OPEN ACCESS

Saudi Journal of Medicine
Abbreviated Key Title: Saudi J Med
ISSN 2518-3389 (Print) | ISSN 2518-3397 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Review Article

Saudi Society of Diabetes Position Statement on Herpes Zoster Vaccination in Adults with Diabetes

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DOI: https://doi.org/10.36348/sjm.2026.v11i08.004 | **Received:** 23.06.2026 | **Accepted:** 15.08.2026 | **Published:** 22.08.2026

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Abstract

Background: Adults with diabetes mellitus (DM) are at increased risk of herpes zoster (HZ) and its complications because of impaired cell-mediated immunity, chronic hyperglycemia, and multiple comorbidities. Despite the availability of highly effective recombinant zoster vaccine (RZV), vaccine uptake remains suboptimal among patients with diabetes in Saudi Arabia. This consensus statement was developed to provide evidence-based recommendations for HZ vaccination in adults with DM within the Saudi healthcare setting. ***Methods:*** A multidisciplinary expert panel convened under the auspices of the Saudi Society of Diabetes conducted structured evidence review and consensus process. A comprehensive literature search of PubMed/MEDLINE, Embase, Scopus, Web of Science, and the Cochrane Library was performed to identify studies published during the previous 10 years on HZ epidemiology, vaccine efficacy and safety, and vaccination strategies in adults with diabetes. Evidence was critically appraised and integrated with expert opinion using a modified Delphi-informed consensus approach. Recommendations were categorized according to evidence strength (Level A–C) and aligned with national immunization policies. ***Results:*** Available evidence consistently demonstrates that diabetes is associated with an increased risk of HZ, postherpetic neuralgia, hospitalization, and other complications. Saudi epidemiological data identified 1,019 HZ cases over a 6-year period, with 31.3% developing complications, 12.5% requiring hospitalization, and 1.2% requiring intensive care. Randomized trials and real-world studies demonstrate that RZV provides approximately 94% efficacy against HZ with durable protection and an acceptable safety profile. The expert panel developed 10 evidence-based recommendations addressing patient selection, vaccination timing, immunocompromised populations, co-administration with other vaccines, risk stratification, healthcare provider education, patient awareness, electronic reminder systems, equitable vaccine access, and pharmacovigilance. The panel emphasized routine assessment of vaccination status during diabetes care and strong physician recommendation as key strategies to improve vaccine uptake. ***Conclusion:*** Adults with diabetes represent a high-risk population for herpes zoster and should be prioritized for recombinant zoster vaccination according to current national recommendations. Integrating vaccination assessment into routine diabetes care, strengthening healthcare provider engagement, and implementing system-level interventions may substantially improve vaccination coverage and reduce the burden of HZ among adults with diabetes in Saudi Arabia.

Keywords: Herpes zoster, Diabetes mellitus, Vaccination, Immunization, Postherpetic neuralgia.

1. INTRODUCTION

Diabetes mellitus (DM) represents a major global public health challenge, with rapidly increasing prevalence and substantial clinical and economic burden. According to the International Diabetes Federation, approximately 589 million adults worldwide are currently living with diabetes, with projections indicating a substantial rise to 163 million cases in the Middle East and North Africa (MENA) region alone by 2050. In the Kingdom of Saudi Arabia, the burden is particularly pronounced, with an adult population of approximately 24.98 million and a diabetes prevalence of 21.4%, corresponding to an estimated 5.34 million affected individuals in 2024. This places Saudi Arabia among the countries with the highest diabetes prevalence globally. The increasing burden is largely driven by rapid urbanization, sedentary lifestyle, and rising obesity rates, and it is associated with significant morbidity, mortality, and healthcare expenditure [1]. Diabetes has risen to become one of the top 10 causes of death on a global scale, mostly as a result of the rapid increase in the incidence of the disease [2,3].

Patients with type 2 diabetes mellitus (T2DM) are at substantially increased risk of a wide range of infections because of impaired immune responses, chronic hyperglycemia, vascular insufficiency, and diabetes-related complications. In a recent systematic review and meta-analysis including 70 studies, Fu *et al.,* reported that severe periodontitis was the most prevalent infection among patients with T2DM, with a pooled prevalence of 33.6%, followed by skin infections (28.6%) and urinary tract infections (9.7%). Regarding incidence rates, lower respiratory tract infections showed the highest pooled incidence at 1409.2 per 10,000 person-years, followed by skin infections (664.1 per 10,000 person-years), upper respiratory tract infections (553.6 per 10,000 person-years), and urinary tract infections (500.6 per 10,000 person-years), highlighting the substantial burden of infectious diseases in diabetic populations [4].

