

## Article

# Influenza and Pneumococcal Vaccination in Non-Infected Cardiometabolic Patients from the Americas during the COVID-19 Pandemic. A Sub-Analysis of the CorCOVID-LATAM Study



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**Abstract:** Background: Influenza vaccination (IV) and Pneumococcus vaccination (PV) are recommended for patients with cardiometabolic diseases. This study aimed to evaluate the immunization rate of ambulatory cardiometabolic patients during the COVID-19 pandemic in the Americas. Methods: Electronic surveys were collected from 13 Spanish speaking countries between 15 June and 15 July 2020. Results: 4216 patients were analyzed. Mean age 60 (±15) years and 49% females. Global IV rate was 46.5% and PV 24.6%. Vaccinated patients were older (IV = 63 vs. 58 years; PV = 68 vs. 59, *p* < 0.01) but without gender difference. Vaccination rates were greater in higher-risk groups (65+, diabetics, heart failure), but not in coronary artery disease patients. In the Southern cone, the rate of IV and PV was approximately double that in the tropical regions of the Americas. In a multivariate model, geographic zone (IV = OR 2.02, PV = OR 2.42, *p* < 0.001), age (IV = OR 1.023, PV = OR 1.035, *p* < 0.001), and incomes (IV = OR 1.28, PV = OR 1.58, *p* < 0.001) were predictors for vaccination. Conclusions: During the COVID-19 pandemic, ambulatory patients with cardiometabolic diseases from the Americas with no evidence of COVID-19 infection had lower-than-expected rates of IV and PV. Geographic, social, and cultural differences were found, and they should be explored in depth.

Keywords: COVID-19; SARS-CoV-2; Influenza vaccination; pneumococcal vaccination; cardio-metabolic



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### 1. Introduction

There is a strong relation between respiratory infections and acute cardiovascular (CV) events. Any Influenza strains and also Streptococcus pneumoniae infections can trigger a variety of CV alterations that may lead to hospitalization or even death [1–5].

The body of evidence confirms that Influenza vaccination (IV) and Pneumococcal vaccination (PV) are related to a decrease in the rate of different CV outcomes, such as myocardial infarction (MI), heart failure (HF) hospitalization, and CV mortality [6–16]. However, some barriers were identified for implementingthese prevention strategies, whichare grouped in patient's decision (vaccine hesitancy, prior experience, fake news), health care providers knowledge and attitude towards vaccination, and health care system barriers, that lead to a lower than expected immunization rate in Latin America and globally [17–25]. In that struggling context, at the end of 2019, a new coronavirus SARS-CoV-2 provoked a pandemic particularly prevalent in the Americas. In North America, it coincided with the end of winter, while in South America, it rose in June and July 2020 [26].

Governmental authorities and health leaders from most countries recommended, on the one hand, to avoid the circulation of people on the streets and in-home confinement, but on the other hand, suggested that vaccination against respiratory pathogens should be kept as usual, and that may have been perceived as a contradictory message. Currently, the information regarding immunization rates for both primary and secondary cardiometabolic disease prevention in the Americas is unknown.

This study aimed to describe the rate of immunization with IV and PV in ambulatory cardiometabolic patients from the Americas with no evidence of infection during the COVID-19 pandemic and to analyze their determinants.

#### 2. Materials and Methods

A pre-specified analysis of the CorCOVID LATAM survey was performed. The rationale and design of the main study have been previously published [27]. It was a survey sponsored by the InterAmerican Society of Cardiology (SIAC) and performed by cardiologists from 13 Spanish-speaking countries to patients older than 18 years with prior CV or metabolic diseases, including arterial hypertension, coronary artery disease, cardiomyopathies, heart failure, valvular disease, pericardial disease, obesity, dyslipidemia, or diabetes, with no evidence or history of COVID-19 infection, with the aim to assess the impact of the COVID-19 pandemic on habits, lifestyle, access to healthcare and treatments, as well as psychological factors [28]. The information was gathered in an online platform (Google Forms platform, Mountain View, CA) between 15 June and 15 July 2020.

