

The effect of physicians' awareness on influenza and pneumococcal vaccination rates and correlates of vaccination in patients with diabetes in Turkey

An epidemiological Study "diaVAX"

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Abbreviations: ACIP, Advisory Committee on Immunization Practices; ADA, American Diabetes Association; CCHS, Canadian Community Health Survey; IPD, invasive pneumococcal disease; MoH, Ministry of Health; NICS, National Immunization Coverage Survey; NVAC, National Vaccine Advisory Committee; OAD, oral anti-diabetic drug; SEMT, Society of Endocrinology and Metabolism of Turkey; TIHUD, Turkish Association of Internal Medicine Specialists; WHO, World Health Organization.

We aimed to examine the effect of increased physician awareness on the rate and determinants of influenza and pneumococcal vaccinations in diabetic patients. Diabetic patients (n = 5682, mean [SD] age: 57.3 [11.6] years, 57% female) were enrolled by 44 physicians between Sept 2010 and Jan 2011. The physicians were initially questioned regarding vaccination practices, and then, they attended a training program. During the last five years, the physicians recommended influenza and pneumococcal vaccinations to 87.9% and 83.4% of the patients, respectively; however, only 27% of the patients received the influenza and 9.8% received the pneumococcal vaccines. One year after the training, the vaccination rates increased to 63.3% and 40.7%, respectively. The logistic regression models revealed that variables which increased the likelihood of having been vaccinated against influenza were: longer duration of diabetes, presence of hyperlipidemia and more use of concomitant medications whereas more use of anti-hyperglycemic medications was associated with increased odds of vaccination. On the other hand, older age, longer duration of diabetes and presence of a cardiovascular disease were variables which decreased the likelihood of having been vaccinated against pneumococcal disease during the past five years. However, during the study period, variables which decreased the odds of having been vaccinated included: older age and anti-hyperglycemic medications for influenza, and presence of hyperlipidemia and a family history of hypertension for pneumococcal disease. While variables which increased the likelihood of vaccination in the same period were: increased number of co-morbidities for influenza, and family history of diabetes for pneumococcal disease. We conclude that increased awareness of physicians may help improve vaccination rates against influenza and pneumococcal disease. However, diabetic patients with more severe health conditions are less likely to having been vaccinated. More structural/systematic vaccination programs are needed to increase the vaccination rates in patients with diabetes.

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Introduction

Immunization is one of the most effective public health interventions, which reduces or eliminates the burden of many infectious diseases; however, adult immunizations generally remain well below proposed levels, even in developed countries.¹ In the Canadian Community Health Survey (CCHS) 2009/2010, the coverage for influenza vaccination was 28.8% in individuals aged over 12 y, and 62.9% in those over 64 y.² According to the data from The Center for Disease Control and Prevention in the US, the vaccination coverage for influenza in the 2009/2010 season was similarly low (41.2% for all ages, and 69.6% for those 64 y and older).³

Various publications have reported that vaccination of patients with diabetes against influenza has been effective in reducing the hospital admissions during influenza epidemics.⁴⁻⁶ Studies show that the pneumococcal vaccine is also effective in reducing the burden of invasive pneumococcal disease (IPD).⁴

According to the Advisory Committee on Immunization Practices (ACIP)⁵ and the American Diabetes Association (ADA),⁶ vaccinating individuals at high risk just before the influenza season each year and the use of the pneumococcal vaccine at least once in a lifetime are the most effective measure in reducing the impact of influenza and IPD. The effective implementation of immunization can reduce the cost of human suffering and community healthcare expenditure in diabetic patients.^{5,6} The current influenza vaccination coverage among individuals with diabetes in our country is far below the recent recommendation goals set by the 'US. National Vaccine Advisory Committee (NVAC: 90% for high risk individuals of all ages and for all individuals > 64 y of age)⁷ and the World Health Organization's (WHO) new Global Vaccine Plan (90% vaccination coverage in all countries by 2015).⁸

The Society of Endocrinology and Metabolism of Turkey (SEMT)'s diabetes guidelines recommend the influenza vaccination on a yearly basis and pneumococcal vaccination once in a lifetime for diabetes patients.⁹ Pneumococcal revaccination is advised in individuals over 65 y of age if the initial vaccination were performed when they were younger than 65, and more than a five-year period has elapsed since the previous vaccination.⁹ Additionally, an effective reimbursement system is in place for both vaccinations by the Social Security Organization, recommended by the Turkish Ministry of Health (MoH) since 2008, as per current practice in 22 European countries.¹⁰⁻¹²

