Immunization and cardiovascular disease in Latin America. The CorVacc study: rationale and design

Inmunización y enfermedad cardiovascular en América Latina. El estudio CorVacc: fundamento y diseño

Fernando Wyss[1]*, Ricardo Lopez-Santi[2], Daniel Piskorz[3], Shyla Gupta[4], Ana Munera-Echeverri[5], Pilar Lopez-Santi[6], Gonzalo Piskorz[7], Vladimir Ulluauri[8], Juan E. Gomez[9], Mildren del Sueldo[10], Claudia Almonte[11], Máxima Mendez[12], Osiris Valdez[13], Carlos I. Ponte-Negreti[14], Iván Romero-Rivera[15], Adriana Puente-Barragan[16], Raúl Villar[17], Julio Effio[18], Daniel Pichel[19], Percy Berrospi[20], Ana I. Barrientos[21], Nancy Silvera[22], Edmundo Jordan[23], Wistremundo Dones[24], Daniel Quezada[25], Ariel Arguello[26], Gonzalo Perez[27], and Adrián Baranchuk[28] on behalf of The CorVacc Study Investigators

[1]Servicios y Tecnología Cardiovascular de Guatemala-CARDIOSOLUTIONS, Guatemala; [2]Hospital Italiano de la Plata, La Plata, Argentina; [3]Unidad de Cardiología Sanatorio Británico, Rosario, Argentina; [4]University of Ottawa, Faculty of Medicine, Ottawa, Canadá; [5]Hospital General de Medellín, Medellín, Colombia; [6]Leiden University Medical Center, Leids Universitair Medish Centrum, Leiden, Holanda; [7]Data IQ, Buenos Aires, Argentina; [8]Hospital Metropolitano de Quito, Quito, Ecuador; [9]Fundacion Valle de Lili, Unidad de Cardiología, Cali, Colombia; [10]Clínica de Especialidades Villa María, Córdoba, Argentina; [11]CEMDOE Unidad de Cardiología, Santo Domingo, República Dominicana; [12]Cli-Lipid, Santo Domingo, República Dominicana; [13]Hospital Central de la Romana, La Romana, Republica Dominicana; [14]Instituto Medico la Floresta, Caracas, Venezuela; [15]Universidade Federal de Alagoas, Alagoas, Brasil; [16]Centro Medico Nacional XX de Noviembre, Ciudad de México, México; [17]BUPA Integra Medica la Serena, La Serena, Chile; [18]Panama Clínic-Hospital Santa Fe, Panamá, Panamá; [19]Universidad de Panamá-Hospital Paitilla, Panamá, Panamá; [20]SANNA Clínica el Golf, Lima, Perú; [21]Hospital Bendaña, San Pedro Sula, Honduras; [22]Sanatorio Santani, Asunción, Paraguay; [23]Hospital Pavía Santurce Cardiology Center, San Juan, Puerto Rico; [24]Hospital Ryder Memorial, Humacao, Puerto Rico; [25]Hospital San Vicente de Paul, San José, Costa Rica; [26]Hospital Vivian Pellas, Managua, Nicaragua; [27]Clinica Olivos, Buenos Aires, Argentina; [28]Kingston Health Sciences Centre, Queens University, Kingston, Canadá

Abstract

Objectives: To determine the rates of vaccination against influenza and pneumococcal disease in the general population of the Americas, both healthy and sick, and to analyze the factors influencing these rates. **Methods:** The Inter-American Vaccination Registry of Influenza and Pneumococcus, (CorVacc Study) is a cross-sectional survey of the general population that will be enacted in 19 Latin American countries. A total of 34 questions will be given to consecutive patients aged 18 years or older through an online survey. **Results:** The data will be analyzed by country and region according to seven clusters: demographics, socioeconomic and educational level, cardiometabolic profile, cardiovascular interventions, medical follow-up and treatments, and COVID-19 vaccination status. The study will be conducted by the Prevention Council of the Inter-American Society of Cardiology. **Conclusions:** This study will provide insight into the impact of influenza and pneumococcus vaccinations in Latin American populations and the barriers preventing the immunization targets from being actualized. Hopefully, this will help to facilitate the development of targeted and focused health prevention strategies.

