SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

Factors associated with influenza vaccination among the elderly and people with diabetes

by Gergő József Szőllősi, MSc

Supervisor: László Kardos, PhD

UNIVERSITY OF DEBRECEN
DOCTORAL SCHOOL OF CLINICAL MEDICINE

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By Gergő József Szőllősi, Expert in Public Health

Supervisor: László Kardos, PhD

Doctoral School of Clinical Medicine, University of Debrecen

Head of the **Defense Committee**:	Mariann Harangi, PhD, DSc
Reviewers:	Anna Páldy, PhD
	Csilla Nagy, PhD
Members of the Defense Committee:	Anna Páldy, PhD
	Csilla Nagy, PhD
	László Pál, PhD
	Tamás Szigeti, PhD

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Introduction

Influenza

Influenza is an infectious respiratory disease that is spread by droplet infection through respiratory droplets. In Europe, infections caused by influenza viruses regularly cause annual epidemics, especially in winter. Literature estimates that approximately 50 million people in Europe are affected each year. In addition to the epidemics that occur, new influenza viruses occasionally emerge to which a significant proportion of the population may be susceptible, potentially creating a pandemic. The most significant complication of the disease is pneumonia. Severe complications are most likely to affect very young infants and the elderly. Another group at increased risk of influenza infection is healthcare workers. The most effective way of preventing influenza is the flu vaccine, which contains two strains A and one B, as defined by the World Health Organisation (WHO). EU Member States strongly recommend vaccination against influenza and subsidise the costs, so that in many cases the vaccine is available free of charge to people at increased risk, but vaccination coverage varies widely, for example among the elderly. The causes of seasonal epidemics are complex and several factors may contribute to their development, such as mutations in influenza viruses, virus transmission routes, the immunological status of the affected population and the general health status of the population.

Public health significance of influenza

Influenza epidemics have a major health and economic impact worldwide. Early detection and effective action can reduce the spread of epidemics and the number of illnesses and deaths caused by the influenza virus. Influenza epidemics have many health, social and economic consequences and affect society as a whole. Since influenza is responsible for a large number of illnesses and deaths, it has a significant health burden. In addition, a significant proportion of patients may require hospitalisation, which also places a burden on the health care system. In addition, influenza epidemics can have a significant impact on society as a whole, and thus have a significant economic impact, as higher rates of absenteeism in schools and workplaces can occur, which can subsequently lead to significant economic losses.

Influenza epidemics

The best way to prevent influenza epidemics is to get vaccinated, and to increase vaccination coverage, many countries are organising flu vaccination programmes to reduce the spread of influenza and prevent serious complications. Influenza outbreaks are monitored by epidemiological investigations, whereby health authorities regularly monitor the frequency of disease occurrence and possible spatial patterns of spread of infectious cases in order to detect influenza outbreaks in time and take appropriate measures to slow down their spread. In addition, the study of genetic variations in influenza viruses allows the prediction of virus transmission patterns and their characteristics, which will help to detect influenza outbreaks in time and to develop effective vaccines against influenza viruses.

Managing and preventing influenza pandemics requires the cooperation and coordinated efforts of all countries around the world.

Antigen shift and drift

Flu viruses are constantly changing, with two main types of change: antigenic shift and antigenic drift. Drift consists of small changes (or mutations) in the genes of influenza viruses that can lead to changes in the surface proteins of the virus. Because of antigenic drift, flu vaccines must be redesigned annually to match current virus strains.

The antigen shift is another process that leads to more radical changes in the genetic material of the influenza virus. An antigenic shift occurs when two or more different strains of influenza viruses fuse in a host cell and exchange genetic material.

Antigenic shift and antigenic drift play an important role in the diversity of influenza viruses and in the emergence and spread of influenza viruses. Continued monitoring of influenza viruses and studying genetic changes in viruses will help to improve the effectiveness of influenza vaccines and other therapies.

Vaccinations

The flu vaccine is one of the most important and effective preventive action against influenza. Vaccination can help to prevent serious illness and complications, but getting vaccinated does not mean that vaccinated people cannot get influenza. Because the influenza virus changes every year, vaccinations should be updated annually. The vaccine contains the flu virus strains for that year and should be given before the flu season, usually before October each year. The vaccine is effective against seasonal influenza viruses in most cases but does not provide complete protection against all types of influenza viruses.

