



# Cardiovascular immunization: a multisociety expert consensus on vaccination as a strategy for cardiovascular prevention in high-risk adults in Mexico<sup>+</sup>

## Immunización cardiovascular: consenso de expertos de múltiples sociedades sobre la vacunación como estrategia para la prevención cardiovascular en adultos de alto riesgo en México

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### Keywords:

Cardiovascular disease, influenza vaccination after myocardial infarction, influenza vaccine to prevent adverse vascular events in heart failure, pneumococcal conjugate vaccine, polysaccharide vaccine.

### Palabras clave:

Enfermedad cardiovascular; vacuna contra la influenza después de infarto de miocardio; vacuna contra la influenza para prevenir eventos vasculares adversos en insuficiencia cardíaca; vacuna neumocócica conjugada; vacuna polisacárida.

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### ABSTRACT

**Introduction:** acute viral and selected non-respiratory infections, including influenza, SARS-CoV-2, and herpes zoster, are increasingly recognized as important triggers of Major Adverse Cardiovascular Events (MACE), including myocardial infarction, stroke, and heart failure decompensation. Infection-related systemic inflammation, endothelial dysfunction, platelet activation, and prothrombotic responses may destabilize atherosclerotic plaques and precipitate cardiovascular complications. **Objective:** to provide evidence-based recommendations for vaccination strategies in adults with cardiovascular disease as part of comprehensive cardiovascular prevention. The concept of cardiovascular immunization represents an emerging paradigm in preventive cardiology, integrating infection prevention with traditional cardiovascular risk reduction

### RESUMEN

**Introducción:** las infecciones virales agudas y algunas infecciones no respiratorias, como la gripe, el SARS-CoV-2 y el herpes zóster, se reconocen cada vez más como desencadenantes importantes de eventos cardiovasculares adversos mayores (MACE, por sus siglas en inglés), como el infarto de miocardio, el accidente cerebrovascular y la descompensación de la insuficiencia cardíaca. La inflamación sistémica relacionada con la infección, la disfunción endotelial, la activación plaquetaria y las respuestas protrombóticas pueden desestabilizar las placas ateroscleróticas y precipitar complicaciones cardiovasculares. **Objetivo:** proporcionar recomendaciones basadas en la evidencia para estrategias de vacunación en adultos con enfermedad cardiovascular como parte de una prevención cardiovascular integral. El concepto de inmunización cardiovascular representa un paradigma

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strategies. **Material and methods:** this expert consensus was developed by a multidisciplinary panel of specialists in cardiology, internal medicine, infectious diseases, and geriatrics under the auspices of AMPAC and ANCAM. A structured literature review of randomized clinical trials, meta-analyses, observational studies, and international clinical practice guidelines was performed, focusing on vaccines against influenza, pneumococcus, SARS-CoV-2, respiratory syncytial virus, and herpes zoster. **Results:** influenza vaccination has the strongest evidence for cardiovascular protection and is recommended as a class I intervention in patients with cardiovascular disease, supported by randomized clinical trials and meta-analyses demonstrating reductions in cardiovascular mortality and major adverse cardiovascular events. Additional vaccines—including pneumococcal, SARS-CoV-2, respiratory syncytial virus, and herpes zoster—may further reduce infection-related cardiovascular complications, particularly in older adults and high-risk populations. **Conclusions:** vaccination should be considered an essential component of comprehensive cardiovascular prevention strategies in patients with cardiovascular disease. Integrating immunization into routine cardiovascular care may reduce infection-triggered cardiovascular events, hospitalizations, and healthcare burden.

*emergente en cardiología preventiva, que integra la prevención de infecciones con las estrategias tradicionales de reducción del riesgo cardiovascular. **Material y métodos:** este consenso de expertos fue desarrollado por un panel multidisciplinario de especialistas en cardiología, medicina interna, enfermedades infecciosas y geriatría bajo los auspicios de AMPAC y ANCAM. Se realizó una revisión estructurada de la literatura de ensayos clínicos aleatorizados, metaanálisis, estudios observacionales y guías de práctica clínica internacionales, centrándose en las vacunas contra la influenza, el neumococo, el SARS-CoV-2, el virus sincitial respiratorio y el herpes zóster. **Resultados:** la vacunación contra la influenza tiene la evidencia más sólida de protección cardiovascular y se recomienda como una intervención de clase I en pacientes con enfermedad cardiovascular, respaldada por ensayos clínicos aleatorizados y metaanálisis que demuestran reducciones en la mortalidad cardiovascular y eventos cardiovasculares adversos mayores. Las vacunas adicionales, incluidas las neumocócicas, SARS-CoV-2, virus sincitial respiratorio y herpes zóster, pueden reducir aún más las complicaciones cardiovasculares relacionadas con la infección, particularmente en adultos mayores y poblaciones de alto riesgo. **Conclusiones:** la vacunación debe considerarse un componente esencial de las estrategias integrales de prevención cardiovascular en pacientes con enfermedad cardiovascular. Integrar la inmunización en la atención cardiovascular de rutina puede reducir los eventos cardiovasculares desencadenados por infecciones, las hospitalizaciones y la carga de atención médica.*

### Abbreviations:

ACC = American College of Cardiology

AHA = American Heart Association

AMPAC = Mexican Association for the Prevention of Atherosclerosis and its Complications

