

# Diabetes and Infectious Disease

- Diabetes complications are looming large and 65% of the reported deaths are due to the cardiovascular complications
- Diabetes also confers an increased risk of developing and dying from infectious diseases and it is now considered an important complication of diabetes
- Indeed, the morbidity and mortality associated with infectious diseases like influenza and pneumonia, which are preventable by appropriate vaccination, are also very high
- Although people of all ages are prone to infectious diseases like pneumonia and influenza, extremes of age and certain underlying medical conditions such as diabetes, asthma, and CVD aggravate the risk

# Diabetes and Influenza

- Diabetes results in increased risk of infections and death associated with infectious disease
- During influenza epidemics, there is 5-15% increase in the mortality among diabetes patients
- Diabetic patients are six fold more likely to require hospitalization with complications of influenza
- Annually 10 to 30 thousand deaths in people with diabetes are associated with respiratory complications such as influenza and pneumonia

# The role of diabetes in the severity of 2009 pandemic influenza.

Year/s observed	Country	Sample size (% diabetes <sup>1</sup> )	Diabetes type <sup>2</sup>	Primary outcome(s) measured	Results <sup>3</sup>	Findings/conclusions
April 2009 – June 2010	USA <sup>4</sup>	668 (2%)	n/a	Hospitalization  ICU admission	ND: 311/658 (47%), D: 5/10 (50%)  ND: 114/658 (17%), D: 2/10 (20%)	Diabetes did not affect the rate of hospitalization or ICU admission
1 January – 1 December 2009	Spain	11,499 (9%)	97 Type I 936 Type II	Death	ND: 244/10,416 (2%), D: 38/1,033 (4%)	No difference in fatality risk in any age group between those with and without diabetes
16 April – 30 August 2009	Canada	716 (7%)	n/a	Hospitalization ICU admission Death	ND: 283/666 (43%), D: 38/50 (76%) ND: 39/666 (6%), D: 8/50 (16%) ND: 12/666 (2%), D: 3/50 (6%)	Diabetes was associated with an increased risk of hospitalization.
26 April – 26 September 2009	Canada	1,479 (9%)	n/a	Non-severe outcome  Non-fatal ICU admission Death	ND: 1,089/1,342 (81%), D: 82/137 (60%)  ND: 194/1,342 (15%), D: 42/137 (31%) ND: 59/1,342 (4%), D: 13/137 (10%)	The risk of a severe outcome was greatest among patients with diabetes

# Animal models of diabetes and influenza

Mouse model	Diabetes type modeled	Influenza A virus subtype	Measure of disease severity	Findings
STZ-induced diabetes in BALB/c mice	I	H1N1	Lung viral titers Lethal dose 50	Diabetic mice had increased influenza virus titers and a lower lethal dose 50 compared to non-diabetic mice.
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RIP-K <sup>b</sup> transgenic diabetic mice	I	H3N2	Lung viral titers Weight loss	There was a significant correlation between blood glucose levels and influenza virus titers in diabetic mice. Diabetic mice had increased influenza virus titers but no difference in weight loss compared to non-diabetic mice.
BKS.Cg-+Leprdb/+Leprdb/Jcl (diabetic mice)	II	H1N1	Lethal dose 50 Death	Diabetic mice had a lower lethal dose 50 and a higher mortality rate compared to non-diabetic mice.

# Recommendations by different organizations for influenza vaccination

Immunization Guidelines 2012.<sup>[23]</sup>

CDCs ACIP 2011-12 Influenza  
Vaccination Guidelines.<sup>[24]</sup>

- a. Routine immunization (annual vaccination) is now recommended for anyone  $\geq 6$  months of age when vaccine is available.
- b. Children aged 6 months to 8 years whose vaccination status is unknown or who have never received seasonal influenza vaccine before as well as children who did not receive at least 1 dose of 2009 (H1N1) monovalent vaccine regardless of previous influenza vaccine history should receive 1 dose of 2010-2011 seasonal influenza vaccine (minimum interval 4 weeks) during the 2010-2011 season.