The effectiveness of the flu vaccine varies from year to year, as the composition of the vaccine is not constant due to the yearly variation of influenza viruses. The effectiveness of the vaccine depends on both the composition of the vaccine in a given year and the strains of influenza virus circulating at that time.
Overall, the effectiveness of the flu vaccine varies, but it remains an effective tool in preventing the disease and reducing the risk of serious complications.

Risk groups

Getting the flu vaccine is highly recommended for people at higher risk of developing serious illnesses, such as the elderly, children, people with chronic illnesses (such as diabetes or cardiovascular disease), pregnant women and health workers. A sufficiently high (~75%) vaccination coverage rate can help to protect not only the health of the individual, but also the whole community by reducing the chances of spreading the infection.

Objective

The main objective of this thesis is to highlight the factors that contribute significantly to the uptake of influenza vaccination, with a particular focus on the factors that influence vaccination uptake among target groups at high risk of health consequences of non-vaccination.

A secondary objective is to show the pattern of influenza vaccination coverage among the main risk groups.

The research questions were:

- What factors contribute to the uptake of influenza vaccination among the elderly population in the country?
- What factors contribute to the uptake of influenza vaccination among the population with diabetes?

The objectives of the research underlying this thesis were:

- To demonstrate the patterns of influenza vaccination coverage in different socio-demographic and other strata of the population aged 65 and over.
- To demonstrate the patterns of influenza vaccination coverage in different socio-demographic and other strata of the self-reported diabetic population.

Data and methodology

European Health Interview Survey

The data used for the study were based on data from the *European Health Interview Survey* (*EHIS*) 2009, 2014 and 2019 databases. In each case, primary data collection was carried out by the Hungarian Central Statistical Office. The data collection was interview-type, which meant that data were collected with the help of interviewers, interviewers who had been trained in advance. The questionnaire survey provides good insights regarding health status, lifestyle factors and characteristics of the inhabitants of a given country, including self-care limitations, but also a picture of physical activity, dietary habits, risk behaviours such as smoking and alcohol consumption. It also presents data on subjective perceptions of satisfaction with the health care system. The survey was conducted among adults aged 15 years and over living in private households. The officially available data are published by Eurostat.

The implementation of the survey based on the public consultation was required by Regulation (EC) No 1338/2008 of the European Parliament and of the Council. The main objective of the survey is to provide a statistical dataset available to all Member States with a common methodology for data collection and analysis, and to make available indicators and health indicators of basic health status. The second round of the Survey took place in 2014 and the third round in 2019. The three surveys were based on three different randomized samples and did not follow the same respondents.

The indicators are based on a set of *European Community Health Indicators (ECHI)*, which have been developed to provide a comprehensive and detailed description of the health status of the population of the Member State collecting the data, the determinants of health, and to provide basic data on health care systems and their use and satisfaction.

The requested database for 2009 contained 384 variables and data on 5051 individuals, with a response rate of 72.2% for that year. The EHIS 2009 data collection took place between 15 September and 30 October 2009, with interviewers visiting a total of 449 municipalities and involving approximately 7000 respondents. The second round of the European Health Interview Survey was conducted in 2014, with primary data collection taking place between 15 September and 15 December. The survey was carried out by contacting 9431 people in 532 municipalities. The survey also covered the population aged 15 and over living in private households. The 2014 database contained 361 variables and the final sample size of the survey was 5826. The response rate for that year was 61.8%.

Primary data collection for the third round of the European Health Interview Survey was carried out between 16 September and 31 December 2019. The survey was conducted by interviewing 12002 people in 510 municipalities. The questionnaire survey covered the population aged 15 years and over living in private households, which means that people living in various institutions, such as nursing homes or residential social care institutions, were excluded from the data collection. The database used contained 541 variables and the final sample size of the survey was 5603. The response rate for that year was 46.7%.

Statistical methodology

The association between the occurrence of response options of categorical variables and data related to influenza vaccination in the matched database of elderly population data was done using chi-square tests. After that data were analysed using multiple logistic regression models, while in the matched database containing data from the diabetic population, data were analysed using univariate and multiple logistic regression analyses.