A recent inquiry by the Turkish Association of Internal Medicine Specialists (TIHUD)—Aegean Study Group, which enrolled 12,235 patients with diabetes, demonstrated that the vaccination rates with pneumococcal and influenza vaccines were very low, being 0.1% and 9.1%, respectively (Unal S. 2011, Personal correspondence).¹³ Despite all efforts, the vaccination rates with the pneumococcal and influenza vaccines remained at low rates in diabetic patients in Turkey, suggesting the need for awareness for immunization in this vulnerable population.

In this epidemiological (diaVAX) study which designed with a non-randomized control group before and after the study, we aimed to examine the effect of a physician training program on

the recommendation and the uptake rates and determinants of influenza and pneumococcal vaccinations in adult patients with diabetes in Turkey. The primary objective was to investigate whether increased physician's awareness can increase the influenza and pneumococcal vaccination rates in patients with diabetes. The secondary objectives were: (1) to determine the factors affecting the physicians' decision on offering influenza and pneumococcal vaccinations in patients with diabetes in the past five years and during the study period, (2) to investigate whether the attitudes of physicians toward influenza and pneumococcal vaccinations could be changed one year after a short training program, and (3) finally, to investigate whether or not there was a relationship between the physicians' self-vaccination against influenza and the vaccination recommendations to their patients with diabetes.

Results

Patient demographics

The demographic characteristics of the study group have been presented in **Table 1**. The study population comprised 5,682 patients > 18 y of age with the diagnosis of type 1 (n = 237) or type 2 diabetes (n = 5,445). The mean (SD) age of the patients was 57.3 (11.6) years, and 57.1% of the patients were female. The mean (SD) duration of diabetes was 8.8 (6.8) years. All of the type 1 diabetes patients were on basal-bolus insulin therapy. The majority of type 2 diabetes patients were under treatment with at least one oral anti-diabetic drug (OAD; 65.5%); metformin (96.4%) was the most frequently used OAD. Sulphonylureas were the most frequently used second add-on drug at a rate of 41.3%, followed by thiazolidinediones at 19.4%, and glinides at 14.9%. Of type 2 diabetes patients, 29.1% were on insulin (28.9% insulin alone and 71.1% combined with OAD), and 5.4% were on a diet only.

The diabetic complications were also questioned; at least one complication was present in 1622 patients (28.5%); retinopathy (41.3%) and peripheral polyneuropathy (39.5%) were the most frequently recorded diabetic complications. The number of patients with two (3.0%) or three (0.5%) diabetic complications was scarce.

The majority of the enrolled patients (61.3%) had at least one co-morbid condition such as hypertension, hyperlipidemia or cardiovascular disease. Of the enrolled patients, 29.7% had only one comorbidity, 20.7% had two and 10.9% had three or more co-morbidities. Anti-hypertensive drugs were the most frequently used medications, followed by lipid-lowering and anti-thrombocyte drugs. Family history was questioned; almost two-thirds of the patients reported hypertension, half of them reported hyperlipidemia and 75% reported diabetes in the family.

Vaccination rates

The data revealed that the participating physicians had recommended influenza and pneumococcal vaccinations to 87.9% and 83.4% of their diabetes patients, respectively during the last five years, but 27% of these patients had received influenza and only 9.8% had received pneumococcal vaccines. During the study period, the physicians had recommended influenza and

Table 1. General demographics and clinical features

	MEN (n = 2438)	WOMEN (n = 3244)	P value
Age (yrs)	57.0 (11.4)	57.5 (11.7)	0.040
Diabetes duration (yrs)	8.5 (7.0)	9.0 (6.9)	< 0.001
BMI (kg/m ²)	28.10 (3.98)	30.53 (5.38)	< 0.001
Waist (cm)	99.7 (11.8)	100.9 (13.9)	< 0.001
Treatment of type 2 DM (%)			
Diet only	5.8	5.0	< 0.001
OADs	69.1	61.9	
Insulin	8.7	8.2	
OAD + Insulin	16.5	24.9	
Microvascular complications (%)			
No complication	73.3	69.7	< 0.001
One complication	22.6	27.4	
Multiple complications	4.2	2.9	

Data are given “mean (SD)” unless otherwise indicated. BMI, body mass index; DM, diabetes mellitus; OAD, oral anti-diabetic drug.

pneumococcal vaccines to 97.6% and 95.1% of the patients, respectively. However, the vaccination uptake rate by the patients was 63.3% for influenza and 40.7% for IPD (Fig. 1). There was a significant association between the rates of two vaccinations ($P < 0.001$).