Specific inclusion criteria were all subjects at cardiology consultation with cardiovascular or metabolic disease and without evidence or suspicion of being sick from SARS-CoV2. Exclusion criteria were patients less than 18 years old, a previous diagnosis of SARS-CoV2, recent hospital stay, or not willing to provide the information contained in the survey. The questionnaire was divided into seven clusters, including basic demographic data and specific vaccine information. A total of 38 questions were performed on each patient. Informed consent was obtained from all the participants in accordance with the requirements of the InterAmerican Society of Cardiology Ethics Committee. Due to government measures to limit population mobilization in some countries, the survey was conducted either by face-to-face visits or by phone or video chat, in which case, informed consent was verbally taken. The basic demographic profile included educational level (illiterate, elementary, high school, tertiary, or university), income (very low, low, middle, and high), occupation, family structure and habitat, cardiovascular disease, and treatments. The second part of the survey examined the patient's behavior during the last 30 days regarding physical activity, nutrition, body weight, alcohol intake and tobacco habits, treatments' accessibility, mood, and quality of sleep. The questions contained multiple answer options and were not forced so that patients were allowed to select multiple responses depending on the question.

The main objective of this sub study was to describe the Influenza and Pneumococcal vaccination rates in cardiometabolic patients from Spanish speaking countries of Latin America. The secondary goals were (1) to assess predictors of IV and PV, (2) to describe the immunization rate in high-risk groups, (3) to analyze geographical, economic, and cultural differences regarding IV and PV within Latin America, (4) to describe predictors of immunization among diabetes, heart failure, and coronary artery disease patients.

The responses of the included patients were classified according to the country of origin in three regions: Mexico, Central America, and the Caribbean (Costa Rica, Cuba, El Salvador, Guatemala, Mexico, Dominican Republic), Andean region (Colombia, Ecuador, Peru, Venezuela), and Southern cone (Argentina, Chile, Paraguay).

IV was considered positive if one dose of any type of IV was received in the last 6 months, while for PV, the time frame was 3 years for at least one dose (without considering different types of PVs). Patients who had received both IV and PV were analyzed in the "double vaccination" group.

IV and PV comparative analyses were performed, stratified by age, sex, and region of inclusion. Specific group aims were elder (65 years or more), patients with known coronary artery disease (CAD), patients with heart failure (HF), and patients with diabetes without prior CV events. In addition, determinants of immunization, such as educational and socioeconomic level, were evaluated in univariate and adjusted models.

Statistical analysis: dichotomic variables are described as numbers and their percentages, and continuous variables are described as mean ( $\pm$ standard deviation) or median (interquartile range) in accordance with their distribution type.  $\chi^2$  and Fisher's tests were used for comparisons between categorical variables, while for comparisons between continuous variables, the Student's t-test or Mann–Whitney U test was used. Bartlett's test was used to determine the normality of the data distribution of the continuous variables. To assess independent predictors of vaccination, multivariate models were performed in the full cohort and stratified by specific at-risk groups (coronary artery disease, heart failure, and diabetes in primary prevention). In the absence of data on any variable, no imputation was made. The Epi Info<sup>®</sup>V7.0 program was used, and a *p*-value of < 0.05 was considered significant. For the multivariate models, variables with a p < 0.1 on univariate analysis were included. Bonferroni correction was used because of the exploratory nature of the analysis and multiple comparisons [29], considering p = 0.00625 for the Influenza vaccine full cohort analysis (8 variables model), and 0.00714 for the Pneumococcal vaccine model (7 variables). Further analyses of predictors of IV, PV, and double vaccination in specific risk-groups of CAD patients, HF patients, and diabetic patients were performed with multivariable models. In them, a *p*-value of 0.0083 was considered significant.

For this study, the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) recommendations [30] were followed.

#### 3. Results

From 4429 surveys, 213 had to be excluded due to incomplete data, inclusion criteria violation, or duplicates. Thus, 4216 remained for analyses. The mean age was 60 ( $\pm$ 15) years, and 49% were females. Immunization variables were complete in all cases. One thousand, seven hundred and sixty-four (42%) patients were older than 65 years, 899 (21.3%) were diabetics, and 606 (14.3%) were smokers (or former smokers). Seven hundred and sixty-nine (18.2%) patients had known CAD, and 538 (12.7%) had HF. The global IV rate was 46.5% (n = 1963), PV 24.6% (n = 1039), and double vaccination 21% (n = 887). Baseline characteristics are shown in Table 1. A homogeneous distribution in the three geographic areas was achieved: 1426 patients were from Mexico and Central America, 1359 from the Andean region, and 1431 from the Southern cone.

