatory cytokines, and disorders of the humoral and T-cell response, failing to overcome the spread of invading pathogens [11]. Accordingly, the Italian national vaccination plan, as well as several programs from other countries, include patients with diabetes in the "at risk" categories for which additional vaccinations are recommended, compared to the general population [12]. The American Diabetes Association (ADA) Standard of Care for diabetes, as well as many other international diabetes guidelines, recommends to provide routinely endorsed vaccinations for children and adults with diabetes as indicated by age [13, 14].

Diabetes is also the most common comorbidity in patients with cancer [15]. Consequently, in the not unusual event of subjects simultaneously affected by diabetes and cancer, the coexistence of the two conditions poses an even more important challenge in the prevention through vaccination of communicable diseases and their potential life-threatening consequences, often capable of nullifying the great results attainable with current anti-tumour treatments. Moreover, the response to some vaccinations in these subjects could be weaker than healthy individuals of the same age: a limitation that can be overcome by reducing the spread of the infective agent, through greater implementation of immunization of both the patients themselves and their caregivers [16]. Consequently, there is a growing need to implement

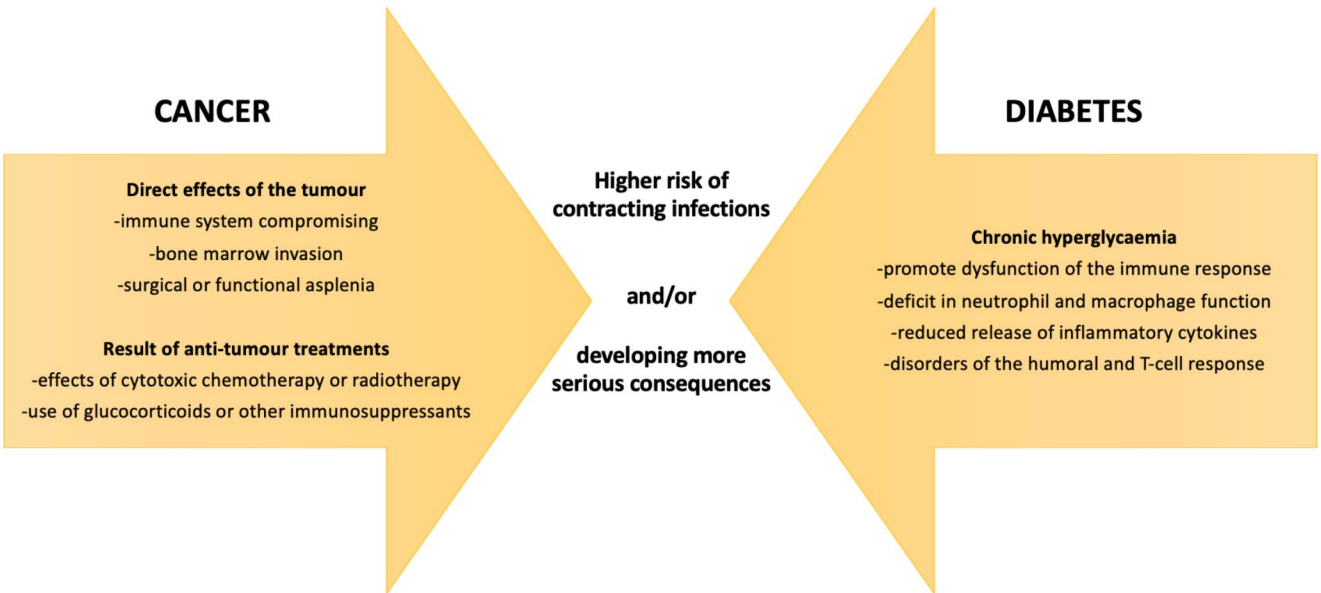

Fig. 1 Mechanisms by which cancer and diabetes can increase the risk of contracting infections or developing more serious consequences

suitable vaccination strategies, through campaigns that must integrate the different healthcare providers and specialties.

The knowledge of this ever-evolving issue, especially if applied to special populations such as patients with diabetes, cancer, or both the diseases, allows Diabetologists and Oncologists (as well as General Practitioners, Internal Medicine specialists, Infective Diseases specialists, and several other healthcare figures) to safeguard the undisputed health and social value of this fundamental preventive strategy.

The purpose of this position statement from a multidisciplinary panel of experts from different Italian scientific societies (AIOM, Italian Association of Medical Oncology; AMD, Italian Association of Medical Diabetologists; SID, Italian Society of Diabetology; SIE, Italian Society of Endocrinology; and SIF, Italian Society of Pharmacology) is to provide a critical overview of vaccination strategies currently recommended for people with diabetes and for cancer patients, paying particular attention to subjects simultaneously suffering from both conditions.

General review of existing guidelines and recommendations

Both in vitro and in vivo studies have shown that diabetes confers an increased susceptibility risk of developing infectious diseases and a higher hazard of death due to more severe course of them. Therefore, besides the microvascular and macrovascular complications of diabetes, infectious diseases must also be taken into highest consideration. Multiple mechanisms, secondary to chronic hyperglycemia, are implicated in the higher frequency and severity of infections in patients with diabetes. Similarly, in patients suffering from malignant tumors, the immune system is compromised due to multiple issues including chronic inflammation, impairment of the hematopoietic system as well as treatments that compromise immune function. Therefore, vaccine-preventable diseases must necessarily represent a focus for oncologists to undertake appropriate interventions in cancer patients.

The Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) provides vaccination schedules specifically for children, adolescents, and adults, and recommends influenza and pneumococcal vaccines for all individuals with diabetes along with Hepatitis B, tetanus, diphtheria, pertussis, meningococcal disease, respiratory syncytial virus, COVID-19 and Herpes Zoster. The ACIP evidence review has evolved over the years and, in 2010, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was adopted, subsequently arriving in 2018 at the Evidence to Decision or Evidence to Recommendation frameworks with the aim of helping to use evidence in a structured and transparent way to make decisions regarding clinical recommendations [17].

The ADA Standards of Medical Care in Diabetes has adopted the same recommendations as the ACIP [14]. Similarly, the 2022 American Association of Clinical Endocrinology (AACE) Diabetes Guideline supports the recommendations of the CDC ACIP, providing, in a paramount section (Question 28), 11 recommendations and the evidence base for each statement on the types of vaccines adults with diabetes should receive [18].

In Italy, in 2018, a consensus statement has been signed by diabetes scientific societies (AMD and SID), General Practitioners associations (FIMMG and SIMG), and Hygienist scientific society (SItI), in order to provide a Recommended Vaccinations Guideline in adult patients with diabetes. The impact and benefits of vaccinations against influenza, pneumococcal, meningococcal, diphtheria-tetanus-pertussis, COVID-19, hepatitis B, mumps-pertussis-rubella (MPS) and Zoster have been traced. The ultimate aim is to increase vaccination coverage which is still far from safety standards [19].

With similar goals, the American Society of Clinical Oncology (ASCO) has stepped into a five-year cooperative agreement with the CDC, supporting guideline development and efforts in providers' and patients' education with the final aim of increasing vaccination rates among cancer patients. For all seasonal vaccines as well as age- and risk-based vaccines (influenza, respiratory syncytial virus, COVID-19, tetanus, diphtheria, pertussis, hepatitis B, Zoster, pneumococcal vaccines, Human Papilloma Virus-HPV), vaccination status of the patient should be settled up, and vaccination should be performed 2–4 weeks before any scheduled cancer treatment and taking into account between live or non-live virus vaccines, too [4].

