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Posted Date: 26 June 2025

doi: 10.20944/preprints202506.2118.v1

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 doi:10.20944/preprints202506.2118.v1

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Examining Vaccination Coverage in Patients with Diagnosis of Chronic Liver Disease and Cirrhosis. A Cross-Sectional Study in Greece

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Abstract

Background/Objectives: Seasonal influenza, pneumococcal disease, and Coronavirus disease (COVID-19) constitute a serious public health concern, as they impact a substantial portion of the population, in particular patients with chronic diseases. The aim of this study was to investigate vaccine coverage in patients with chronic liver disease and cirrhosis, about influenza, pneumococcal, and COVID-19 vaccines, and to identify the sociodemographic and clinical factors affecting it. **Methods:** A cross-sectional study was conducted. The study population consisted of patients with a diagnosis of chronic liver disease and liver cirrhosis. The study was conducted from March 2022 to July 2023. **Results:** A convenience sample size of 300 patients (age ≥ 30) participated. Regarding their vaccination, 88.3% were vaccinated against SAR-Covid-19, 44.8% against pneumococcus, and 54.7% against seasonal influenza this year. Patients' belief that annual vaccination is the best method for influenza prevention was found to be significantly higher among older patients and those with comorbidities. Also, patients who had been vaccinated against seasonal influenza (this year or every year), against pneumococcus, or SAR-Covid-19 agreed significantly that annual vaccination is the best method for influenza prevention. In addition, patients who were informed about vaccination by their doctor/ nurse agreed significantly more with that. Multiple logistic regression found that a four times greater probability of being fully vaccinated according to the national vaccination program was found in patients who were informed about vaccination by a doctor/nurse. Moreover, as patients' age increased, so did the probability of being fully vaccinated. **Conclusions:** The study's findings can be utilized in public health initiatives and by healthcare practitioners addressing patients with low vaccination adherence.

Keywords: Beliefs; cirrhosis; COVID-19; disease; influenza; liver; pneumococcal; uptake; vaccine

1. Introduction

Seasonal influenza, pneumococcal disease, and Coronavirus disease (COVID-19) constitute a serious public health concern, as they impact a substantial portion of the population and frequently have considerable effects on patients. The estimated incidence of influenza across all age groups varied from 3.0% to 11.3% per season, with a median of 8.3%, while the rate for individuals aged 18 to 64 was 8.9% [1]. Seasonal influenza accounts for over 5 million hospital admissions, with elevated hospitalization rates among elderly patients (≥65 years) [2]. The estimated mean annual influenza-associated respiratory excess mortality rates ranged from 0.1 to 6.4 per 100,000 individuals for people younger than 65 years, with rates increasing in older people, reaching 17.9 to 223 per 100.000 for people older than 75 years [3]. The burden of pneumococcal community-acquired pneumonia (CAP) in Europe is also high, with older people with co-morbidities being the most vulnerable groups in

 doi:10.20944/preprints202506.2118.v1

the population. What is particularly important is that most cases of pneumococcal CAP (30%-78%) were caused by serotypes covered by the PCV13 vaccine [4]. The risk of invasive pneumococcal disease is demonstrated to be 2 to 13 times greater in individuals with chronic liver disease relative to the general population, contingent upon age. The likelihood of complications is markedly elevated in cirrhosis, encompassing severe infection, bacteremia, and mortality [5]. In the US, it is estimated that in 5% of adult patients hospitalized for CAP, the responsible pathogen is pneumococcus [6]. The COVID-19 epidemic in recent years has caused millions of infections and fatalities globally, rendering it the most critical public health concern of recent decades. Populations at heightened risk for severe disease and mortality comprised the elderly and individuals with underlying comorbidities, including hypertension, diabetes, obesity, chronic lung conditions, and disorders of the heart, liver, and kidneys [7].

The fundamental public health intervention to safeguard the population against the aforementioned three diseases is vaccination [8]. Patients with liver disease, particularly those with cirrhosis, are a vulnerable population for seasonal influenza infection. Vaccination provides substantial protection by enhancing seroconversion rates, ensuring strong immunogenicity, and reducing the risk of hospital admission, without there being patient safety issues [9,10]. Patients with chronic liver disease exhibited elevated seroconversion rates and substantial protection against COVID-19 infection following vaccination [11]. It is projected that COVID-19 vaccinations have preserved about 1.5 million lives in European countries from December 2020 to March 2023 among individuals aged 25 and older [12]. Despite the absence of extensive studies on the efficacy of the pneumococcal vaccine in individuals with liver diseases, it is advised for this cohort of chronic patients.