These international findings are consistent with data from Saudi Arabia. In a Saudi single-center study involving 300 diabetic patients with disease duration exceeding five years, the overall prevalence of infections reached 57.6%. Bacterial infections were the most common, affecting 46.7% of patients, followed by fungal infections (12%) and viral infections (4.7%), while serious infections accounted for 21% of cases. Importantly, the presence of diabetic complications and hypertension were identified as significant risk factors for infection development. These findings emphasize the high infectious burden among diabetic patients in Saudi Arabia and support the need for preventive strategies, early infection screening, vaccination programs, and optimization of glycemic control to reduce morbidity and healthcare burden [5].

Patients with diabetes are at increased risk of infections due to multiple pathophysiological mechanisms, including impaired innate and adaptive immune responses, chronic inflammation, and vascular dysfunction. In Saudi Arabia, infections—particularly respiratory infections such as influenza, pneumonia, and COVID-19—are more frequent and severe among individuals with diabetes, leading to higher rates of hospitalization, intensive care unit admission, and mortality [6–10].

Also, diabetic patients with inadequately managed hyperglycemia face elevated risks for several complications that substantially increase the disease's mortality rate. Significantly, these patients exhibit heightened vulnerability to infections from bacteria, viruses, or fungi, attributable to compromised immune system control [11–13].

In addition, infections can destabilize glycemic control and precipitate acute metabolic complications such as diabetic ketoacidosis and hyperosmolar hyperglycemic state, thereby creating a bidirectional relationship that further worsens outcomes [14].

Given this heightened susceptibility, preventive strategies—particularly vaccination—are essential components of comprehensive diabetes care. In Saudi Arabia, several vaccines are recommended for adults with diabetes in accordance with national policies and international guidelines [10,15]. These include seasonal influenza vaccines, pneumococcal vaccines, coronavirus disease 2019 vaccines, and herpes zoster vaccines, in addition to vaccines indicated in specific contexts such as meningococcal vaccination for Hajj and Umrah and emerging vaccines such as those targeting respiratory syncytial virus [10,15–17].

Despite robust evidence supporting their efficacy and safety, vaccine uptake among patients with diabetes remains suboptimal, underscoring the need for targeted strategies to enhance awareness, accessibility, and implementation in routine clinical practice [10,17,18].

2. METHODOLOGY

This consensus-based position statement aims to provide evidence-based recommendations regarding herpes zoster vaccination in adult patients with diabetes mellitus, with particular emphasis on the Saudi Arabian healthcare setting.

A. Study Design and Objective

The development of this consensus-based position statement was conducted under the auspices of the Saudi Society of Diabetes and involved structured input from multidisciplinary experts across the Kingdom of Saudi Arabia. The process incorporated evidence reviews and expert discussion conducted through a single expert panel meeting that included

endocrinologists, diabetes specialists, obesity medicine specialists, infectious diseases specialists, internal medicine specialists, and primary care health professionals.

The primary objective was to formulate evidence-based, context-specific recommendations for herpes zoster vaccination in adults with diabetes mellitus, with a focus on reducing infection-related morbidity and complications in this high-risk population. Particular emphasis was placed on the burden of herpes zoster among patients with diabetes, vaccine efficacy and safety, and implementation of vaccination strategies within routine diabetes care in Saudi Arabia.

B. Literature Search

A targeted and comprehensive literature review was conducted to identify evidence regarding herpes zoster infection and vaccination in adults with diabetes mellitus. Key databases included PubMed/MEDLINE, Embase, Scopus, Web of Science, and the Cochrane Library. The search strategy combined terms related to herpes zoster and vaccination (e.g., "herpes zoster", "shingles", "varicella-zoster virus", "herpes zoster vaccine", "recombinant zoster vaccine", "Shingrix") with diabetes-related terms ("diabetes mellitus", "type 1 diabetes", "type 2 diabetes", "glycemic control", "diabetes complications", and "infection risk in diabetes").

The search was restricted to studies published within the last 10 years to ensure contemporary relevance, with no language restrictions applied. Reference lists of relevant studies and review articles were also screened to identify additional publications. All study designs were considered; however, priority was given to high-quality evidence, including randomized controlled trials, systematic reviews, meta-analyses, and well-designed observational studies.

Evidence synthesis balanced global data with regional applicability. International studies provided robust evidence on herpes zoster vaccine efficacy and safety, while regional and local data were emphasized to reflect epidemiological patterns, healthcare infrastructure, and vaccination practices specific to Saudi Arabia. Discrepancies in evidence were resolved through expert panel discussion.

C. Expert Panel and Consensus Process

A multidisciplinary expert panel from multiple regions within Saudi Arabia was convened. The consensus process was conducted through structured expert discussion during a single consensus meeting. The meeting involved critical appraisal of the literature, formulation of preliminary recommendations, and refinement and validation of the final statements.