Vaccination coverage rates of influenza and IPD during the past five years and in the study period were evaluated according to the most relevant variables as shown in Table S1. No gender difference was observed in the rate of influenza or pneumococcal vaccination except that a slightly higher rate of female had received influenza vaccine during the study period ($P = 0.035$). During the past five years the frequency of older patients (≥ 65 y) who received influenza and pneumococcal vaccines was higher than those < 65 y of age ($P < 0.001$ for both). This trend continued during the study period for pneumococcal vaccine only ($P = 0.002$). Patients with longer duration of diabetes were more likely to having been vaccinated for influenza ($P < 0.001$) and IPD ($P < 0.001$). The mean duration of diabetes was significantly longer in patients who had received influenza (10.2 vs. 8.2 y, $P < 0.010$) and pneumococcal vaccines (10.4 vs. 8.6 y, $P < 0.010$) during the last five years, a fact that was not observed during the study period (data not shown).

During the study period diabetic patients who used more than three anti-diabetic medications were more likely to having been vaccinated for influenza ($P = 0.001$) and IPD ($P < 0.001$). Whereas in the same period patients who used less number of concomitant medications were more frequently to having been vaccinated for IPD ($P = 0.033$) but not for influenza.

The uptake of influenza vaccination was significantly increased as the number of co-morbidities and the number of anti-hyperglycemic medications increased ($P < 0.001$ for both), whereas the uptake of pneumococcal vaccination was correlated with the presence of cardiovascular disease only ($P = 0.002$). Patients with family history of diabetes were less frequently to having been

vaccinated against influenza during the past five years, the same trend was observed for IPD during the study period. Similarly, during the same period patients with family history of hyperlipidemia received vaccination against influenza less frequently than those who had other diseases in their family (Table S1).

Patients who had received influenza and pneumococcal vaccination in the past five years had a significantly higher mean number of co-morbid conditions (vaccinated vs. not-vaccinated; influenza vaccine 1.83 vs. 1.69, $P < 0.010$; pneumococcal vaccine 1.90 vs. 1.71, $P = 0.020$), which persisted during the study period (influenza: $P = 0.019$, IPD: $P < 0.001$; data not shown).

For the previous five years, the logistic regression model revealed that the duration of diabetes, the number of concomitant medications and the presence of hyperlipidemia were inversely and significantly associated factors, while the number of anti-diabetic medications was the only positive factor linked to being vaccinated for influenza. Accordingly, every single year of increase in diabetes duration, every single increase in the number of concomitant medications, and the presence of hyperlipidemia were associated with a 5%, 8%, and 28% decrease in the odds of vaccination against influenza, whereas every single increase in the number of anti-diabetic medications was linked with a 1.11-fold increase in the odds of influenza vaccination. During the study period, aging and anti-diabetic medications were inversely associated factors, but co-morbidities and a family history of cardiovascular disease were positively associated significant factors with influenza vaccination. In this case, every single year of increase in age and every single increase in the number of anti-diabetic medications were associated with a 2% and 12% decrease, whereas every single increase in the number of co-morbidities and a family history of cardiovascular disease were linked to a 1.16- and 1.27- fold increase in the odds of influenza vaccination (Table 2).

A similar model indicated that in the past five years; aging, diabetes duration and presence of cardiovascular disease were