Despite the safety and efficacy of these vaccinations, vaccination rates among people with liver disease remain significantly low. Concerning seasonal influenza, vaccination rates among patients with liver cirrhosis approximate 40%. Concerning pneumococcal disease vaccination in individuals with liver disease, rates begin at 3.7% at diagnosis and increase to 10.8% after five years, underscoring the exceedingly low acceptance of this vaccine [13,14]. The vaccination rates for COVID-19 among individuals with liver cirrhosis differ by country, ranging from 31.7% to 89.7% [15]. Detrimental factors influencing the vaccination of individuals with liver disease encompass insufficient knowledge about the vaccine, age under 65 years, apprehension regarding post-vaccination consequences, and perceived vaccine inefficacy [15–17]. Factors that enhance the probability of vaccination acceptance comprise increased interaction with healthcare professionals, prior vaccination history, age (≥65 years), current tobacco use, poor health status, inadequate self-reported household income, and the presence of comorbidities [14,18].

Highlighting vaccination coverage and the factors influencing it is an important factor in designing effective public health programs. The body of literature regarding vaccination coverage in patients with chronic liver disease, particularly those with cirrhosis, is scarce. To examine the factors influencing patients' vaccination behavior, an extensive investigation of the demographic and clinical characteristics of patients should be conducted, as has been chosen in the present study.

In this context, this study aimed to investigate vaccine coverage in patients with chronic liver disease and cirrhosis, to influenza, pneumococcal, and COVID-19 vaccines, and to identify the sociodemographic and clinical factors affecting it.

2. Materials and Methods

2.1. Study Design

A cross-sectional study was conducted. The study population consisted of patients with a diagnosis of chronic liver disease and liver cirrhosis, who visited the outpatient hepatology clinics of two university hospitals in Athens, Greece. A convenience sample size of 300 patients participated. The study was conducted from March 2022 to July 2023. The inclusion criteria were patients over 30 years of age, diagnosed with chronic liver disease and cirrhosis, absence of psychiatric diseases, and

 doi:10.20944/preprints202506.2118.v1

proficient in reading and speaking Greek. The prevalence of chronic liver disease and cirrhosis markedly escalates post the age of 30. The primary etiologies, including alcoholic liver disease, non-alcoholic fatty liver disease, and chronic viral hepatitis, necessitate prolonged exposure and time for progression. Moreover, individuals over 30 years of age with cirrhosis or chronic liver disease face an elevated risk of severe consequences from influenza due to diminished liver and immunological reserves. Vaccination in this demographic is essential for averting hospitalizations and fatalities. Those who did not meet the study inclusion criteria and those who did not give their consent or withdrew their consent during the study were excluded from the study.

2.2. Data Collection

The initial patient interaction was conducted by a medical team member, who introduced the researcher. Following verbal assent, the researcher, also part of the medical team, proceeded with the procedure. The researcher clarified the study's goal, addressed any inquiries, and distributed the consent forms and questionnaires at varying intervals to maintain participant anonymity. The anonymity of participants was safeguarded, with no interaction occurring among them, as the survey was administered in a designated room within the Outpatient Clinics. The data gathering method employed was convenience sampling. All patients who solicited for participation in the study consented to engage, resulting in a 100% response rate.

The survey instrument was a structured questionnaire developed specifically for this study, informed by data from international scientific literature. A literature review was undertaken on vaccine coverage in both healthy adults and patients with chronic disease, chronic liver disease, and cirrhosis, regarding influenza, pneumococcal, and COVID-19 vaccines [8,13,15–17,19–24]. This questionnaire was developed by the research team in alignment with the study's objectives; thus, no approval is necessary. The expertise of academics and professors in communicable diseases, infection control, public health, community nursing, and vaccinations, alongside statistical science, substantially aided in the development of the questionnaire. The initial questionnaire consisted of 100 items. A panel of nursing professors and four specialists in infection control and vaccinations was briefed about the tool's aim to ensure clarity and suitability. After careful review of the questionnaire, they provided feedback, categorizing each item as "essential," "useful but inadequate," or "unnecessary." Following the evaluation of expert feedback, 38 items were integrated into the final questionnaire, with the support of a statistical scientist. A pilot study involving 42 patients was conducted before the main study to identify potential comprehension challenges with the questions.