Consensus was achieved using a structured consensus meeting. The expert panel consisted of 9 experts representing endocrinology, infectious diseases, internal medicine and obesity. Consensus was predefined as ≥80% agreement. Each recommendation was anonymously voted on during the consensus meeting. The percentage agreement achieved for each recommendation is presented in Supplementary Table 1.

All recommendations were reviewed to ensure alignment with national healthcare policies and immunization strategies, including those endorsed by the Saudi Ministry of Health. Special consideration was given to high-risk diabetic populations, aging adults, patients with diabetes-related complications, and implementation barriers affecting vaccine uptake.

To maintain transparency and minimize bias, all panel members disclosed potential conflicts of interest prior to participation. The consensus process was conducted independently of external funding influences, and emphasis was placed on prioritizing high-quality, peer-reviewed evidence over individual expert opinion. This work is based entirely on previously published studies and does not involve any new research on human or animal subjects.

D. Evidence Hierarchization and Integration

Evidence Hierarchization

The identified evidence was systematically appraised and categorized according to the principles of the Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence (2011), taking into account study design, methodological quality, consistency of findings, and clinical relevance. Randomized controlled trials, systematic reviews, and meta-analyses were considered the highest level of evidence, followed by well-conducted observational studies and real-world evidence. Where high-quality evidence was lacking, recommendations were informed by expert consensus based on the best available evidence and clinical expertise [19].

For clarity and consistency throughout this position statement, the supporting evidence for each recommendation was summarized using three evidence categories adapted from the OCEBM framework:

Level A, representing high-certainty evidence derived from randomized controlled trials, systematic reviews, or meta-analyses.
Level B, representing moderate-certainty evidence derived primarily from observational studies or limited clinical investigations.
Level C, representing expert consensus or limited evidence where robust clinical data were unavailable.

This approach provides a transparent and pragmatic summary of the evidence while maintaining consistency with internationally recognized evidence-based medicine principles.

3. Diabetes and Infections:

Diabetes mellitus is associated with a well-documented increase in susceptibility to infections, as well as greater severity and poorer outcomes once infection occurs. Chronic hyperglycemia impairs multiple components of the immune system, including neutrophil chemotaxis, phagocytosis, and intracellular killing, in addition to altering cytokine responses and cellular immunity. Microvascular and macrovascular complications further compromise tissue perfusion, thereby limiting the delivery of immune cells and antimicrobial agents to sites of infection. Collectively, these mechanisms predispose individuals with diabetes to a broad spectrum of bacterial and viral infections, including respiratory, urinary tract, and skin and soft tissue infections [20,21].

Conversely, infections can significantly disrupt glycemic control, creating a bidirectional and self-amplifying relationship. Acute infections trigger stress responses characterized by increased secretion of counter-regulatory hormones such as cortisol and catecholamines, leading to insulin resistance and hyperglycemia. In severe cases, infections may precipitate acute metabolic decompensation, including diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state (HHS). This interplay underscores the clinical importance of infection prevention and early management in patients with diabetes, particularly among older adults and those with poorly controlled diseases or multiple comorbidities [20,21].

Patients with diabetes are at increased risk of invasive pneumococcal disease and its complications, including pneumonia, bacteremia, and meningitis. Impaired immune responses and comorbid conditions contribute to higher morbidity and mortality in this population [22].

Seasonal influenza infection is associated with increased hospitalization and mortality among individuals with diabetes. Infection may precipitate acute metabolic complications and exacerbate underlying comorbidities [23,24].

The COVID-19 pandemic has highlighted the vulnerability of patients with diabetes, who exhibit higher rates of severe disease, hospitalization, intensive care admission, and mortality [25,26].

Respiratory syncytial virus is increasingly recognized as a significant cause of lower respiratory tract infections in older adults and those with chronic diseases, including diabetes [27].

4. Herpes Zoster Among Patients with Diabetes in Saudi Arabia:

A multicenter retrospective chart review of electronic medical records from five Saudi National Guard hospitals and affiliated primary care centers, including all documented herpes zoster (HZ) cases between January 2017 and December 2022. A total of 1,019 HZ cases were identified, corresponding to an estimated 6-year prevalence of 0.12%, with annual cases increasing from 89 in 2017 to 279 in 2022. The mean patient age was 52.8 years, more than half were female, and 73.9% had at least one comorbidity, most commonly hypertension (38.9%) and diabetes (37.7%). HZ-related complications occurred in 31.3% of patients, including post-herpetic neuralgia (17.6%) and disseminated HZ (5.6%). Overall, 12.5% required hospitalization, 1.2% were admitted to the intensive care unit, and the mean hospital stay was 10.1 days. Multivariable logistic regression identified age ≥60 years (OR=1.42; p=0.03), autoimmune disease (OR=2.45; p<0.01), depression (OR=2.68; p=0.02), and chronic lung disease (OR=1.95; p=0.04) as significant predictors of complicated HZ[28].

