



## Survey of vaccination practices in patients with diabetes: A report examining patient and provider perceptions and barriers



Carlos E. Alvarez<sup>a</sup>, Luciana Clichici<sup>a</sup>, Angela Patricia Guzmán-Libreros<sup>a</sup>, Mariola Navarro-Francés<sup>a</sup>, Javier Ena<sup>b,\*</sup>

<sup>a</sup> Centro de Salud de Alfaz del Pi, Alicante, Spain

<sup>b</sup> Hospital Marina Baixa, Villajoyosa, Alicante, Spain

### ARTICLE INFO

#### Article history:

Received 13 May 2017

Received in revised form 19 June 2017

Accepted 21 June 2017

#### Keywords:

Diabetes

Vaccine

Seasonal influenza vaccine

Pneumococcal vaccine

Hepatitis B vaccine

### ABSTRACT

In a cross-sectional study involving 279 patients with diabetes attending a primary care center the proportion of patients vaccinated for seasonal influenza, pneumococcus and hepatitis B was 40%, 2% and 2%, respectively. We found significant barriers for vaccination in 24% of patients and in 42% of providers.

© 2017 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Diabetes is one of the leading causes of morbidity and mortality in the world. Although prevention and treatment of cardiovascular complications is well established, there is less robust information on the prevention of infectious complications in patients with diabetes. Like the general population, children and adults with diabetes must complete the mandatory vaccination schedule according to age-related recommendations [1,2]. In addition, annual vaccination against influenza is recommended for all persons with diabetes equal or greater than 6 months of age [3]. In the case of influenza, patients with diabetes have been found to have a fourfold higher risk of death from influenza than the general population adjusted for age [3]. Case-control studies show that influenza vaccine reduces hospital admissions of patients with diabetes by up to 79% during influenza epidemics [4]. Like influenza, pneumococcal pneumonia is a preventable disease and in patients with diabetes the incidence of pneumococcal bacteremic pneumonia is higher than the general population, with mortality rates as high as 50% [5]. The US Centers for Disease Control and Prevention (CDC) recommends vaccination against pneumonia for all people with diabetes 2 through 64 years of age with 23-valent pneumococcal polysaccharide vaccine (PPSV23). In patients aged 65 years or older it is recommended the 13-valent pneumococcal conju-

gated vaccine (PCV13), that it should be administered at least 1 year after the PPSV23 vaccine [1]. On the other hand, hepatitis B virus vaccination is also recommended by the US Centers for Disease Control and Prevention to unvaccinated adults with diabetes mellitus due to higher rates of infection and progression to cirrhosis than in the general population [6]. For these reasons we wanted to review the proportion of patients with diabetes who have a history of vaccination against influenza, PPCV23 and hepatitis B virus in our health area. Moreover, we wanted to know the possible barriers, either by the patients or by the health-care professionals that make difficult the administration of such vaccines.

We carried out a cross-sectional study at a primary care health center located in Alfaz del Pi in the province of Alicante (Spain), serving a population of 21,700 inhabitants of the Spanish National Health System, of which approximately 1757 adult patients have known diabetes. Since the coverage probability for influenza in Spain is around 56%, a 2-sided 95% confidence interval with  $\pm 6\%$  precision gives an effective sample size  $n \geq 230$ .

The study was conducted between October and December 2016. A total of 279 consecutive adult patients with diabetes seen at the primary care center gave their informed consent for data collection. The study was approved by the Institutional Review Board of our Center. Data collected for the analysis were age, sex, cigarette smoking, history of cardiovascular or cerebrovascular disease, chronic kidney disease, chronic respiratory disease, hospital admission in the last 12 months and the most recent

\* Corresponding author at: Servicio de Medicina Interna, Hospital Marina Baixa, Av Alcalde Jaime Botella Mayor, 7, 03570 Villajoyosa, Alicante, Spain.

E-mail address: [ena\\_jav@gva.es](mailto:ena_jav@gva.es) (J. Ena).

HbA1c value. The use of seasonal influenza, PPSV23 and hepatitis B vaccine for every patient included in the study was assessed through electronic health record review. A survey of attitudes about vaccination inquiring about vaccine safety and perception of effectiveness was carried out among patients and health care workers.