The final questionnaire included the socio-demographic characteristics of the participants that encompassed 10 variables on gender, age, height, weight (body mass index), ethnicity, marital and work status, educational attainment, and habits regarding smoking and alcohol usage. The influenza vaccination section comprises 11 items addressing vaccination status, duration since vaccination, annual administration, reasons for non-vaccination, and additional inquiries regarding pneumococcal and SARS-CoV-2 vaccinations. Additionally, if individuals contracted influenza post-vaccination, please specify the frequency of illness, instances of hospitalization, duration of hospitalization, and predominant symptoms experienced, including fever, headache, diarrhea, vomiting/nausea, sleepiness, myalgia/arthralgia, irritability, etc. This section also encompasses four additional items regarding participants' beliefs about influenza vaccination, including whether annual vaccination is the most effective method for preventing influenza, whether it is detrimental to patients with pre-existing conditions, whether they receive all vaccines recommended by the National Immunization Program, and their primary source of information regarding the influenza vaccine.

The third component of the questionnaire has 13 items on the clinical features of individuals. Initially, it comprises six questions detailing general data, including year of diagnosis, disease duration, disorder type (liver cirrhosis, hepatocellular carcinoma, hepatitis), etiological factors (hepatitis B, hepatitis C, alcohol), Child-Pugh score classification (A, B, C), and co-morbidities. Subsequently, four items about the type of drug therapy administered in the past six months are

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specified, including corticosteroid preparations such as cortisol, prednisolone, and methylprednisolone, as well as immunosuppressants like interferon A-IFN-α, pegylated interferon (Peg-IFN-α), lamivudine, and entecavir. The results of laboratory tests were documented, including platelet levels (x104/mm3), albumin levels (3.5g/dl), and prothrombin (80%).

2.3. Ethical Issues

The study was approved by the Ethics Committee of the two hospitals (approval number: 24286, 16/09/2021; 986, 26/10/2021). Signed informed consent has been obtained from all participants after informing them about the purpose of the study, confidentiality, and the voluntary nature of participation. Moreover, we conducted our study in accordance with the Declaration of Helsinki [25].

2.4. Statistical Analysis

Quantitative variables were expressed as mean values (Standard Deviation) and as median (interquartile range), while categorical and ordinal variables were expressed as absolute and relative frequencies. For the comparison of proportions, chi-square tests were used. Mann-Whitney or Kruskal-Wallis tests were used for the comparison of ordinal variables among two or more than two groups, respectively. Student's t-test was used for the comparison of continuous variables between two groups. Spearman correlation coefficients (rho), were used to explore the association between ordinal and continuous variables. The coefficient is considered very high when it is above 0.9, high when it is 0.7-0.9, moderate when it is 0.5-0.7, low when it is 0.3-0.5, and very low when it is below 0.3 [26]. Logistic regression analysis in a stepwise method (p for entry 0.05, p for removal 0.10) was used to find independent factors associated with being fully vaccinated according to the national vaccination program. Adjusted odds ratios (OR) with 95% confidence intervals (95% CI) were computed from the results of the logistic regression analyses. Multiple linear regression analysis was used with dependent the variables presented patients' beliefs on vaccination against influenza, in a stepwise method. Adjusted regression coefficients (β) with standard errors (SE) were computed from the results of the linear regression analyses. All reported p values are two-tailed. Statistical significance was set at $p<0.05$ and analyses were conducted using SPSS statistical software (version 26.0).

3. Results

The sample consisted by 300 patients (56.3% males), with mean age 61.4 years (SD=12.1 years). Their characteristics are presented in Table 1. Most patients had normal BMI (47.8%), were Greeks (82.9%), were married (63.5%) and were middle/high school graduates (50.7%). Also, 65.6% smoked, 59% consumed alcohol and 70.3% had a concomitant disease. Regarding their vaccination, 88.3% were vaccinated against SAR-Covid-19, 44.8% against pneumococcus and 54.7% against seasonal influenza this year. Moreover, 52.2% believe very much that annual vaccination is the best method for influenza prevention and 78.3% did not think at all that vaccination against influenza is harmful in patients with their disease. All vaccinations according to the national vaccination program had done 55.9% of the sample and main source about vaccination was their doctor/ nurse (54.7%). From hepatitis suffered 55.0% of the sample, from liver cirrhosis 39% and from hepatocellular carcinoma 11.3%.

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Table 1. Sample characteristics.