In a recent paper, the Italian Association of Medical Oncology (AIOM) has strongly reinforced the recommendations on seasonal influenza, pneumococcal infection and SARS-CoV-2 vaccinations, underlining the deleterious effects of vaccine hesitancy in patients with malignancies [3].

Vaccinations in cancer patients

Specific challenges of vaccinating patients with cancer

It is important to provide cancer patients with direct protection against infectious agents through immunization, and oncologists should provide adequate counselling and encourage adherence to vaccination. However, considering

that the cancer patient's immune system, due to the state of immunosuppression, may respond sub-optimally to vaccination, it is necessary to consider vaccinating also people who are in close contact, such as cohabitants, caregivers, and the healthcare personnel in charge of the patient (doctors, nurses, social and healthcare workers). Close family members or persons in close contact with the patient should be assessed for their actual vaccination status and possibly be (re)vaccinated [20].

ASCO recommends vaccinating all family members and close contacts, if possible [4]. The Infectious Diseases Society of America (IDSA) 2013 guidelines state that immunocompetent individuals living in a household with immunocompromised patients can safely receive all recommended live and non-live vaccines, with some exceptions and precautions [21]. IDSA guidelines recommend against administering oral polio vaccine to contacts/family members of immunocompromised patients and against administering live attenuated influenza vaccine (LAIV vaccine administered by intranasal spray) to contacts/family members of patients who have recently received a bone marrow transplant or who develop graft versus host disease (GVHD). Vaccination against Rotavirus is strongly discouraged in family members of cancer patients [20].

The Italian Ministry of Health, for the 2024–2025 season, recommends seasonal influenza vaccination for cancer patients undergoing chemotherapy, for family members and contacts (adults and children) of cancer patients, and for physicians and health care/social care staff, since they can transmit influenza to those at high risk of influenza complications [22].

Efficacy of vaccinations on immune response in cancer patients

In cancer patients, non-live vaccines (inactivated vaccines, subunit vaccines, including recombinant polysaccharide vaccines and polysaccharide-protein conjugate vaccines, toxoids and mRNA vaccines) can be safely used. In contrast live vaccines, containing an attenuated but replication-capable virus or bacterium, may represent a risk of uncontrolled infection by the vaccine strain and are therefore to be avoided in cancer patients [4] (Fig. 2).

The effectiveness of vaccination is primarily assessed by the reduction in the incidence of infections. However, such studies do not usually provide detailed information on the reduction of infection rates due to the specific serum/genotype against which patients have been immunized [20]. This represents an important limitation. Furthermore, most data on vaccination in cancer patients derive from underpowered studies that include subjects with different tumor types and chemotherapy treatments and use different definitions of vaccine response. The efficacy of vaccination in cancer patients is related to the type of disease and the degree of immunosuppression [4], but also to the dosage and number of vaccine administrations [23].

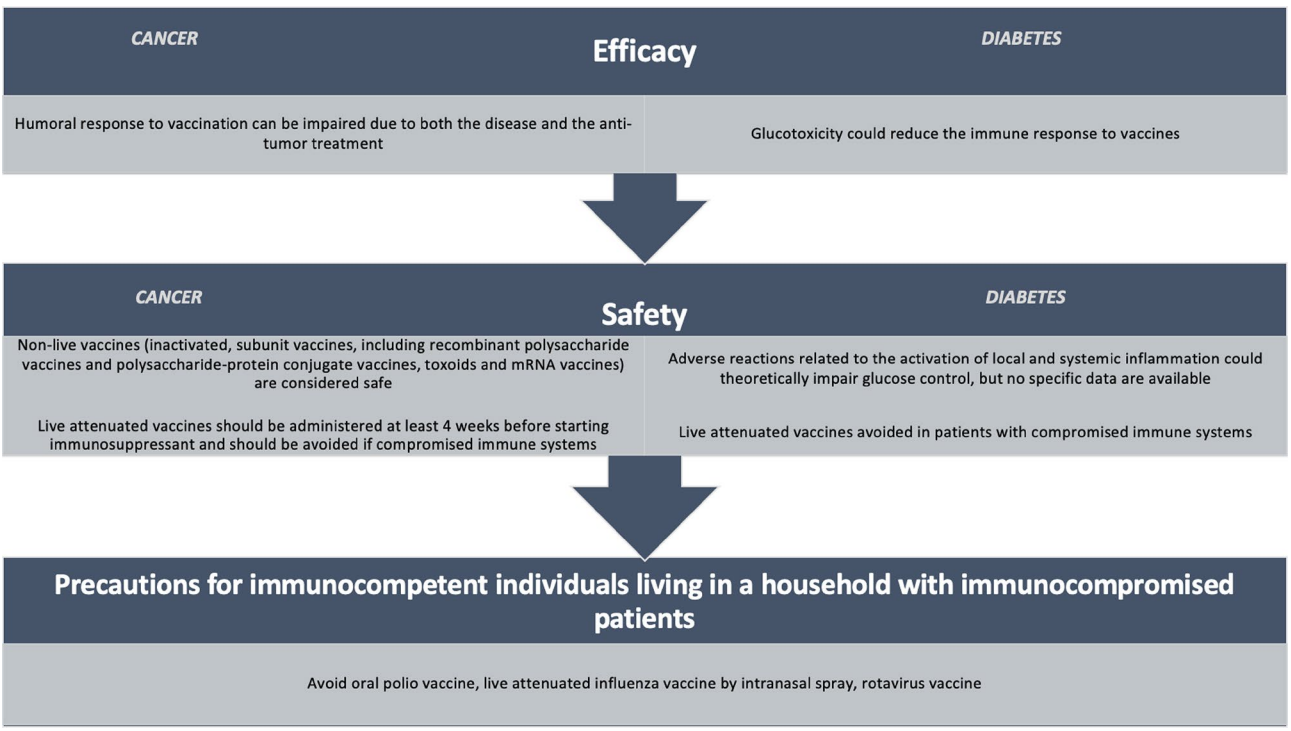

Fig. 2 Efficacy, safety and precautions of vaccination in patients with cancer and diabetes

Classically, vaccine response is measured by assessing antibody titers (immunoglobulin G) before and after vaccination [23]. In cancer patients, the humoral response to vaccination is often impaired due to both the disease and the anti-tumor treatment. However, other studies have recently found that the cellular response, and in particular the T-cell response, would be stronger than the humoral response, and possibly even more predictive of protection [24]. Regarding influenza vaccination, it has been reported that the response to the vaccine in cancer patients is similar to that of healthy patients [23]. Chiou WY et al. [25] demonstrated the efficacy of pneumococcal vaccination in elderly patients with colorectal cancer, with a significant reduction in the risk of hospital admission for pneumonia. The ASCO guidelines [4] on anti-COVID-19 vaccination state that seroconversion rates in adults with solid tumors tend to be lower than in those without tumors. Seroconversion rates are even lower in hematological diseases. Piubelli et al. [26] verified that COVID-19 vaccination is able to elicit a significant humoral response in patients with solid tumors, independent of tumor type and therapy. Furthermore, five non-randomized studies demonstrated that vaccination is useful in reducing severe COVID-19 disease in cancer patients (reduction in COVID-19 hospitalizations and death within 30 days compared to unvaccinated cancer patients) [27–31].

Regarding herpes zoster vaccination, the best humoral and cellular response after administration of the recombinant vaccine is expected immediately after tumor diagnosis and before the start of immunosuppressive therapy [4].

Safety of vaccinations during cancer treatment

In general, inactivated vaccines are considered safe and should be administered at least 2 weeks before the start of chemotherapy and not during radiotherapy, to trigger an effective immune response. However, concomitant administration of inactivated vaccines with chemotherapy and radiotherapy is not harmful [23] (Fig. 2).

