Original Paper

Seasonal Influenza Vaccination Coverage in Greece in 2009 and 2014

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Key words:
- Seasonal influenza
- Vaccination coverage rates (VCRs)
- Chronic illness
- Older populations

SUMMARY

BACKGROUND: Prevention of seasonal influenza is the most effective public health intervention to control epidemics, largely dependent on influenza vaccination coverage rates (VCRs). The current study aimed to summarize characteristics of VCRs in the general population and among vulnerable populations in Greece. **METHODS:** Data from the Hellenic Statistical Authority Health Information Survey in 2009 (n=6,172) and 2014 (n=8,223) was analyzed using weighted sample size for VCRs in the general population as well as a sub-analysis for vulnerable populations for those with chronic disease and predictive models for those over 60 years of age. A two-samples proportion test, logistic regression and Walds test with p-value threshold <0.05 were used to analyze the data. **RESULTS:** VCRs from 2009 to 2014 increased significantly (p <0.05) by 9.8% in the Greek population. Those with asthma and COPD younger than age 60 showed lower VCRs than the older age group and those with hypertension, diabetes and back problems had significant (p <0.05) increased VCRs from 2009 to 2014. In addition, among those over 60 years of age, factors associated with being vaccinated included having a chronic illness, health status, last doctor's visit, education and geographical location while smoking status was associated with not being vaccinated. **CONCLUSION:** In a country that faces a prolonged economic crisis, prevention is key to relieving the burden. Influenza vaccination is the only cost-effective and preventive measure to control flu epidemics. It could be extremely beneficial to invest in communication strategies to increase VCRs and prevent disease, as opposed to managing expensive and devastating epidemics.
Pneumon 2017, 30(1):41-48.

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INTRODUCTION

According to the World Health Organization (WHO), influenza is responsible for 3 to 5 million hospitalizations and up to 500,000 deaths every year

worldwide[1]. Seasonal influenza is a threat to all, with most vulnerable populations being children age 6-59 months, pregnant women, elderly and those with chronic illnesses[1]. Prevention of seasonal influenza is the most effective public health intervention to control epidemics, largely dependent on influenza vaccination coverage rates (VCRs) among those at risk and those who are in close contact with vulnerable people[2].

An unpredictable virus, influenza is constantly evolving through antigenic shift and drift[3] and requires constant global monitoring in order to reformulate vaccines that are effective against the flu[4]. It is unknown what each flu season strain will present, therefore annual flu vaccination is the best mode for prevention of outbreaks and death[4].

In Greece, recommendations for seasonal influenza vaccination are inclusive, with specific consideration and recommendations given to those over age 60 years, those with chronic illness or obesity, pregnant woman at all stages, all healthcare workers, and those living in households with elderly or children[2]. Seasonal flu shots are available with or without prescription to all insured people belonging to vulnerable groups under the national health system[5]. For those uninsured, the cost of the shot is on average, six euros[5]. Epidemiological data on incidence and deaths of seasonal influenza and information on vaccination and healthcare professionals exists in Greece, however nationally representative VCRs for the general and vulnerable populations have not been previously examined in the Greek population[6].

The purpose of the current study was to summarize influenza VCRs in 2008-2009 and 2013-2014 periods of the total Greek population by demographic, social and chronic illnesses as well as identify common characteristics of those vaccinated for seasonal influenza in older age population using the 2009 and 2014 Hellenic Statistical Authority (ELSTAT) European Health Interview Surveys (HIS).

METHODS

Study Design

Secondary data analysis was conducted using data collected by ELSTAT for the HIS 2009[7] and 2014[8]. The HIS is a cross-sectional population health survey conducted every five years using a standardised protocol outlined by the European Union (EU) and Eurostat, following Regulation EC No. 1338/2008[8] and Implementing Regulation EC No. 141/2013[8]. A multi-stage stratified sample design was used and is outlined in detail in the Final Quality Reports for 2009[7] and 2014[8]. The survey gathers information on demographics, health status, health services and factors that influence health as well as income information[7] via questionnaires[9,10]. The questionnaire was administered through in-person interviews in the local language, Greek[7,8].

The HIS is conducted in the last quarter of the survey year, in all four major regions of Greece and was inclusive of all private households[8]. A weighted data set was used for all analyses (weighted, clustered and stratified dataset provided by ELSTAT), generating nationally representative results with 95% confidence intervals (CI) for both 2009 and 2014. The total population in Greece as of 2011 was 10, 816,286[11]. The HIS data included only those aged 15 years and over and included 6, 172 respondents in 2009[7] and 8, 223 in 2014[8]. A sub-analysis for persons vaccinated was used and identified using information from the question that asked the respondent the date of their last flu shot. A respondent's answer (having had the shot in the previous or current year) was totaled in each HIS year.