Age	60.35 (SD 15.39)				
Female sex	49.07% (2069)				
Region					
-Mexico, Central America	33.82% (1426)				
-Andean	32.23% (1359)				
-Southern cone	33.94% (1431)				
Educational Level					
-None (analphabet)	2.28% (96)				
-Primary	19.14% (807)				
-Secondary (high school)	32.14% (1355)				
-Tertiary	15.32% (646)				
-University	31.12% (1312)				
Incomes					
-Very low (needs external support)	10.01% (422)				
-Low (covers basic needs)	35.53% (1498)				
-Middle (can save)	48.55% (2047)				
-High	5.91% (249)				
Coronary artery disease	18.24% (769)				
Diabetes	21.32% (899)				
Hypertension	72.84% (3071)				
Heart failure	12.70% (538)				
Current or past smokers	14.3% (616)				
Increased smoking during pandemic	17.00% (103)				
Influenza vaccination in the last 6 months	46.56% (1963)				
Pneumococcal vaccination in the last 3 years	24.64% (1039)				

Table 1. Clinical characteristics of the population.

We found no gender difference in vaccination uptake (Influenza vaccination: 46.8% in females and 46.4% in males, OR = 1.01, CI 95% 0.89–1.14, p = 0.8; Pneumococcus vaccination: 23.9% in females vs. 25.4% in males, OR = 0.92, CI 95% 0.80–1.06, p = 0.25). Vaccinated patients were older for IV (63 (±15) vs. 58 (±14) years, p < 0.001), PV (68 (IQR 58–75) vs. 59 (IQR 48–70) years, p < 0.001), and double vaccination (69 (70–76) vs. 59 (49–70) years, p < 0.001). Table 2 shows that vaccination rates were greater in specific high risk groups, such as elder (65+), diabetics, and HF patients. However, the vaccination rate was similar in CAD in comparison with non-CAD patients. Current smokers or past smokers had a lower immunization rate for Influenza, Pneumococcus, and double vaccination.

On exploratory analyses, differences in immunization rates between geographic regions, educational level, and economic strata were analyzed. Patients from the Southern cone had vaccination rates of approximately double than the tropical regions (Figure 1): Influenza vaccination 69% in Southern cone, 34% in Andean region, and 35% in Mexico, Central America and Caribbean ( $\chi^2 = 452$ , df = 2, p < 0.001); Pneumococcus vaccination 43%, 20%, and 11%, respectively ( $\chi^2 = 406$ , df = 2, p < 0.001); and double vaccination 40%, 11%, and 9%, respectively ( $\chi^2 = 458$ , df = 2, p < 0.001).

The specific countries with higher immunization rates were Argentina (65%), Peru (54%), and Chile (36%) for PV, and for IV: Chile (91%), Argentina (87%), and Paraguay (70%). Patients from the Southern cone within the high-risk population (65+, CAD, HF) had the highest Influenza immunization rates (87%, 80%, and 78%, respectively), and it doubled the rate to other regions (Figure 1, all *p* < 0.001)