A cross-sectional study conducted in Al-Ahsa by Ahmed Alhaid *et al.,* (2023) evaluated the prevalence and awareness of HZ among patients with diabetes mellitus attending outpatient clinics. The study included 224 participants with a mean age of 61.1 ± 8 years, of whom 54.5% were female. More than half of the participants (56.7%) had heard of HZ, and 62.1% demonstrated overall awareness, while 55.8% expressed a positive attitude toward the disease. However, only 6.7% had been diagnosed with HZ, and 23.7% reported knowing someone affected. Healthcare providers were identified as the primary source of information (80.8%), followed by friends and relatives (37.9%), highlighting the central role of clinicians in patient education [29].

Despite relatively moderate awareness levels, vaccination uptake remained low, with only 18.8% of participants reporting having received the HZ vaccine. Awareness was significantly associated with higher educational level, higher income, shorter duration of diabetes, prior exposure to HZ (personal or through acquaintances), and prior vaccination. Importantly, the study underscores a persistent gap between awareness and preventive action. The findings emphasize the need for targeted educational interventions using accessible language and multiple communication channels, alongside proactive healthcare provider engagement to improve vaccination uptake among patients with diabetes in Saudi Arabia [29].

According to data from the Saudi Ministry of Health, the reported annual incidence of herpes zoster (HZ) in Saudi Arabia was 13.1 cases per 100,000 population in 2018 (30). However, these administrative data are likely to represent minimum estimates of the true disease burden because passive surveillance systems may be affected by under-ascertainment and under-

reporting, particularly among patients managed in outpatient settings or private healthcare facilities. Consequently, the actual incidence of HZ in Saudi Arabia is likely to be substantially higher and more consistent with estimates reported internationally. The risk of HZ increases markedly with advancing age and is further amplified by comorbid conditions, including diabetes mellitus, autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis, chronic respiratory diseases (e.g., asthma and chronic obstructive pulmonary disease), hematologic and solid malignancies, human immunodeficiency virus infection, and hematopoietic stem cell or solid organ transplantation [29,31].

Why Patients with Diabetes Are at Increased Risk of Herpes Zoster

Herpes zoster results from reactivation of latent varicella-zoster virus (VZV) and is associated with increased incidence and severity in individuals with diabetes. Complications such as postherpetic neuralgia can significantly impair quality of life [32,33].

A comprehensive meta-analysis of observational studies, including four case–control and twelve cohort studies, demonstrated that individuals with diabetes mellitus have a significantly higher risk of developing herpes zoster compared with the general population, with a pooled relative risk of 1.38 (95% confidence interval: 1.21–1.57). This increased risk was consistent across subgroups stratified by diabetes type, age, and study design, highlighting the robustness of the association. Furthermore, the presence of cardiovascular disease exerted an additive effect, further elevating the risk (pooled relative risk: 1.19, 95% confidence interval: 1.11–1.28). A clear linear relationship between advancing age and HZ risk was also observed among individuals with diabetes. These findings underscore the heightened vulnerability of this population and support the prioritization of preventive strategies, particularly vaccination, with emphasis on older adults and those with comorbid cardiovascular disease [34].

Patients with diabetes are at increased risk of HZ due to multiple immunological and metabolic mechanisms that impair host defense against latent viral infections. Reactivation of VZV is primarily controlled by cell-mediated immunity, which is often compromised in individuals with diabetes. Chronic hyperglycemia leads to dysfunction of both innate and adaptive immune responses, including impaired neutrophil chemotaxis and phagocytosis, reduced T-cell proliferation, and altered cytokine production. These immune abnormalities reduce the ability to maintain viral latency, thereby increasing the likelihood of VZV reactivation [18,35].

In addition, diabetes is associated with chronic low-grade inflammation and microvascular dysfunction, which further impair tissue perfusion and immune surveillance. The presence of comorbidities frequently associated with diabetes—such as cardiovascular disease, chronic kidney disease, and obesity—may further exacerbate immune dysregulation. Epidemiological studies have consistently shown that patients with diabetes have a significantly higher risk of developing herpes zoster compared with the general population, with a pooled relative risk of 1.38. This risk is further amplified in older adults and those with poor glycemic control [36].

Complications of Herpes Zoster in Patients with Diabetes

Herpes zoster in patients with diabetes is associated with increased severity, prolonged disease course, and a higher risk of complications. One of the most common and debilitating complications is postherpetic neuralgia (PHN), characterized by persistent neuropathic pain lasting months or even years after resolution of the rash. Patients with diabetes are particularly susceptible to PHN due to underlying diabetic neuropathy and heightened nerve vulnerability [37,38].