Australian Technical Advisory  
Group on Immunization.<sup>[26]</sup>

- a. All individuals aged 65 years and over.
- b. All Aboriginal and Torres Strait Islander peoples aged 15 years and over.
- c. Pregnant women.
- d. Individuals aged 6 months and over with medical conditions predisposing to severe influenza complications such as cardiac disease, chronic respiratory disease, diabetes and other metabolic disorders, renal disease, etc.

Canadian National Advisory  
Committee on Immunization for  
the 2011-2012 Season.<sup>[27]</sup>

- a. Influenza vaccine may be administered to people of any age who are residents of nursing homes, long-term care facilities, other chronic care facilities, people  $\geq 65$  years of age and healthy children 6-23 months of age.
- b. Adults (including pregnant women) and children with the following chronic health conditions are recommended recipients of Influenza Vaccine like cardiac or pulmonary disorders, diabetes, chronic kidney disease, other metabolic diseases, renal disease, etc.

# Influenza vaccine

Evidence of vaccine efficacy in elderly diabetics and very young children is not established

However vaccination in diabetics is still justified due to

- Good safety profile of vaccine

- Absence of effective preventive interventions for influenza

- Risk of diabetics for developing severe disease

ARTICLE

# **Working-age adults with diabetes experience greater susceptibility to seasonal influenza: a population-based cohort study**

## **Key points**

- Guidelines calling for influenza vaccinations in diabetic, in addition to elderly, adults implicitly single out working-age adults with diabetes
- Working age adults with diabetes experience a greater burden of influenza than similar non-diabetic adults

# **Diabetes and the Severity of Pandemic Influenza A (H1N1) Infection**

**Diabetes triples the risk of hospitalization after influenza A (H1N1)p and quadruples the risk of ICU admission once hospitalized**



# IDF Key facts about influenza for diabetes patient

- A dangerous complication of the flu is pneumonia and people with diabetes are more at risk of developing this complication than people without diabetes.
- Flu, and other viral infections, can lead to higher blood sugar levels.
- People with diabetes are six times more likely to be hospitalized with influenza during flu outbreaks.
- Diabetes guidelines issued by the World Health Organization (WHO), the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) and RSSDI recommend diabetes patients to get their flu vaccine at the start of every flu season.
- A recently published review study confirms that vaccinating people with diabetes against influenza is indeed the sensible thing to do (Vaccine Journal, 12 September 2017)
- But people with diabetes seem to be unaware of the potential risk of an influenza infection. In Germany, only 40% of the people with diabetes gets an annual flu vaccine. In Poland, the rate drops to 10%.

# Vaccination of Influenza in Diabetes Patient

- Influenza prevention is being treated as an integral part of a 'healthy ageing' strategy
- Overall influenza vaccination rates in high-risk groups continue to remain below target worldwide
- Vaccination coverage in household contacts of persons with diabetes mellitus of type 2 is 30% lower than in diabetes mellitus patients

Contents lists available at [ScienceDirect](#)

# Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)

Influenza vaccination in people with type 2 diabetes, coverage, predictors of uptake, and perceptions. Result of the MADIABETES cohort a 7 years follow up study



## Results

- Most patients (90%) agreed to be vaccinated following their physician's advice because of their age or their chronic conditions.
- The most common reason for refusal among men was the belief that they were not at risk (41.6% vs. 29.79% in women);
- The most common reason for refusal among women was fear of adverse reactions (32.53% vs. 20.23% in men).

**The uptake of influenza vaccination among diabetic patients was below desirable levels. The main barrier to vaccination was lack of knowledge regarding the need, risks and advantages of influenza vaccination**

# Influenza vaccine

## Modes of administration:

### Injectable

Can be used in 6 months & older individuals

Given SC or IM

### Nasal spray vaccine

Live attenuated vaccine, administered by spraying into the nose

Can be given to healthy persons between ages 2 and 49

Pregnant women cannot receive the nasal vaccine

## Contraindications for influenza vaccine

Severe allergy to chickens or egg protein

During viral illness/ fever

Hypersensitivity to flu vaccine

This vaccine has a very small chance of a serious reaction or even death

# ADA Rationale for immunization

- Patients with diabetes may have abnormalities in immune function and presumed increased morbidity and mortality from infection.
- Epidemiological studies support the fact that patients with diabetes (in particular those with end organ complications of cardiac and renal disease) are at high risk for complications, hospitalization, and death from influenza and pneumococcal disease.
- There is sufficient evidence that people with diabetes generally have appropriate humoral immune responses to vaccination.
- Subgroup analysis of patients with diabetes reported in clinical narrative and case-control studies support the fact that vaccination against influenza has been effective in reducing hospital admissions during influenza epidemics.
- Immunization against influenza and pneumococcal disease is an important part of preventive services for many chronic diseases such as diabetes.