Selected Variables

Both 2009 and 2014 demographic variables were used in their original categories with the exception of the sub-population (vaccinated persons) in which was created into a binary outcome variable and age in which was categorized into an ordinal categorical variable as follows: 15-25; 26-44; 45-59 and 60+. Level of education was grouped into less than primary schooling, completed primary school, lower secondary school, upper secondary school, post-secondary school, a short-cycle schooling, tertiary education including three levels (Bachelor, Master and Doctoral) modeling the 2014 questionnaire. Marital status was grouped into single, married and widowed in which included separated and divorced. For employment categories, employed included unpaid, practicum, and leave-of-absence, while student included further training, unpaid work and military service and retired included early retirement or given up business. A sub-analysis on chronic diseases and vaccination rates included asthma, chronic obstructive pulmonary disease (COPD), myocardial infarction (MI), coronary heart disease (CHD), hypertension, stroke, osteoarthritis, back problems, diabetes, allergies, cirrhosis and depression.

Statistical Analysis

Data analysis was completed using STATA 13.1. Descrip-

tive statistics for flu vaccination on demographic as well social factors were summarized in nationally representative proportions for both surveys. A two-sample proportions test with a significance threshold p<0.05 was used to test significance of the change over time (2009 versus 2014) for VCRs for flu in the overall population and among various chronic illnesses. For those who had chronic illness, those under 60 years old and those over 60 were also sub-analyzed, as older people tend to account for most of the population who has a chronic disease[12].

A sub-analysis for predicting characteristics of older adults who got vaccinated in 2009 and 2014 were also completed with a threshold to reject the null hypothesis for initial association was a p-value<0.25. Variables were then evaluated for correlation using a Pearson's R correlation matrix and variables with an R >0.5 were evaluated for validity as predictors for influenza vaccination. A final explanatory model was built using backwards stepwise multiple logistic regression and Wald's test for both years (final threshold, p-value<0.05).

RESULTS

Answers, "don't know and refused", were dropped from analysis as they accounted for <0.5% of the population in 2009 and 2014 which included the variables vaccinated persons, employment, having a chronic illness, asthma, COPD, MI, CHD, hypertension, osteoarthritis, back problems, diabetes, allergies, cirrhosis, and depression.

VCRs in General Population

Influenza VCR in the Greek population was 22.7% (95% CI: 21.5- 23.9) in 2008-2009 and increased significantly by 9.8% (p-value <0.001) to 32.5% (95% CI: 30.5- 34.5) in 2013-2014. Among those that had gotten the seasonal influenza vaccine in 2008-2009, 81.8% (CI: 79.1- 84.2) reported their last shot in the same year (2009) while the 2014 survey showed similar results with 89.5% (CI: 87.9- 90.9) of the population reporting having had their last influenza shot within the current season (2014). As seen in Table 1, gender distribution was similar between 2009 and 2014 while older age, living in urban are, being married and being retired had the highest proportions of those vaccinated in both years. Social factors that had higher proportions of those vaccinated in 2009 and 2014 included having a chronic illness, being a nonsmoker, reporting better health, having the support of 1-2 persons, and having had a doctor's visit within the past year (Table 2).

TABLE 1. Demographic proportions for the Greek population who was vaccinated for seasonal influenza, with 95% Confidence Interval (CI)