n=300	n (%)
Gender	
Male	169 (56.3)
Female	131 (43.7)
Age (years), mean (SD)	61.4 (12.1)
BMI levels	
Underweight	20 (6.7)
Normal	143 (47.8)
Overweight	94 (31.4)
Obese	42 (14)
Nationality	
Greek	248 (82.9)
Other	51 (17.1)
Married	190 (63.5)
Employed	93 (31.0)
Educational level	
None/ Primary school	93 (31)
Middle/ High school	152 (50.7)
University/ MSc/ PhD	55 (18.3)
Smoking	196 (65.6)
Alcohol consumption	177 (59)
Comorbidities	211 (70.3)
Vaccinated against seasonal influenza this year	164 (54.7)
Vaccinated against seasonal influenza every year	159 (53.2)
Vaccinated against pneumococcus	134 (44.8)
Vaccinated against SAR-Covid-19	264 (88.3)
Do you believe that annual vaccination is the best method for influenza prevention?	
Not at all	17 (5.7)
A little	20 (6.7)
Moderately	49 (16.4)
Much	57 (19.1)
Very much	156 (52.2)
Do you think that vaccination against influenza is harmful in patients with your disease?	
Not at all	234 (78.3)
A little	26 (8.7)
Moderately	25 (8.4)
Much	10 (3.3)
Very much	4 (1.3)
Have you had all vaccinations according to the national vaccination program?	167 (55.9)
The main information source about vaccination	
Doctor/ Nurse	164 (54.7)
Pharmacist	44 (14.7)
Media	76 (25.3)
Conferences / Informative events	2 (0.7)
Friends/ Family	21 (7)
Printed material	1 (0.3)
Other	9 (3)
Diagnosis	
Liver cirrhosis	117 (39)

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Hepatocellular carcinoma	34 (11.3)
Hepatitis	165 (55)

The association of patients' beliefs that annual vaccination is the best method for influenza prevention with their characteristics is provided in **Table 2**. Significantly higher levels of agreement were found among married patients, those who were not employed, older patients, and those who had a comorbidity. Also, patients who had been vaccinated against seasonal influenza (this year or every year), against pneumococcus, or SAR-Covid-19 agreed significantly that annual vaccination is the best method for influenza prevention. In addition, patients who were informed about vaccination by their doctor/ nurse agreed significantly more with that, while those who were informed by their friends/family agreed significantly less.

Table 2. Association of belief that annual vaccination is the best method for influenza prevention with patients' characteristics.

		Do you believe that annual vaccination is the best method for influenza prevention?[1]		
		Mean (SD)	**Median (IQR)**	**P**
Gender	Male	4.14 (1.13)	5 (3 — 5)	0.241[+]
	Female	3.94 (1.30)	4 (3 — 5)	
BMI levels	Underweight	4.25 (1.07)	5 (3.5 — 5)	0.891[++]
	Normal	4.03 (1.21)	5 (3 — 5)	
	Overweight	4.11 (1.17)	5 (4 — 5)	
	Obese	3.95 (1.38)	5 (3 — 5)	
Nationality	Greek	4.09 (1.20)	5 (3 — 5)	0.284[+]
	Other	3.88 (1.29)	4 (3 — 5)	
Married	No	3.92 (1.20)	4 (3 — 5)	0.050[+]
	Yes	4.13 (1.22)	5 (3 — 5)	
Employed	No	4.25 (1.13)	5 (4 — 5)	<0.001[+]
	Yes	3.62 (1.28)	4 (3 — 5)	
Educational level	None/ Primary school	4.28 (1.08)	5 (4 — 5)	0.085[++]
	Middle/ High school	3.93 (1.29)	4 (3 — 5)	
	University/ MSc/ PhD	4.02 (1.16)	4 (3 — 5)	
Smoking	No	4.08 (1.22)	5 (3 — 5)	0.722[+]

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	Yes	4.04 (1.21)	5 (3 — 5)	
Alcohol consumption	No	4.10 (1.18)	5 (3 — 5)	0.610+
	Yes	4.02 (1.23)	5 (3 — 5)	
Concomitant disease	No	3.80 (1.30)	4 (3 — 5)	0.012+
	Yes	4.16 (1.16)	5 (3 — 5)	
Vaccination information				
Vaccinated against seasonal influenza this year	No	3.35 (1.29)	3 (3 — 4)	<0.001+
	Yes	4.64 (0.74)	5 (5 — 5)	
Vaccinated against seasonal influenza every year	No	3.44 (1.30)	4 (3 — 5)	<0.001+
	Yes	4.59 (0.80)	5 (4 — 5)	
Vaccinated against pneumococcus	No	3.67 (1.28)	4 (3 — 5)	<0.001+
	Yes	4.53 (0.92)	5 (4 — 5)	
Vaccinated against SAR-Covid-19	No	3.06 (1.39)	3 (2 — 4)	<0.001+
	Yes	4.19 (1.12)	5 (4 — 5)	
Main information source about vaccination				
Doctor/ Nurse	No	3.81 (1.25)	4 (3 — 5)	<0.001+
	Yes	4.26 (1.14)	5 (4 — 5)	
Pharmacist	No	4.02 (1.25)	5 (3 — 5)	0.334+
	Yes	4.27 (0.95)	5 (3.5 — 5)	
Media	No	4.12 (1.20)	5 (3 — 5)	0.062+
	Yes	3.86 (1.24)	4 (3 — 5)	
Friends/ Family	No	4.09 (1.21)	5 (3 — 5)	0.005+
	Yes	3.50 (1.10)	4 (3 — 4)	
Disease		4.1 (1.19)		
Liver cirrhosis	No	4.04 (1.22)	5 (3 — 5)	0.806+
	Yes	4.08 (1.20)	5 (3 — 5)	
Hepatocellular carcinoma	No	4.02 (1.22)	5 (3 — 5)	0.099+
	Yes	4.36 (1.08)	5 (4 — 5)	