Patients included in the study had a mean age of 67 years, being 54% male and 25% presenting with severe comorbidity. A proportion of 15% of patients had suffered hospitalization in the last 12 months. A total of 57 (20%) received insulin treatment. The mean value of HbA1c was 7.0% (Table 1).

The proportion of patients vaccinated with seasonal influenza, PPSV23 and hepatitis B vaccines were 40%, 2% and 2%, respectively. There was a higher frequency of influenza vaccination in subjects older than 65 years, but vaccination was not associated with smoking, presence of cardiovascular, respiratory or renal comorbidity, recent hospitalization, poor glycemic control nor insulin use (Table 1). PPSV23 and hepatitis B vaccinations were anecdotal precluding any statistical analysis.

Regarding beliefs and attitudes for vaccination, a total of 67 (24%) of the patients did not believe in the effectiveness of the vaccination or feared side effects. However, there were only 4 (1%) patients who experienced mild adverse reactions to influenza vaccination. As for health-care workers (n = 12), only 7 (58%) had been vaccinated against seasonal influenza in the previous year. In the primary care center influenza vaccination had been promoted with advertising posters, but the same was not the case for PPSV23 or hepatitis B vaccine. All studied vaccines are administered at no cost for patients belonging to the Spanish National Health System.

In our study we observed low vaccine coverage against influenza virus in patients with type 2 diabetes. The rate of PPSV23

and hepatitis B vaccination was practically anecdotal. The results obtained are even lower than a study of similar characteristics carried out in a public hospital in the United States in which the proportion of vaccine coverage against influenza, PPSV23 and hepatitis B, was 41%, 37% and 39% [7]. In a nationwide study in the United States, vaccination coverage for influenza, PPSV23, and hepatitis B in patients with diabetes was 62%, 53%, and 17%, respectively [8]. Failure to immunize patients with diabetes with pneumococcal and hepatitis B vaccine are probably unawareness of vaccination recommendations for this population in spite of the position of the US Centers for Disease Control and Prevention. The International Diabetes Federation did not establish a level of recommendation for vaccine preventable diseases [9]. The American Diabetes Association categorized recommendation for immunization in patients with diabetes as level of evidence C (conflicting evidence with the weight of evidence supporting the recommendation) [10]. Such level of evidence for pneumococcal vaccine probably was based on a randomized trial in which the 14-valent pneumococcal polysaccharide vaccine showed lack of efficacy in US Veterans [11]. However, the 13-valent pneumococcal conjugate-vaccine showed recently a vaccine efficacy of 89% in patients with diabetes [12]. Similarly, a meta-analysis of 17 studies (only 2 randomized trials) showed that hepatitis B vaccine produced seroprotection proportions from 31.3 to 100.0% (median, 73.4%) among persons with diabetes and 35.2 to 100.0% (median, 87.1%) for those without diabetes [13]. This wide range of seroprotection variation was due to different vaccine dosage (from 3 to 40 µg) and schedules (from 0-, 1-, and 2-month schedule to 0-, 1-, 2-, and 12-month schedule). It was confirmed that administration of 4th additional hepatitis B vaccine dose improved immune response among adults with diabetes. Douvin et al. [14] reported seroprotective anti-HBs levels in 91.5% when using a 20µg vaccine dosage.