Other complications include herpes zoster ophthalmicus, which can lead to serious ocular involvement and potential vision loss, as well as secondary bacterial infections due to impaired wound healing. Systemic complications, such as VZV-associated vasculitis, may increase the risk of cerebrovascular and cardiovascular events. In addition, HZ can precipitate acute metabolic decompensation in diabetic patients, including diabetic ketoacidosis and hyperosmolar hyperglycemic state, particularly in severe or disseminated cases [37–41].

Beyond physical complications, herpes zoster significantly impacts quality of life, with increased rates of chronic pain, sleep disturbance, anxiety, and depression. The combination of increased susceptibility, more severe clinical manifestations, and higher complication rates underscores the importance of preventive strategies, particularly vaccination, in patients with diabetes [42].

5. Vaccines for Herpes Zoster

Two vaccines are currently available for the prevention of varicella and herpes zoster. The first is the live attenuated zoster vaccine (ZVL), commercially known as ZOSTAVAX (Oka/Merck), which is administered as a single-dose regimen and is indicated for immunocompetent individuals aged 60 years and older. The second is the recombinant subunit glycoprotein E vaccine (RZV), known as SHINGRIX, which is administered in a two-dose schedule and is recommended for individuals aged 50 years and above. SHINGRIX has been approved for use in Saudi Arabia, and the Saudi Ministry of Health has recently made it available across primary healthcare centers for adults aged ≥50 years, as well as for individuals aged ≥18 years with immunocompromising conditions [43–45].

Efficacy and Safety

Both vaccines have demonstrated efficacy and safety in clinical trials and real-world studies, although important differences exist in their immunogenicity, durability, and safety profiles. The live-attenuated vaccine, administered as a single dose, was the first licensed vaccine for HZ prevention and has shown moderate efficacy, particularly in younger older adults. However, its effectiveness declines with increasing age and over time. In contrast, the recombinant zoster vaccine is a non-replicating, adjuvanted subunit vaccine administered in a two-dose schedule and has demonstrated substantially higher and more sustained efficacy across all age groups, including older adults and immunocompromised populations [46–48].

High-quality evidence from a large systematic review and network meta-analysis including over 2 million participants demonstrated that the recombinant zoster vaccine provides superior protection compared with both the live-attenuated vaccine and placebo. Specifically, RZV showed a vaccine efficacy of approximately 94% (95% credible interval 79%–98%) versus placebo and 85% (95% credible interval 31%–98%) compared with ZVL in preventing herpes zoster. In contrast, the live-attenuated vaccine did not demonstrate statistically significant superiority over placebo in some analyses for laboratory-confirmed HZ outcomes (47). These findings are supported by clinical trials and real-world effectiveness data indicating that RZV consistently provides higher protection against both herpes zoster and its most debilitating complication, PHN (46,48). Importantly, RZV maintains high efficacy even in older populations, where vaccine performance is most clinically relevant.

Regarding safety, both vaccines are generally well tolerated, with no major safety concerns identified in clinical trials or post-marketing surveillance (46,48). However, differences exist in reactogenicity profiles. The recombinant zoster vaccine is associated with a higher rate of local and systemic adverse events compared with both ZVL and placebo. Meta-analysis data indicate that RZV increases the risk of injection-site reactions (relative risk 1.79, 95% credible interval 1.05–2.34) and systemic adverse events (relative risk 2.28, 95% credible interval 1.45–3.65) compared with placebo [47]. These adverse events are typically mild to moderate and transient, including pain, redness, fatigue, and fever. In contrast, the live-attenuated vaccine is associated with fewer adverse reactions but carries limitations related to its live viral nature, including contraindications in immunocompromised individuals [48]. The recombinant vaccine, being non-replicating, is considered safe for use in immunocompromised populations and individuals with immune-mediated diseases, further expanding its clinical utility [46,48].

Current evidence strongly supports the use of recombinant zoster vaccine as the preferred strategy for prevention of herpes zoster due to its superior efficacy, durable protection, and broader applicability across high-risk populations. Although associated with higher reactogenicity, its favorable benefit–risk profile makes it the cornerstone of herpes zoster prevention strategies in adults, particularly those with chronic conditions such as diabetes mellitus [48–50]

Contraindications and Precautions

The recombinant zoster vaccine (RZV) is generally well tolerated and has no live virus component, making it suitable for a broad range of adults, including many immunocompromised individuals. However, RZV is contraindicated in individuals with a history of severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine or following a previous dose of RZV. Vaccination should be deferred in individuals experiencing a moderate or severe acute illness, with or without fever, until recovery. Mild acute illnesses, such as an uncomplicated upper respiratory tract infection or low-grade fever, are not contraindications to vaccination. RZV is not indicated for the treatment of active herpes zoster or postherpetic neuralgia and should not be administered during an episode of acute herpes zoster; vaccination should be postponed until the acute illness has resolved. Healthcare providers should assess each individual's clinical status and vaccination history before administration in accordance with national recommendations and the manufacturer's prescribing information [46–49].