ANCAM = National Association of Cardiology of Mexico

ANCCMR = National Association of Cardiologists of Centro Médico La Raza

ANCISSTE = National Association of Cardiologists of ISSSTE

CVD = Cardiovascular Disease

ESC = European Society of Cardiology

IAMI = Influenza Vaccination After Myocardial Infarction

IVVE = Influenza Vaccine to Prevent Adverse Vascular Events in Heart Failure

MACE = Major Adverse Cardiovascular Events

PCV20 = Pneumococcal Conjugate Vaccine

PPSV23 = Polysaccharide Vaccine

RSV = Respiratory Syncytial Virus

SIAC = Inter-American Society of Cardiology

SMC = Mexican Society of Cardiology

WHO = World Health Organization

### KEY MESSAGES

1. Acute viral and selected non-respiratory infections, including influenza, SARS-CoV-2, and herpes zoster, represent important triggers of cardiovascular events.<sup>1-7</sup>
2. Influenza vaccination has the strongest evidence for cardiovascular protection, reducing cardiovascular mortality and major adverse cardiovascular events.<sup>8-10</sup>
3. Vaccination against pneumococcus, SARS-CoV-2, RSV, and herpes zoster may reduce infection-related cardiovascular complications in high-risk populations.<sup>3,6,7,11-17</sup>
4. Cardiovascular immunization represents an emerging paradigm in preventive cardiology and should be integrated into cardiovascular prevention strategies.<sup>4,5,18-21</sup>

### CLINICAL PERSPECTIVES

#### What is new

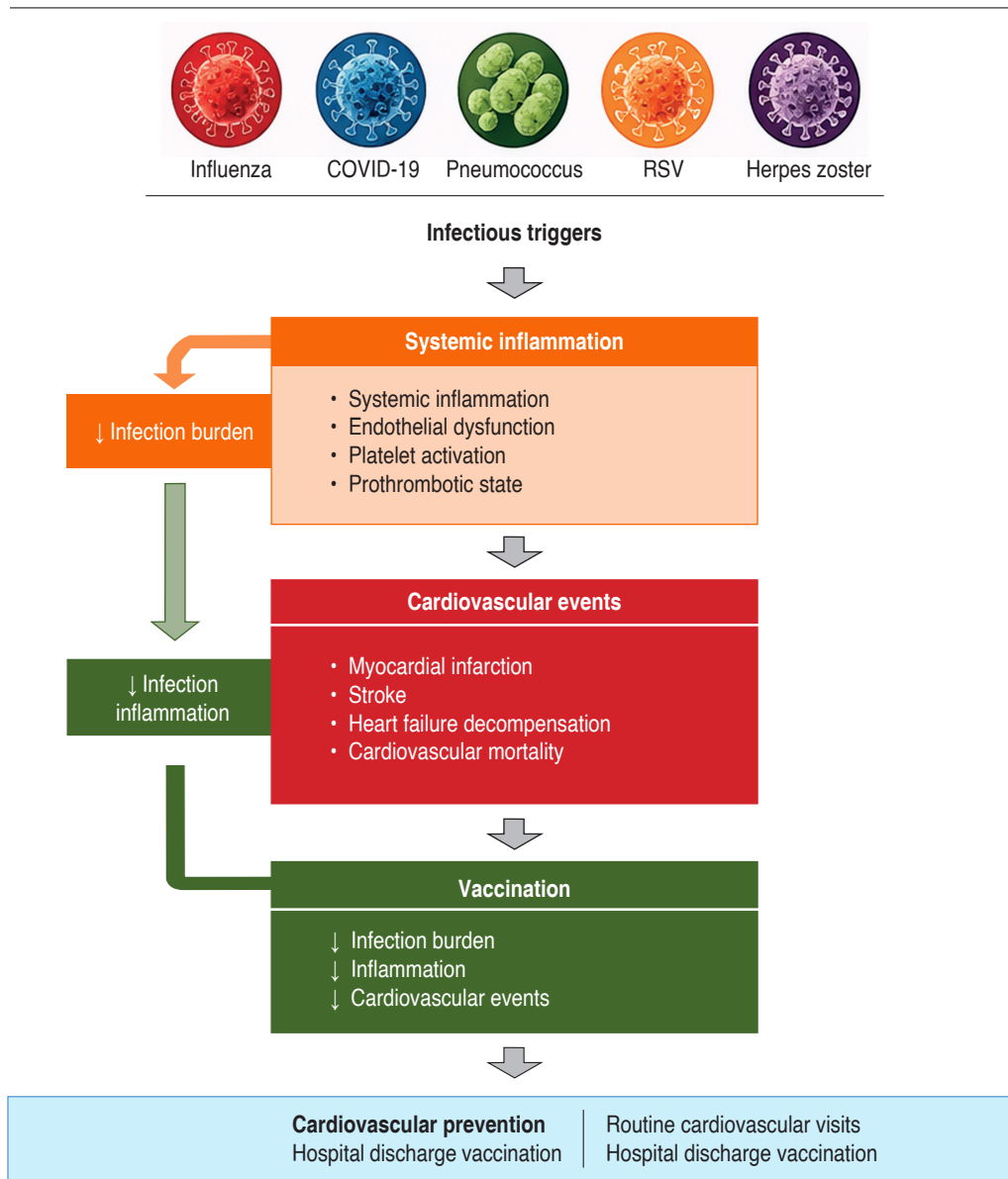
1. Several infectious diseases—including respiratory viral infections and herpes zoster—act as triggers of major adverse cardiovascular events.<sup>1-7</sup>
2. Influenza vaccination reduces cardiovascular mortality and major cardiovascular events in randomized trials and meta-analyses.<sup>4,12,13</sup>
3. Vaccination broadens the scope of cardiovascular prevention beyond traditional therapies.