 doi:10.20944/preprints202506.2118.v1

Hepatitis	No	4.18 (1.16)	5 (4 — 5)	0.084+
	Yes	3.95 (1.24)	4 (3 — 5)	
			rho	
Age (years)			0.30	<0.001

[1]values range from 1(not at all) to 5(very much) +Mann-Whitney test; ++Kruskal-Wallis test; rho: Spearman's correlation coefficient.

The association of patients' belief that vaccination against influenza is harmful in patients with their disease, with their characteristics, is provided in Table 3. Significantly higher levels of agreement were found among female patients, younger patients, and those with higher educational levels. Also, patients who had been vaccinated against seasonal influenza (this year or every year), against pneumococcus, or SAR-Covid-19 agreed significantly less that vaccination against influenza is harmful in patients with their disease.

Table 3. Association of belief that vaccination against influenza is harmful in these specific patients with their characteristics.

		Do you think that vaccination against influenza is harmful in patients with your disease?[1]		
		Mean (SD)	**Median (IQR)**	**P**
Gender	Male	1.30 (0.78)	1 (1 — 1)	0.005+
	Female	1.54 (0.98)	1 (1 — 2)	
BMI levels	Underweight	1.35 (0.67)	1 (1 — 1.5)	0.562++
	Normal	1.48 (0.96)	1 (1 — 1)	
	Overweight	1.32 (0.78)	1 (1 — 1)	
	Obese	1.36 (0.88)	1 (1 — 1)	
Nationality	Greek	1.41 (0.89)	1 (1 — 1)	0.920+
	Other	1.37 (0.85)	1 (1 — 1)	
Married	No	1.40 (0.85)	1 (1 — 1)	0.889+
	Yes	1.41 (0.90)	1 (1 — 1)	
Employed	No	1.36 (0.84)	1 (1 — 1)	0.216+
	Yes	1.51 (0.96)	1 (1 — 2)	
Educational level	None/ Primary school	1.24 (0.70)	1 (1 — 1)	0.031++
	Middle/ High school	1.45 (0.91)	1 (1 — 1)	
	University/ MSc/ PhD	1.56 (1.01)	1 (1 — 2)	
Smoking	No	1.39 (0.87)	1 (1 — 1)	0.832+
	Yes	1.42 (0.89)	1 (1 — 1)	
Alcohol consumption	No	1.46 (0.92)	1 (1 — 2)	0.252+
	Yes	1.37 (0.85)	1 (1 — 1)	
Concomitant disease	No	1.48 (0.92)	1 (1 — 2)	0.257+
	Yes	1.38 (0.86)	1 (1 — 1)	
Vaccination information				
Vaccinated against seasonal influenza this year	No	1.68 (1.03)	1 (1 — 2)	<0.001+
	Yes	1.18 (0.65)	1 (1 — 1)	
Vaccinated against seasonal influenza every year	No	1.64 (1.02)	1 (1 — 2)	<0.001+
	Yes	1.21 (0.68)	1 (1 — 1)	
	No	1.55 (1.00)	1 (1 — 2)	0.002+

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Vaccinated against pneumococcus	Yes	1.24 (0.68)	1 (1 — 1)	
Vaccinated against SAR-Covid-19	No	2.00 (1.33)	1 (1 — 3)	<0.001+
	Yes	1.33 (0.77)	1 (1 — 1)	
The main information source about vaccination				
Doctor/ Nurse	No	1.50 (0.95)	1 (1 — 2)	0.102+
	Yes	1.34 (0.81)	1 (1 — 1)	
Pharmacist	No	1.37 (0.85)	1 (1 — 1)	0.075+
	Yes	1.61 (1.04)	1 (1 — 2)	
Media	No	1.39 (0.89)	1 (1 — 1)	0.182+
	Yes	1.47 (0.84)	1 (1 — 2)	
Friends/ Family	No	1.41 (0.87)	1 (1 — 1)	0.555+
	Yes	1.40 (1.05)	1 (1 — 1)	
Disease		1.31 (0.73)		
Liver cirrhosis	No	1.47 (0.97)	1 (1 — 1)	0.246+
	Yes	1.31 (0.71)	1 (1 — 1)	
Hepatocellular carcinoma	No	1.44 (0.91)	1 (1 — 1)	0.137+
	Yes	1.18 (0.53)	1 (1 — 1)	
Hepatitis	No	1.29 (0.69)	1 (1 — 1)	0.102+
	Yes	1.50 (1.00)	1 (1 — 1)	
		rho		
Age (years)		-0.13		0.030

[1]values range from 1(not at all) to 5(very much) +Mann-Whitney test; ++Kruskal-Wallis test; rho: Spearman's correlation coefficient.