Herpes zoster vaccination in Saudi patients

A cross-sectional study conducted in Riyadh by Haytham I. AlSaif *et al.,* (2025) evaluated the uptake, willingness, and determinants of HZ vaccination among adults aged ≥50 years with chronic diseases attending a tertiary care hospital. The study included 333 participants and demonstrated a notably low vaccine uptake rate of only 12%. Among those who had not been vaccinated, nearly half (45.7%) expressed willingness to receive the vaccine. However, overall knowledge regarding HZ and the RZV was limited, with a mean score of 3.84 out of 14, indicating substantial knowledge gaps within this high-risk population [50].

Importantly, physician recommendation emerged as the strongest predictor of vaccine uptake (OR: 7.5; 95% CI: 2.79–20.11), followed by higher levels of knowledge (OR: 1.42; 95% CI: 1.19–1.67). Willingness to vaccinate was primarily influenced by positive attitudes toward vaccination (OR: 1.28; 95% CI: 1.12–1.48). The most reported barrier was low perceived risk of HZ (27%), underscoring a critical mismatch between actual risk and patient perception. These findings highlight that, despite low uptake, there is a substantial opportunity to improve vaccination coverage through targeted educational interventions and stronger physician–patient communication strategies, particularly in high-risk populations with chronic diseases such as diabetes in Saudi Arabia [50].

Another cross-sectional study conducted in the Qassim region of Saudi Arabia by Dawood Al-Orini *et al.,* evaluated the acceptability of HZ vaccination among patients with diabetes mellitus. The study included 410 participants with a median age of 56 years and found that only 25% expressed willingness to receive the HZ vaccine. Acceptability was significantly associated with male gender (AOR 2.01, 95% CI 1.01–4.00, p = 0.047), belief in vaccine effectiveness (AOR 3.94, 95% CI 2.25–6.90, p < 0.001), and awareness that immunocompromised individuals are at increased risk of HZ (AOR 2.32, 95% CI 1.37–3.93, p = 0.002). These findings indicate that both knowledge and perception of risk play a central role in shaping vaccination decisions among diabetic patients[51].

Importantly, the study demonstrated a substantial increase in vaccine acceptability when physician recommendation was introduced, with 74.2% of participants willing to be vaccinated if advised by their healthcare provider. Predictors of this increased willingness included male gender (AOR 2.37, 95% CI 1.18–4.79, p = 0.016) and prior history of varicella vaccination (AOR 4.50, 95% CI 1.02–19.86, p = 0.047). These findings underscore the critical influence of healthcare providers in improving vaccine uptake and highlight the need for targeted awareness campaigns focusing on vaccine effectiveness and risk perception to enhance acceptance of HZ vaccination among patients with diabetes in Saudi Arabia [51].

6. Clinical Practice Recommendations

The following clinical practice recommendations are intended to support healthcare providers in implementing evidence-based herpes zoster vaccination strategies for adults with diabetes mellitus in routine clinical care across the Kingdom of Saudi Arabia. These recommendations are aligned with national immunization policies and are endorsed in principle by the Saudi Society of Diabetes, Figure 1.

Recommendation 1:

Herpes zoster vaccination status should be routinely assessed, documented, and updated as part of standard diabetes care visits. Vaccination review should be incorporated into routine diabetes follow-up, annual health assessments, hospital admissions, influenza vaccination campaigns, and pre-Hajj/Umrah medical evaluations to maximize vaccination opportunities. *(Evidence Level: C – Expert consensus and best clinical practice)*

Recommendation 2:

Adults aged ≥50 years with diabetes should receive should receive two doses of the recombinant zoster vaccine (RZV), with the second dose administered 2–6 months after the first (0- and 2–6-month schedule), to achieve optimal and durable protection against herpes zoster, regardless of prior history of herpes zoster infection or previous receipt of live zoster vaccine, unless contraindicated. *(Evidence Level: A – High efficacy demonstrated in randomized controlled trials)*

Recommendation 3:

Adults with diabetes who are immunocompromised or receiving immunosuppressive therapies should receive recombinant herpes zoster vaccination according to current national and international recommendations, including vaccination beginning at 19 years of age when indicated. *(Evidence Level: B – Evidence from subgroup analyses and expert guidance)*

