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The impact of seasonal influenza vaccination uptake on COVID-19 vaccination attitudes in a rural area in Greece

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ABSTRACT

Introduction: Promoting vaccination for coronavirus disease 2019 (COVID-19), especially for high-risk groups such as the elderly and persons with comorbidities, is important for reducing the incidence of severe disease and death.
Methods: Retrospective cross-sectional study of factors associated with COVID-19 vaccination, including previous influenza vaccination, among all persons who received medical services in a rural area in Crete, Greece, between October 2020-May 2021.
Results: Among 3129 participants, receipt of influenza vaccination in 2020–21 was strongly associated with COVID-19 vaccination, as was influenza vaccination in 2019–20, albeit to a lesser extent. In addition, persons older than 59 years (with exception of those 90 + years old) and those who lived closer to the hospital/health center, were more likely to vaccinate for COVID-19. Persons younger than 40 years of age, females, persons with mental illness or neurologic disease, were also less likely to vaccinate for COVID-19 (all $p < 0.001$).
Conclusions: COVID-19 vaccination was more likely among those who were vaccinated for influenza before and during the pandemic. Access to healthcare services and specific comorbidities, were important influencers for vaccination, underlying the importance of tailored interventions to enforce vaccination in high-risk groups.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a highly transmissible respiratory infection caused by the severe acute respiratory syndrome coronavirus 2 virus (SARS-CoV-2). The first COVID-19 case in Greece was confirmed in February 2020, with data reporting a total of 5,188,890 cases and 33,750 deaths by 8 November 2022 in the country [1].

Promoting primary prevention through vaccination, especially for high-risk groups such as the elderly and persons with comorbidities, is crucial for reducing the incidence of severe disease and death [2]. In Greece, vaccinations for COVID-19 commenced in late December 2020 and by end of October 2022, a total of 7,910,910 people (74.1 % of the total population) had received at least one vaccine dose [3]. Despite vigorous efforts to achieve high vaccine coverage worldwide through organized vaccination programs and public awareness campaigns, compliance was suboptimal for a significant proportion of the general population [4].

Understanding the barriers to and predictors of COVID-19 vaccination is important to improve coverage and protect public health. Studies have previously sought to juxtapose compliance with and hesitancy about the COVID-19 and influenza vaccines [5]. We therefore hypothesized that acceptance of influenza vaccination might be associated with subsequent COVID-19 vaccination.

The aim of our study was to identify individual predictors of COVID-19 vaccination, including past receipt of the seasonal influenza vaccine during the preceding two winter seasons, in a large population sample of a rural area in Greece.

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2. Methods

2.1. Study aims

The specific aims of this study were to evaluate:

a) the rates of influenza vaccination in a large population sample of a rural area in the periods before (influenza vaccination period 2019–2020) and after (influenza vaccination period 2020–2021) the initiation of the COVID-19 vaccination period in Greece.
b) the association between influenza vaccination and full COVID-19 vaccination.
c) factors associated with COVID-19 vaccination.

2.2. Study design and setting

A retrospective cross-sectional study among all adults who visited or were admitted to the General Hospital/Community Health Center and public peripheral medical centers of Sitia, Crete, Greece, from October 2020 through May 2021. This network of public health centers provides health services to a population of more than 18,000 people, with a 75-bed capacity, 15 medical specialties, a 24-hour emergency department and 6 peripheral medical centers.

2.3. Data collection and definitions

Demographics, comorbidities, medications, vaccination status for influenza (2019–20 and 2020–21 seasons) and for COVID-19 were retrieved during patient interviews, from clinical records and from the national electronic prescription system.

Polypharmacy was defined as concomitant receipt of 5 or more drugs. Immune compromise was defined as a person receiving immunosuppressive agents or corticosteroids > 20 mg/day for more than two weeks, and transplant patients. Malignancy was defined as a person receiving treatment for malignancy or with a current history of malignancy. A person was considered vaccinated for COVID-19 if they had received two vaccine doses by 15 July 2021, which was the last day of data collection. The reason for stopping the collection of data at this specific date was that on that day, the mandatory vaccination of certain professional groups was announced by the Greek government.

2.4. Statistical analysis

Individual-level characteristics were compared between participants vaccinated and unvaccinated against COVID-19 using the Mann-Whitney and Pearson chi-squared tests for continuous and categorical variables respectively. Influenza vaccination rates in the 2019–20 and 2020–21 seasons were compared with the McNemar paired test. The association between full COVID-19 vaccination and influenza vaccination during 2019–20 and 2020–21 was examined in a multivariate logistic regression model, adjusted for age, sex, individual comorbidities and distance between the person's residence and the General Hospital/Health Center. We further attempted to include in the model an indicator for polypharmacy (receipt of five or more drugs regularly), and an interaction term between influenza vaccination during the two seasons (to assess whether regular receipt of the seasonal influenza vaccine during both seasons is a stronger predictor of COVID-19 vaccination); model comparison was performed with a likelihood ratio test. Potential collinearity in all models was examined by calculating Variance Inflation Factors for each covariate. All analyses were performed using the R software environment, version 4.2.