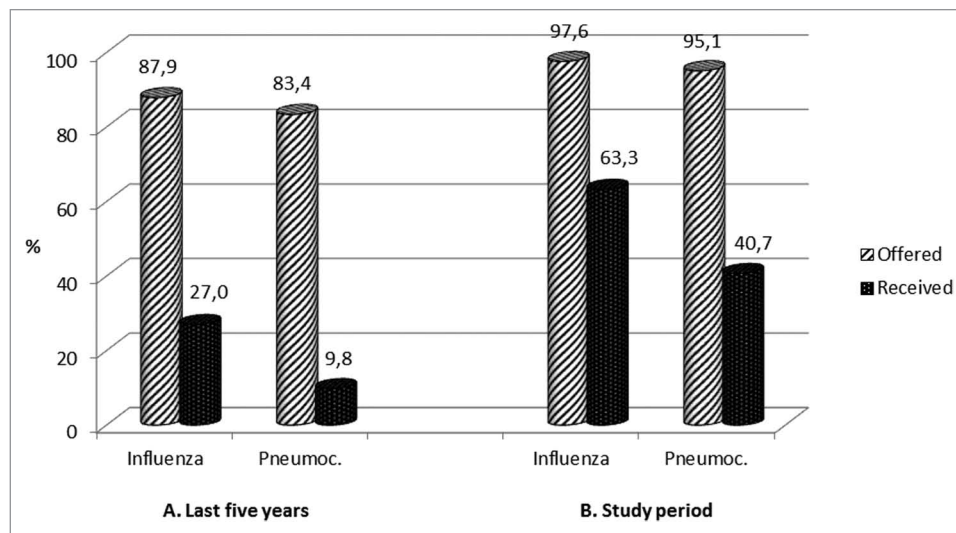


Figure 1. Vaccination coverage within last five years and during the study period.

inversely related factors to having been vaccinated for pneumococcal disease. Correspondingly, every single year of aging, every single year of increase in diabetes duration, and the presence of cardiovascular disease were related to a 1%, 3%, and 23% decrease in the odds of pneumococcal vaccination. However, during the study period, the presence of hyperlipidemia and family history of hypertension were inversely related to having been vaccinated for pneumococcal disease, but the number of comorbidities and family history of diabetes were positively associated factors to having been vaccinated for pneumococcal disease. Thus, hyperlipidemia and a family history of hypertension were associated with a 37% and 21% decrease, whereas every single increase in the number of co-morbid diseases, and a family history of diabetes were linked to a 1.23- and 1.48- fold increase in the odds of pneumococcal vaccination (Table 3).

Physician questionnaire outcomes

The rates of physicians' self-vaccination in this study showed an increasing trend from 41.5% in 2006 to a peak of 78% in 2009 when the influenza vaccination season coincided with the H1N1 pandemic. Nevertheless, the rate of self-vaccination of physicians decreased to 63.4% in 2010. The physicians were also asked regarding the main reasons for not having received the influenza vaccination themselves; the foremost reason appeared as not being in a risk group (17.1%) and not being sure about the safety of the influenza vaccine (9.8%). The self-vaccination of physicians against influenza was associated with prescription of each of the vaccinations for their patients separately. However, this was not a determining factor for prescribing both vaccines together.

In addition, physicians questioned patients who had not received vaccination during the previous year. Strikingly, the patients' own fears and/or hesitations were the most frequent reasons given for not having received the influenza and the pneumococcal vaccines (61% and 53.7%, respectively). In 34.1% of the cases, the out-of-stock status for the influenza vaccine during the H1N1 pandemic was stated as the reason for not having been

vaccinated (14.6% for pneumococcal vaccine). For the influenza vaccine, another 19% of the enrolled patients reported that they neglected in getting the vaccine despite having a prescription (this rate was 17.1% for the pneumococcal vaccine).

Discussion

Vaccination of patients with diabetes against influenza and IPD prevents disease-associated morbidity and mortality, and it is one of the key public health issues in Turkey.

Apart from two studies (Unal S. 2011, Personal correspondence),¹³ one of which has not been published, until recently there have been no significant data regarding the rates of immunization against influenza and pneumococcal vaccines in patients with diabetes in Turkey. A recent study conducted to evaluate the burden of pneumococcal infections suggested that pneumococcal vaccination of elderly and adults at risk is cost-saving in Turkey.¹⁴ Therefore, we chose a non-randomized control group before-and-after study design in order to see the coverage of influenza and pneumococcal disease vaccination in people with diabetes at the baseline, and to compare the differences in vaccination practices if any, a year after the physician training program.