Factors associated with vaccination uptake were identified using multiple logistic regression models adjusted for confounders and including interactions, where the outcome variable in each case was a binary variable of vaccination uptake. In all cases, interactions between explanatory variables were identified in the models.

The descriptive data are presented with raw case numbers and percentages, with corresponding p-values. Multiple models are presented with adjusted odds ratios and their corresponding p-values. The goodness of fit of the regression model was tested using the Hosmer-Lemeshow test.

Statistical analysis of the data was performed using Stata statistical software (version 9.0, Stata Corp, College Station, TX, USA), and the p-value from the statistical procedures was considered significant if the p-value was less than 0.05.

Results

An Exploratory Assessment of Factors with Which Influenza Vaccine Uptake Is Associated in Hungarian Adults 65 Years Old and Older: Findings from European Health Interview Surveys

The primary objective of this study was to identify factors that are significantly associated with uptake of the influenza vaccine, and the secondary objective was to identify additional target groups related to vaccination uptake.

The analysis is based on EHIS databases from 2009, 2014 and 2019. The EHIS sample size was 5051 in 2009, 5826 in 2014 and 5603 in 2019. The 2009 survey had 1046 respondents aged 65 and over (21%); the 2014 and 2019 databases had 1216 (21%) and 1628 (29%) respondents aged 65 and over. After the age filtering, the databases (n=3890) were merged and during the data cleaning process, respondents (n=535; 14%) who did not answer the relevant questions were excluded as they would not have contributed to the multiple regression analysis; the final sample size was 3355.

The sample for the elderly group consisted of 1269 (38%) men and 2086 (62%) women. The most common level of education was secondary with 1807 respondents (54%), followed by primary with 1019 respondents (30%). Tertiary education was the least common with a prevalence of 16% (n=529). In terms of marital status, 1656 respondents (49%) had a partner, and 1699 had no partner (unmarried, divorced or widowed). In terms of self-assessed health, 2392 (71%) perceived their own health as good and 963 (29%) as poor. Approximately 65% of the elderlies (n=2181) felt that they could do "a lot" about their health. The survey identified 2357 people (70%) as overweight or obese. The prevalence of smoking was 40% in the sample, which meant that 1348 people in the merged database were classified as smokers. In terms of satisfaction with a specialist, 2524 people (75%) were satisfied and 2945 people (88%) were satisfied with their GP. For the question on most recent doctor appointment, 3082 (92%) had seen their GP in the last year and 2461 (73%) had seen a specialist in the last year. Respiratory diseases affected 449 people (13%) aged 65 or over, cardiovascular diseases affected 2623 (78%) and endocrine diseases affected 1262 (38%). The number and proportion of respondents varied by region, with the lowest proportion of respondents from South Transdanubia (n=322, 10%) and the highest proportion from Central Hungary (n=938, 28%).

Influenza vaccination coverage among people aged 65 and above

The influenza vaccination coverage of 3355 participants aged 65 years and older was 37% (n=352) in 2009, 32% (n=348) in 2014 and 28% (n=366) in 2019. Approximately 32% of participants aged 65 years or older in the merged database were properly vaccinated and thus classified as protected during the previous influenza season relative to the year of the European Health Interview Survey. There was a significant and decreasing trend in vaccination coverage over the years of the survey ($p<0.001$), indicating that the level of influenza vaccination coverage has been decreasing over time among people aged 65 years and older. Influenza vaccination rates were higher among men (n=429, 34%) compared to women (n=637, 31%) ($p=0.049$). In terms of educational attainment, the highest vaccination rates were observed among respondents with tertiary education (n=211, 40%), followed by those with secondary (n=554, 31%) and primary (n=301, 30%) educational level ($p<0.001$). There was no statistical difference ($p=0.086$) of higher vaccination coverage (n=563, 33%) among persons with social support (married or had a partner) than among persons living alone (n=503, 30%). Respondents with self-rated poor health status (n=335, 35%) had significantly ($p<0.017$) higher vaccination coverage than those with rated good health (n=731, 31%). Respondents who said they could do a lot for their health had a non-significantly higher ($p=0.436$) rate of influenza vaccination coverage (n=703, 32%) compared to respondents who said they could not do much for their health. There was a significantly higher ($p=0.029$) level of influenza vaccination coverage (n=344, 34%) among respondents with a normal BMI compared to those who were obese or overweight (n=722, 31%). Non-smokers tended to be vaccinated at a higher rate (n=651, 32%) than smokers (n=415, 31%), but the association was not statistically significant ($p=0.314$). Respondents who were satisfied with their GP (n=955, 32%) were significantly ($p=0.029$) more likely to be vaccinated than respondents who were not satisfied with their GP (n=111, 27%). Satisfaction with the specialist did not show a significant correlation with the level of vaccination ($p=0.301$), however, a higher proportion of those who were satisfied (n=814, 32%) were vaccinated compared to those who were not satisfied (n=252, 30%). Respondents who had visited their GP (n=1028, 33%) or specialist (n=860, 35%) in the past year had significantly higher vaccination rates than those who had not visited their GP or specialist ($p<0.001$). Respondents who had respiratory (n=173, 39%), cardiovascular (n=886, 34%) or endocrine (n=464, 37%) diseases had significantly higher influenza vaccination rates compared to respondents who did not have these diseases ($p<0.001$). There was spatial heterogeneity in