Live attenuated vaccines should be administered at least 4 weeks before the start of immunosuppressive therapy and should be avoided in patients with compromised immune systems [4]. The CDC and the IDSA recommend against vaccination with live attenuated vaccines for at least 3 months after stopping immunosuppressive therapy. Some chemotherapeutic agents cause immunosuppression beyond 3 months. For patients receiving regimens that include anti-B-cell antibodies, vaccination should be delayed for at least 6 months after the end of treatment. The ASCO guidelines [4] report that, in patients receiving immune checkpoint inhibitor (ICI) therapy, COVID-19 vaccination has similar seroconversion rates as in patients without cancer, with mild to moderate side effects (local pain and fatigue), and without any increase in immune-related adverse reactions in vaccinated patients. Influenza vaccination in patients undergoing ICI therapy also does not show an increased risk of immune-related adverse reactions compared to non-vaccinated patients undergoing therapy.

Vaccinations in patients with diabetes

Specific challenges in vaccinating patients with diabetes

Infections are associated with more severe complications in people with diabetes, compared to the general population, and may also increase blood glucose levels, thus making diabetes more difficult to manage. People with diabetes have a higher risk to be hospitalized for such complications [10]. In particular, a 6% increased risk of hospitalization was reported for seasonal influenza [32]. Conversely, patients who received influenza vaccination showed a lower risk of hospitalization for pneumonia [33]. In addition, in a retrospective study, influenza vaccination in patients with type 2 diabetes (T2D) was associated with a significant reduction in the risk of hospitalization for stroke, heart failure or pneumonia [34].

Therefore, children and adults with diabetes should receive all recommended vaccinations according to age-appropriate recommendations [12, 14, 35]. The European health authorities and the World Health Organization (WHO) set the target objective of 75% of vaccination coverage in the diabetic population [36]. The Italian Ministry of Health recommends and offers free influenza vaccination for people with diabetes, indicating a minimum vaccination coverage goal of at least 75% as desirable and 95% as the optimal goal. In the 2022–2023 flu vaccination campaign, vaccination coverage in the diabetic population was only 38%. The percentage improves when assessing the category of diabetic patients over 65 old years, reaching 72% coverage [37]. Although rates differ across nations, it has been reported that regular visits to primary care providers were associated with higher influenza vaccination rates among subjects with diabetes [38, 39]. Pneumococcal vaccine coverage data are not routinely collected. In elderly subjects coverage was relatively low, ranging from 0.7 to 50%, in different Italian regions [12]. Furthermore, despite the heavy burden of herpetic infection in immunocompromised people, current levels of anti- herpes zoster vaccine coverage in different countries are low in people with diabetes [40].

Elderly age, the presence of comorbidities, frequent primary care visits, and a previous history of vaccination have all been associated with greater vaccination adherence.

Conversely, poor perception of the risk of infection complications, fear of adverse events, and a self-rated good health status have all been associated with lower vaccination adherence [41].

These considerations underline the specific challenges in vaccinating patients with diabetes.

Considering the gaps between recommendations and the real vaccination coverage, the following actions could be implemented to improve the compliance to vaccination in people with diabetes:

- analyzing the reasons why some people do not wish to receive vaccinations;
- removing barriers through education and providing information on the risks associated with infections and their effective prevention by vaccination;
- improving the dissemination work directed to both healthcare workers and people with diabetes, as well as their families.

A central role should be played by the collaboration of general practitioners with diabetologists in promoting access to vaccination. Various methods may be used to inform diabetic population, such as displaying posters in the waiting areas, providing adequate health education by healthcare professionals (physicians, nurses, and pharmacists), and sending vaccination reminders to both patients and their primary care providers.

Finally, national health institutions and scientific societies should collaborate to promote independent scientific research and information on vaccines, and on appropriate level of immunization in people with diabetes.

Efficacy of vaccinations on immune response in patients with diabetes

Given the high risk for morbidity and mortality from infective diseases that people with diabetes experience, the WHO [42] and some international guidelines [14, 19] decided to strongly recommend several vaccinations in patients with diabetes.

One of the possible mechanisms underlying the greater susceptibility of patients with diabetes to infective diseases and their complications can be directly related to glucotoxicity [43]. Glucotoxicity could reduce the immune response to vaccines, as suggested by some human studies [44, 45]. An example of this putative lower efficacy of vaccination among patients with diabetes derives from hepatitis B vaccination, but several studies have shown reduced immunogenicity in patients with diabetes [46]. Nevertheless, some other authors reported that the humoral response of subjects with diabetes was not dissimilar from that of the general population [47, 48]. Moreover, some issues have been raised about vaccine safety in patients with diabetes [16]. Most adverse reactions are related to the activation of local and systemic inflammation, which could theoretically impair glucose control (Fig. 2). However, a recent observational study, performed on patients with type 1 diabetes (T1D) and assessing the effectiveness of mRNA-based anti-COVID-19 vaccine (Moderna), did not report any increase in glucose levels as shown by interstitial glucose monitoring data [49]. To further complicate the overall picture, the efficacy and safety of vaccines in people with diabetes could be theoretically different in distinct subpopulations (e.g., T1D vs. T2D, or different age groups); therefore, it would be very important to collect data on subgroups in order to issue evidence-based recommendations. Unfortunately, available studies do not report such subgroup analyses, limiting the information that can be collected in systematic reviews for clinical decision-making.

Pneumococcal infections

Nowadays, two types of vaccines are available for protection against pneumococcal infections in adults: polysaccharide (23-valent: PPSV23) and conjugate (13-valent: PCV13; 15-valent: PCV15; 20-valent: PCV20) vaccines. All these vaccines fully demonstrated their efficacy in reducing pneumonia among immunocompetent adults [50, 51].

Little evidence is available on the effectiveness of anti-pneumococcal vaccination in patients with diabetes. A post hoc analysis of the only available randomized clinical trial [52] suggested that pneumococcal conjugate vaccine PCV13 is effective in reducing hospitalizations for pneumonia. On the other hand, a recent meta-analysis of observational studies failed to demonstrate the effectiveness of the pneumococcal vaccines in reducing hospitalizations and mortality in this population, irrespective of the type of vaccine used (PPSV23 and PCV13) [53]. Moreover, the same meta-analysis showed a likely reduction in the efficacy of the PPSV23 vaccine over time among patients with diabetes [53]. A previous systematic review exploring differences in pneumococcal-related outcomes in vaccinated adults with and without diabetes also provided conflicting results [54], and a previous meta-analysis including only patients with diabetes [55] raised some doubts about the efficacy of pneumococcal vaccines in this population. However, the only available randomized trial seems to suggest an effective protection of this vaccine also in patients with diabetes [52]. Moreover, it should be noted that all available evidence on the effectiveness of anti-pneumococcal vaccination derive from studies performed with PPSV23 and PCV13 vaccines. PCV15 and PCV20 are well-known to be more effective

than previous vaccines [56]. Unfortunately, data on these vaccines among patients with diabetes are not yet available.

Influenza

Data on the effectiveness of vaccination for influenza in patients with diabetes are more robust and convincing in comparison with those obtained for other vaccinations. There are several meta-analyses [33, 57] suggesting a similar efficacy in preventing adverse outcomes among individuals with diabetes. In particular, a recent systematic review and meta-analysis reported favorable results deriving from observational studies including a large cohort of patients with T2D, with long follow-up time, and with data on laboratory and clinical parameters [33]. This study observed an overall wide reduction in all-cause mortality associated with influenza vaccination, partly explained by the reduction in the risk of complications of influenza, such as pneumonia. In this analysis, influenza vaccination was associated with a reduced risk of hospitalization for pneumonia. However, other mechanisms cannot be ruled out: for example, among patients with cardiovascular disease, influenza vaccination can reduce cardiovascular mortality and morbidity [58]. Moreover, infections such as influenza can increase blood glucose levels, acutely worsening diabetes and its intercurrent complications [59].