2.5. Ethics

Performance of the study and access to patient data was approved by the General Hospital/ Community Health Center of Sitia Scientific Council (decision 5494/20–10-2021).

3. Results

During the 8-month study period, a total of 3129 patients visited the General Hospital/Community Health Centers of Sitia and comprise the study population (Table 1). Approximately half (1640 persons, 52.4 %) were female, 12.1 % were younger than 60 years old, 45.1 % were 60–79 years old, and 42.8 % were older than 79 years. The most common comorbidities were hypertension (66.0 %), dyslipidemia (60.4 %), diabetes (29.5 %), chronic heart failure (26.4 %) and mental illness (23.5 %).

A total of 2070 study participants (66.2 %) were vaccinated for seasonal influenza in the 2019–20 season, rising significantly to 2665 (85.2 %) in 2020–21 ($p < 0.001$). Among the 1059 participants not vaccinated during 2019–20, 668 (63.1 %) received an influenza vaccine the following season, whereas nearly all influenza vaccine recipients in 2019–20 were vaccinated again in 2020–21 (1997/2070 participants, 96.5 %).

A total of 2399 participants (76.7 %) had been vaccinated for COVID-19 with 2 doses until 15 July 2021; the 730 (23.3 %) unvaccinated participants include 86 partially vaccinated with 1 dose (11.8 %) and 644 completely unvaccinated (88.2 %). A comparison of demographic characteristics and comorbidities between COVID-19 fully vaccinated and unvaccinated (or not fully vaccinated) persons is presented in Table 1. The age distribution was similar ($p = 0.12$) but there were fewer women among the fully vaccinated participants ($p < 0.001$). Participants fully vaccinated for COVID-19 were more commonly vaccinated for influenza both in 2019–20 and 2020–21, lived closer to the hospital/health center, were more likely to have hypertension and dyslipidemia, but less likely to suffer from mental illness or neurologic disease (all $p < 0.001$, Table 1).

Table 2 presents the results of the multivariable logistic analysis. Receipt of influenza vaccination in 2020–21 was strongly associated with COVID-19 vaccination (Odds Ratio, OR, 2.44, 95 % CI: 1.90–3.13), as was influenza vaccination in 2019–20 albeit to a lesser extent (OR 1.30, 95 % CI: 1.05–1.60). Compared to the 50–59 years age group, people younger than 40 years were less likely to be fully vaccinated against COVID-19, while people older than 59 years more likely to be vaccinated, with the exception of the 90 + years age group (Table 2). Female sex and the presence of diabetes, atrial fibrillation or other arrhythmias, mental illness and neurologic disease, were all independently associated with reduced odds of COVID-19 vaccination, while dyslipidemia was associated with increased odds. Finally, living farther from the hospital/health center decreased the odds of vaccination by about 11 % for every 10 km of distance (Table 2). There was no evidence of collinearity in the model, with all Variance Inflation Factors under 1.6 (data not shown). Adding the variable for polypharmacy in the model did not result in an improved fit ($p = 0.18$), nor did addition of an interaction term between influenza vaccination during the two seasons ($p = 0.7$). A sensitivity analysis excluding the 86 persons vaccinated with 1 dose did not meaningfully alter the results (online supplement).

4. Discussion

Our study population comprises all persons who sought health services in an 8-month period during the first months of the COVID-19 vaccination program in Greece. The study cohort covers

Table 1
Demographic characteristics, comorbidities of study population and univariate comparisons between participants fully vaccinated (with 2 doses as of 15 July 2021) and unvaccinated (or partially vaccinated) for COVID-19.