vaccination coverage, with vaccination rates ranging from 28% to 35%, but these differences were not statistically significant ($p>0.05$).

Multiple logistic regression model results for the population aged 65 and above

The fit of the multiple logistic regression model was considered adequate ($p=0.551$). Results of the regression showed that respondents who had visited their GP in the past year in 2019 were significantly less likely to have received the flu vaccine than respondents who had visited their GP in the previous year in 2009 (OR=0.56, $p<0.001$). Respondents who had visited their GP within one year in 2009 were significantly more likely to have received the flu vaccine compared to those who had not visited their GP within the previous year (OR=4.70, $p<0.001$). A similar association was observed in 2014, with people aged 65 years and over who had visited their GP in the past year being 2.81 times more likely to have received the flu vaccine compared to those who had not visited their GP in the past year (OR=2.81, $p=0.002$). Respondents who had seen their specialist in the previous year were more likely to have received the flu vaccine compared to those who had not seen their specialist in the past year (OR=1.48, $p<0.001$). Receiving the flu vaccine was significantly associated with educational attainment among those perceived to be in poor health, with respondents with a higher educational level had higher chance of being vaccinated compared to those with primary education (OR=3.67, $p<0.001$). This relationship was also observed for good self-assessed health, where respondents with tertiary education were 46% more likely to be vaccinated compared to those with primary education (OR=1.46, $p=0.011$). Respondents with good self-reported health and secondary education were significantly less likely to be vaccinated against influenza compared to respondents with poor self-reported health and secondary education (OR=0.40, $p<0.001$). Among population aged 65 years and over who had not seen their GP in the past year, those with a partner were significantly more likely to have been vaccinated than those who did not have a partner and also rarely visited their GP (OR=2.76, $p=0.010$). Among single respondents, those who had seen their doctor in the past year were 4.33 times more likely to have received the flu vaccine than those who had not seen a doctor in the past year (OR=4.33, $p<0.001$). Being overweight or obese was significantly associated with not receiving the flu vaccine; that is, obese or overweight respondents were significantly less likely to receive the vaccine within one year than those with a normal body mass index (OR=0.76, $p=0.004$). A significant association was found between vaccination coverage and self-reported diseases; those aged 65 years and over with respiratory disease (OR=1.29, $p=0.019$) or cardiovascular disease (OR=1.35,

p=0.004) or endocrine disease (OR=1.25, p=0.005) were more likely to be vaccinated compared to respondents who did not have these diseases. No statistically proven association between sex and vaccination was found, but men were more likely to be vaccinated than women (OR=1.17, p=0.077). An association was found with borderline significance between responses to the question 'How much can you do for your health' and the odds of receiving the vaccination: people who thought they could do a lot for their health were 19% more likely to receive the flu vaccine (OR=1.19, p=0.056). Smoking status (p=0.082) and satisfaction with GP (p=0.065) showed no clear statistically proven association with vaccination. Among older people with a partner, respondents who saw their GP more often (within one year), were 56% more likely to have been vaccinated than those who saw their GP less often, but this association was borderline significance (OR=1.56, p=0.056). Satisfaction with specialists did not have a significant effect on vaccination uptake (p=0.843) but seeing a specialist within a year had a positive effect on vaccination uptake (OR=1.48, p<0.001). No spatial heterogeneity was observed between regions in terms of adequate vaccination uptake (p>0.05).