# ADA immunization strategy

- Educate staff/patients to increase the awareness of the risks of influenza and pneumococcal disease among people with diabetes and the efficacy of vaccine in reducing disease.
- Educate staff/patients to reduce the fears and perceptions concerning adverse events associated with vaccination.
- Create a diabetes registry, systematic tracking system, and effective reminder system as part of a successful implementation strategy
- Health care providers in episodic or acute care settings should offer vaccination to all individuals with diabetes
- Empower staff (to include the medical and administrative health care team) to identify people with diabetes.
- Empower staff to offer vaccination to residents of nursing homes and other residential care settings and to those hospitalized

**Influenza vaccination helps  
reduce complications from  
chronic diseases**



**World health organization considers  
influenza Vaccination the most effective  
way to prevent infection**

**RESEARCH ARTICLE**

**Open Access**

# Vaccines for the prevention of seasonal influenza in patients with diabetes: systematic review and meta-analysis

- The WHO and several NITAGs recommend seasonal influenza vaccination of patients with diabetes, regardless of age and severity of the diabetic disease
- For NITAGs, knowledge about the strength of the vaccine effect and the quality of the underlying evidence are crucial for decision making
- Other relevant key criteria such as disease severity, burden of the disease in a population, and the availability of other preventive measures
- Due to strong residual confounding in most of the identified studies, the available evidence is insufficient to determine the magnitude of benefit that diabetic people derive from seasonal influenza vaccination.



## **Effectiveness of the influenza vaccine in preventing admission to hospital and death in people with type 2 diabetes**

**People with type 2 diabetes may derive substantial benefits from current vaccines, including protection against hospital admission for some major cardiovascular outcomes and underlines the importance of influenza vaccination as part of comprehensive secondary prevention in this high-risk population.**

# Influenza vaccination in diabetes patients

Age group	Dosage (ml)	Number of doses	Route
6–35 months	0.25	2 doses at the first time* 1 dose annually	IM
3–8 years	0.50	2 doses at the first time* 1 dose annually	IM
≥9 years	0.50	1 dose annually	IM

\*Children 6 months through 8 years of age receiving influenza vaccine for the first time should receive two doses administered at least 1 month apart

**The recommendation of compulsory immunization with anti-influenza vaccines is essential because of their impact on the reduction of respiratory infections, the number and length of hospitalizations and the number of deaths related to respiratory tract diseases.**

# Predictors of the antibody response to influenza vaccination in older adults with type 2 diabetes

- Older adults with well-controlled T2DM mount antibody responses to influenza vaccination similar to those of healthy age-matched controls
- Less frailty and improved control of diabetes may be the important determinants of vaccine responsiveness
- The study suggests that influenza vaccine should be administered to elderly patients with T2DM

# South Asian Recommendations for Vaccination Against Seasonal Influenza

- Every one with diabetes over the age of six month are strongly advised to maintain good glycemic control and to take influenza vaccination yearly for minimizing infective episodes, except who are allergic to eggs.
- Influenza immunization is strongly recommended yearly in all people with diabetes with renal failure, immunocompromised state due to concomittant illness and comorbidities, chronic respiratory diseases like bronchial asthma and COPD, smokers, poor hygenic conditions (like slum dwellers) and those who frequently travel to high risk areas.
- In younger persons with diabetes (18-50 years) counseling should be done about influenza vaccination. People with diabetes with long duration of disease and poor control have greater susceptibility to infection by Influenza virus hence should be vaccinated
- Elderly people with diabetes above 50 years of age and with co-morbidities should be strongly motivated for mandatory vaccination against influenza.

Thank you!

Email: [drjayantpanda@gmail.com](mailto:drjayantpanda@gmail.com)  
Mobile: 9437028282