		Influenza Vaccination				Pneumococcal Vaccination			Both Vaccines				
		Yes ( <i>n</i> = 1963)	No $(n = 2253)$	OR (CI)	p	Yes ( <i>n</i> = 1963)	No ( <i>n</i> = 3177)	OR (CI)	p	Yes $(n = 887)$	No ( <i>n</i> = 3329)	OR (CI)	p
Age > 65y	Yes ( <i>n</i> = 1764)	1048 (59%)	716 (41%)	2.45 (2.16–2.77)	<0.001	624 (35%)	1140 (65%)	2.68 (2.32–3.1)	<0.001	565 (32%)	1199 (68%)	3.12 (2.67–3.64)	<0.001
	No $(n = 2442)$	913 (37%)	1529 (63%)			413 (16%)	2029 (64%)			320 (13%)	2122 (87%)		
T2DM	Yes ( <i>n</i> = 899)	456 (51%)	443 (49%)	1.23 (1.06–1.43)	0.002	245 (27%)	654 (73%)	1.19 (1.01–1.41)	0.023	216 (24%)	683 (76%)	1.24 (1.04–1.48)	0.008
	No ( <i>n</i> = 3317)	1507 (45%)	1810 (55%)			794 (24%)	2523 (76%)			671 (20%)	2646 (80%)		
Smoking	Yes ( <i>n</i> = 616)	237 (39%)	369 (61%)	0.7 (0.59–0.83)	<0.001	77 (13%)	529 (87%)	0.43 (0.31–0.51)	<0.001	65 (11%)	541 (89%)	0.41 (0.31–0.53)	< 0.001
	No ( <i>n</i> = 3610)	1726 (48%)	1884 (52%)			962 (27%)	2648 (73%)			822 (23%)	2788 (77%)		
Heart Failure	Yes ( <i>n</i> = 538)	302 (56%)	236 (44%)	1.55 (1.29–1.86)	<0.001	160 (30%)	378 (70%)	1.34 (1.1–1.64)	0.002	142 (26%)	396 (74%)	1.41 (1.14–1.73)	<0.001
	No ( <i>n</i> = 3687)	1661 (45%)	2017 (55%)			879 (24%)	2799 (76%)			745 (20%)	2933 (80%)		
Coronary Disease	Yes ( <i>n</i> = 769)	381 (50%)	388 (50%)	1.15 (0.99–1.35)	0.06	182 (24%)	587 (76%)	0.93 (0.78–1.12)	) 0.48	159 (21%)	610 (79%)	0.97 (0.8–1.18)	0.78
	No ( <i>n</i> = 3477)	1582 (46%)	1865 (54%)			857 (25%)	2590 (75%)			728 (21%)	2719 (79%)		

Table 2. Rate of immunization with Influenza vaccine, Pneumococcal vaccine, and double vaccination in specific risk groups.

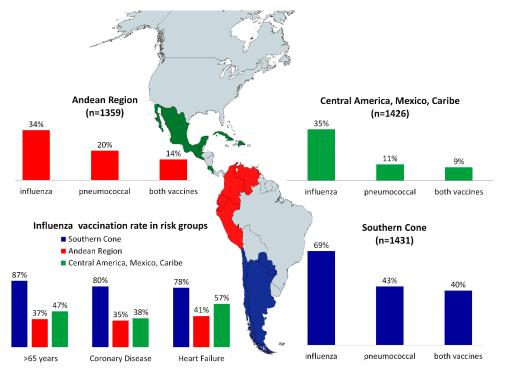


Figure 1. Immunization rate by geographic zone.

We found an incremental correlation between economic strata and vaccines uptake in this cohort, in spite being free of charge in most countries (Figure 2): for IV, 40%, 45%, 48%, and 55%, in very low, low, middle, and high incomes, respectively ( $\chi^2 = 18.9$ , df = 3, p < 0.001). For PV, 12%, 22%, 27%, 41%, ( $\chi^2 = 84.1$ , df = 3, p < 0.001), and for double vaccination the rates were 10%, 18%, 23%, and 37%, respectively ( $\chi^2 = 77.3$ , df = 3, p < 0.001). On the other hand, we found significant differences regarding educational level (IV,  $\chi^2 = 61.9$ , df = 4, p < 0.001), (PV,  $\chi^2 = 29.4.9$ , df = 4, p < 0.001) (double vaccination,  $\chi^2 = 33.4$ , df = 4, p < 0.001), but it did not follow an incremental correlation, lowering the immunization rates among mostly educated patients (Figure 2). The rate of IV was 40% in illiterate patients and 38% in university level patients.

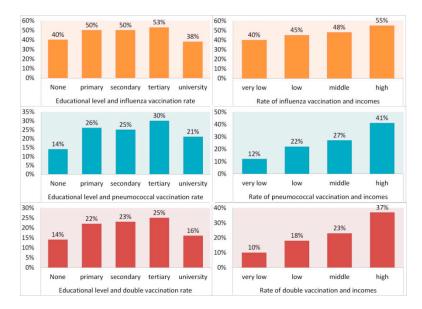


Figure 2. Relation between educational and economic levels and immunization rates.