Herpes Zoster

Patients with T2D show an increased risk of both herpes zoster (HZ) infection and complications, and a further increase in risk has been observed in older people, especially with associated cardiovascular disease [60, 61]. A recent systematic review and meta-analysis of the few available clinical trials and observational studies assessed the efficacy and effectiveness of HZ vaccines in people with diabetes. According to this analysis, the quality of evidence for efficacy of the recombinant zoster vaccine (RZV) was higher than that for the live attenuated vaccine, even if no head-to-head comparison between the two available vaccines has been performed in people with diabetes [62].

Patients with cancer and diabetes

Immunological vulnerabilities in patients with cancer and diabetes

Diabetes and cancer are among the leading causes of death worldwide, and their incidence and prevalence have progressively increased in recent years [63]. A strong interconnection between these two medical conditions has been described, with patients with diabetes being at higher risk to develop some malignancies [64], on the one hand, and anti-cancer treatments potentially leading to iatrogenic hyperglycemia and/or diabetes-related complications [15, 65], on the other. A negative impact of diabetes on cancer-related mortality has also been reported [65, 66]. A common denominator between diabetes and cancer is represented by immune system disfunction, which exposes affected patients to higher risk of infections.

Indeed, cancer patients often have a compromised immune system due to various factors, such as chronic inflammation and toxicities from anti-cancer treatments (e.g. chemotherapy and radiotherapy) [4]. Diabetes, as well, is associated with impaired T-cell responses, decreased neutrophil function, and reduced humoral immunity [67]. Several studies have demonstrated that patients with T2D and hyperglycemia show increased rates of bacterial infections, fungal infections such as candidiasis and mucormycosis, as well as shorter remission periods, shorter median survival times, higher rates of hospital admissions, more infection-related admissions, and higher mortality rates [68, 69]. A systematic review and meta-analysis revealed that preexisting diabetes in cancer patients was associated with an increased risk of all-cause mortality compared to cancer patients without diabetes [70].

The immune system function is a major factor in determining the spectrum of infections to which cancer patients are more vulnerable. Host defense mechanisms are mediated by the immune system, which is traditionally divided into the innate (general or non-specific) compartment and the adaptive (specialized or specific) one [71–73]. The former is constitutively present, not antigen-specific, and able to mobilize rapidly, thus providing the first line of defense for invading microorganisms. The innate immune system is comprised of anatomical barriers, humoral factors that aid in the inflammatory response, and cellular components that facilitate phagocytosis. In cancer patients, these barriers can be compromised by malignant invasion, mechanical obstruction, or treatments such as radiation and cytotoxic chemotherapy. The adaptive immune system is antigen-specific and exhibits immunological memory. Therefore, it requires time to react but can react more rapidly, although not as quickly as innate immunity, on repeated exposure to the same organism [72]. Adaptive immunity includes both humoral and cellular components mediated by B and T lymphocytes, respectively.

Both the innate (general) and the adaptive (specialized) immune systems may be altered in cancer patients. Factors that predispose to infection are divided into “host-associated” and “treatment-associated”. Host-associated factors include underlying immune deficiencies, medical comorbidities, past infections, poor nutritional status, presence of

foreign bodies, and psychological stress. Treatment-associated factors include surgery, radiation, immunosuppressant therapies, antimicrobial use, and invasive procedures [71].

For instance, chemotherapy and radiation therapy may result in decreased number of circulating neutrophils. A subset of solid tumor patients receives intensive chemotherapy that is complicated by neutropenia. Moreover, anticancer therapy further increases the risk of infection by causing delayed wound healing and mucosal lesions [74].

Finally, recent evidence suggests that the patient's microbiota could also affect different aspects of carcinogenesis, favoring the proliferation of epithelial cells, establishing inflammatory microenvironment, and promoting treatment resistance [75].

Impact on oncological outcomes

In the last few decades studies on the relationship between diabetes and cancer have increased exponentially [76–80]. A meta-analysis of 151 cohorts indicated a strong causal association between T2D and the incidence of liver, pancreatic, and endometrial cancer, and a reduced risk of prostate cancer [81]. Less clear is the relationship between T1D and the incidence of cancers, with more controversial data [82]. Cancer patients with diabetes have a worse prognosis [65, 83], probably also because high glucose levels induce an intracellular signaling alteration in tumor cells with a consequent more aggressive behavior [84]. Several studies in different types of cancer demonstrated that hyperglycemia can upregulate the VEGF/VEGFR pathway and promote neoangiogenesis [85]. Moreover, high glucose promotes the upregulation of epithelial-mesenchymal transition (EMT) transcription factors in different modalities depending on the specific type of cancer [86, 87]. Finally, hyperglycemia influences the chemoresistance in various cancers via multiple modalities, such as the upregulation of insulin-like growth factor binding protein-2 (IGFBP-2) in breast cancer [88] and the SMAD3 and MYC phosphorylation in colorectal cancer [89]. The impact of diabetes on cancer therapies also seems to apply to immunotherapy. A recent study has revealed that ICIs seem less beneficial in patients with non-small cell lung cancer (NSCLC) and diabetes with a significantly shorter median progression-free survival (PFS) and overall survival (OS), as compared to patients without diabetes [90].

Impact on diabetes outcomes

In recent years, advances in diabetes management and the resulting increase in life expectancy of patients with diabetes have allowed to identify new comorbidities, defined as emerging complications of diabetes, including cancer [91]. Furthermore, the increase in the incidence of diabetes is paralleled by the increasing incidence of cancer [92] and it is estimated that approximately 20% of people with cancer have or will develop diabetes, more than double the incidence of diabetes in the global adult population [93, 94]. As a consequence, in some countries, cancer has become the leading cause of mortality in people with diabetes [95, 96].

The presence of cancer in patients with diabetes also has a significant impact on diabetic outcomes. For instance, tumor cachexia, defined as a multifactorial syndrome characterized by loss of skeletal muscle (a crucial organ in the maintenance of glucose homeostasis and among the main targets of insulin action), is often associated with glucose intolerance, insulin resistance, and inflammation, which predispose to T2D development or worsening [97, 98]. In addition, cancer-related stress (especially due to acute illnesses, recurrent hospitalizations, surgeries, infections, and hemorrhages) can also induce or worse hyperglycemia and inflammation [97]. Finally, when cancer affects organs involved in glycemic homeostasis, such as pancreas and the liver, it can cause diabetes as a direct consequence of the altered functioning of these organs or secondary to the resection of the tumor (e.g., after partial or total pancreatectomy) [92]. In patients with diabetes and cancer, management of diabetes should be tailored to the patient, individualizing glycemic targets, glucose monitoring, and treatment goals, usually prioritizing the continuation of cancer treatment [99–101]. Indeed, cancer treatment is associated with decreased diabetes medication adherence and self-management behaviors, such as blood glucose monitoring [102, 103]. In addition, several anti-cancer therapies, such as corticosteroids [104], somatostatin analogs (SSAs) [92], mTOR inhibitors [15, 101], and ICIs can directly affect glucose homeostasis, thus increasing the risk of new-onset hyperglycemia or worsening of pre-existing diabetes, posing significant difficulties for its management [105, 106]. The mechanisms underlying these effects are variable. Corticosteroids can cause hyperglycemia and diabetes by increasing hepatic gluconeogenesis and inhibiting glucose uptake into adipose tissue [104]. SSAs, acting on somatostatin receptors, induce hyperglycemia and diabetes through a direct suppression of insulin secretion by pancreatic beta-cells and of GLP-1 by enteroendocrine L cells [92, 107, 108]. Although it is not entirely known how ICIs can determine the onset of diabetes, it has been proposed that these drugs evoke an immune response against pancreatic beta-cells by activating the immune system [109].