Influenza Vaccination Coverage and Its Predictors among Self-Reported Diabetic Patients-Findings from the Hungarian Implementation of the European Health Interview Survey

During influenza epidemics morbidity and mortality are significantly higher among people with diabetes - a significant proportion of which could be considered as preventable by vaccination - and therefore increasing influenza vaccination coverage is a public health priority, not only among the general population but also among target groups at increased risk.

Understanding the factors that could contribute to influenza vaccination uptake is a priority to reduce the significant economic and health burden caused by influenza.

The primary objective of this study was to identify the factors that are significantly associated with uptake of the influenza vaccine, and an additional objective was to identify additional target groups at increased risk of vaccination uptake.

Influenza vaccination coverage among people with diabetes

Based on self-report, 426 people with diabetes were identified in 2009, 474 in 2014 and 547 in 2019, with a prevalence of 9% in 2009, 8% in 2014 and 10% in 2019. No significant difference was detected in the rates of influenza vaccination between diabetic and non-diabetic participants ($p=0.282$). In 2009, 111 of 426 self-reported diabetic participants (26%) had received the influenza vaccine, in 2014, 132 of 474 diabetic participants (28%) had received the vaccine, and in 2019, 139 of 547 diabetic participants (n=25%) had received the influenza vaccine within the year prior to the study. Among people with diabetes aged 65 years or older (n=745), vaccination coverage was 35%, which was significantly higher than the 17% vaccination coverage in the 18-64 age group (n=702, $p<0.001$). In terms of gender, there was no statistically detectable difference in vaccination uptake rates between men and women in the diabetic group, although vaccination uptake rates were higher among men (28%) compared to women (25%) ($p=0.186$). There was no significant difference in vaccination between primary (n=343, vaccination rate=25%) and secondary (n=892, vaccination rate=24%) educational level respondents ($p=0.691$); however, a significant difference was observed between tertiary (n=211, vaccination rate=39%) and primary respondents in terms of influenza vaccination uptake ($p=0.001$). The proportion vaccinated was significantly ($p=0.034$) lower (25%) in participants

with self-reported good health (n=949) than in the group considered to be in poor health (n=496; vaccination coverage=30%). People with diabetes who had seen their GP for less than 1 year (n=1380; vaccination coverage=27%) did not have significantly higher vaccination coverage than people with diabetes who had seen their GP less frequently (≥12 months) (24%; p=0.632). A similar but non-significant association was observed for the most recent GP visit: the group of diabetics who consulted a GP frequently (n=1202) had a higher proportion of vaccinated individuals (27%) compared to the group who consulted a GP infrequently (n=244; vaccination coverage=22%) (p=0.073). In addition, comorbidities such as cardiovascular, musculoskeletal or gastrointestinal diseases were significantly associated with vaccination status. Diabetic patients with cardiovascular or cerebrovascular disease had significantly higher vaccination coverage (28%; n=1184) than those without such disease (21%; n=263) (p=0.026). The same association was observed for musculoskeletal disorders (n=955, 29% vs. n=492, 21%; p=0.001) and gastrointestinal disorders (n=112, 36% vs. n=1332, 26%; p=0.020). In terms of self-reported co-morbidities, diabetics with co-morbidities had higher rates of influenza vaccination than diabetics without co-morbidities.

Results of a multiple logistic regression model among people with diabetes

Self-reported diabetics aged 65 years or older with secondary educational level were significantly more likely to be vaccinated against influenza compared to those aged 18-64 years with the same educational level (OR=3.67, p<0.001). Furthermore, respondents in the age-group of 18-64 with secondary education had significantly lower odds of receiving the influenza vaccine within one year compared to participants in the same age-group with primary education (OR=0.53, p=0.038). Respondents aged 65 years or older with tertiary education were significantly more likely to be vaccinated against influenza within one year compared to respondents aged 18-64 years with the same educational level (OR=2.41, p=0.005). Respondents aged 65 years or older with secondary education had significantly higher odds of being properly vaccinated compared to diabetics of the same age-group with primary education (OR=1.58, p=0.035). A similar association was found for respondents aged 65 years or older and with tertiary education compared to those with primary education, indicating that older diabetics with tertiary education had significantly higher odds of receiving influenza vaccination compared to those with primary education (OR=2.49, p=0.001). In 2019, diabetics with tertiary education were 2.65 times more likely to be vaccinated compared to diabetics with