In a multivariate analysis, after adjustment for the factors found in the bivariate model and the exploratory socio-demographic analysis, the stronger predictors of vaccines rates in all groups were the geographic zone (Southern cone having the highest odds), age (approximately 3% increase per aging year), and income level (Table 3), both for IV and PV. Heart failure was associated with IV only, and diabetes was not associated with IV or PV after Bonferroni's adjusted *p*-value. Smoking was an independent predictor of non-vaccination for IV and PV.

**Table 3.** Multivariate analysis, independent predictors of Influenza vaccination and Pneumococcal vaccination.

Independent Predictors of Influenza Vaccination, Full Cohort (n = 4216)										
Term	Odds Ratio	95% C.I.	Coefficient	S. E.	Z-Statistic	<i>p</i> -Value				
Age (per year)	1.023	1.018-1.028	0.023	0.002	9.558	0.0000				
Heart failure	1.360	1.097-1.686	0.308	0.109	2.81	0.0049				
Diabetes	1.214	1.037-1.423	0.194	0.080	2.410	0.0159				
Coronary artery disease	0.993	0.836-1.180	-0.006	0.087	-0.070	0.9441				
Smoking	0.762	0.632-0.919	-0.271	0.095	-2.846	0.0044				
Educational level	0.989	0.925-1.058	-0.010	0.034	-0.304	0.761				
Income level	1.283	1.162-1.415	0.249	0.050	4.966	0.0000				
Geographic Zone	2.012	1.854-2.184	0.699	0.041	16.721	0.0000				
Independent Predictors of Pneumococcal Vaccination, Full Cohort (n = 4216)										
Term	Odds Ratio	95% C.I.	Coefficient	<b>S.</b> E.	<b>Z-Statistic</b>	<i>p</i> -Value				
Age (per year)	1.035	1.029-1.041	0.035	0.003	11.709	0.0000				
Heart Failure	1.386	1.087 - 1.767	0.326	0.123	2.637	0.0084				
Diabetes	1.203	1.003-1.446	0.184	0.094	1.963	0.0496				
Smoking	0.451	0.346-0.587	-0.796	0.134	-5.194	0.0000				
Educational level	1.077	0.994-1.167	0.074	0.040	1.832	0.0668				
Income level	1.582	1.405 - 1.782	0.459	0.060	7.566	0.0000				
Geographic Zone	2.472	2.234-2.737	0.905	0.051	17.483	0.0000				

Note: With Bonferroni correction, a *p* level of 0.00625 was considered for the Influenza vaccine full cohort analysis (8 variables model), and 0.00714 for the Pneumococcal vaccine model (7 variables). Statistical significative results are shown in bold.

An analysis of specific risk groups was performed. Among CAD patients (n = 769), geographic zone, age, and incomes level were the stronger predictors for PV and for IV (OR = 2.3289, 95% CI = 1.913-2.8351; OR = 1.0385, 95% CI = 1.0236-1.0535; OR = 1.6188, 95% CI = 1.2643-2.0727, respectively, for IV),

(OR = 1.9265, 95% CI = 3.1583–5.4228; OR = 1.034, 95% CI = 1.016–1.0523; OR = 1.5372, 95% CI = 1.1392–2.0743, respectively, for PV). In patients with diabetes but without HF or CAD (n = 460), geographic zone, and age were independent predictors of IV and PV. (OR = 1.9265, 95% CI = 1.5077–2.4617; and OR = 1.0266, 95% CI = 1.0103–1.0432, respectively, for IV) (OR = 2.4263, 95% CI = 1.8359–3.2065; and OR = 1.0348, 95% CI = 1.0155–1.0545, respectively, for PV). However, for HF patients (n = 538) independent predictors were the same for IV but for PV the predictors were geographic zone, income level, and educational level (OR = 1.8039, 95% CI = 1.3591–2.3944; OR = 1.0189, 95% CI = 1.0044–1.0336; and OR = 1.5697, 95% CI = 1.10189, 95% CI = 1.1014–2.0684, and OR = 1.3809, 95% CI = 1.1026–1.7294, respectively, for PV).