In Table 4 are presented patients percentages that had been fully vaccinated according to the national vaccination program and their association with their characteristics. The percentage of full vaccination was significantly greater in Greek patients, in those who were not employed, in older patients, in those who did not consume alcohol, and in those who had a concomitant disease. Furthermore, the percentage of full vaccination was significantly greater in patients who had been vaccinated against seasonal influenza (this year or every year), against pneumococcus, or SAR-Covid-19. Being informed about vaccination from a doctor/nurse resulted in significantly greater percentage of having done all vaccinations according to the national vaccination program, while being informed from the media or friends/family resulted in significantly lower percentages of being fully vaccinated.

Table 4. Association of having had all vaccinations according to the national vaccination program with patients' characteristics.

		Have you had all vaccinations according to the national vaccination program?		**P**
		No	**Yes**	
		n (%)	**n (%)**	
Gender	Male	80 (47.3)	89 (52.7)	0.205+
	Female	52 (40.0)	78 (60.0)	
BMI levels	Underweight	8 (40.0)	12 (60.0)	0.981+
	Normal	63 (44.4)	79 (55.6)	
	Overweight	42 (44.7)	52 (55.3)	
	Obese	18 (42.9)	24 (57.1)	
Nationality	Greek	96 (38.9)	151 (61.1)	<0.001+
	Other	36 (70.6)	15 (29.4)	

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Married	No	51 (47.2)	57 (52.8)	0.443+
	Yes	81 (42.6)	109 (57.4)	
Employed	No	71 (34.3)	136 (65.7)	<0.001+
	Yes	61 (66.3)	31 (33.7)	
Educational level	None/ Primary school	41 (44.1)	52 (55.9)	0.069+
	Middle/ High school	74 (49.0)	77 (51.0)	
	University/ MSc/ PhD	17 (30.9)	38 (69.1)	
Smoking	No	43 (41.7)	60 (58.3)	0.576+
	Yes	88 (45.1)	107 (54.9)	
Alcohol consumption	No	44 (36.1)	78 (63.9)	0.019+
	Yes	88 (49.7)	89 (50.3)	
Concomitant disease	No	52 (58.4)	37 (41.6)	0.001+
	Yes	80 (38.1)	130 (61.9)	
Vaccination information				
Vaccinated against seasonal influenza this year	No	112 (83.0)	23 (17.0)	<0.001+
	Yes	20 (12.2)	144 (87.8)	
Vaccinated against seasonal influenza every year	No	113 (81.3)	26 (18.7)	<0.001+
	Yes	19 (11.9)	140 (88.1)	
Vaccinated against pneumococcus	No	118 (71.5)	47 (28.5)	<0.001+
	Yes	14 (10.5)	119 (89.5)	
Vaccinated against SAR-Covid-19	No	31 (91.2)	3 (8.8)	<0.001+
	Yes	100 (37.9)	164 (62.1)	
The main information source about vaccination				
Doctor/ Nurse	No	85 (62.5)	51 (37.5)	<0.001+
	Yes	47 (28.8)	116 (71.2)	
Pharmacist	No	113 (44.3)	142 (55.7)	0.889+
	Yes	19 (43.2)	25 (56.8)	
Media	No	85 (38.1)	138 (61.9)	<0.001+
	Yes	47 (61.8)	29 (38.2)	
Friends/ Family	No	115 (41.4)	163 (58.6)	<0.001+
	Yes	17 (81.0)	4 (19.0)	
Disease				
Liver cirrhosis	No	79 (43.4)	103 (56.6)	0.748+
	Yes	53 (45.3)	64 (54.7)	
Hepatocellular carcinoma	No	120 (45.3)	145 (54.7)	0.269+
	Yes	12 (35.3)	22 (64.7)	
Hepatitis	No	54 (40.0)	81 (60.0)	0.190+
	Yes	78 (47.6)	86 (52.4)	
		Mean (SD)	Mean (SD)	
Age (years)		57.0 (11.7)	64.9 (11.2)	<0.001++

+Pearson's chi-square test; ++Student's t-test.