primary education (OR=2.65; p=0.002). Male diabetic respondents who had seen their GP within one year were 39% more likely to be vaccinated against influenza compared to women who had seen their GP within one year (OR=1.39, p=0.014). However, male respondents who had not seen their GP within one year were 74% less likely to be vaccinated compared to women (OR=0.26, p=0.033) in this stratum. In terms of co-morbidities, diabetics with musculoskeletal conditions were significantly more likely to be vaccinated against influenza compared to diabetics without the condition (OR=1.43, p=0.015)

Discussion

Summary of the results of the studies

The main focus of the research is on influenza vaccination uptake and identifying factors that significantly contribute to vaccination uptake in the elderly and diabetic groups using EHIS data. Both scientific articles presented the variation in vaccination coverage and factors that may be associated with vaccination uptake, based on data from a national, representative and cross-sectional database with a relatively large number of respondents.

While it is important to highlight the fact that the influenza vaccine is available free of charge to both the elderly – population over 65 –, and people with diabetes, both studies highlighted that the level of vaccination coverage is significantly below the ideal. The situation is further exacerbated by the worsening trend, as the influenza vaccination coverage among the elderly population was 37% in 2009, 32% in 2014, which decreased to 28% by 2019. At the same time, the vaccination coverage among those identified as diabetic by self-report was 26% in 2009, followed by a slight increase in 2014, as the vaccination coverage changed to 28%, but decreased to 25% in 2019, which can be considered lower than both years studied. There was a statistically proven ($p<0.001$) decrease in vaccination coverage among the elderly population from 2009 to 2019, while a slight decrease in vaccination coverage was also observed among diabetics, but this trend was not significant ($p>0.05$). Older people and people with diabetes are more likely to receive regular care and monitoring by health care providers, yet organised interventions should also be targeted to increase vaccination uptake among younger and disease-free populations beyond the at-risk groups. Diabetes itself is a significant risk factor for subsequent cardiovascular complications, and therefore the promotion of free vaccination is a priority for the health care system.

Among diabetics, older age was associated with higher vaccination uptake ($p<0.001$), which may be due to the additional risk of serious complications later in life due to age and co-morbidities, which put this group at increased risk of serious complications. In terms of vaccination uptake, older diabetics with secondary and tertiary education were more likely to be vaccinated.

There was a gender difference in influenza vaccination coverage, with higher vaccination rates among men aged 65 years ($p<0.05$) compared to women, but this association was not statistically confirmed in the confounder-adjusted analysis. Nevertheless, a difference ($p<0.05$)

was observed in the likelihood of vaccination uptake between men and women among both those with diabetes who saw their GP less frequently and those who saw their GP within a year. These differences may indicate the need for gender-specific approaches to promote vaccination, as gender differences may contribute to vaccination uptake.

Educational attainment was found to be a significant determinant of vaccination uptake, with the highest vaccination uptake among the elderly in the country among those with tertiary education ($p<0.001$). In terms of vaccination uptake, respondents with both good and poor self-reported health status were more likely to be vaccinated compared to those with primary education and the same self-reported health status ($p<0.05$). This result is in line with international findings, although other study authors have found that primary education has a protective effect compared to persons without primary education, so higher education had a more favourable effect on vaccination uptake. Analyses adjusted for confounders showed that higher education had a positive effect on vaccination uptake among older people with diabetes ($p<0.05$), whereas this association was not clear in the younger age group. Overall, these results suggest that higher education was associated with a higher likelihood of vaccination, highlighting the importance of programmes to promote the benefits of vaccination among people with lower education levels, which would be expected to increase knowledge levels and health awareness. These results are well correlated with the scientific literature.

Regarding marital status, there was no significant association between vaccination uptake and marital status among those who met their GP more often, while marital status showed a statistically significant positive association with vaccination uptake among older respondents who met their GP less often.