#### 4. Discussion

The main findings of this study were that during the COVID-19 pandemic, immunization against Influenza was low and against Pneumococcus was very low in ambulatory cardiometabolic patients from the Americas, and there were significant socio-cultural and geographic differences in vaccination rates among them. The risk group with a higher immunization rate was the elder group (65+ years). That may be related to the wider knowledge from doctors and patients regarding the general benefits of immunization in this group, opposite to immunization for younger patients with HF, diabetes, or CAD. As mentioned before, there is a strong correlation between respiratory infections and CV events, as well as a clear cut down with vaccination, and currently, vaccines are recommended in several cardiology guidelines [31–35]. It is possible that the COVID-19 pandemic had an impact on these low rates, something that needs further exploration.

Immunization rates were higher in the Southern cone zone compared to the other regions. Knowledge about respiratory viruses' circulation, the attack rate of Influenza, and seasonality may be lower by doctors and patients from tropical countries, and then immunization may not be taken into account as a CV prevention strategy among them. Regarding differences in immunization rates among regions and countries analyzed, IV is recognized in the essential medicines list (EML) only in 4 out of 13 countries (Argentina, Dominican Republic, El Salvador, Mexico), and PV in 8 countries (Argentina, Colombia, Dominican Republic, Ecuador, El Salvador, Mexico, Paraguay, and Peru). Being listed in the EML is the first step towards improvement in availability and access.

Due to the nature of this survey, a transversal cut trial during the COVID-19 pandemic, we compared the immunization rates with the Pan American Health Organization (PAHO) reported rates of immunization in high-risk groups from prior years, and noted that, as an example, IV rates were near 100% in several regions of the Americas for 65+ group in the pre-pandemic years [36], and thus, we assume that we are probably facing a strong decrease in immunization rates against respiratory pathogens this season, with potential adverse consequences on public health for further months or years, indirectly related to the COVID-19 pandemic. Other preventive health measures, such as cancer screening, also had modifications during the pandemic, with unknown later outcomes [37–42].

By the time WHO declared the pandemic, several restrictive measures were taken, including the suspension of non-urgent medical care and CV disease care. As an example, in prior publications, we noted more than a 70% reduction in elective CV procedures during March and April of 2020 (compared to an average from 2010–2019) in Buenos Aires, as well as a fall in hospitalizations for acute CV events, such as coronary syndromes or HF hospitalizations [43]. In Latin America, the low rate of availability and use of telehealth and digital prescriptions before the COVID-19 pandemic, together with the lack of access to clinics and cardiologic follow-up (related to each country's restrictive governmental measures), may have contributed, at least in part, to lower access to vaccines.

Pneumococcal vaccination rates were very low in all high-risk groups. Pneumococcus and PV do not follow a seasonal pattern, but IV campaigns are an opportunity for PV uptake. Fifty-one percent of the included patients had a prior CV hospitalization, and half of them had a hospitalization in 2019–2020, making a stronger case for the PV prescription during the analyzed time frame and possibly reflecting a low prescription or acceptance by patients of PV during the pandemic. Although some patients may have received the complete PV scheme before the last three years, these results are alarming. In the surveys from the tropical countries, the rate was as low as 10%. The later development and knowledge about CV benefits of PV in comparison to IV [44] recall bias, direct cost, and lack of coverage in some national immunization programs, as well as its availability and distribution issues during the COVID-19 pandemic, may have been determinants of this low rate.

Heart failure is a usual indication for Influenza and Pneumococcus immunization, irrespective of the age of the patients, who usually live with dyspnea and are at higher risk of pneumonia and developing in-hospital complications [14–16]. Our data showed that HF was indeed a predictor of the use of vaccines. However, the proportional weight was milder than socio-demographic predictors than income level, age, or geographic area. Although the number of HF patients in this survey was low, this may reflect that in the HF population, age surpasses HF itself as the main reason for immunization. Of note, in the largest cohorts, HF average age was around 70 years [45,46].

Several ecologic and molecular studies found that patients with coronary artery disease are vulnerable and at risk of respiratory infections [1–4]. Then, randomized clinical trials, retrospective studies, and metanalyses have shown that immunization reduces mortality and morbidity among them [11–13,47–50]. However, in this cohort, known

CAD was not associated with increased rates of immunization. Knowledge, attitude, and behavior both by patients and physicians may play a role in this finding, as well as psychological aspects of CAD patients after an acute coronary event [51].