	Total (N = 3129)	COVID fully vaccinated (N = 2399)	COVID unvaccinated / partially vaccinated (1-dose) (N = 730)	p-value
Females	1640 (52.4)	1213 (50.6)	427 (58.5)	**<0.001**
Age*	76.0 (66.0–84.0)	77.0 (67.0–84.0)	75.0 (63.0–85.8)	0.12
Age < 40	50 (1.6)	24 (1.0)	26 (3.6)	**<0.001**
Age 40–49	91 (2.9)	60 (2.5)	31 (4.2)	0.02
Age 50–59	237 (7.6)	154 (6.4)	83 (11.4)	**<0.001**
Age 60–69	649 (20.7)	516 (21.5)	133 (18.2)	0.06
Age 70–79	763 (24.4)	598 (24.9)	165 (22.6)	0.22
Age 80–89	1075 (34.4)	883 (36.8)	192 (26.3)	**<0.001**
Age 90+	264 (8.4)	164 (6.8)	100 (13.7)	**<0.001**
Influenza vaccination in 2019	2070 (66.2)	1667 (69.5)	403 (55.2)	**<0.001**
Influenza vaccination in 2020	2665 (85.2)	2135 (89.0)	530 (72.6)	**<0.001**
Distance to center (km)*	9.4 (1.3–23.9)	7.4 (1.3–23.9)	16.8 (1.3–27.3)	**<0.001**
Comorbidities				
Diabetes mellitus	922 (29.5)	699 (29.1)	223 (30.5)	0.5
Heart failure	826 (26.4)	624 (26.0)	202 (27.7)	0.4
Other cardiovascular disease	706 (22.6)	552 (23.0)	154 (21.1)	0.3
AF or other arrhytmia	723 (23.1)	535 (22.3)	188 (25.8)	0.06
Hypertension	2063 (66.0)	1620 (67.6)	443 (60.7)	**<0.001**
Dyslipidemia	1889 (60.4)	1500 (62.6)	389 (53.3)	**<0.001**
Pulmonary disease	350 (11.2)	256 (10.7)	94 (12.9)	0.11
Gastrointestinal disease	59 (1.9)	43 (1.8)	16 (2.2)	0.59
Mental illness	736 (23.5)	516 (21.5)	220 (30.1)	**<0.001**
Dementia	483 (15.4)	376 (15.7)	107 (14.7)	0.54
Rheumatologic / Connective tissue disease	212 (6.8)	164 (6.8)	48 (6.6)	0.87
Thyroid disease	319 (10.2)	248 (10.3)	71 (9.7)	0.68
Osteoporosis / osteopenia	684 (21.9)	527 (22.0)	157 (21.5)	0.83
Malignancy	147 (4.7)	106 (4.4)	41 (5.6)	0.22
Immunocompromise	264 (8.4)	201 (8.4)	63 (8.6)	0.89
Neurologic disease	210 (6.7)	138 (5.8)	72 (9.9)	**<0.001**
Polypharmacy > 4 drugs	1112 (35.5)	843 (35.2)	269 (36.8)	0.43

* Median (IQR) and Mann-Whitney test. For all other variables: number (percentage) and Fisher's test.

Table 2
Multivariate logistic model for predictors of COVID-19 vaccination.

	Odds Ratio	p-value
Age < 40	**0.49 (0.25–0.94)**	**0.032**
Age 40–49	1.05 (0.61–1.81)	0.86
Age 50–59	Reference	
Age 60–69	**1.56 (1.10–2.21)**	**0.013**
Age 70–79	**1.44 (1.02–2.03)**	**0.039**
Age 80–89	**1.86 (1.32–2.63)**	**<0.001**
Age 90+	0.66 (0.44–1.01)	0.05
Females	**0.70 (0.58–0.85)**	**<0.001**
Influenza vaccination in 2019–20	**1.30 (1.05–1.60)**	**0.015**
Influenza vaccination in 2020–21	**2.44 (1.90–3.13)**	**<0.001**
Diabetes mellitus	**0.80 (0.65–0.97)**	**0.027**
Heart failure	0.92 (0.76–1.12)	0.42
Other cardiovascular disease	0.93 (0.74–1.16)	0.51
AF or other arrhythmia	**0.77 (0.62–0.96)**	**0.018**
Hypertension	1.11 (0.90–1.35)	0.33
Dyslipidemia	**1.34 (1.10–1.62)**	**0.003**
Pulmonary disease	0.80 (0.61–1.05)	0.11
Gastrointestinal disease	0.82 (0.44–1.52)	0.52
Mental illness	**0.68 (0.55–0.83)**	**<0.001**
Dementia	1.28 (0.97–1.71)	0.09
Rheumatologic / Connective tissue disease	1.01 (0.66–1.56)	0.95
Thyroid disease	1.15 (0.85–1.55)	0.36
Osteoporosis / osteopenia	1.06 (0.85–1.33)	0.6
Malignancy	0.65 (0.38–1.11)	0.12
Immunocompromise	1.22 (0.75–1.99)	0.42
Neurologic disease	**0.58 (0.41–0.81)**	**0.001**
Distance to center (per 10 km)	**0.89 (0.84–0.94)**	**<0.001**

a notable proportion of the local population (>17 %) who sought care during the study period. The importance of our study lies in confirming that influenza vaccination (both during seasons 2019–20 and 2020–21) is associated with full COVID-19 vaccination, whereas accessibility is an important driver of vaccination, as longer distance was associated with lower odds of COVID-19 vaccination. The fact that persons older than 89 years were less likely to get vaccinated against COVID-19 compared to persons aged 60–89, can also be considered affirmative of access issues.