After multiple linear regression, it emerged that age and being informed by a doctor/nurse were significantly associated with believing that annual vaccination is the best method for influenza prevention (Table 5). More specifically, greater age and being informed about vaccination by a doctor/nurse were significantly associated with greater belief. With the belief that vaccination against influenza is harmful in patients with the specific disease, it was found that gender and age were significantly associated with. More specifically, females agreed more with this statement, as well as younger patients.

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Table 5. Multiple linear regression results, in a stepwise method, with the belief that annual vaccination is the best method for influenza prevention and that vaccination against influenza is harmful in patients with the specific disease, as dependent variables.

Dependent variable	Independent variables	β+	SE++	P
Do you believe that annual vaccination is the best method for influenza prevention?	Age (years)	0.003	0.001	<0.001
	Main information source about vaccination: Doctor/ Nurse (yes vs no)	0.045	0.021	0.032
Do you think that vaccination against influenza is harmful in patients with your disease?	Gender (Females vs Males)	0.058	0.022	0.009
	Age (years)	-0.002	0.001	0.032

Note. Logarithmic transformations of the dependent variables were used for the regression analyses +regression coefficient; ++Standard Error.

From multiple logistic regression, it was found that non-Greek (only Greek-speaking individuals of non-Greek ethnicity) patients had by 59% lower probability of being fully vaccinated according to the national vaccination program compared to Greek patients (Table 6). Also, employed patients had by 49% lower probability of being fully vaccinated according to the national vaccination program. A four times greater probability of being fully vaccinated according to the national vaccination program was observed in patients who were informed about vaccination by a doctor/nurse. Moreover, as patients' age increased, so did the probability of being fully vaccinated.

Table 6. Multiple logistic regression results, in a stepwise method, with being fully vaccinated according to the national vaccination program as a dependent variable.

	OR (95% CI)+	P
Nationality (Other vs Greek)	0.41 (0.19 — 0.87)	0.020
Employed (yes vs no)	0.51 (0.27 — 0.99)	0.046
Main information source about vaccination: Doctor/ Nurse (yes vs no)	4.00 (2.37 — 6.76)	<0.001
Age (years)	1.04 (1.01 — 1.07)	0.005

+Odds Ratio (95% Confidence Interval).

4. Discussion

The current study demonstrated elevated vaccination rates among individuals with liver disease and cirrhosis for COVID-19, while indicating low rates for seasonal influenza and pneumococcal disease. The study indicated that elderly patients, individuals with comorbidities, and those who received information about vaccination from healthcare providers regarded annual vaccination as the most effective way for influenza protection. Female patients, younger patients, and individuals with higher educational attainment perceived the influenza vaccine as detrimental. Moreover, individuals who received vaccination information from a physician or nurse, patients with Greek nationality, as well as older patients, exhibited a higher likelihood of receiving all their vaccinations under the national vaccination policy.

The elevated vaccination rates for COVID-19 suggest that study participants exhibit confidence in the vaccinations four years post-release, particularly as they are among vulnerable demographic groups at increased risk for severe disease. Despite apprehensions over the safety and efficacy of COVID-19 vaccinations, initial post-marketing studies have demonstrated elevated acceptance rates [27,28]. Despite influenza being a severe infectious disease that significantly affects the population every year, especially vulnerable groups, vaccination rates are persistently low. The current study indicates that influenza vaccination rates slightly surpassed 50%, aligning with findings from the

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literature concerning patients diagnosed with cirrhosis or liver disease [9,16]. Individuals may not perceive seasonal influenza as very hazardous and may believe they are not at risk of it. A crucial determinant for the adoption of the influenza vaccination and all recommended vaccines, as indicated by the current study, is the information conveyed to patients by healthcare professionals (physicians or nurses). This finding aligns with earlier studies indicating that trust in physicians for vaccine information and their recommendations are significant predictors of vaccine adoption [21,29]. Healthcare professionals should, during patient consultations, allocate time to advocate vaccination, elucidate the risks associated with non-vaccination, and address any inquiries or concerns patients may have regarding the safety and efficacy of vaccinations. Individuals frequently opt to obtain information regarding vaccines via social media or the internet. Nonetheless, there exists a risk that the information acquired from these sources may lack validity and may not be grounded in scientific fact. The content of social media posts or internet uploads frequently lacks a credible source. Social networks frequently serve as instruments for the anti-vaccine movement, disseminating misinformation and conspiracy theories [30,31]. As misinformation on social media increases, vaccination coverage decreases [32]. The delivery of accurate information to patients by healthcare professionals and public health campaigns will improve vaccination rates, regardless of the disease addressed by the vaccine. Increased acceptance will provide future benefits for the implementation of all vaccinations under national vaccination programs.