	2009		2014		
	VCR %	95% CI	VCR %	95% CI	Diff.
Gender					
Male	46.8	43.8-49.7	46.3	43.8-48.9	-0.4
Female	53.2	51.3-57.6	53.7	51.1-56.2	0.4
Age, Categorical					
15-25	6.3	4.6-8.6	7.8	6.3-9.7	1.5
26-44	17.1	14.7-19.8	21.5	19.3-23.9	4.4
45-59	14.4	12.3-16.7	20.4	18.5-22.4	6.0
60+	62.2	59.1-65.2	50.3	47.4-53.2	-11.9
Education					
<Primary	16.2	14.4-18.3	12.4	10.9-14.0	-3.9
Primary	30.3	27.9-32.9	26.8	24.6-29.2	-3.5
Secondary	30.1	27.4-33.0	37.0	34.4-39.8	6.9
Non-tertiary	3.7	2.6-5.2	3.5	2.7-4.7	-0.1
Tertiary	19.6	17.1-22.4	20.2	17.9-22.7	0.6
Urbanization					
Urban	45.0	42.0-47.9	34.2	30.3-38.3	-10.8
Semi-urban	12.2	10.3-14.5	28.1	24.4-32.1	15.8
Rural	42.8	40.0-45.6	37.7	33.7-41.9	-5.1
Continued... Region					
Northern	28.0	25.5-30.6	28.1	24.5-31.9	0.1
Central	21.0	18.9-23.4	24.0	20.7-27.8	3.0
Attica	41.6	38.6-44.6	35.3	31.2-39.5	-6.3
Islands[1]	9.4	8.0-11.1	12.6	10.1-15.7	3.2
Marital status					
Single	14.0	11.7-16.7	17.0	14.9-19.2	3.0
Married	65.9	63.1-68.7	65.2	62.8-67.5	-0.7
Widowed[2]	20.0	18.2-22.0	17.8	16.3-19.4	-2.2
Employment					
Employed[3]	24.7	22.0-27.6	29.3	26.8-31.9	8.0
Unemployed	3.9	2.7-5.6	9.7	8.0-11.6	7.6
Student[4]	3.6	2.4-5.6	4.6	3.4-6.3	1.9
Retired[5]	50.3	47.3-53.2	40.7	38.1-43.4	-14.4
Disabled	2.2	1.5-3.2	3.7	3.0-4.7	1.4
Domestic tasks	15.3	13.5-17.3	12.0	10.6-13.5	-4.2

Note: Diff, differences between 2009 and 2014; 1, includes Crete; 2, includes divorced or separated; 3, includes unpaid, practicum, and leave; 4, includes further training, unpaid work and military service; 5, includes early retirement or given up business;

TABLE 2. Proportions for social factors among those vaccinated for seasonal flu in the Greek Population, with 95% Confidence Intervals (CI)

	2009		2014		
	VCR%	95% CI	VCR%	95% CI	Diff.
Chronic Illness					
Yes	67.0	64.0-69.9	60.8	57.7-63.7	-6.3
No	33.0	30.1-36.0	39.2	36.3-42.3	
Smoking Status					
Nonsmoker	73.1	70.3-75.8	74.2	72.0-76.3	1.1
Smoker	26.9	24.2-29.7	25.8	23.7-28.0	
Health Status					
Very good	21.0	18.4-23.8	28.8	26.1-31.6	7.8
Good	30.9	28.2-33.7	34.5	32.0-37.2	3.7
Fair	30.0	27.5-32.6	25.0	22.9-27.1	-5.0
Bad	12.5	11.0-14.3	8.6	7.5-9.8	-3.9
Very Bad	5.7	4.6-7.0	3.1	2.4-4.0	-2.5
People who Support					
None	4.4	3.5-5.5	5.4	4.5-6.6	1.1
1-2	54.7	51.8-57.7	58.7	56.0-61.4	4.0
3-5	34.3	31.5-37.2	31.3	28.8-33.9	-3.0
>6	6.6	5.3-8.3	4.5	3.4-6.0	-2.1
Continued... Last visit to Doctor					
Past year	46.3	43.3-49.3	68.2	65.5-70.7	21.9
>12 months ago	49.6	46.6-52.5	28.9	26.5-31.5	-20.6
Never	4.1	3.1-5.5	2.9	2.0-4.2	-1.2

Note: CI, confidence interval; diff, differences between 2009 and 2014.

Chronic Illness

The general population who reported having a chronic illness had a VCR of 38.2% (95% CI: 36.1-40.3) in 2008-2009 and 40.2% (95% CI: 37.8- 42.6) in 2013-2014. Those with chronic illness under the age of 60 had a VCR of 19.4% (95% CI: 16.6-22.7) in 2008-2009 and 23.4% (95% CI: 20.5-26.5) in 2013-2014 while those over 60 had VCRs of 54.1% (95% CI: 51.4-56.7) in 2008-2009 and 55.4% (95% CI: 52.5-58.3) in 2013-2014. VCRs among those with various chronic diseases increased slightly over time with a significant increase for hypertension, diabetes and back problems ($p < 0.05$) while those under age 60 years had generally lower VCRs (Figure 1). Among the total population with asthma, VCRs were 45.9% (95% CI: 38.8-53.2) in 2008-2009 and 48.0% (95% CI: 41.4-54.7) in 2013-2014 and slightly higher for those who had COPD with VCRs of 57.4% (95% CI: 49.5-65.0) and 60.0% (95% CI: 52.2-67.1), respectively. In those with asthma less than 60 years old, VCRs were 27.9% (95% CI: 18.8-39.2) in 2008-2009 and 30.1% (95% CI: 21.7-40.2) in 2014 while the same age group with COPD had VCRs between 35.3% (95% CI: 24.5-47.8) and 35.7% (95% CI: 22.8-51.0), respectively (Figure 1). An overall increase in VCR trend was observed in the population with asthma and COPD regardless of age.