Keywords: Vaccines. Influenza. Pneumococcus.

Resumen

Objetivos: *Determinar las tasas de vacunación contra la influenza y la enfermedad neumocócica en la población general de las Américas, tanto en personas sanas como enfermas, y analizar los factores que influyen en estas tasas.* **Métodos:** *El Registro Interamericano de Vacunación contra la Influenza y el Neumococo (Estudio CorVacc) es una encuesta transversal dirigida a la población general que se llevará a cabo en 19 países de América Latina. Se aplicará un total de 34 preguntas a pacientes consecutivos de 18 años o más mediante una encuesta en línea.* **Resultados:** *Los datos serán analizados por país y región según siete grupos: demografía, nivel socioeconómico y educativo, perfil cardiometabólico, intervenciones cardiovasculares, seguimiento médico y tratamientos, y estado de vacunación contra la COVID-19. El estudio será llevado a cabo por el Consejo de Prevención de la Sociedad Interamericana de Cardiología.* **Conclusiones:** *Este estudio proporcionará información sobre el impacto de las vacunas contra la influenza y el neumococo en las poblaciones de América Latina y las barreras que impiden alcanzar los objetivos de inmunización. Se espera que estos hallazgos contribuyan al desarrollo de estrategias de prevención de la salud más enfocadas y efectivas.*

Palabras clave: Vacunas. Influenza. Neumococo.

Introduction

Cardiovascular (CV) disease is the leading cause of morbidity and mortality worldwide. The current global health policy goals include a 25% reduction in premature mortality from non-communicable diseases by 2025[1].

There is a strong association between respiratory infections and acute CV events. All strains of influenza and *Streptococcus pneumoniae* infections can trigger a variety of CV alterations that may lead to hospitalization or death[2-6].

Evidence has shown that influenza vaccination (IV) and pneumococcus vaccination (PV) are associated with a reduction in the rate of several CV outcomes, such as myocardial infarction (MI), heart failure (HF) hospitalization, and CV mortality[7-17]. However, several challenges have been identified in the implementation of these prevention strategies. These challenges include patient decisions (vaccine hesitancy, previous experience, and misinformation), healthcare providers' knowledge and attitudes toward vaccination, and healthcare system barriers. All these factors contribute to lower-than-expected immunization rates in Latin America and globally[18-28].

Despite the efforts by the World Health Organization, government authorities, and health leaders in most countries to encourage compliance with vaccination recommendations, uptake remains low. At present, there is no accurate information on vaccination rates among patients undergoing primary or secondary prevention of cardiometabolic diseases in the Americas[29].

The aim of this study is to determine the rates of vaccination against influenza and pneumococcal disease in the general population of the Americas, both healthy and sick, and to analyze the factors influencing these rates.

Methods and design

Study population

The registry for this study is observational. A total of 19 countries will be prospectively enrolled in the Inter-American Vaccination Registry of Influenza and Pneumococcus (CorVacc Study). Eligibility for the registry includes ambulatory patients over 18 years of age who provide their informed consent to participate in the survey. Patients under the age of 18 years and those unable to provide informed consent will be excluded from the study.

Informed consent

Patients will be informed about the survey's objective and the anonymity of their responses. No identifiable personal data will be collected. Ethics approval was obtained from the Inter-American Society of Cardiology (SIAC) Research Ethics Board.

Study design

A cross-sectional online survey comprising 34 questions will be developed using Google Forms (Mountain View, CA). The research team will invite patients to complete the questionnaire in person or through email, social media, telephone calls, and paper questionnaires.

The survey will be divided into three sections: (i) questions that examine a patient's demographic profile;

(ii) questions that examine their CV risk profile; and (iii) questions that examine their vaccination profile.

The questionnaire consists of a variety of question types, including dichotomous, Likert-type, multiple-option, and open-ended response choices. The respondents will not be obligated to provide a response and they may select multiple responses, in accordance with the content of the question.