Synergistic effects of cancer and diabetes on the immune response

To the best of our knowledge, there are no studies investigating the potentially negative and synergistic effect of diabetes and cancer on the immune response, and on vaccination effects. Efficacy and safety of vaccines are often analyzed independently in the two conditions. Indeed, a large cohort study showed that the humoral immune response to COVID-19 mRNA vaccines was good both in patients with cancer and in those with diabetes. Compared to the control group, however, the strength of the humoral neutralizing response in these two categories was reduced [110]. Another cohort study investigated the immunogenicity of the ChAdOx1 nCoV-19 vaccines in subjects with different comorbidities, finding cancer -but not diabetes- to significantly impair immune response [111]. However, a group of patients with both diabetes and cancer was not included in these studies, and cellular mechanisms were not investigated. Nevertheless, an interconnection between diabetes, cancer, and immune response has been hypothesized. A cohort study showed that annual flu vaccine significantly reduced the risk of lung cancer in patients with diabetes, with a dose-dependent protective effect [112] (Fig. 3A). This evidence was further supported by a preclinical study, where administration of flu vaccine by intra-tumor injection

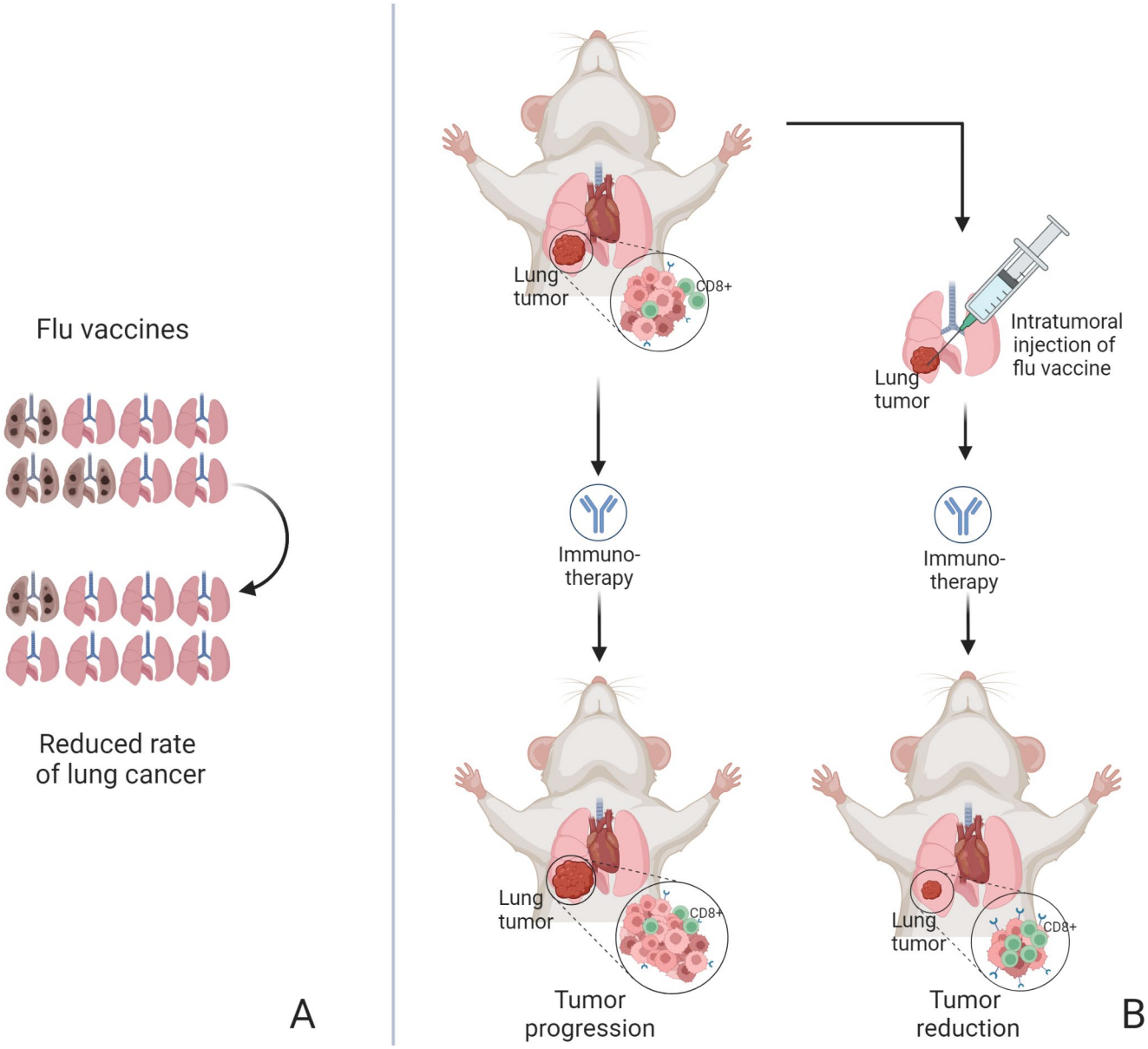

Fig. 3 (**A**) Flu vaccine significantly reduces the risk of lung cancer in patients with diabetes. (**B**) Administration of flu vaccine by intra-tumor injection in mice with lung cancer sensitizes tumors to PD-L1 checkpoint inhibitors. Created with BioRender.com

in mice with lung cancer increased CD8 + T cells within the tumor microenvironment, reduced tumor growth, and sensitized these tumors to PD-L1 checkpoint blockade treatment [113] (Fig. 3B). In keeping with this evidence, the CD8 + T lymphocytes role seems crucial. Indeed, circulating CD8 + PD-1 T lymphocytes display lower basal mitochondria respiration, reduced glycolysis, and lower count in T2D patients. These latter findings could be implicated in greater tumor progression and susceptibility to viral infections in T2D patients, as compared to the general population [114].

Table 1 Recommended immunizations for adults affected by Diabetes and cancer

Vaccines	Recommended ages	Schedule
Influenza	All ages	Annual, with (preferably high dose) inactivated quadrivalent vaccine. Live-attenuated vaccines are contraindicated
COVID-19	All ages	Initial vaccination and booster, according with National Health Care System schedule*
Pneumonia	19 years and older	Initial priming with a conjugate vaccine (15-valent pneumococcal conjugate vaccine, PCV15, or 20-valent pneumococcal conjugate vaccine, PCV20) followed at least 8 weeks later by a dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23)
Zoster	19 years and older	Two doses at least 4 weeks apart
RSV	60 years and older	Single dose
Hepatitis B**	All people 19–59 years old	Three-dose Recombivax HB series (0, 1, 6 months) can be proposed
	60 years and older: immunize those with other risk factors	Check antibody surface titer 1–2 month after the last dose; if < 10 mUI/ml, repeat vaccination schedule
Tetanus, diphtheria, pertussis (Tdap)	All adults	One dose of Tdap, followed by Td or Tdap booster every 10 years
HPV	19–26 years: eligible	Two or three doses schedule
	27–45 years: *shared decision making*	

The table summarizes disease, age, and schedule of administration of vaccines that should be offered to patients with Diabetes and cancer. When differences have been found among available guidelines, the working group discussed the evidence and provide a final recommendation, according to a prudent principle and giving greater consideration to the condition (i.e. Diabetes or cancer) with higher potential clinical impact in the specific VPD

*Evaluate immunosuppression grade; **if negative screening for HBV

In addition, tumor-infiltrating CD8 + T cells in patients with diabetes and colorectal cancer display a different transcriptomic profile, as compared to those of non-diabetic patients with colorectal cancer, involving genes in common between diabetes, cancer, and immune response such as LGALS1, CDKN2 A, B3GALT4 [115].