### CLINICAL IMPLICATIONS

1. Cardiologists should routinely assess vaccination status in patients with cardiovascular disease.<sup>14,18-21</sup>
2. Hospitalization for acute coronary syndromes or heart failure represents an opportunity to administer vaccines before discharge.<sup>8,19,22</sup>
3. Vaccination should be integrated alongside lipid lowering, blood pressure control, **metabolic control**, antithrombotic therapy, and lifestyle modification.
4. The contemporary cardiologist should actively **recommend, prescribe, and facilitate vaccination** as part of cardiovascular care.

CENTRAL ILLUSTRATION (Figure 1)

**Cardiovascular immunization: an expert consensus on vaccination for cardiovascular prevention**



**Figure 1:** Central illustration. Cardiovascular immunization and cardiovascular prevention.

Infections such as influenza, SARS-CoV-2, pneumococcus, Respiratory Syncytial Virus (RSV), and herpes zoster can trigger cardiovascular events through systemic inflammation, endothelial dysfunction, platelet activation, and prothrombotic states that promote destabilization of atherosclerotic plaques. These mechanisms may precipitate acute cardiovascular complications including myocardial infarction, stroke, and heart failure decompensation. Vaccination against these pathogens reduces infection burden and systemic inflammatory activation and may therefore represent a complementary strategy for cardiovascular prevention in patients with cardiovascular disease.

## INTRODUCTION

Cardiovascular Disease (CVD) remains the leading cause of mortality worldwide, accounting for a substantial proportion of global morbidity and healthcare burden.<sup>23</sup> Despite major advances in pharmacologic therapies and preventive strategies, patients with established cardiovascular disease continue to experience high rates of recurrent cardiovascular events.

In recent years, increasing attention has been directed toward the role of infections as triggers of cardiovascular events. Infections—including influenza, SARS-CoV-2, herpes zoster, Respiratory Syncytial Virus (RSV), and bacterial pneumonia—have been associated with increased risks of myocardial infarction, stroke, and heart failure exacerbation.<sup>1,2</sup> Large epidemiological studies have demonstrated strong temporal associations between infections and acute cardiovascular events.

In a landmark study, Kwong and colleagues demonstrated that the risk of acute myocardial infarction increased nearly six-fold during the first week following laboratory-confirmed influenza infection.<sup>2</sup> These findings support the concept that respiratory infections may act as important triggers of cardiovascular events in susceptible individuals.

The mechanisms underlying this association involve several interconnected biological pathways. Acute infections induce systemic inflammatory responses characterized by increased cytokine production, endothelial dysfunction, platelet activation, and a prothrombotic state.<sup>4,5</sup> These mechanisms may destabilize pre-existing atherosclerotic plaques

and promote thrombus formation, leading to acute cardiovascular events such as myocardial infarction or ischemic stroke.

In addition to inflammatory activation, acute infections increase metabolic demand and oxygen consumption, potentially precipitating myocardial ischemia in patients with underlying coronary artery disease. Hypoxemia and sympathetic activation during infection may further exacerbate cardiovascular instability.

These observations have led to the concept that preventing infections may represent an additional strategy for reducing cardiovascular risk. Vaccination represents the most effective strategy for preventing many respiratory infections.

By preventing infection-induced inflammation and thrombosis, vaccination may reduce the incidence of infection-triggered cardiovascular events. This paradigm has been referred to as **cardiovascular immunization**, highlighting the emerging role of vaccines as complementary interventions in cardiovascular prevention.<sup>4,5</sup>

The concept of cardiovascular immunization proposes that preventing infections through vaccination may reduce inflammation-mediated cardiovascular complications and improve outcomes in patients with cardiovascular disease.

The mechanisms linking infection, inflammation, and cardiovascular events are summarized in [Table 1](#).

**Transition to methods.** Given the growing recognition of infections as triggers of cardiovascular events and the expanding role of vaccination in adult preventive medicine, this expert consensus was developed to review the available scientific evidence and provide practical recommendations for vaccination strategies in adults with cardiovascular disease.