Age was identified as a significant determinant influencing the identification of the benefits of the influenza vaccine and the acceptance of vaccination, according to the findings of this study. Older adults, particularly those with chronic diseases, like our study participants, constitute a vulnerable population and opt for vaccination to safeguard themselves [19,33]. Younger patients tend to be in good health, exhibit poor vaccine uptake rates, perhaps due to their perception of minimal danger or a low probability of severe illness. Nonetheless, their health status as chronic patients categorizes them within vulnerable populations for severe illness, a fact that should be particularly underscored by their attending physician. Health education initiatives should not solely focus on the elderly but must also address the dangers faced by the younger population, particularly those with comorbidities.

Our findings revealed that the percentage of full vaccination according to the national vaccination program was significantly greater in patients who had been vaccinated against seasonal influenza (this year or every year), against pneumococcus, or SAR-Covid-19. This finding aligns with past studies indicating that those vaccinated for one disease are more likely to accept further vaccines, and vaccine refusal and hesitance correlate with non-compliance to vaccination recommendations [34–36]. Consequently, the endeavors of healthcare professionals and public health initiatives to enhance vaccination adherence must be maintained, since this might provide multiplicative advantages, with vaccine acceptance fostering overall compliance with vaccination guidelines.

Non-Greek citizens participating in our study exhibited significantly lower immunization rates in accordance with the national vaccination program. This finding aligns with research from other countries indicating that immunization rates among adults and children of a nationality distinct from that of the host country are lower [37–39]. This finding can be elucidated by the challenges faced by residents of different nationalities in accessing health services, encountering financial and insurance obstacles, or experiencing communication difficulties stemming from language hurdles. This finding highlights the importance of including citizens of different ethnicities and minority populations in health promotion and vaccination programs.

Compared to non-working patients, employed patients in this study were found to be much less likely to be fully vaccinated according to the national vaccination program. Employees, who come into constant contact with many people, are at high risk of infection, and therefore vaccination would be an important preventive measure for them. According to the findings of other studies, those who consider themselves to be at high risk of infection and employees have higher vaccination rates [40,41]. Therefore, this finding is not consistent with those of other studies. Our finding can probably be interpreted as random due to the small sample size of the study. Furthermore, we did not record

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the perceptions of employees as to whether they considered themselves to be at high risk of infection. Perhaps a perception that they do not belong to a high-risk group for infection may explain this finding.

This research possesses certain limitations. The study is cross-sectional using a convenience sampling method; thus, a causal relationship between the variables cannot be established, and the findings may not be generalized to the broader population. The study was limited to two university hospitals; hence, the findings are not generalizable to all individuals with liver disease. Moreover, the limited sample size and dependence on self-reported data, which may induce self-report bias, are two additional limitations of the study. In addition, important variables that could significantly influence the outcomes, including medication adherence, socioeconomic status, access to healthcare services, and the etiology of liver disease, were not examined.

5. Conclusions

This study emphasized the inadequate vaccination rates for influenza and pneumococcus among individuals diagnosed with chronic liver disease and cirrhosis, contrasted with elevated rates for COVID-19. These findings are significant and can be utilized within national public health initiatives and by healthcare professionals during patient interactions, ensuring that younger patients and those apprehensive about vaccine efficacy and safety receive focused attention to facilitate adherence to annual vaccinations and all vaccines included in national programs. More large-scale studies on patients with chronic liver disease, and in particular cirrhosis, are necessary to confirm the findings of this study and to investigate the effect of other variables that influence vaccination coverage and were not included in this study.

Author Contributions: Conceptualization, P.D. and E.D.; methodology, P.D., T.A., N.M., L.K., K.G. and E.D; software, N.M.; validation, P.D., T.A., S.P., K.G. and E.D.; formal analysis, N.M.; investigation, P.D., T.A. N.M., K.G.; resources, P.D., T.A., N.M., K.G. and E.D.; data curation, P.D. and N.M.; writing—original draft preparation, P.D., T.A., N.M., L.K., K.G. and E.D.; writing—review and editing, P.D., T.A., N.M., S.P., K.G. and E.D.; visualization, P.D. and supervision, E.D.; project administration, P.D. and E.D.

Funding: The publication of this study (APC) was funded by the Special Account for Research Grants (ELKE), University of West Attica, Athens, Greece. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; in the decision to publish the results. This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of General Oncology Hospital Of Kifisia "Agioi Anagyroi" (approval number 986, 26 October 2021), and General Hospital of Athens "G. Genimmatas (approval number 24286, 16 September 2021).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

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