Self-assessed health status was significantly ($p<0.05$) associated with vaccination uptake, with participants with poor self-assessed health status among older people with secondary education and among people with diabetes being more likely to have received the flu vaccine than those who assessed their health as good. It is important to mention the perception of illness and burden of disease, as these factors may contribute to health-related decisions, including vaccination uptake. Hence, raising health awareness can significantly increase influenza vaccination coverage.

There was no statistically proven ($p>0.05$) association between how much a person in the study could do for their health and vaccination uptake, although people who thought they could do a lot for their health had higher vaccination uptake. In a study with a similar focus, a nearly identical association was found, whereby an important factor for vaccination uptake was the opinion about previous vaccinations administered.

The presence of obesity or overweight was found to be a significant ($p<0.05$) determinant of vaccination uptake among the elderly, with higher vaccination coverage among people with normal BMI compared with obese or overweight respondents. Despite the higher risk of developing more severe complications among people who are obese or overweight, an inverse association was seen when compared with literature data.

Among the elderly, satisfaction with the general practitioner was considered as a determinant of influenza vaccination uptake, but satisfaction with the specialist was not found to be a factor which influencing uptake.

Smoking among the elderly was not significantly associated with vaccination uptake, although non-smokers had slightly higher influenza vaccination uptake, but this association was not significant ($p>0.05$). However, literature suggests that smoking may have a negative impact on vaccination uptake.

Meeting the GP and the specialist helped to get the vaccination. The gatekeeping role of general practitioners, as well as higher doctor-patient contact during possible specialist care, is assumed to be associated with an increase in the odds of vaccination uptake. This association is supported by literature data. Analyses adjusted for confounding factors showed that more frequent contact with a general practitioner or specialist was significantly ($p<0.001$) associated with vaccination uptake among older people in both 2009 and 2014, and that more regular contact with a doctor was also associated with a positive effect on vaccination uptake among older people without a partner. These associations were not significant ($p>0.05$) in the self-reported diabetic group, but the trend was still similar, with those who had relatively more frequent visits to a specialist reporting higher vaccination uptake.

In relation to comorbidities, it was clearly outlined that the population affected by diseases had higher rates of vaccination coverage, which is in line with literature. It is important to note that the desired vaccination coverage rates among the target groups with co-morbidities and at increased risk of complications and mortality were not ideal. Therefore, increasing vaccination coverage among people at increased risk remains a major public health task and challenge.

There was clear regional heterogeneity in influenza vaccination coverage among the elderly, but differences between regions were not significant ($p>0.05$).

Despite the fact that the influenza vaccine is available free of charge to residents aged 65 years and above and to diabetic respondents, and that it is clearly recommended by public health institutions and health professionals, vaccination coverage was still considered insufficient in both risk groups in Hungary in the years covered. Based on our research, influenza vaccination coverage and the factors influencing vaccination uptake were investigated from two aspects

using a database representative of the Hungarian population, one among the elderly and the other among self-reported diabetic individuals. The main finding is that, despite the fact that influenza vaccination is available free of charge to both high-risk target groups, vaccination uptake was extremely low. The situation is further exacerbated by the fact that even after stratification within each risk group, vaccination coverage did not reach the ideal level. This is a clearly negative public health indicator, as the influenza vaccination coverage rate, with a particular focus on groups at increased risk, can be considered as an effective indicator of a country's public health preparedness and awareness. This unfavourable situation is exacerbated by the fact that a primary care monitoring indicator on vaccination uptake has only been developed for the elderly and is not available for people with diabetes and other risk groups, thus making it difficult to assess the potential health gains from vaccination.

In addition, our studies have identified and delineated factors that may significantly contribute to vaccination uptake and non-vaccination in two groups at increased risk. In the older age group, factors influencing willingness to vaccinate included educational level, marital status, perceived health status, frequency of visits regarding general practitioners and specialists, and co-morbidities. Higher educational level and the presence of co-morbidities clearly increased the likelihood of vaccination uptake, but obesity or overweight and less frequent GP appointments decreased the likelihood of vaccination uptake. Vaccination coverage among the population with diabetes was extremely low and there was no statistically proven improvement over the years. Older age and higher education had a positive effect on vaccination uptake, while female gender was a risk factor among those who saw their GP more often, and musculoskeletal conditions had a significant effect on uptake among co-morbidities.