The Canadian Adult National Immunization Coverage Survey (NICS) in 2009 showed low vaccination rates for influenza at all age groups across ethnic populations (34–50%).¹⁵ In a survey, including 11 European countries, the vaccination coverage levels in the general population ranged from 9.5% (Poland) to 28.7% (UK) during the 2007/2008 season. The coverage in the elderly target group was highest at 70.2% in the UK and lowest at 13.9% in Poland.¹⁶ In the US the influenza coverage in the general population aged between 18 and 64 y was only 25% compared with coverage in the elderly population, which was achieved at the level of 67%.⁷

In 2003, the World Health Assembly¹⁷ recommended to increase the seasonal influenza vaccination coverage of the elderly population and all individuals at high risk to at least 75% by

2010. The New Global Vaccine Action Plan was endorsed during the 65th World Health Assembly recommending that all countries should achieve at least 90% coverage of all vaccines at national level by 2015.⁸ According to the recommendations by NVAC in the US, the vaccination coverage of influenza in high risk individuals aged 18–64 y and in all individuals aged > 64 y was aimed to reach 90% each. The corresponding goals for pneumococcal vaccine are 60% and 90%.⁷ However, the baseline (2008) vaccination uptake in high risk individuals between 18–64 y was only 39%, and in older individuals (> 64 y), this rate was 67%. Similarly, the corresponding data from the year 2006 for pneumococcal vaccine uptake revealed 17% and 60%, respectively.⁷ In the above-mentioned multinational European study, the vaccination rate for influenza in the 2007/2008 season in chronically ill individuals (including diabetes mellitus) ranged from 11.1% (Poland) to 56.0% (UK).¹⁶ In Spain, the coverage among adults with diabetes in 2010 was 65.0%, compared with 41.2% for those without diabetes.¹⁸ In a computer-assisted telephone survey performed in Australia, 47% and 31% of high-risk individuals were immunized against influenza and pneumococcus, respectively, and among chronic conditions, only diabetes was found to be associated with having been vaccinated.¹⁹ In parallel with international data, our results confirmed that immunization in the high risk diabetic patient population is still low in Turkey despite the current strict guidelines.

The physician-filled data pointed out that despite the considerably high recommendation rates during the past five years, the vaccination uptake by the patients remained at low levels. Previously, the influenza vaccination rate was very low (27%), in nearly one in every four patients with diabetes; however, this rate was increased to 63.3% during the study period. The pneumococcal vaccination rates were also very low, in nearly one in every 10 patients with diabetes, which has increased 4-fold (from 9.8% to 40.7%). In a study investigating the recommendations and vaccinations for the pneumococcal vaccine, a tracking and reminder system resulted in high vaccination rates, both in the adult population and the elderly with diabetes.²⁰ Another UK study revealed that an educational outreach visit may improve the influenza and pneumococcal vaccination rates in primary care.²¹ Our results were in the same line with the last two studies.

The data have also suggested that various factors carry a negative impact on the prescriptions of influenza and pneumococcal vaccinations in Turkey. It is believed that more complicated or older diabetes patients have more contact with their doctors. Therefore, these patients may have an increased chance of vaccination. In a study investigating the influenza vaccination among the elderly population in Spain, the influenza coverage increased from 50.1% in 1993 to 63.7% in 2003, and to 65% in 2010.²² Elderly age, being male, suffering from a chronic disease, and a visit to the physician in the last two weeks were found to be significantly associated with a higher likelihood of being vaccinated. However, this was not observed in our study. Our results from five years back revealed that those who had more co-morbidities and/or familial risk factors had a lower chance of being vaccinated against influenza or IPD. Although the results in the study period indicated some improvement in the uptake of the

Table 2. Factors associated with influenza vaccination during five years prior to the study and during the study period (multiple logistic regression model)

Associated parameters	p value	OR (95% CI)
A. Previous five years		
DM duration (year)	< 0.001	0.951 (0.938–0.965)
Anti-hyperglycemic medication (n)	0.042	1.111 (1.004–1.230)
Concomitant medication (n)	0.017	0.922 (0.862–0.985)
HL (in patient)	0.001	0.721 (0.592–0.877)
B. During study period		
Age (year)	< 0.001	0.983 (0.976–0.990)
Co-morbidity (n)	< 0.001	1.162 (1.078–1.252)
Anti-hyperglycemic medication (n)	0.003	0.879 (0.807–0.957)
Family history of CVD	0.004	1.269 (1.078–1.494)

Variables entered in the model at step one: age, gender, BMI, duration of DM; HT, CVD and HL (in patient); family history of HT, CVD, HL and DM; number of co-morbidities, anti-hyperglycemic and concomitant medications. CI, confidence interval; DM, diabetes mellitus; n, number; BMI, body mass index; HT, hypertension; CVD, cardiovascular disease; HL, hyperlipidemia.

influenza vaccine in particular, the pneumococcal vaccine is still less likely to be offered to high risk patients with diabetes.

