Background:

- Persons living with diabetes experience high rates of cardiovascular disease, microvascular complications, and neurovascularities, and are at greater risk of serious complications leading to hospitalization and death due to influenza infection compared to non-diabetic population.
- The WHO and multiple National Immunization Technical Advisory Groups recommend seasonal influenza vaccination for persons with diabetes, recommendations that are supported by 38% reduction of mortality and 23% reduction of hospitalization in elderly patients, and 58% hospitalization reduction in non-elderly patients.
- Despite recommendations from global health authorities to administer influenza vaccines annually to all diabetic patients, coverage is often suboptimal, reaching 75% target as recommended by the European Union Council, with vaccination rates even decreasing over time in some countries worldwide.
- This work represents the first major systematic review and meta-analysis of influenza vaccination uptake in the diabetes population, and qualifies the evidence gap in this population.

Methods:

- A systematic literature review was conducted using predefined criteria for population, intervention, comparator, outcome, timing, setting, and study design (PICTOS) criteria to identify and include eligible studies (Table 1).
- Medline (PubMed), Embase (OVID), Cochrane CENTRAL, and Medline (PubMed) databases were searched using specific terms to identify and include eligible studies (Table 1).
- Data extraction was conducted using the DCMC Data Version 2.0 software platform (Doctor Evidence, LLC, Santa Monica, CA, USA) and its universal electronic extraction form, based on a standardized data configuration protocol. Each collected data point was extracted by two highly trained and proctored evidence analysts. All terms (characteristics and outcomes) were collected as reported in each paper and the coordinate points were “bound” before analysis using the DCMC Ontology System.
- Analyses tested the effect of age, sex, and previous vaccination as predictors of vaccination rates.

Table 1.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Eligible Studies (n)</th>
<th>Excluded Studies (n)</th>
<th>Reasons for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Sex</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Previous vaccine</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Diabetes</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Socioeconomic</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Education</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Income</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Eligibility</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Setting</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Study design</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Compliance</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Randomization</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Enrollment</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
<tr>
<td>Follow-up</td>
<td>53</td>
<td>11</td>
<td>Not available</td>
</tr>
</tbody>
</table>

- The association of any baseline patient characteristics on receipt of influenza vaccination was assessed in a univariate or multivariate model.

Results:

- A search of 736 unique references yielded 51 studies meeting PICTOS criteria for predictors. Of the 51 studies, 16 were analyzed for the most common predictors (Figure 1).

Socioeconomic Factors

- Patients who were low-income and had diabetes were significantly less likely to receive the influenza vaccine than high-income patients with diabetes (Odds Ratio 0.79; 95% CI 0.87-0.94, p < 0.0001) (Figure 3).
- Patients who had less than a high school education and had diabetes were significantly less likely to receive the influenza vaccine than persons with more than a high school education (Odds Ratio 0.87; 95% CI 0.82-0.93, p < 0.0001) (Figure 3).

Comorbidity Factors

- Patients who had cancer and had diabetes were significantly more likely to receive the influenza vaccine than diabetes patients without cancer (Odds Ratio 1.22; 95% CI 1.01-1.47, p = 0.0417) (Figure 4).
- Patients who had respiratory disease and had diabetes were significantly more likely to receive the influenza vaccine than diabetes patients without respiratory disease (Odds Ratio 1.60; 95% CI 1.23-2.09, p = 0.0005) (Figure 5).
- Patients with cardiovascular disease and diabetes were significantly more likely to receive the influenza vaccine than patients without cardiovascular disease (Odds Ratio 1.62; 95% CI 1.45-1.81, p<0.001) (Figure 6).

Other Factors

- Of patients who had received an influenza vaccination in a previous season, 90.2% (90.0-90.4) were vaccinated again during the current study period (Figure 7).
- Persons with diabetes aged >=65 had a significantly greater rate of influenza vaccine uptake than younger adults with diabetes (Odds ratio 2.57, 95% CI 1.99 to 3.31, p<0.001) (Figure 8).

Applications for Healthcare Practitioners:

- Patients with diabetes are at increased risk for complications resulting from influenza, including mortality and hospitalization.
- Within the diabetic population, there are certain groups that are less likely to become vaccinated, including younger patients, those with less education, and those with lower income.
- These patients may require particular attention with regard to influenza vaccine education and outreach, including improved knowledge of the risks of influenza with diabetes.

Conclusions:

- This first ever systematic review of predictors of influenza vaccination in patients with diabetes identified similar factors to patients without diabetes reported in the literature.
- Several significant predictors for influenza vaccine in patients with diabetes, including socioeconomic factors (lower income and education), comorbidities (cancer, respiratory disease, and cardiovascular disease), and age, were associated with influenza vaccination uptake in this population.
- Similar factors have been found to influence the general population as well as persons with diabetes, including age and education.
- A better understanding of holistic predictors will inform interventions to increase influenza vaccination in patients with diabetes. Because these predictors (socioeconomic, comorbidity, and age) affect patient health at large, interventions and educational programs that target these groups (e.g. low-income patients) could be extended to include influenza vaccination.
- These conclusions are limited by those data that have been published, which contain a certain amount of heterogeneity and inconsistency. Further investigation with large randomized trials with borderline significance (cancer and cardiovascular disease) is necessary to confirm the effect of these risk factors regarding influenza vaccine uptake.

Limitations:

- The literature available for analysis is limited to select countries, as influenza vaccination is not consistently reported around the world.
- As this analysis is limited by the available literature, there is the possibility that other predictors exist that have not yet been explored and/or published.

References:

8. Favors less than high school Favors more than high school
9. Favors no cardiovascular disease Favors cardiovascular disease Favors <65 years Favors >= 65 years
10. Patients who had cancer and had diabetes were significantly more likely to receive the influenza vaccine than diabetes patients without cancer (Odds Ratio 1.22; 95% CI 1.01-1.47, p = 0.0417) (Figure 4).
11. Patients who had respiratory disease and had diabetes were significantly more likely to receive the influenza vaccine than diabetes patients without respiratory disease (Odds Ratio 1.60; 95% CI 1.23-2.09, p = 0.0005) (Figure 5).
12. Patients with cardiovascular disease and diabetes were significantly more likely to receive the influenza vaccine than patients without cardiovascular disease (Odds Ratio 1.62; 95% CI 1.45-1.81, p<0.001) (Figure 6).
13. Patients with diabetes aged >=65 had a significantly greater rate of influenza vaccine uptake than younger adults with diabetes (Odds ratio 2.57, 95% CI 1.99 to 3.31, p<0.001) (Figure 8).
14. This work represents the first major systematic review and meta-analysis of influenza vaccination uptake in the diabetes population, and qualifies the evidence gap in this population.

Disclosures:

The study was sponsored by Sanofi. Jan Liska, Olivia Banyon, Sandrine Samson, and Anne C. Beal are employed by Sanofi. Tobias Sayre and Roshan Shah report employment by Doctor Evidence, who is contracted by Sanofi.

Figures:

- Figure 1. PRISMA diagram showing study selection process for predictors of vaccine uptake.
- Figure 2. Vaccine uptake in patients with low-income vs. high-income.
- Figure 3. Vaccine uptake in patients with more or less than high school education.
- Figure 4. Vaccine uptake in patients with cancer vs. no cancer.
- Figure 5. Vaccine uptake in patients with respiratory disease vs. no respiratory disease.
- Figure 6. Vaccine uptake in patients with cardiovascular disease vs. no cardiovascular disease.
- Figure 7. Proportion of patients receiving vaccination who were vaccinated again.
- Figure 8. Vaccine uptake in patients >=65 vs. <65.