Older population

In 2009, 49.6% (CI: 47.2-52.0) of those aged 60 and over were vaccinated against the seasonal flu whereas an increase was observed among the same age group with 52.7% (CI: 50.0-55.5) in 2014. A bivariate analysis in 2009

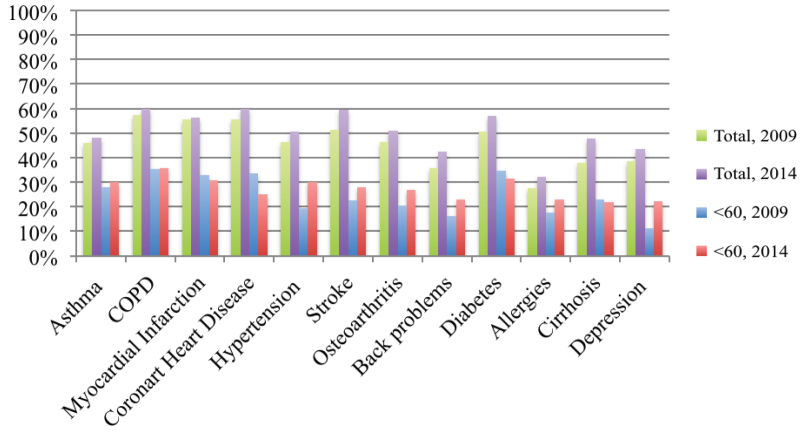

FIGURE 1. Vaccination Coverage Rates for those with chronic diseases in 2009 and 2014 by total and those <60 years of age. Note: COPD-Chronic Obstructive Pulmonary Disease, MI-Myocardial Infarction, CHD- Coronary Heart Disease. Total refers to the total population with various chronic diseases.

showed an initial association (p <0.25) of being vaccinated with chronic illness, smoking status, health status, education, employment, the degree of urbanization, gender, and number of people who support and were included for correlation analysis. 2014 showed the same initial associations as 2009 in addition to region and last doctor's visit. A correlation analysis did not show any correlated variables (Pearson's R <0.5). A final predictive model was created for those aged 60 years and older for 2009 and 2014 and can be seen in Table 3 and 4, respectively.

TABLE 3. Final logistic regression model for 2009 data of older adults (>60 years) who were vaccinated for seasonal influenza in Greece

	VCR%	OR	95% CI	P-value	Wald's
General pop.	49.6				
Chronic illness					
No	17.4	1.0			
Yes	82.6	1.6	1.2- 2.1	**0.001**	
Smoking Status					
Nonsmoker	84.4	1.0			
Smoker	15.6	0.6	0.4- 0.7	**0.000**	
Health Status					0.002
Very good	7.5	1.0			
Good	28.7	1.5	1.0- 2.2	**0.040**	
Fair	37.7	1.9	1.2- 2.8	**0.003**	
Bad	18.2	2.3	1.5- 3.6	**0.000**	
Very Bad	7.9	2.3	1.4- 3.8	**0.002**	
Employment					0.001
Employed	4.8	1.0			
Unemployed	0.5	1.6	0.4- 6.3	0.508	
Student[1]	0.2	5.5	0.6- 50.8	0.130	
Retired[2]	76.1	2.1	1.3- 3.4	**0.001**	
Disability[3]	2.3	1.4	0.6- 3.2	0.440	
Domestic	16.2	1.4	0.9- 2.3	0.179	
Degree of Urbanization					0.025
Urban	37.6	1.0			
Semi-urban	9.2	0.6	0.4- 0.9	**0.008**	
Rural	53.2	1.0	0.8- 1.2	0.661	
People Support					0.029
None	4.7	1.0			
1 to 2	58.2	1.3	0.9- 2.0	0.171	
3 to 5	32.0	1.1	0.7- 1.6	0.745	
More than 5	5.1	0.8	0.4- 1.4	0.360	