Based on the reported evidence, we can hypothesize that in patients with both diabetes and cancer the immune response to vaccines could be reduced, as compared to patients without these two conditions. However, studies considering patients with both conditions undergoing vaccinations are lacking and strongly warranted, since these patients are frequent in daily clinical practice. Vaccine pleiotropic effects should be investigated to evaluate their efficacy, safety, and adverse events in this setting, since they could modify patient's outcome.

Recommendations and guidelines

Recommended immunization strategies

A strong mutual relationship exists among most of vaccine preventable diseases (VPDs) and disease course of both diabetes and cancer [3]. In recent years, medical oncology and diabetology international scientific societies published several guidelines to define and promote vaccination strategies in patients, respectively, with cancer or diabetes. Nonetheless, the patient's adherence to these recommendations, as well as clinician's perception of the clinical relevance of this topic, are still scant [116].

Many vaccination schedules are substantially similar in both people with cancer and with diabetes. Disease, age, and schedule of administration of vaccines that should be offered to patients with both diabetes and cancer are summarized in Table 1, as finally agreed by the working group from a multidisciplinary panel of Italian scientific societies.

Both cancer and diabetes can be considered as chronic disease, inducing frailty and disability in affected subjects and with increasing impact on health care systems [117]. A clear and tailored communication can be of great value to resolve patients and caregivers doubts and increase the acceptance of vaccines. This effort could represent a valid tool to help health care systems to mitigate the negative impact of VPDs on patients with cancer and diabetes.

Oncological guidelines

AIOM was one of the first scientific societies to publish recommendations on vaccination against VPDs in cancer patients, specifically flu, in 2014 [5]. Since then, AIOM has continued to promote vaccinations, increasing

oncologists' awareness of anti-pneumococcal [3, 118], anti-SARS-CoV-2 [3], and anti-Herpes Zoster [119] vaccines. Moreover, AIOM has recently investigated oncologists' knowledge of this issue with a survey with disappointing results: only 30% of respondents discuss vaccinations with patients during the first oncological visit and only 44% of them consider vaccination an issue of their pertinence in clinical practice [116].

The main European and international scientific societies agree that vaccination counseling is important at the time of patient referral with vaccine schedule planning, ideally before the initiation of cancer treatments [3, 4]. Scientific societies recognize that the diagnosis of cancer is a devastating event and that vaccination is not perceived as an immediate priority by the patient (and often not even by the oncologist). However, several studies demonstrated that, when vaccines are administered before starting oncological treatment, the best protection is achieved. To achieve this outcome, vaccination counseling should represent an integral part of the management of cancer patients, through multidisciplinary team and allocated resources.

Vaccination history should be mandatorily listed on the medical record, in order to easily identify which vaccinations are missing or which need to be updated with seasonal booster shots (e.g. anti-flu and anti-SARS-CoV-2).

Active collaboration with general practitioners, hygienists, and pharmacists is necessary to implement the vaccination offer, possibly by organizing dedicated outpatient facilities within the same hospital, if feasible.

Vaccination counseling should also be extended to family contacts (caregivers) to better protect patients (cocooning vaccination).

Live-attenuated vaccines should be avoided in cancer patients because they may induce uncontrolled infection from the vaccine strain. For this reason, measles, mumps, and rubella (MMR) vaccine, oral typhoid, and Monkeypox and smallpox (ACAM2000) vaccines are contraindicated during cancer treatment. Non-live vaccines are safe for use in cancer patient and can be administered before and/or during oncological treatments. Examples of non-live vaccines are inactivated vaccines, recombinant and polysaccharide-protein conjugate subunit vaccines, and mRNA vaccines.

Influenza vaccines

Most infection-related deaths are attributed to influenza and pneumonia deaths that can be prevented by vaccination. The mortality rate of fatal infections in cancer patients is nearly three times that of the general population [SMR, 2.92; 95% (confidence interval) CI 2.91–2.94] [120]. Studies support the safety and benefits of influenza vaccination in reducing the severity of infections and associated hospitalizations, while recognizing a lower rate of seroconversion compared to immunocompetent individuals [121, 122]. Cancer patients should annually receive one of the preferentially recommended high-dose or adjuvanted vaccine formulations (high-dose Quadrivalent vaccine, and Quadrivalent adjuvanted flu vaccine) according to their availability [123, 124].

COVID-19 vaccines

Cancer patients show a higher rate of complications and mortality during COVID-19 compared to healthy subjects, with poorer outcomes in hematologic malignancies and lung cancer [125, 126].

In cancer patients, there is a suboptimal seroconversion rate after COVID-19 vaccination when compared with immunocompetent subjects [127, 128]. According to the diminished immunogenicity and the continuous evolution of the virus into new variants, several studies state that annual boosting may assure the optimal protection in immunocompromised patients [129, 130]. The vaccination can reduce the risk of severe COVID-19 illness [27], the rates of hospitalization and mortality [28], and the risk of COVID-19 sequelae (long COVID) [29]. The VAX4 FRAIL study reported clinically manageable adverse events toxicities [131]. Transient axillary adenopathy can appear after COVID-19 vaccination, for this reason the Society of Breast Imaging has published recommendations on this topic [132].

Pneumococcal vaccines

Streptococcus pneumoniae (*S. pneumoniae*, pneumococcus) can cause severe pneumonia and meningitis in immunocompromised subjects [133]. The spread of pneumococcal resistant clones to the common antibiotics represents a growing issue [134]. The immune response to the pneumococcal vaccine on the day of chemotherapy or 2 weeks before has been demonstrated similar in a small prospective randomized controlled trial in patients with gastrointestinal cancer undergoing chemotherapy [135]. The pneumococcal vaccine is useful to reduce the risk of pneumonia-related hospitalization in cancer patients aged ≥ 75 years [136].

The currently recommended approach is an initial priming with a conjugate vaccine (15-valent pneumococcal conjugate vaccine, PCV15), followed at least 8 weeks later by a dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23) [12] or a single dose of 20-valent pneumococcal conjugate vaccine (PCV20) only [12].

Recombinant Zoster vaccines

The incidence of HZ is high in the first 2 years after cancer diagnosis, especially in patients younger than 50 years of age. Complications of HZ, such as post-herpetic neuralgia (PHN), can negatively impact quality of life [137].

The approval of the adjuvanted, RZV by the US Food and Drug Administration (FDA) in 2017 converted HZ into a VPD [138]. The vaccine schedule consists of two doses at least 4 weeks apart. Humoral responses are higher when RZV is administered before chemotherapy, rather than on therapy [139]. An increase of T cell response was observed in 67.5% cancer patients undergoing immunotherapy both 28 days after the second dose and six months after the second dose [140], confirming the immunogenicity of the vaccine even during ICIs treatment.

Respiratory syncytial virus (RSV) vaccines

RSV clinical manifestation ranges widely from mild upper respiratory infections to severe lower respiratory tract infections (LRTIs) [141]. There are no specific studies on this vaccine in patients with cancer. Therefore, awaiting specific data on this population, the recommendation for the general population remains valid. Patients with lung and mediastinal cancer and patients with lung metastases are at increased risk, so it is recommended to prioritize this population.