One of the key discussion points concerned whether adults with diabetes younger than 50 years should receive RZV. Although diabetes is associated with an increased risk of HZ, PHN, and hospitalization due to impaired cell-mediated immunity, current recommendations continue to advise routine vaccination for immunocompetent adults aged ≥50 years, reserving vaccination for adults aged ≥19 years only when immunocompromising conditions are present. Consequently, routine vaccination of immunocompetent adults with diabetes aged <50 years remains unsupported by direct clinical trial evidence and requires further evaluation through prospective effectiveness and cost-effectiveness studies [49]. *The expert panel identified this as a priority area for future research in Saudi Arabia and recommends conducting prospective real-world effectiveness, safety, epidemiological, and cost-effectiveness studies to determine the clinical and economic value of extending RZV vaccination to adults with diabetes younger than 50 years. Such evidence will be essential to inform future updates of national vaccination recommendations.*

Immunocompromise refers to a state of impaired immune function resulting from an underlying disease or immunosuppressive therapy, leading to reduced cell-mediated and/or humoral immune responses and an increased susceptibility to infections, including reactivation of latent VZV. Current international recommendations consider immunocompromised adults to include patients with hematologic malignancies (e.g., leukemia, lymphoma, multiple myeloma), solid tumors receiving chemotherapy, recipients of hematopoietic stem cell or solid organ transplantation, advanced or untreated HIV infection, primary immunodeficiency disorders, and individuals receiving immunosuppressive therapies, such as high-dose systemic corticosteroids, biologic agents (e.g., tumor necrosis factor inhibitors or anti-CD20 monoclonal antibodies), Janus kinase inhibitors, calcineurin inhibitors, antimetabolites (e.g., azathioprine or mycophenolate mofetil), or other disease-modifying immunosuppressive drugs. These individuals are at substantially increased risk of herpes zoster and its complications and are therefore recommended to receive the recombinant zoster vaccine beginning at 19 years of

age, in accordance with current international recommendations [49].

Recommendation 4:

Herpes zoster vaccination should not be delayed because of mild or moderate hyperglycemia. Vaccination may be administered regardless of glycemic control in clinically stable patients, provided there is no acute febrile illness or other temporary contraindication. *(Evidence Level: B – Observational studies and clinical guidance)*

Recommendation 5:

Recombinant herpes zoster vaccine may be safely co-administered with other recommended adult vaccines using separate anatomical injection sites, according to national immunization schedules and clinical judgment. *(Evidence Level: A – Established evidence from immunization studies)*

Recommendation 6:

Vaccination efforts should prioritize adults with diabetes who are at increased risk of herpes zoster and its complications, including older adults, individuals with long-standing diabetes, suboptimal glycemic control, diabetes-related complications, multiple comorbidities, autoimmune diseases, chronic kidney disease, or other conditions associated with impaired immunity. Clinical algorithms and risk-stratification tools should be developed and implemented to facilitate identification of high-risk patients who would benefit most from vaccination. *(Evidence Level: B – Observational studies, subgroup analyses, and expert consensus)*

Recommendation 7:

Healthcare professionals should proactively recommend herpes zoster vaccination during routine diabetes care. Educational initiatives should be implemented to improve healthcare providers' knowledge of adult immunization recommendations, while culturally appropriate patient education and targeted public awareness campaigns should be developed to improve vaccine confidence, address vaccine hesitancy, and increase vaccination uptake. *(Evidence Level: A – Strong evidence supporting provider recommendation as a major determinant of vaccine acceptance)*

Recommendation 8:

Electronic health systems should incorporate vaccination reminders, clinical decision support tools, and standardized vaccination tracking to facilitate identification of eligible patients, improve completion of the two-dose vaccination schedule by receiving the second dose 2–6 months after the first, and ensure continuity of care across primary care, specialty diabetes clinics, hospitals, and private healthcare facilities. Vaccination records should be integrated into national electronic health systems under the supervision of the Saudi Ministry of Health. *(Evidence Level: C – Expert consensus and health system best practice)*

Recommendation 9:

Healthcare systems should improve equitable access to recombinant herpes zoster vaccination across all healthcare sectors, including primary healthcare centers, specialty diabetes clinics, hospitals, and private healthcare providers, while ensuring adequate vaccine availability and streamlined referral pathways. *(Evidence Level: C – Expert consensus and health system implementation guidance)*

Recommendation 10:

Adverse events following herpes zoster vaccination should be documented and reported through the Saudi national pharmacovigilance system to support continuous vaccine safety surveillance, quality improvement initiatives, and public confidence in adult immunization programs. *(Evidence Level: C – Regulatory and expert consensus guidance)*

Recommendation 11 (Research Agenda):

The Saudi Society of Diabetes recommends prioritizing prospective epidemiological, real-world effectiveness, safety, and cost-effectiveness studies evaluating recombinant zoster vaccination in adults with diabetes younger than 50 years. The findings from these studies should inform future updates to national vaccination policies and recommendations. *(Evidence Level: C – Regulatory and expert consensus guidance)*

Declarations

Conflicts of Interest

Ali Albarrak, Amani Alhozali, Lamya Alzubaidi, Ali Alshehri, Emad R. Issak, Fahad Alsabaan, Hussein Elbadawi, Nasser Aljuhani, Abdulrahman Alshaikh, Saud Alsifri, and Mahmoud Amer declare no conflicts of interest.