TABLE 4. Final logistic regression model for 2014 data of older adults (>60 years) who were vaccinated for seasonal influenza in Greece

	VCR %	OR	95% CI	P-value	Wald's
General pop.	52.7				
Smoking Status					
Nonsmoker	86.1	1.0			
Smoker	13.9	0.7	0.6- 1.0	**0.030**	
Health Status					0.001
Very good	6.0	1.0			
Good	35.2	1.7	1.2- 2.5	**0.003**	
Fair	38.7	2.0	1.4- 2.9	**0.000**	
Bad	14.7	2.4	1.6- 3.7	**0.000**	
Very Bad	5.4	2.4	1.3- 4.6	**0.007**	
Last Doctors visit					0.000
Last 12 months	79.8	1.0			
>12 months	19.6	0.6	0.4- 0.7	**0.000**	
Never	0.6	0.4	0.2- 1.0	**0.047**	
Education					0.007
<Primary	23.2	1.0			
Primary	41.1	0.8	0.6- 1.1	0.126	
Secondary	21.9	0.7	0.5- 1.0	**0.033**	
Non-tertiary	1.3	0.6	0.3- 1.5	0.300	
Tertiary	12.5	1.3	0.9- 1.9	0.208	
Region					0.044
Northern	31.6	1.0			
Central	25.4	1.3	1.0- 1.8	**0.045**	
Attica	32.8	1.5	1.1- 2.0	**0.010**	
Islands	10.3	1.3	0.9- 1.8	0.205	
Degree of Urbanization					0.010
Urban	33.6	1.0			
Semi-urban	24.7	1.2	0.9- 1.6	0.220	
Rural	41.7	1.6	1.2- 2.1	**0.003**	

In 2009, those over 60 years of age who had a chronic disease were 1.6 times (p=0.001) more likely to have been vaccinated than those who did not. A smoker was significantly less likely (p=0.000) than nonsmokers to be vaccinated for the seasonal flu. For health status, the worse someone rated their health, the more likely they were to have been vaccinated than someone who had

rated it "very good" (Wald's test, p=0.002). Those who were retired were 2.1 times more likely (Retired, p=0.001) than those employed to be vaccinated in 2009. Living in semi-urban areas of Greece were less likely (Semi-urban, p=0.008) to be vaccinated than those living in urban areas; however living in rural areas did not show any difference in VCRs than those living in urban areas. Logistic regression analysis did not show significant differences between number of people supporting an individual compared to those who did not have any, a Wald's test revealed the overall factor was important to include in the model for predicting vaccination among those older than 60 years of age (Wald's, p <0.05; Table 4).

Similar patterns for 2014 for smoking and health status were found for VCRs among older people. Having last seen by a physician over a year ago (p=0.000) or never (p=0.047) was significantly less likely to have been vaccinated than those who had seen one within the past 12 months. Those with secondary education were significantly less likely (p <0.05) to have been vaccinated than those with a primary education or less. Those living in Central Greece or Attica were significantly more likely to be vaccinated for the flu as compared to those living in Northern Greece. At the same time, those living in rural areas were significantly more likely (p=0.003) than those living in urban areas to be vaccinated in 2014 (Table 5).

DISCUSSION

The current study aimed to summarize influenza VCRs of those who got vaccinated in Greece in 2009 and 2014. It further aimed to identify coverage rates among those with chronic illness and those vaccinated over the age of 60. As previously mentioned, in Greece, seasonal vaccination is recommended and covered for all vulnerable populations. The current analysis showed that VCRs for seasonal influenza in Greece are low, including in vulnerable populations who also represented the largest proportions of those who get vaccinated. Following the 2009 H1N1 pandemic, a significant increase (p<0.001) in VCRs occurred in 2014 in the general population.

VCRs among those who had a chronic illness was 40.2% (in 2013-2014), well below the recommended EU coverage of 75% by 2014-2015[2]. Those under 60 years old with chronic disease had an even lower VCR of 23.4% (in 2013-2014), being half of those over 60 years old, signifying that although this group is considered a vulnerable population, those younger are not being vaccinated for the seasonal flu. Greece's VCRs among those with chronic disease in 2013-2014 were similar to VCRs of the 2012-2013 season in Germany, France and Norway[2]. A study on ICU admissions in 2009 for the H1N1 pandemic showed that 41% of the population admitted had at least one chronic illness, mainly asthma and COPD[13]. Considering this, VCRs for influenza among those who had asthma and COPD were alarmingly low in Greece and even more so in the age group under 60 years old. It is important this population has high VCRs for seasonal flu, especially those with respiratory conditions who carry the greatest risk for complications and death.