Study organization

A call for cardiologists and other physicians from Latin American countries to join a team of collaborators for the CorVacc Study was conducted. A total of 19 countries were represented by cardiologists who registered to participate in the study. The countries will be divided according to a prespecified geographic distribution (Fig. 1), as follows:

- North, Central, and Caribbean region: Mexico, Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica, Panama, Cuba, Puerto Rico, and Dominican Republic
- Andean region (AR): Venezuela, Colombia, Ecuador, Bolivia, and Peru
- Southern Cone region: Paraguay, Chile, Uruguay, Brazil, and Argentina.

The total population within Latin American countries is estimated to be approximately 662 million. A sample size of 20,000 surveys was calculated to achieve a margin of error of 5%, a confidence level of 90%, and an error of distribution of 50%.

Survey

The survey platform will be made for enrolling patients. To enhance the response rate, periodic reminders will be sent through mail, text message, or social media. In addition, information about the progression of surveys by country will be made available. The survey is comprised of 34 questions (Table 1), which address the following topics:

Population demographics

It is crucial to ascertain the factors that may influence behavior, such as age and gender. It is important to characterize the country in which patients reside, considering factors such as income, education, and health coverage. There are significant differences between the three regions with regard to environmental and cultural factors. Furthermore, some countries have experienced migratory flows, particularly from Europe, resulting in ethnic differences, in contrast to other countries with larger native and black populations.

Socioeconomic status and education level

The Prospective Urban and Rural Epidemiological study demonstrated that socioeconomic status is associated with differences in risk factors for CV disease incidence and outcomes, including mortality[30]. According to this study, individuals with a lower level of education in low-and middle-income countries, such as the Latin American community, experience higher incidence and mortality rates from CV diseases[30]. Factors such as access to health services, treatments, and vaccination against influenza and pneumonia are crucial for understanding the true situation of patients with cardiometabolic diseases.

Cardiometabolic profile

Patients will be characterized by their history of cardiometabolic diseases, and the time elapsed since their last admission to hospital due to CV events. It is well established that individuals who have survived a MI or ischemic stroke, particularly those with diabetes, are at higher risk of subsequent CV events. These patients would potentially benefit from intensified treatment and comorbidities management[31].

Medical controls and treatments

Suboptimal adherence to medications prescribed chronically for secondary prevention of CV and metabolic diseases continue to burden the healthcare system, despite the well-established prevention benefits of adherence[32]. Potential barriers to optimal adherence include the number of pills per day, access to healthcare systems, and the availability of drugs and medical prescriptions[33]. Therefore, evaluating the percentage of the population receiving treatment according to medical recommendations is extremely valuable. Furthermore, assessing adherence to recommended immunizations against influenza and pneumococcus is crucial, as vaccines are particularly indicated in this group of patients[33].