Both scientific articles identified priorities in the field of public health, such as the influence of education and the need for personalised interventions to increase vaccination coverage. Both studies pointed to the desirability of establishing on future research not only to understand the factors influencing vaccination uptake in high-risk target groups, but also to further increase overall vaccination coverage in the general disease-free population, which is an essential element of an effective public health strategy on this issue.

On the issue of influenza vaccination, it is important to note the relationship between public opinion and vaccine safety. Understanding and exploring this relationship can be key to improving public perceptions and attitudes towards vaccination.

The administration and management of vaccines is mainly done at the primary care level in Hungary, so it is important that health care professionals have the right knowledge and attitude towards the impact of influenza on elderly people and people with diabetes. Education and

vaccination campaigns clearly have an important role, as clear and easy-to-understand communication can help to dispel misconceptions about vaccination, therefore encourage vaccination uptake. No specialised vaccination centres have been established in Hungary so far, although literature suggests that these facilities could contribute to increasing vaccination coverage. The lack of such specialised vaccination centres could be a potential barrier to increasing vaccination coverage. Infrastructural improvements, as well as increased access to vaccination services and easier access to and promotion of vaccination, could presumably contribute to an increase in vaccination coverage.

As a final conclusion, the two published scientific articles have clearly highlighted the importance of understanding the factors influencing influenza vaccination among the elderly and diabetic patients. They suggest the need for tailored interventions, a more effective public health strategy, with vaccination campaigns as key elements to promote vaccination and to increase vaccination uptake in order to achieve higher vaccination coverage rates in Hungary. The results of these studies underline the importance of understanding the factors influencing influenza vaccination uptake. Improving vaccination coverage in high-risk groups is a priority, not only in the field of public health in Hungary, but also a major challenge globally, and it is essential to understand the variables that may contribute to vaccination uptake or non-vaccination.

In summary, our research highlights the importance of using comprehensive strategies for influenza vaccination management, particularly in the older age group and in the diabetic population.

Key findings

- Increasing influenza vaccination coverage: despite the fact that vaccination is available free of charge for high-risk target groups, the vaccination coverage among both the elderly and people with diabetes is still very low, significantly below the WHO-defined and ideal 75% coverage rate.
- Frequency of seeing a specialist among the elderly population, frequency of seeing a general practitioner in 2009 and 2014, and frequency of seeing a GP among those not in a couple relationship clearly had a favourable effect on vaccination uptake. Higher educational level, worse self-assessed health status, normal body mass index and the presence of co-morbidities were also positively associated with vaccination uptake. Thus, in order to increase vaccination uptake among the elderly, primary care should pay further attention to those with primary education and obesity, who do not have co-morbidities and have less frequent contact with health professionals such as GPs or specialists.
- Among people self-identified as having diabetes, older age was significantly associated with vaccination uptake among people with secondary and tertiary educational level. Furthermore, gender, co-morbidities and last meeting with the GP was associated with vaccination. In order to increase influenza vaccination coverage, it would be a priority for public health programmes to target the younger age group within the diabetic population with lower education level, where the presence of co-morbidities is not yet explicitly known.
- Significantly more efforts should be made in order to increase influenza vaccination coverage not only among groups at increased risk, but also among the general population.

Limitations

The questionnaires were completed voluntarily and anonymously, so the results presented by the surveys may under-represent the actual/real data and associations.

A limitation of the analyses is that the meeting with the specialist as a study parameter was not accurately presented, as the data were not queried in this way.

In the analyses, mild and severe diseases were not distinguished in the questions on co-morbidities due to lack of data collection.

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List of publications

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List of publications related to the dissertation

1. **Szőllősi, G. J.**, Nguyen, C. M., Santoso, C. M. A., Zsuga, J., Nagy, A. C., Kardos, L.: An Exploratory Assessment of Factors with Which Influenza Vaccine Uptake Is Associated in Hungarian Adults 65 Years Old and Older: findings from European Health Interview Surveys. *Int. J. Environ. Res. Public Health. 19* (12), 1-12, 2022.
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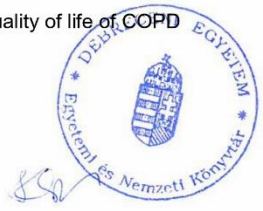

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