## MATERIAL AND METHODS

### Consensus development process

This expert consensus document was developed by a multidisciplinary panel including specialists in cardiology, internal medicine, infectious diseases, and geriatrics under the auspices of the Mexican Association for the Prevention of

**Table 1: Mechanisms linking infection and cardiovascular events.**

Mechanism	Cardiovascular consequence
Systemic inflammation	Plaque destabilization
Endothelial dysfunction	Impaired vascular regulation
Platelet activation	Increased thrombosis
Prothrombotic state	Acute coronary syndrome or stroke
Hypoxemia	Heart failure decompensation
Immunothrombosis	Increased thrombosis through immunological pathway

**Table 2: Major clinical studies evaluating influenza vaccination and cardiovascular outcomes.**

Study	Population	Study design	Key findings
IAMI trial	Post-myocardial infarction	Randomized clinical trial	↓ Cardiovascular mortality and ↓ MACE
IVVE trial	Heart failure	Randomized clinical trial	↓ Hospitalizations
PANDA II	Acute heart failure	Cluster randomized trial	↓ Cardiovascular events
Udell et al.	Cardiovascular disease	Meta-analysis	↓ Major cardiovascular events

Atherosclerosis and its Complications (AMPAC), the National Association of Cardiology of Mexico (ANCAM), the Mexican Society of Cardiology (SMC), the National Association of Cardiologists of ISSSTE (ANCISSSTE), and the National Association of Cardiologists of *Centro Médico La Raza* (ANCCMR), with participation of national cardiovascular institutions.

The objective of this document was to review the available scientific evidence linking vaccination to cardiovascular outcomes and to provide practical recommendations for implementing vaccination strategies in adults with cardiovascular disease. This document represents an expert consensus based on available evidence and multidisciplinary discussion, without a formal Delphi process.

A structured literature review was performed in PubMed/MEDLINE, Scopus, and Google Scholar, including studies published between January 2013 and December 2025. Search terms included combinations of: influenza vaccination, pneumococcal vaccination, COVID-19 vaccination, respiratory syncytial virus vaccine, herpes zoster vaccine, cardiovascular disease, myocardial infarction, stroke, heart failure, major adverse cardiovascular events, and prevention.

The literature search included randomized clinical trials, systematic reviews, meta-analyses, observational studies, and international clinical practice guidelines.

Evidence was evaluated for:

1. Influenza
2. Pneumococcal
3. SARS-CoV-2
4. Herpes zoster.
5. RSV

Recommendations were formulated based on available evidence and expert consensus.

## RESULTS

### Influenza vaccination and cardiovascular prevention

Among currently available vaccines, influenza vaccination has the strongest evidence supporting cardiovascular protection, supported by randomized clinical trials and meta-analyses demonstrating reductions in cardiovascular mortality and major adverse cardiovascular events.<sup>8-10,24-28</sup>

The principal randomized clinical trials and meta-analyses evaluating influenza vaccination and cardiovascular outcomes are summarized in [Table 2](#), and the corresponding published effect estimates are visually summarized in [Figure 2](#).

### Pathophysiological background

Influenza infection has long been associated with increased cardiovascular risk. Viral respiratory infections trigger systemic inflammatory responses characterized by increased cytokine production, endothelial dysfunction, platelet activation, and prothrombotic states.<sup>4,5</sup>

These processes may destabilize atherosclerotic plaques and promote thrombosis, ultimately precipitating acute cardiovascular events such as myocardial infarction or stroke.

Furthermore, infections increase metabolic demand and oxygen consumption, potentially precipitating myocardial ischemia in patients with underlying coronary artery disease.

In patients with heart failure, respiratory infections may exacerbate hemodynamic stress and precipitate decompensation.

### Epidemiological evidence

Several epidemiological studies have demonstrated a strong temporal relationship between influenza infection and cardiovascular events.

In a landmark study, Kwong et al. reported that the risk of acute myocardial infarction increased nearly six-fold during the first week following laboratory-confirmed influenza infection.<sup>2</sup>

These findings support the concept that influenza infection may act as a trigger for cardiovascular events in susceptible individuals with underlying atherosclerotic disease.

### Randomized clinical trials

#### IAMI trial

The **Influenza Vaccination After Myocardial Infarction (IAMi) trial** represents one of the most important randomized clinical trials evaluating the cardiovascular benefits of influenza vaccination.<sup>8</sup>

This multicenter randomized trial evaluated influenza vaccination administered shortly after hospitalization for myocardial infarction.

The study demonstrated that influenza vaccination significantly reduced the composite endpoint of:

1. Cardiovascular death.
2. Recurrent myocardial infarction.
3. Stent thrombosis.

Importantly, vaccination was associated with:

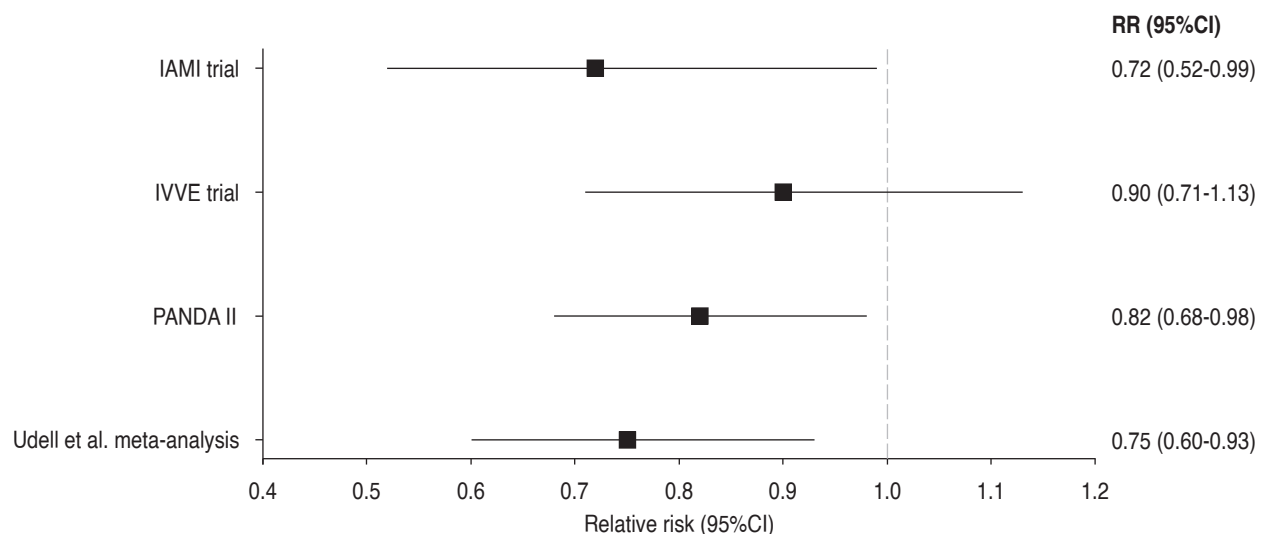
1. 28% reduction in major adverse cardiovascular events.
2. 42% reduction in cardiovascular mortality.

These findings provided strong evidence supporting influenza vaccination as a cardioprotective intervention in patients with coronary artery disease.

#### IVVE trial

The **Influenza Vaccine to Prevent Adverse Vascular Events in Heart Failure (IVVE) trial** evaluated influenza vaccination in patients with symptomatic heart failure.<sup>22</sup>

Although the primary composite outcome of cardiovascular death, myocardial infarction, or stroke did not reach statistical significance, influenza vaccination was associated with reductions in:



**Figure 2:** Forest plot of influenza vaccination and cardiovascular outcomes.

Author-generated forest plot based on published effect estimates from the IAMi trial, IVVE trial, PANDA II, and the meta-analysis by Udell et al.<sup>4,5,12,14</sup> Squares represent individual study estimates with horizontal lines indicating 95% confidence intervals. The diamond represents the pooled effect estimate.

1. Hospitalizations.
2. Respiratory complications.

Subgroup analyses suggested greater benefits during periods of high influenza circulation.

#### *PANDA II trial*

The **PANDA II trial** evaluated influenza vaccination strategies in patients hospitalized with acute heart failure.<sup>24</sup>

This cluster-randomized trial demonstrated that influenza vaccination was associated with reductions in cardiovascular events and hospitalizations during follow-up.

These findings further support the potential role of influenza vaccination in high-risk cardiovascular populations.

#### *Meta-analyses*

Several meta-analyses have evaluated the cardiovascular effects of influenza vaccination.

The meta-analysis conducted by **Udell et al.** demonstrated that influenza vaccination was associated with a significant reduction in major cardiovascular events among patients with established cardiovascular disease.<sup>9</sup>

More recent meta-analyses incorporating randomized trials and observational studies have confirmed reductions in:

1. Cardiovascular mortality.
2. Major adverse cardiovascular events.
3. Hospitalizations.<sup>10,24-28</sup>

In patients with heart failure, pooled analyses have reported reductions in hospitalizations with influenza vaccination, with relative risks of approximately **0.86 (95%CI 0.76-0.97)**.<sup>25-28</sup>

The principal randomized clinical trials and meta-analyses evaluating influenza vaccination and cardiovascular outcomes are summarized in *Table 2*, and the corresponding pooled effects are illustrated in *Figure 2*.

Forest plot summarizing randomized clinical trials and meta-analyses evaluating the association between influenza vaccination and cardiovascular outcomes. The figure illustrates relative risk estimates for major adverse cardiovascular events and cardiovascular

mortality among vaccinated individuals with cardiovascular disease. Most studies demonstrate a consistent protective effect of influenza vaccination, particularly in patients with recent myocardial infarction or established coronary artery disease.

#### **Guideline recommendations**

The cardiovascular benefits of influenza vaccination are now recognized in major clinical practice guidelines.

The **2023 ACC/AHA guideline for chronic coronary disease** recommends annual influenza vaccination in patients with cardiovascular disease as part of comprehensive preventive care.<sup>18</sup>

Similarly, the **ACC/AHA guideline for acute coronary syndromes** supports influenza vaccination during or shortly after hospitalization for myocardial infarction.<sup>19</sup>

The **European Society of Cardiology (ESC)** also recommends influenza vaccination in patients with cardiovascular disease to reduce infection-triggered cardiovascular events.

#### *Consensus recommendation*

Annual influenza vaccination is recommended in all adults with **established cardiovascular disease**, including chronic coronary syndrome, prior myocardial infarction or acute coronary syndrome, heart failure, peripheral arterial disease, atherosclerotic cerebrovascular disease, significant valvular heart disease, and cardiomyopathies.

In adults without established cardiovascular disease but with **high cardiometabolic risk**—including advanced age, diabetes mellitus, obesity, chronic kidney disease, or multiple cardiovascular risk factors—vaccination should follow national immunization schedules and may also confer cardiovascular benefit. Indicated for individuals aged > 6 months. Nasal vaccine not recommended for those > 50 years. Specific recommendations for those > 65 years with inactivated quadrivalent vaccine or high dose.