Hepatitis B vaccines

All cancer patients should be tested for Hepatitis B Virus (HBV) before starting any systemic oncological therapy by 3 tests (hepatitis B surface antigen [HBsAg], hepatitis B core antibody [anti-HBc], and antibody to hepatitis B surface antigen). HBV reactivation risk assessment is based on the diagnosis of chronic HBV (HBsAg-positive) or past HBV (HBsAg-negative and anti-HBc-positive) infection [142]. If serologic assessment for HBV infection is negative, a three-dose Recombivax HB series (0, 1, 6 months) can be proposed to the patient [143]. Post-vaccination anti-surface antibody titers should be checked 1–2 months after the last dose, and if hepatitis B surface antibody concentrations are lower than 10 mUI/mL, the entire vaccine schedule should be repeated.

Monkeypox

Mpox (formerly monkeypox) is a viral disease caused by monkeypox virus (MPXV), genus Orthopoxvirus. The clinical manifestation of the disease includes general symptoms such as fever and headache, and a frequent and characteristic rash (papules, vesicles, and pustules), often with concomitant mucous (oral cavity) lesions. Severe pictures of the disease may manifest as visceral localization and bacterial superinfection. Immunocompromised people, especially untreated HIV-infected persons with low CD4 counts, are at risk of developing complications and death due to mpox. The only mpox vaccine authorized by the EMA is the modified live Ankara vaccine virus - Bavarian Nordic (MVA-BN). It is safe to administer in immunocompromised patients, such as people with cancer and/or HIV.

Mass vaccination for mpox is currently neither required nor recommended. At present, vaccination is offered to some at-risk groups and travelers to endemic areas [144].

Diphtheria, tetanus, pertussis (Tdap)

Diphtheria-tetanus-pertussis vaccination (Tdap) is recommended for people aged 7 and over. Adults should receive a booster dose of Tdap every 10 years, or after 5 years in case of severe or dirty wounds [145].

Human papillomavirus (HPV)

Persistent infection with HPV strains with a high carcinogenic risk, in particular HPV 16 and HPV 18, is responsible for the occurrence of carcinomas of the anogenital and oropharyngeal region. Infections with low-risk carcinogenic strains, such as HPV 11, are responsible for more than 90% of condylomas in the anogenital area. Most HPV-associated cancers are preventable by vaccination [146]. The target populations for HPV vaccination are all subjects of both sexes aged between 9 and 12 and 26 years. The indication may be extended up to the age of 45 for subjects with low HPV exposure, with a previous incomplete vaccination cycle, sex workers, men who have sex with men, and transgender and gender-diverse. The HPV vaccine is most effective if administered before the start of sexual activity [147].

Diabetological guidelines

People with diabetes are at higher risk for developing infections compared to the general population, and the course of the infection is more complicated [148, 149]. The recent COVID-19 pandemic has corroborated the close association between infections and diabetes, following observations that people with diabetes are more likely to progress to severe COVID-19 disease and die than those with normal glucose metabolism [150]. Some common infections are preventable through vaccination and international guidelines recommend routine vaccination for adults with diabetes [14].

Influenza vaccines

Influenza is a common and preventable infectious disease associated with high mortality and morbidity, particularly among the elderly and individuals with chronic conditions. Influenza vaccine reduces all-cause mortality by 50% and lowers the risk of hospitalization for pneumonia by 11% [33, 151]. Consequently, the ADA recommends annual influenza vaccination for all individuals with diabetes [14].

Influenza vaccination is recommended for all individuals ≥6 months of age without contraindication, preferably using an inactivated quadrivalent vaccine (QIV). The live attenuated influenza vaccine, which is delivered by nasal spray, is an option for people who are aged 2–49 years, but people with diabetes are cautioned against taking the live attenuated influenza vaccine and are instead recommended to receive the inactive or recombinant influenza vaccination. For individuals >65 years, the high-dose quadrivalent inactivated influenza vaccine may offer additional benefits [124].

COVID-19 vaccines

People with diabetes are more likely to develop severe symptoms and complications in case of SARS-CoV-2 infection [152]. Hospitalization and mortality rates are higher than the general population and further worsened in the event of poor glucose control [153]. Therefore, subjects with diabetes should receive all recommended doses of SARS-CoV-2 vaccine including the required boosters [14, 35].

Pneumococcal vaccines

People with diabetes show higher rates of pneumococcal infection as well as a higher risk of pneumonia-related hospitalization and mortality [154]. Both the pneumococcal conjugate vaccine (PCV) and the polysaccharide vaccine (PPV) have been shown to be effective in subjects with diabetes [52, 155, 156]. Both the ADA and the Italian diabetes societies [35] recommend that adults aged 65 or older, as well as adults aged 19–64 with underlying risk factors or severe comorbidities, whose vaccine status is unknown or who have not received pneumococcal vaccine, should receive one dose of PCV15 o PCV20. According to the recommendations of the CDC, If PCV15 is used, it should be followed by PPSV23 after at least one year [14, 35]. Adults previously immunized with PCV13 should receive one dose of PPVS23 after one year, too [157, 158].

Recombinant Zoster vaccines

People with diabetes are at a higher risk of HZ infection, particularly women, elderly individuals, and those with T1D [40]. Two HZ vaccines are currently available: the RZV and the zoster vaccine live (ZVL). Both vaccines are effective in preventing HZ, with ZVL additionally reducing the risk of postherpetic neuralgia [159]. RZV [160] is recommended for individuals over 50 years of age, with two doses administered within two months [14]. Additionally, it is advisable to consider revaccination with RZV for individuals who have already been vaccinated with the live attenuated vaccine, after a minimum interval of eight weeks [160].

RSV vaccines

RSV infection is an important illness in elderly and high-risk adults. Patients with diabetes aged 60 or older are considered as a high-risk group [161]. According to the recommendations of the ACIP Respiratory Syncytial Virus Vaccines Adult Work Group and to the ADA, all adults aged 60 or older should receive a single dose of an RSV vaccine [162].

DPT vaccine

There are no specific indications regarding this vaccination for individuals with diabetes. DPT vaccination is recommended for adults aged 19 to 64 years, with periodic administration every 10 years. Additionally, the vaccine is recommended during pregnancy, and the booster dose should be repeated with each pregnancy, even if pregnancies are closely spaced. The presence of diabetes in pregnant women is not a contraindication for vaccination [163].

Hepatitis B vaccine

Compared with the general population, people with diabetes have higher rates of hepatitis B infection [14]. According to the ADA, the hepatitis B vaccine is recommended for adults with diabetes aged <60 years. For adults aged ≥60 years, hepatitis B vaccine may be administered at the discretion of the treating clinician.

The Italian SID-AMD standards recommend vaccination for all unvaccinated individuals with diabetes. Additionally, periodic screening of the anti-HBs antibody titer is advised, along with the administration of booster doses for those with a decline in antibody levels [164]. Some studies indicate that patients with diabetes may achieve a lower protective antibody response or produce a quantitatively lower antibody response to the hepatitis B vaccine compared to healthy individuals [165, 166].

Papilloma virus vaccine

There are no specific indications regarding this vaccination for individuals with diabetes. HPV vaccination is recommended for individuals <26 years, with three doses for males and two doses for females over a six-month period. Individuals >26 years may receive the HPV vaccine after consulting with healthcare professionals [167].

Strategies for overcoming challenges to vaccination in patients with cancer and diabetes

Patients with cancer and diabetes face unique challenges regarding vaccination due to their compromised immune systems, and overcoming these challenges requires a multifaceted approach. Raising concerns for vaccine hesitancy are multifactorial, including the optimal timing of vaccination, doubts about efficacy, and potential adverse effects of vaccines in immunocompromised patients. It has been widely recognized that both cancer treatments and diabetes can weaken the immune system, leading patients and/or caregivers to worry about vaccine efficacy and safety. Accordingly, it is widely recognized that patients with B cell malignancies (particularly myeloma) and those receiving anti-CD20 monoclonal antibodies have the weakest humoral responses. Although international guidelines recommend inactivated influenza vaccination in this specific population based on data supporting efficacy and excellent safety profiles, outcome has often been suboptimal due to persisting hesitancy among both patients and oncologists regarding the optimal vaccine schedule and timing, and the best method to assess response in immunocompromised populations.