**Table 1**  
Characteristics of patients included in the study.

	All patients (N = 279)	Influenza Vaccination YES(N = 112)	Influenza Vaccination NO (N = 167)	P value	PPSV23 vaccination YES(N = 6)	PPSV23 vaccination NO(N = 273)	P value	Hepatitis B vaccination YES(N = 5)	Hepatitis B vaccination NO (N = 274)	P value
Age (years)	67.3 ± 12.3	71.8 ± 9.9	64.4 ± 12.8	<0.001	74.3 ± 12.8	67.2 ± 12.3	0.157	70.20 ± 5.4	67.2 ± 12.4	0.596
Age ≥ 65 years	179 (64)	85 (76)	94 (56)	<0.001	5 (83)	174 (64)	0.610	4 (80)	175 (64)	0.822
Age < 65 years	100 (36)	25 (22)	75 (45)		1 (17)	99 (36)		1 (20)	99 (36)	
Sex (%)				0.543			0.573			0.492
Male	152 (54)	64 (57)	88 (53)		4 (67)	148 (54)		4 (80)	148 (54)	
Female	127 (46)	48 (43)	79 (47)		2 (33)	125 (46)		1 (20)	126 (46)	
Smoker (%)				0.341			0.473			0.286
Yes	59 (21)	20 (18)	39 (23)		0	59 (22)		2 (40)	57 (21)	
No	220 (79)	92 (82)	128 (77)		6 (100)	214 (78)		3 (60)	217 (79)	
Comorbidity (%)										
Stroke	33 (12)	12 (11)	11 (7)	0.314	1 (17)	32 (12)	1.000	0	33 (2)	1.000
Coronary artery disease	69 (25)	31 (28)	38 (23)	0.169	2 (33)	67 (24)	0.921	1 (20)	68 (25)	1.000
COPD	42 (15)	18 (16)	24 (14)	0.734	2 (33)	40 (15)	0.447	0	42 (15)	0.879
Chronic kidney disease	34 (12)	14 (13)	20 (12)	1.000	1 (17)	33 (12)	1.000	1 (20)	34 (12)	1.000
Hospital admission in the past 12 months (%)				0.613			0.098			1.000
Yes	43 (15)	19 (17)	24 (14)		3 (50)	40 (15)		1 (20)	42 (15)	
No	236 (84)	93 (83)	143 (86)		3 (50)	233 (85)		4 (80)	232 (85)	
Treatment with insulin (%)				0.001			0.711			0.547
Yes	57 (20)	20 (18)	37 (22)		2 (33)	55 (20)		2 (40)	55 (20)	
No	222 (80)	92 (82)	130 (78)		4 (67)	218 (80)		3 (60)	219 (80)	
HbA1c (%)	7.0 ± 1.4	7.1 ± 1.5	6.8 ± 1.3	0.101	7.9 ± 2.5	6.9 ± 1.4	0.085	7.4 ± 1.9	7.0 ± 1.4	0.519
HbA1c (mmol/mol)	53 ± 7.0	54 ± 7.5	51 ± 6.5		63 ± 12.5	52 ± 7.0		57 ± 9.5	53 ± 7.0	
HbA1c ≥ 7% (53.0 mmol/mol)	92 (48)	47 (42)	45 (27)	0.009	3 (50)	89 (33)	0.623	2 (40)	90 (33)	1.000
HbA1c < 7% (53.0 mmol/mol)	187 (52)	65 (58)	122 (73)		3 (50)	184 (67)		3 (60)	184 (67)	

COPD: Chronic obstructive pulmonary disease. PPSV23: 23-valent pneumococcal polysaccharide vaccine. The results are expressed as mean ± SD or frequency (percentage).

Since data from studies suggest that adults with diabetes have a reduced response to vaccination, administration of a double strength vaccine (40 µg per dose) or extending the interval to the final 4th dose (using 20µg per dose) may achieve seroprotection in most adults with diabetes.

In parallel to the lack of unequivocal support by scientific associations for diabetes, we have found significant attitude barriers in patients and health-care workers for vaccination against these preventable diseases.

Multiple strategies have been proposed in order to increase vaccine coverage in at-risk populations. But foremost, significant national and international scientific associations for the study of diabetes should modify their position regarding the strength of recommendations for vaccination. At a local level, the strategies that have proven to be useful to increase the vaccination rates have been the use of memory systems for prescribing physicians through medical records or electronic records. Reminders increased the percentage of vaccination rate by an average of 22 points [15].

In summary, we observed very low vaccine coverage rate against preventable diseases in patients with type 2 diabetes. The lack of full support for vaccine recommendation in standards of care and guidelines of well known scientific associations for diabetes constitute an important barrier. In addition, among patients and health-care workers there is a belief that vaccines are infective or cause significant adverse effects. Since convincing effectiveness is essential in prescribing physicians, it is necessary to implement guideline modification, and incorporate the most updated information on the efficacy and safety of vaccines. Subsequently, the use of recall systems in electronic history could improve adherence rates to vaccination.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Conflicts of interest

None.