Opposite to previously described predictors of IV and PV, smoking status had a strong, independent, and inverse relationship with vaccination. Even under cardiac care, smokers are a known group of non-adherence to preventive health measures. The risk of severe pneumonia, as well as the benefit of vaccination, is neglected by them [52–56].

Beyond direct pandemic effects regarding immunization rates, this study revealed inequities in the access to IV and PV as preventive CV measures in the Americas. Low income patients and low educational level patients had significantly lower rates of vaccination in spite of vaccines being incorporated in most national immunization programs free of charge. Knowledge, information in mass media, access to consultation and prescriptions, should be reviewed as barriers in achieving greater vaccination rates in this vulnerable cohort. During the COVID-19 pandemic, this inequity in access to healthcare was more visible, according to several studies [57–61]. Even more, global gross domestic product shrinkage of 3.2% in 2020 was predicted by the United Nations, and that will push 34 million more people into extreme poverty [62] with a potentially worse scenario for IV and PV rates for the next years if proper measures are not taken by stakeholders.

On the other edge, the immunization rate for both IV and PV declined in the stratum of the higher educational level (university level). This phenomenon may be attributed to chance and the low number of surveys, but unfortunately, we found similar reports regarding lower vaccination levels in the most educated participants [63], attributed to skeptical views and sentiments related to vaccine safety and efficacy. Of note, that study also included patients from the Americas. The low immunization rate, even in the context of a pandemic caused by a new respiratory virus, is a call to action for the development of strategies to increase the rate of Influenza and Pneumococcal vaccination for the vulnerable population of the Americas.

This survey was performed at the half of 2020 when COVID-19 was increasing in the Americas, and information regarding circulating Influenza was limited due to redirection of resources to the care of the pandemics, and epidemiological surveillance for other viruses was halted. Currently, we know that the Influenza rate during 2020 was 0.2% in Southern Cone, 4.4% in the Andean region, 2.7% in Central America, 4.8% in the Caribbean region, and 6.4% in North America (PAHO report) [64]. Influenza A H1N1pdm09 and B Yamagata were the predominant strains during 2020. By week 51, there were 28,281 CRP confirmed H1N1pdm09 cases, 112,415 Influenza B cases, and 139,655 Influenza A not subtyped in the Americas, but at the same time, there were 13,351,225 SARS-CoV-2 confirmed cases. The uptake of SARS-CoV-2, social distancing, and the use of masks may have contributed to this phenomenon, being the lowest Influenza season in decades. There is uncertainty regarding the uptake of Influenza once SARS-CoV-2 diminishes (naturally or due to vaccination) or when social distancing measures reduce.

Finally, the world is in need of rapid development and access to COVID-19 vaccines. In the race, mRNA-based and adenovirus-based vaccines have been in use since December 2020. The long-term duration of immunity of the vaccines or the diseases themselves, as well as developing mutations of the virus, are not well documented so far. Thus, there is a potential need for repeated SARS-CoV-2 vaccination, and in that context, prior experience of IV campaigns and fusion of efforts towards an improvement in adult vaccinations may contribute to global health.

#### Limitations

For IV, the 6 months window analyzed included the usual Influenza season and the IV campaign months for Southern Cone, Andean countries, and some Central American countries. However, it is possible that for Mexico and the Dominican Republic, the period analyzed captured only the last part of the winter and IV prescription, which may have biased the results of part of Central America, Mexico, and the Caribbean region.

It is possible that patients who agreed to participate and are under cardiac followup are more adherent to health care strategies, including immunization, compared to the general population. Despite this, immunization levels were lower than in the years before the pandemic and much lower than recommended levels. Regarding predictors of immunization in the specific subgroup analyses (patients with CAD, with HF, or with diabetes), geographic zone and age were again independent predictors of IV and PV in all, and income level in some subgroups. In spite of being similar to the findings from the whole cohort multivariable analyses, these results should be taken with caution, as the number of cases included for each specific analysis was low.

#### 5. Conclusions

During the COVID-19 pandemic, ambulatory patients with cardiometabolic diseases from the Americas had lower-than-expected rates of Influenza and Pneumococcal vaccination, both in primary and secondary prevention of CV disease. Geographic, social, and cultural differences were found, and they should be explored in depth.

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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.

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