**Class of recommendation: I**  
**Level of evidence: A**

### Additional vaccines for cardiovascular prevention

Although influenza vaccination has the strongest evidence supporting cardiovascular protection, additional vaccines may contribute to reducing infection-triggered cardiovascular complications in high-risk populations.

These vaccines (Table 3) include pneumococcal, SARS-CoV-2, Respiratory Syncytial Virus (RSV), and herpes zoster vaccines, which have demonstrated benefits in preventing severe infections associated with systemic inflammatory responses and cardiovascular complications.<sup>3,6,7,11-17</sup>

### Pneumococcal vaccination

#### Biological rationale

*Streptococcus pneumoniae* infection remains a major cause of community-acquired pneumonia in adults and is associated with substantial morbidity and mortality. Pneumonia induces systemic inflammatory responses that may increase cardiovascular risk through endothelial dysfunction, activation of coagulation pathways, and plaque destabilization.

Severe pneumococcal infection is characterized by elevated inflammatory

mediators, which may promote thrombotic events and contribute to acute coronary syndromes or cerebrovascular events.<sup>12,13</sup>

Additionally, pulmonary infections increase myocardial oxygen demand while impairing oxygen delivery, potentially precipitating myocardial ischemia in patients with pre-existing coronary artery disease.

#### Epidemiological evidence

Several observational studies have evaluated the association between pneumococcal vaccination and cardiovascular outcomes.

Population-based cohort studies suggest that pneumococcal vaccination may reduce the risk of myocardial infarction and cardiovascular mortality in older adults and individuals with chronic diseases.<sup>12,13</sup>

Although randomized trials specifically designed to evaluate cardiovascular endpoints following pneumococcal vaccination are limited, the biological plausibility and epidemiological evidence support vaccination in high-risk populations.

#### Guideline context

Current vaccination guidelines recommend pneumococcal vaccination for adults aged  $\geq 65$

**Table 3: Vaccination strategies for cardiovascular prevention.**

Vaccine	Target population	Potential cardiovascular impact	Recommendation (class)	Evidence (level)
Influenza	All adults with cardiovascular disease or cardiovascular risk factors	↓ MACE and ↓ cardiovascular mortality	I	A
Pneumococcal	$\geq 65$ years or high-risk individuals	↓ Infection-triggered cardiovascular events	I	B
SARS-CoV-2	All patients with cardiovascular disease or cardiovascular risk factors	↓ Severe infection and cardiovascular complications	I	B
Herpes zoster	$\geq 50$ years with cardiovascular disease or cardiovascular risk factors	↓ Infection-related vascular inflammation	I	B
RSV	18-50 years with conditions that could decrease immune capacity $\geq 60$ years with comorbidities or cardiovascular risk factors	↓ Prevent infection-triggered cardiovascular events ↓ Respiratory infection burden	IIa	B

MACE = Major Adverse Cardiovascular Events. RSV = Respiratory Syncytial Virus.

years and individuals with chronic medical conditions, including cardiovascular disease.<sup>14</sup>

The introduction of newer conjugate vaccines with broader serotype coverage has simplified vaccination schedules and may improve adherence.

#### *Consensus recommendation*

Pneumococcal vaccination is recommended in adults  $\geq 65$  years or those with high cardiovascular risk 18-64 years. In pregnant individuals, vaccination with PCV20 (Pneumococcal Conjugate Vaccine) and PPSV23 (Polysaccharide Vaccine).

**Class of recommendation: I**  
**Level of evidence: B**

#### **SARS-CoV-2 vaccination**

##### *Cardiovascular implications of COVID-19*

The COVID-19 pandemic highlighted the strong relationship between viral infections and cardiovascular complications.

SARS-CoV-2 infection has been associated with:

1. Myocardial injury.
2. Myocarditis.
3. Thromboembolic complications.
4. Arrhythmias.
5. Heart failure exacerbation.

Large cohort studies have demonstrated increased risks of myocardial infarction, stroke, and heart failure among individuals infected with SARS-CoV-2 during both the acute phase and long-term follow-up.<sup>3</sup>

Persistent inflammatory and immune-mediated mechanisms may contribute to long-term cardiovascular risk following infection.

##### *Evidence supporting vaccination*

Vaccination against SARS-CoV-2 significantly reduces the risk of severe infection, hospitalization, and systemic inflammatory responses.<sup>15</sup>

By preventing severe infection and reducing inflammatory activation, COVID-19 vaccination

may indirectly reduce cardiovascular complications associated with infection.

Population studies have demonstrated lower rates of cardiovascular complications among vaccinated individuals compared with unvaccinated individuals following infection.

#### *Consensus recommendation*

COVID-19 vaccination with mRNA vaccines is recommended in all patients  $> 6$  months and adults  $> 65$  years with cardiovascular disease or cardiovascular risk factors.

**Class of recommendation: I**  
**Level of evidence: B**

#### **Respiratory Syncytial Virus (RSV) vaccination**

##### *Clinical relevance in older adults*

Respiratory syncytial virus infection is increasingly recognized as an important cause of respiratory morbidity in older adults.