One of the reasons for this paradigm may be connected with the lack of knowledge (unawareness of guidelines or unfamiliarity with recommended practices). Nevertheless, we think that this is not the case in our study. According to the physicians' self-perception questionnaire, 97.6% of participating physicians in our study indicated that they recommend the influenza vaccine to all patients with diabetes. In a Canadian study which examined the influenza and pneumococcal vaccination rates in the elderly population, more than 90% of unvaccinated participants had visited a physician within the past year.²³ In a study looking for the reasons for the low vaccination rate in the elderly in the US, 61% of the patients vaccinated during the previous year had paid multiple visits to physicians.²⁴ Reluctance to change practice (clinical inertia, disbelief in vaccine effectiveness in patients with more severe health conditions, or disagreement with guidelines), time constraints, lacking of effective recall systems to keep track of prescriptions and deficiencies in the healthcare system are some of the barriers affecting the physicians' adherence to guidelines.²⁵ In the above-mentioned US study, it was found that physicians appeared to know the indications for the use of vaccination, but failed to translate this knowledge into clinical practice.²⁴ We also revealed in a previous study that physicians were aware of guidelines for standard care in patients with diabetes, but adherence to these guidelines was poor.²⁵

The physicians' self-vaccination rate may also be related to offering the vaccination to their patients. In the 2005–2006 NICS study in Canada, the physician coverage of the influenza vaccine was close to the vaccination coverage of elderly patients (physicians: 74.3%, patients: 69.9%).²⁶ In a study researching the

Table 3. Factors associated with pneumococcal vaccination within previous five years and during the study period (multiple logistic regression model)

Associated parameters	p value	OR (95% CI)
A. Within previous five years		
Age (year)	0.033	0.989 (0.979–0.999)
DM duration (year)	< 0.001	0.973 (0.958–0.987)
CVD (in patient)	0.046	0.771 (0.598–0.995)
B. During the study period		
Co-morbidity (n)	0.002	1.228 (1.076–1.402)
HL (in patient)	< 0.001	0.633 (0.535–0.750)
Family history of DM	< 0.001	1.483 (1.225–1.795)
Family history of HT	0.013	0.794 (0.662–0.952)

Variables entered in the model at step one: age, gender, BMI, duration of DM; HT, CVD and HL (in patient); family history of HT, CVD, HL and DM; number of co-morbidities, anti-hyperglycemic and concomitant medications. CI, confidence interval; DM, diabetes mellitus; n, number; BMI, body mass index; HT, hypertension; CVD, cardiovascular disease; HL, hyperlipidemia.

attitudes and practices of vaccination among healthcare workers, 51% of the staff were found to have received the influenza vaccine.²⁷ Self-vaccination was associated with recommending the vaccine to patients, and providers who did not believe the vaccine was protective or effective were less likely to recommend it to patients. In our study, the self-vaccination rate of the physician was 63.4% during the study period, and this was closely related to the prescription of each of the vaccinations.

Another important issue is the patients' non-compliance as it has been shown in our study. For several reasons, some of the patients may not get the vaccine shot even if they would have the prescription. In the above-mentioned Canadian study, most vaccinations occurred in a physician's office, suggesting a role for physician advocacy to improve the immunization rates.²³ Furthermore, some of our patients may have been confused due to some debates on the effectiveness of vaccination raised during the H1N1 pandemic a year ago. In the CCHS between 2007/2008 and 2009/2010, the coverage rates for influenza vaccination decreased from 31.6% to 28.8% in individuals aged over 12 y, and from 67.8% to 62.9% in those over 64 y.² In our study, the patients' own fears and/or hesitations were the most frequent reasons for not being vaccinated. Nevertheless, vaccination opportunities through vaccination programs should not be missed in a country with low adult vaccination rates.²⁸