Previous studies have shown an association between previous influenza vaccination and COVID-19 vaccine willingness and/or acceptance [6,7]. Our findings add to the literature, by confirming the association between influenza vaccination and vaccination for COVID-19. It is worth noting that a higher proportion of participants were vaccinated for influenza during the 2020–21 season (85.2 %) compared to the 2019–20 season (66.2 %, p < 0.001) and influenza vaccination during the 2020–21 season had a stronger association with COVID-19 vaccination. This could be either due to timing as these persons were closer to their COVID-19 vaccination, thus increasing the odds of vaccine acceptance, or due to more effective health communication provided by healthcare workers [8].

Access, convenience and distance, are important drivers of vaccination, particularly during public health crises [9–11]. Our findings corroborate those of previous studies that highlighted these factors as important influencers of vaccine acceptance. However, to our knowledge, specific age-stratified determinants of accessibility have not been defined. It is a fact that elderly patients are usually less mobile or rely on their caregivers to reach a health service. From a social perspective, altered risk perception could also be an influencing factor, attributed to social isolation of the elderly during the pandemic, which aimed to minimize contacts and thus decrease their risk of infection. In addition, avoidance of crowded public settings due to fear of contracting COVID-19 might have

counterintuitively played a role in avoiding vaccination clinics. Ineffective communication, such as lack of information and misinformation, was also found to be an important contributor in the decision for vaccination among older adults. Hence, in such situations and when specific age groups are considered high risk for severe infection, it is important to address access issues to vaccines with tailored interventions, including improvement of access (e.g., increasing vaccination sites, providing at-home vaccination services) and enhancing communication by providing prompt and accurate information on the usefulness and effectiveness of vaccines.

We detected several other factors that lowered the odds of COVID-19 vaccination; specifically, persons younger than 40 years of age, females, persons with mental illness, neurologic disease, diabetes mellitus, and persons with atrial fibrillation or other cardiac arrhythmias. Young adults, probably due to higher confidence and lower risk perception in association with COVID-19, as well as females, are known to have lower rates of COVID-19 vaccination [9,12–14]. Mental illness was recorded in a high proportion of our population (23.5 %), which leads us to believe that they represent an heterogenous group of conditions. Therefore, different reasons might have accounted for their lower propensity to vaccinate, such as altered risk perception, altered health beliefs, ineffective communication, and fewer options of access to health services. Given the higher mortality risk due to COVID-19 in persons with severe mental illness compared to the general population, strategies to enhance vaccination acceptance are imperative, including targeted communication and improved access [15]. Similar reasons for lower vaccination might be related to persons with neurologic disease, where another factor could be the general perception that vaccines are associated with neurological adverse events. Persons with dyslipidemia and hypertension typically have frequent visits and contacts with healthcare services and thus, their higher rates of vaccination might reflect effective communication and better access to health centers. In addition, hypertension was found to be associated with severe COVID-19 early during the pandemic, which might have prompted these patients to vaccinate [16]. On the other hand, we were unable to explain the reason why persons with diabetes mellitus and atrial fibrillation/other arrhythmias had lower uptake of COVID-19 vaccination in our study.

Certain limitations should be acknowledged in our study. Single country setting and the rural location limit generalizability of our findings. The retrospective manner of the study might have impacted the quality of data, despite the fact that we used various sources to retrieve information. We analyzed partially vaccinated participants together with the unvaccinated, even though their motivations and rates of vaccine acceptance might differ; nevertheless, excluding the partially vaccinated did not meaningfully alter our results and conclusions. We did not have information on past COVID-19 incidence; participants with previous infection might have deferred or avoided vaccination altogether. Finally, although our findings confirm the association between influenza and COVID-19 vaccination and, despite the high influenza vaccination rate among our population, our study was not designed to detect specifically those who were consistently vaccinated every year.

In conclusion, the current study provides meaningful information on factors that affected COVID-19 vaccination in a rural area in Greece. The odds of COVID-19 vaccination were higher among those who were vaccinated for influenza before and during the pandemic and those who lived closer to the vaccination center, whereas younger persons and persons with specific underlying conditions such as mental illness and neurologic disease, were less likely to vaccinate. In order to increase vaccine acceptance and vaccination rates, future strategies should be appropriately tailored to the characteristics and needs of different patient groups and geographic situations, whereas ease of access should be taken into account, particularly in rural areas and among populations with accessibility issues.

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Data availability

Data will be made available on request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.12.024.

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