RSV infection may lead to severe lower respiratory tract disease and has been associated with increased hospitalization among older individuals with chronic cardiovascular conditions.<sup>16</sup>

Patients with heart failure or chronic cardiopulmonary disease appear particularly vulnerable to RSV-associated complications.

##### *Evidence from clinical trials*

Recent phase III clinical trials evaluating RSV vaccines have demonstrated significant reductions in RSV-associated lower respiratory tract disease among adults aged  $\geq 60$  years.<sup>11</sup>

Although cardiovascular outcomes were not primary endpoints in these trials, preventing severe respiratory infections may reduce cardiovascular stress and prevent decompensation in patients with underlying cardiovascular disease.

#### *Consensus recommendation*

RSV vaccination may be considered in adults  $\geq 60$  years. Recommended options include: RSVPref3 (Arexvy) and Nirsevimab (Beyfortus).

**Class of recommendation: IIa**  
**Level of evidence: B**

### Herpes zoster vaccination

#### *Cardiovascular risk associated with herpes zoster*

Herpes zoster infection has been associated with increased risk of stroke and myocardial infarction.

The proposed mechanisms include vascular inflammation, immune-mediated endothelial injury, and systemic inflammatory responses.<sup>6,7</sup>

The risk of stroke appears to be highest during the first weeks following herpes zoster infection but may remain elevated for several months.

#### *Evidence supporting vaccination*

The recombinant herpes zoster vaccine demonstrates high efficacy in preventing herpes zoster infection and post-herpetic neuralgia.<sup>17</sup>

Meta-analysis, observational, and case-control studies suggest that vaccination may also reduce cardiovascular risk by preventing infection-associated inflammatory responses that could lead to cardiovascular events.

#### *Consensus recommendation*

Herpes zoster vaccination is recommended in adults  $\geq 50$  years and adults between 18-50 years with increased risk (conditions that could decrease immune capacity) with recombinant zoster vaccine (Shingrix).

**Class of recommendation: I**  
**Level of evidence: B**

## DISCUSSION

The concept of cardiovascular immunization represents a novel approach to cardiovascular prevention, expanding traditional risk reduction strategies beyond pharmacologic and lifestyle interventions to include prevention of infection-triggered cardiovascular events. The growing recognition of infections as triggers of cardiovascular events has important

implications for preventive cardiology. The present expert consensus highlights vaccination as an important and often underrecognized strategy for reducing infection-triggered cardiovascular complications in patients with cardiovascular disease.

Evidence for cardiovascular benefit is strongest for influenza vaccination, supported by randomized clinical trials demonstrating reductions in cardiovascular mortality and major adverse cardiovascular events. For other vaccines, available data are derived primarily from meta-analysis and observational studies that reflect the indirect effects related to the prevention of infection-triggered inflammatory responses.

### Infection as a trigger of cardiovascular events

A substantial body of epidemiological evidence supports the concept that acute infections may precipitate cardiovascular events in susceptible individuals. Respiratory infections—including influenza, SARS-CoV-2, and bacterial pneumonia—have consistently been associated with increased risks of myocardial infarction, stroke, and heart failure exacerbation.<sup>1-3</sup>

The biological mechanisms underlying these associations involve multiple interconnected pathways. Acute infections induce systemic inflammatory responses characterized by increased levels of pro-inflammatory cytokines and inflammatory mediators. These responses promote endothelial dysfunction and increase platelet reactivity, thereby creating a prothrombotic environment.<sup>4,5</sup>

Systemic inflammation may also destabilize pre-existing atherosclerotic plaques, increasing the likelihood of plaque rupture and thrombus formation. Hypoxemia, increased metabolic demand, and sympathetic activation during acute infections may further contribute to myocardial ischemia and cardiovascular instability.

These mechanisms collectively explain why respiratory infections can act as a «second hit» in patients with underlying cardiovascular disease.

### Cardiovascular benefits of vaccination

Among currently available vaccines, influenza vaccination has the most robust evidence

supporting cardiovascular protection. Randomized clinical trials and meta-analyses have consistently demonstrated reductions in cardiovascular events among vaccinated individuals with cardiovascular disease.<sup>8-10,24-28</sup>

The IAMI trial provided strong evidence supporting influenza vaccination as a cardioprotective intervention in patients hospitalized with myocardial infarction.<sup>8</sup> In this study, influenza vaccination administered shortly after hospitalization significantly reduced cardiovascular mortality and recurrent cardiovascular events.

Similarly, the IVVE trial evaluated influenza vaccination in patients with heart failure.<sup>22</sup> Although the primary composite outcome did not reach statistical significance, the trial demonstrated reductions in hospitalizations and respiratory complications among vaccinated patients.

Meta-analyses further support the cardiovascular benefits of influenza vaccination. The meta-analysis conducted by Udell et al. demonstrated a significant reduction in major cardiovascular events among vaccinated patients with cardiovascular disease.<sup>9</sup> More recent analyses incorporating additional randomized trials and observational studies have confirmed reductions in cardiovascular mortality, major adverse cardiovascular events, and hospitalizations.<sup>10,24-28</sup>

These findings support influenza vaccination as an effective strategy for reducing infection-triggered cardiovascular complications.