According to the regression results, we assumed that previously, the physicians were less likely to offer the influenza vaccine to patients with longer diabetes duration, and to those who use a higher number of medications and those with hyperlipidemia; similarly, elderly patients, those with longer diabetes duration and those on more complicated treatments had a less likelihood of being offered pneumococcal vaccination. However, the results of the study period suggested that after the training, there may be some improvement in physicians' behavior toward vaccination. As indicated, patients with a higher number of co-morbid conditions and family history of cardiovascular disease are more likely to be offered the influenza vaccine, and correspondingly, patients with a higher number of co-morbidities and family history of diabetes are more likely to be offered the pneumococcal vaccine by their physicians. Nevertheless, in elderly patients and

those under multiple anti-diabetic medications, the vaccination offer for influenza may not reach a satisfactory level. Similarly, in the case of pneumococcal vaccination, the offer may be still low, particularly in patients with hyperlipidemia and in those with a family history of hypertension (Tables 2 and 3). On the other hand, published literature has indicated that having one or more co-morbid conditions is an important predictor in receiving the pneumococcal²⁹ as well as the influenza vaccines.³⁰ However, a study from Taiwan found that older adults with a greater number of chronic diseases had a higher likelihood of missing vaccination against influenza.³¹ The contradicting findings of our study with the majority of international published data may bring into the open a few major issues: First, during daily routine diabetes care, the participating physicians may not be sufficiently concerned about the preventive measures in patients with poor health outcomes due to time constraints. Second, considering that physicians are mostly concerned with the treatment of presenting symptoms, they may forget to apply preventive measures such as recommending vaccinations during the busy daily practice. Third, physicians had considerably low levels of tracking for their patients' vaccinations, which may have resulted in low levels of vaccinations in the long run. To support this, our study may have acted as a new form of tracking activity which resulted in considerable increases in both vaccinations during the study period.

The most prominent strengths of our study are its large sample size, the high response rate by the patients, and the inquired physician self-perception on vaccination. Nevertheless, the study had some limitations: Despite an initial selection of 70 physicians for a better representation of the Turkish primary and secondary healthcare system, only 44 physicians provided data. Second, the study protocol lacked a method for patient registration, and the physicians enrolled patients without a systematic approach. However, the findings from the study certainly addressed the extent of the public health issue and thus, the study may have a promising positive impact on future immunization strategies in Turkey.

In spite of all the concerns, the results of our study highlighted a short training program, which after a year could help increase the physicians' awareness, and may result in increased

vaccination rates in diabetic patients, as opposed to the low vaccination levels of the past five years. Due to the pilot nature of the study, our results may not be considered as generalized to all physicians caring for patients with diabetes in Turkey. Moreover, we cannot rule out the positive feedback on the raised physicians' perception by having participated in the study.

In summary, the increased coverage rate of influenza vaccination in our study remains below the level recommended by the WHO¹⁷ (63.3% in our sample vs. 75.0%); besides, the rate for pneumococcal vaccine is even poorer than the above. This study identified some critical factors, including the demographics and co-morbidities to be associated with low influenza and pneumococcal vaccination rates among the adult population with diabetes. Patients in older age, those with longer disease duration, those with more complicated treatment, more co-morbid disease and unfavorable family history are more likely to miss the opportunities to receive vaccination. We conclude that free vaccine coverage does not always result in increased vaccination rates, particularly in elderly diabetic individuals with multiple co-morbid conditions and worse health outcomes.

Therefore, further research is needed to find solutions to increase the vaccination rate in this population. Policy makers should consider establishing an electronic system that allows physicians to monitor the immunization history of their patients when the health records are electronically retrieved during their visits. On the other hand, physicians may wish to see progresses in the development of vaccines with better safety and efficacy, and they may also benefit from being reminded of the importance of vaccination in this vulnerable population. Finally, patients with poor health may need to have extra social support i.e., reminding calls and home visits. Such efforts may help increase the vaccination coverage and better protect the health of the population at risk.

Materials and Methods

This epidemiological study was designed with retrospective and prospective arms for exploring the vaccination rates against influenza and IPD during the past five years and during the study period one year after a physician training program. A flow diagram of the study has been presented in **Figure S1**. The study protocol was approved by the central ethics board and subjected to the regulatory review of the MoH of Turkey (diaVAX TRSP 001 approval no. 060809/01 Sept 2009).

Selection of physicians

Initially, a representative sample of 70 physicians from 50 sites was randomly selected; 44 physicians from 43 sites agreed to participate and provided data for this study (response rate: 62.9%). No financial incentive was provided to physicians for participation in the study. There was no difference in terms of regional and/or specialty distribution of physicians between those who did not agree to participate and those who participated.

Physician questionnaire

The physicians' knowledge and perception about influenza and pneumococcal vaccinations was evaluated via the questionnaire where the physicians' self-vaccination rate against influenza was also investigated.