The lowest VCRs in the general population were among those aged 15-25. As this age group represents the majority of school and university students and those serving in the military resulting in their spending a bulk of their time in areas with high crowd density, they have an increased risk for infection and transmission of the influenza virus. During the 2009 H1N1 pandemic youth between 12 and 22 years were the most affected, a reminder that seasonal influenza is unpredictable, and that younger adults are not exempt from the risk of seasonal influenza[14].

In the current study, those aged 45-59 years of age also had very low VCRs in both years. This is in agreement with previous findings in which found that those aged 30-64 were more likely to have an intention to decline getting vaccinated for H1N1 than those aged 15-29 in 2009[15]. Epidemiological data from the Greek European Centre for Disease Control (KEELPNO) as well as a previous study by Rovina et al. showed that this age group has had the highest rates of intensive care units (ICU) and deaths among the entire population[13,16,17]. With approximately 59% of ICU cases in 2010-2011[16] and approximately 41% in 2013-2014[17] being between the ages of 30-59 years of age and an ICU stay in Greece costing approximately 4,300 euros per patient[18], it would be beneficial from an economic standpoint to protect this group, in addition to achieving improved health and prevention of transmission to others. Furthermore, this age group accounted for 94 of 180 deaths in 2010-2011[16] and 47 of 145 deaths in 2013-2014[17] flu seasons further highlighting the preventable loss of life from seasonal influenza in what is considered a non-high risk population.

Those older than age 60, who accounted for most of the population vaccinated, had a VCR of 52.7% in 2014, also below the recommended EU target of 75% by 2014-2015[2]. The VCR for older people in 2014, were similar to that in Malta, France, Germany, Norway and Denmark while above Central and Eastern European countries

such as Lithuania, Romania, Hungary, Slovenia Slovakia, Latvia and Estonia[2].

Studies in Greece have shown that the primary reason given by the public and healthcare practitioners for intention not to be vaccinated was the belief that the vaccine might not be safe[15,19,20]. Other reasons for non-intention have included the vaccine not being effective or perception that flu is not a threat[15,21,22]. With low VCRs that remain low over time and the concerns surrounding vaccine safety and effectiveness or a lack of perceived threat from influenza altogether, reveal gross misinformation among the general public and healthcare practitioners driving the need for more accurate and effective public health communication strategies surrounding the seasonal flu.

In agreement with this study's findings, previous studies have also shown that among the older population, being married, use of medical services, having a chronic disease are more likely to be vaccinated[23]. Perceived health status was also significantly associated with being vaccinated among the older population and can be explained by the likeliness that having a chronic illness influences self-perceived health status. An interesting behavioral result is that smokers were less likely to be vaccinated. As smoking is known to compromise respiratory system defense by impairing mucociliary clearance mechanism, increasing the permeability of respiratory epithelial cells, and decreasing humoral-mediated and cell-mediated immunity[24], smokers are at higher risk for respiratory infections with increased severity and risk for complications and would therefore benefit from receiving the annual flu shot.

The results of the current study widen the understanding of VCRs in Greece and support vaccination strategies for controlling influenza epidemics and protecting the public. The results of this study also align with previous research evidence on reasons for non-vaccination in Greece and Europe. Further research is needed to explore healthcare workers' practices on recommending vaccination as well as VCRs in other vulnerable populations. Limitations to the current study included structure of the question on flu vaccination, as it was not possible to assess and compare flu seasons. The current study is cross-sectional and cannot assume inference.

CONCLUSION

In a country that faces a prolonged economic crisis that has exhausted its health system's resources, prevention is key to relieving the burden of disease. Influenza vaccination is the only cost-effective and preventive measure to control seasonal influenza epidemics. Addressing this public health issue by improving VCRs would decrease transmission and incidence rates, ICU admissions and deaths and consequently relieve costs while also reducing loss in productivity in the workforce[1]. It could be extremely beneficial to invest in communication strategies aimed at increasing the public's capacity in order to increase VCRs and prevent influenza, as opposed to managing expensive and devastating epidemics.

Statement of Conflict of interest:

The authors declare no potential conflicts of interest.

Funding information:

The current study was funded by the George D. Behrakis Foundation.

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