Coordination between diabetologists and oncologists is essential for determining the best timing for vaccination. Indeed, scheduling vaccinations during periods of lower immunosuppression and routine diabetes check-ups can increase patients' compliance while optimizing vaccine efficacy. Furthermore, well-controlled blood glucose levels before vaccination can also improve outcomes [168] (Fig. 4). Cancer treatments often involve a complex regimen of medications, including drugs used to mitigate side effects and/or to treat comorbidities other than diabetes. This can increase hesitation since some patients believe that vaccines might affect their treatment outcomes. Strategies to improve vaccination rates may also rely on tailored communication with and education of patients. Healthcare providers should have empathetic conversations with patients to address their specific concerns, use simple, non-technical language to explain the benefits and safety of vaccines, and provide easily understandable evidence-based written materials and visual aids. Training healthcare providers on vaccination guidelines for immunocompromised patients may also ensure they will be well-equipped to address patient concerns and questions.

Using inactivated vaccines instead of live vaccines and choosing vaccines with a proven safety record in immunocompromised populations will significantly reduce the risk of infection, while ensuring safe and effective vaccination practices. These vaccines should be part of immunization programs for patients undergoing cancer treatment and those with chronic conditions like diabetes. Health organizations (e.g., CDC and WHO) and scientific societies (e.g., ADA, ASCO, and IDSA) provide guidelines for vaccinating immunocompromised individuals that emphasize the preference for inactivated vaccines, offering recommendations on timing and dosing to optimize safety and efficacy.

Other important issues are closely monitoring patients after vaccination for adverse reactions and communication with patients about recognizing potential adverse events, and how to manage them. Improving access to vaccination using mobile units and home vaccination programs is pivotal to reaching patients with limited access to healthcare facilities. Finally, supportive policies that ensure insurance coverage for recommended vaccines and funding of vaccination programs targeting high-risk populations may remove financial barriers and improve access to needed vaccines.

With the increase in life expectancy of cancer patients, it is important for oncologists to preserve the best quality of life of their patients. Effective prevention of the main VPDs through vaccinations is important from an oncological, social-health, and economic standpoint. Oncologists have a key role in educating their patients on the importance of vaccinations to prevent VPDs and ensuring the effectiveness and safety of oncological treatments. Targeted education campaigns and multidisciplinary collaboration between oncologists and diabetologists would be paramount to filling gaps in current evidence and areas while improving vaccination uptake.

Conclusions

Diabetes and cancer are becoming more and more common worldwide and, given their involvement in multiple aspects and functions of the body, their management implies a "holistic" approach by different professional figures. Prevention of communicable infectious diseases represents one of these aspects, considering the deep impact of both diabetes and cancer (and their therapies) on the immune system and, consequently, on the infection risk. Vaccination proved safe and effective in reducing the risk of infection

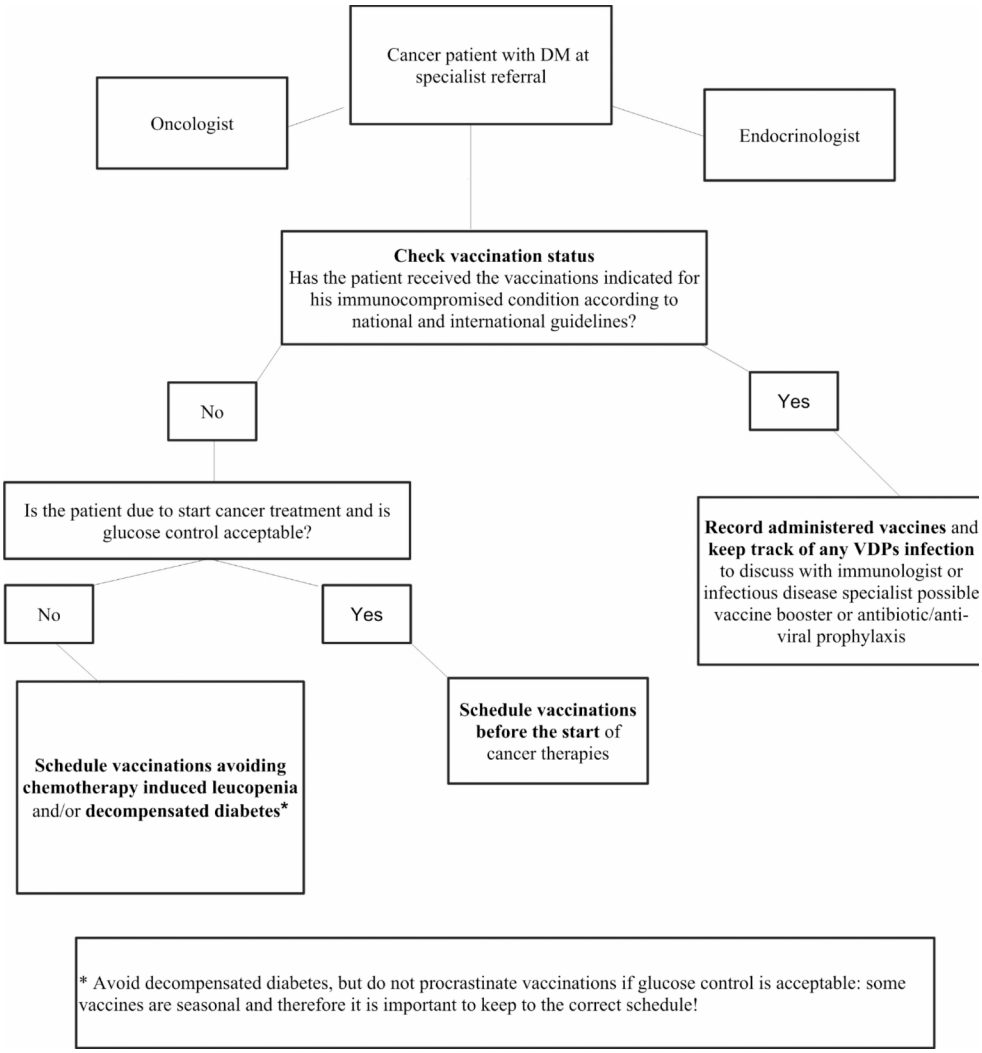

Fig. 4 Tentative decision-making algorithm for vaccinating cancer patients with diabetes

and adverse consequences of infectious diseases, both in people with diabetes and in patients with cancer. Taking into account the synergistic negative effect on the immune system of both conditions, vaccination in cancer patients with diabetes represent an even more important aspect of clinical management.

This position statement summarizes both oncological and diabetological guidelines in order to provide clinicians (oncologists, diabetologists, and every professional figure involved in the management of these patients) a concise and helpful outline of the main vaccinations recommended for patients with cancer and diabetes. Many aspects of this matter are, however, still controversial, like the optimal administration schedule (particularly in relation to chemo/radiotherapy schedules or other oncological therapies that could further derange the immune system function), the strategies for overcoming potential suboptimal response in immunocompromised patients, and the logistic challenges faced by health institutions for organizing vaccination sessions for a vast number of patients and their caregivers. New research findings will be important for overcoming these challenges and controversies, with the aim of further optimizing the management of cancer patients with diabetes and improving their outcomes.

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