## References

- [1] Kim DK, Bridges CB, Harriman KH, Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) ACIP Adult Immunization Work Group. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older United States, 2015. *MMWR Morb Mortal Wkly Rep* 2015;64:91–2.
- [2] Ministerio de Sanidad, Servicios Sociales e Igualdad. Recomendaciones de vacunación en adultos año 2004. In: <https://www.msssi.gob.es/ciudadanos/proteccionSalud/vacunaciones/docs/recoVacunasAdultos.pdf>. Access March 17, 2017.
- [3] Valdez R, Narayan KM, Geiss LS, Engelgau MM. Impact of diabetes mellitus on mortality associated with pneumonia and influenza among non-Hispanic black and white US adults. *Am J Public Health* 1999;89:1715–21.
- [4] Colquhoun AJ, Nicholson KG, Botha JL, Raymond NT. Effectiveness of influenza vaccine in reducing hospital admissions in people with diabetes. *Epidemiol Infect* 1997;119:335–41.
- [5] Smith SA, Poland GA. Use of influenza and pneumococcal vaccines in people with diabetes. *Diabetes Care* 2000;23:95–108.
- [6] Centers for Disease Control and Prevention. Use of hepatitis B vaccination for adults with diabetes mellitus: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2011;60:1709–11.
- [7] Alcusky MJ, Pawasauskas J. Adherence to guidelines for hepatitis B, pneumococcal, and influenza vaccination in patients with diabetes. *Clin Diab* 2015;33:116–22.
- [8] Villarroel MA, Vahratian A. Vaccination coverage among adults with diagnosed diabetes: United States, 2015. NCHS data brief, no. 265. Hyattsville, MD: National Center for Health Statistics. 2016. In: <https://www.cdc.gov/nchs/data/databriefs/db265.pdf>. Access March 17, 2017.
- [9] Dunning T, Sinclair A, Colagiuri S. New IDF guideline for managing type 2 diabetes in older people. *Diabetes Res Clin Pract* 2014 Mar;103(3):538–40.
- [10] American Diabetes Association. Standards of Medical Care in Diabetes-2017. Comprehensive Medical Evaluation and Assessment of Comorbidities. *Diabetes Care* 2017;40(Suppl 1):S25–32.
- [11] Simberkoff MS, Cross AP, Al-Ibrahim M, Baltch AL, Geiseler PJ, Nadler J, et al. Efficacy of pneumococcal vaccine in high-risk patients. Results of a Veterans Administration Cooperative Study. *N Engl J Med* 1986;315:1318–27.
- [12] Huijts SM, van Werkhoven CH, Bolkenbaas M, Grobbee DE, Bonten MJM. Post-hoc analysis of a randomized controlled trial: Diabetes mellitus modifies the efficacy of the 13-valent pneumococcal conjugate vaccine in elderly. *Vaccine* 2017;30:151–2. <http://dx.doi.org/10.1016/j.vaccine.2017.01.071>. pii: S0264-410X(17)30151-2. [Epub ahead of print] PubMed PMID 28410813.
- [13] Schillie SF, Spradling PR, Murphy TV. Immune response of hepatitis B vaccine among persons with diabetes: a systematic review of the literature. *Diabetes Care* 2012;35:2690–7.
- [14] Douvin C, Simon D, Charles MA, Deforges L, Bierling P, Lehner V, et al. Hepatitis B vaccination in diabetic patients. Randomized trial comparing recombinant vaccines containing and not containing pre-S2 antigen. *Diabetes Care* 1997;20:148–51.
- [15] Willis BC, Ndiaye SM, Hopkins DP, Shefer A, Task Force on Community Preventive Services. Improving influenza, pneumococcal polysaccharide, and hepatitis B vaccination coverage among adults aged years at high risk: a report on recommendations of the Task Force on Community Preventive Services. *MMWR Recomm Rep* 2005;54(RR-5):1–11.