### **Expanding the concept of cardiovascular immunization**

Although influenza vaccination currently has the strongest evidence base, other vaccines may also contribute to reducing cardiovascular risk, primarily through prevention of infection-triggered inflammatory and thrombotic pathways.

Pneumococcal vaccination may reduce cardiovascular events by preventing severe bacterial pneumonia and the associated inflammatory cascade. Observational studies have suggested protective associations between pneumococcal vaccination and cardiovascular outcomes in older adults.<sup>12,13</sup>

Similarly, vaccination against SARS-CoV-2 reduces the risk of severe infection and systemic inflammatory responses associated with COVID-19.<sup>15</sup> Given the substantial cardiovascular burden associated with COVID-19 infection, vaccination may indirectly reduce cardiovascular complications by preventing severe disease.

Herpes zoster infection has also been associated with increased risk of stroke and myocardial infarction.<sup>6,7</sup> Preventing herpes zoster infection through vaccination may therefore reduce infection-related vascular inflammation.

New vaccines targeting Respiratory Syncytial Virus (RSV) represent another important development in adult vaccination. RSV infection can cause severe respiratory illness in older adults and has been associated with exacerbations of heart failure and other cardiovascular conditions.<sup>11,16</sup>

These observations collectively support the concept of cardiovascular immunization, which integrates infection prevention into cardiovascular risk reduction strategies.

### **Integration into cardiovascular guidelines**

The growing recognition of vaccination as a cardiovascular preventive strategy is reflected in contemporary clinical practice guidelines and international consensus statements.

The American College of Cardiology and American Heart Association (ACC/AHA) recommend annual influenza vaccination for patients with cardiovascular disease as part of comprehensive preventive care.<sup>18,19</sup> Similarly, the European Society of Cardiology (ESC) emphasizes vaccination as a strategy to reduce infection-triggered cardiovascular events.

In the Americas, the Inter-American Society of Cardiology (SIAC) and the World Heart Federation have issued a consensus supporting influenza vaccination as a cardiovascular preventive strategy, reinforcing its relevance in Latin American clinical practice.<sup>20</sup>

In parallel, the World Health Organization (WHO) recommends annual influenza vaccination for high-risk populations, including older adults and individuals with chronic medical conditions, highlighting its importance

from both cardiovascular and public health perspectives.<sup>21</sup>

These recommendations highlight the increasing recognition of vaccination as an integral component of preventive cardiology.

### Clinical implications

From a clinical perspective, cardiologists are uniquely positioned to promote vaccination among patients with cardiovascular disease.

Routine cardiovascular visits provide an opportunity to assess vaccination status and ensure that patients receive recommended vaccines. Hospitalization for acute coronary syndromes or heart failure represents another critical opportunity to administer vaccines before discharge.

Integrating vaccination into cardiovascular care pathways may represent a practical, scalable, and cost-effective strategy for reducing infection-related cardiovascular events and improving clinical outcomes.

### Public health implications

Increasing vaccination coverage among patients with cardiovascular disease may have important public health implications.

Patients with cardiovascular disease represent a high-risk population for both infectious complications and cardiovascular events. Improving vaccination coverage in this population may reduce hospitalizations, healthcare costs, and mortality.

In regions with high cardiometabolic disease burden, vaccination strategies may represent a scalable intervention for reducing infection-triggered cardiovascular complications. These findings are particularly relevant in low- and middle-income countries, where cost-effective preventive strategies are critically needed.

### Limitations

Although the evidence supporting influenza vaccination as a cardioprotective intervention is strong, evidence for other vaccines remains less robust in terms of randomized controlled trials with respect to cardiovascular outcomes.

Most studies evaluating pneumococcal, RSV, or herpes zoster vaccines were not specifically designed to assess cardiovascular endpoints. Therefore, the magnitude of cardiovascular protection associated with these vaccines remains less well defined.

Future randomized clinical trials specifically designed to evaluate cardiovascular outcomes following vaccination would help clarify the magnitude of cardiovascular benefits associated with these vaccines.

### Future directions

Future research should focus on evaluating vaccination strategies in high-risk cardiovascular populations through randomized clinical trials designed to assess cardiovascular outcomes.

Advances in immunology and vaccine technology may further expand the role of vaccination in preventive cardiology. In addition, improving vaccination uptake through integrated healthcare strategies represents an important area for future investigation.

These findings are particularly relevant in regions with a high burden of cardiometabolic disease, where scalable and cost-effective preventive strategies such as vaccination may have substantial impact.

Clinical impact across diverse healthcare settings and patient populations. The incorporation of vaccination into routine cardiovascular care pathways may contribute to reducing the burden of cardiovascular events and healthcare utilization in high-risk conditions, highlighting its importance from both cardiovascular and public health perspectives.<sup>21</sup>

These recommendations highlight the increasing recognition of vaccination as an integral component of preventive cardiology.

### CONCLUSIONS

Vaccination represents an important and often underrecognized strategy for cardiovascular prevention. Preventing infections that trigger systemic inflammation may reduce cardiovascular events and improve outcomes in patients with cardiovascular disease. Integrating immunization into routine cardiovascular care should

therefore be considered part of comprehensive cardiovascular prevention strategies. The concept of cardiovascular immunization highlights the emerging role of vaccines as complementary interventions alongside traditional therapies for cardiovascular risk reduction.

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