Training program

After collection of self-completed questionnaires, all of the participating physicians attended a face-to-face or received an online half-a-day training session on 07 Sept 2009. During the session, the study protocol was also explained. Those who did not attend this activity provided a training DVD before any patient enrollment. The training program was specifically designed in accordance with the immunization recommendations of the 'SEMT Clinical Practice Guidelines on Diabetes and its Complications'.⁹ Topics included the burden of diabetes, the increased risk of hospitalization and death due to influenza and IPD, the effectiveness and safety of the influenza and pneumococcal vaccines, vaccination recommendations, and the possible reasons for the low rate of vaccination in patients with diabetes. The ultimate aim of the training program was to recall the physicians' knowledge, and thus increase the awareness regarding vaccination.

Sample size determination

The sample size calculation for this study was based on the above mentioned TIHUD study (Unal S. 2011, Personal correspondence). Accordingly, in 12 235 patients, pneumococcal vaccination was performed at a level of 0.1%. We hypothesized an increase in the rate of vaccination to 65% after a training program which aimed for increased awareness. Thus, to recover the rate of pneumococcal vaccination to 65% with a confidence level of 95% ($\alpha = 0.05$), a power of 90% and an error rate of 2%, approximately 5900 patients were planned to be enrolled. Taking into account the approximate 10% rate of non-responders, 6490 patients with diabetes were invited to participate in the study. Consecutive patients who turned up for routine follow-up and/or for other medical reasons, and signed an informed consent between Sept 2010 and Jan 2011 were enrolled in this epidemiological registry study.

Retrospective phase

The influenza and pneumococcal vaccination histories of all enrolled patients for the past five years were obtained from the physicians' records and/or by asking the patients.

Prospective phase

The original registry period was planned as 9 mo, but in order to avoid potential biases caused by uncertainty about the H1N1 vaccine in the public and also due to shortage of the pneumococcal vaccine, the Steering Committee decided to stop the registry after three months. The study was re-launched in the following season. Thus, here we presented the results of the study period between Sept 01 2010 and Jan 12 2011 (4.5 mo).

Data collection

The data were collected during a single registry visit by means of a basic data collection form. The physicians recorded the patients' demographic data (i.e., age, gender, diabetes duration), current treatment for diabetes and complications if present, family history (diabetes, hypertension, hyperlipidemia, and cardiovascular diseases—including coronary artery disease, peripheral vascular disease, and stroke), co-morbid diseases of the patient (hypertension, hyperlipidemia, and cardiovascular disease) and their treatment if applicable.

Vaccinations with the influenza and the pneumococcal vaccines during the study period were entirely left up to the

physicians' discretion without imposing any special requirements. Therefore, this study could also be considered in a semi-observational design. The participating physicians indicated that they followed-up their prescriptions in most of the cases. Generally, the physicians requested from their patients to be informed by phone when they had received the vaccine. However, in 58.3% of the prescribed patients, a nurse asked them by phone whether they had received the vaccine during the study period.

Statistical analysis

All statistical analyses were performed using a validated statistical software, Stata Version 10.0. The descriptive statistics for the categorical variables were tested using the Chi-square or the Fisher's exact test, and the continuous variables using the Student's t or the Mann Whitney-U tests whenever applicable. Two separate multiple logistic regression models were generated to identify the influential factors on the uptake of influenza or pneumococcal vaccines in the past five years and during the study period. The dependent factors were set as receiving the influenza or pneumococcal vaccine during the past five years, and during the study period. The univariate analysis included the variables that were found to be significant in the models. The independent variables entered in the model at step one were: gender, age and body mass index; presence of hypertension, cardiovascular disease and hyperlipidemia; family history of diabetes, hypertension, cardiovascular disease and hyperlipidemia; duration

of diabetes, number of co-morbid conditions, and the number of anti-hyperglycemic and concomitant medications. The non-significant predictors ($P > 0.05$) were subsequently removed on a backward stepwise basis. The Hosmer-Lemeshow test was used to examine how well the model accounted for the outcome. A P value of less than 0.05 was considered statistically significant.

Disclosure of Potential Conflicts of Interest

The authors declared no conflict of interest, except for Dr Serdar Altinel having been an employee at Sanofi-Pasteur, Turkey, at the time of conduction of the study.

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Supplemental Materials

Supplemental materials may be found here:

www.landesbioscience.com/journals/vaccines/article/25826

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