Funding: No funding

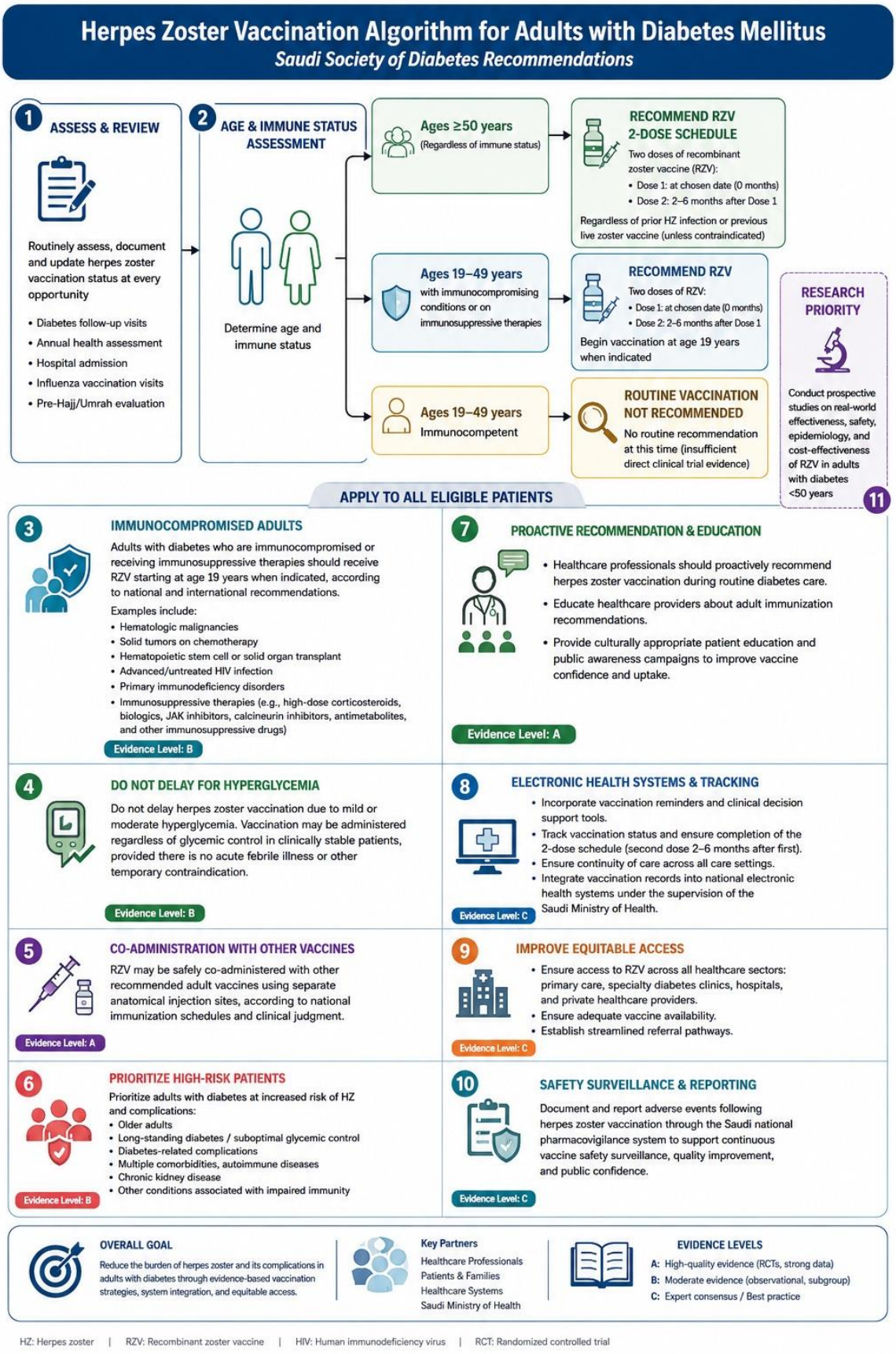

Figure 1: Herpes Zoster Vaccination Algorithm for Adults with Diabetes Mellitus

Supplementary Table 1

Recommendation	Agreement (%)
Recommendation 1	100%
Recommendation 2	89%
Recommendation 3	89%
Recommendation 4	100%
Recommendation 5	100%
Recommendation 6	100%
Recommendation 7	89%
Recommendation 8	100%
Recommendation 9	100%
Recommendation 10	89%
Recommendation 11	100%

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