Discussion

In 2021, the SIAC published an article evaluating the status of cardiometabolic patients without COVID-19
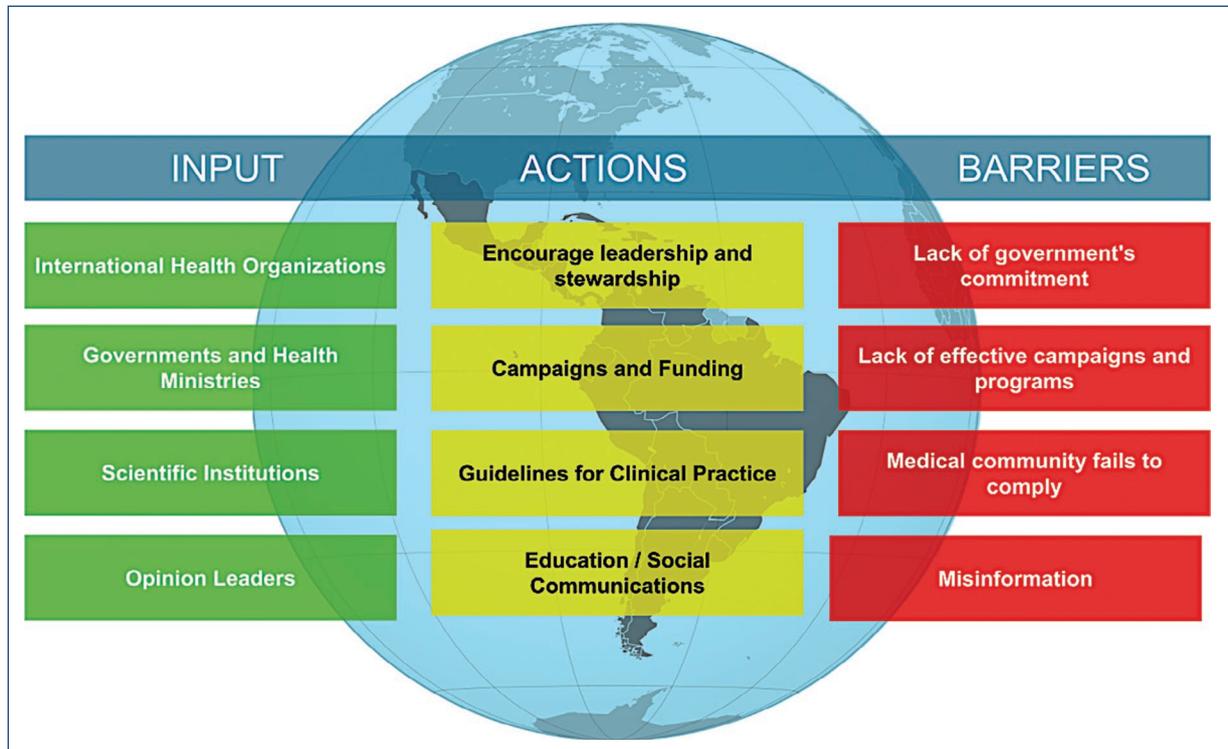
Figure 1. Key factors influencing immunization rates, actions for improvement and barriers encountered.

infection during the pandemic, including their immunization profile against influenza and pneumococcus[34]. A total of 4216 subjects were included in the study, where the mean age was 60 (± 15) years, and 49% of patients were females. The study population comprised of 1764 patients (42%) aged 65 years or above, 899 patients (21.3%) with diabetes, and 606 patients (14.3%) who were current or former smokers. A total of 769 (18.2%) patients had a known history of computer-aided design, while 538 patients (12.7%) had a history of HF. The global IV rate was 46.5% (n = 1963), PV 24.6% (n = 1039), and double vaccination rate was 21% (n = 887)[29].

The immunization rate was found to be lower than expected for this population. Furthermore, no significant sex differences in vaccination rates were identified by the authors[35].

In the same cohort, the impact of different variables on immunization rates was analyzed, including geographic region. The vaccination rates of patients from the Southern cone (Argentina, Paraguay, and Chile) were approximately double those of patients from the tropical regions. The IV rate was 69% in the Southern cone, 34% in AR (Peru, Ecuador, Colombia, and Venezuela), and 35% in Central America and the Caribbean (Costa Rica, Cuba, El Salvador, Guatemala, Mexico

and Dominican Republic) (χ = 452, df = 2, p < 0.001). The rates of PV were 43%, 20%, and 11%, respectively (χ = 406, df = 2, p < 0.001). The rates of double vaccination were 40%, 11%, and 9%, respectively (χ^2 = 458, df = 2, p < 0.001)[36].

In this context, several variables influence the decision to be vaccinated or not in the continent. These variables are presented in figure 2.

Despite the advantages associated with IV and PV, the recommendations for its prescription by scientific societies and health regulatory agencies, the vaccination rates globally, as well as in the Americas, appear lower than expected. This phenomenon can be attributed to the existence of implementation barriers affecting doctors, patients, and the broader health system. Recognizing these barriers is crucial for developing strategies to achieve vaccination targets[37].

A thorough understanding of these implementation barriers, which involve doctors, patients, and their context, is essential when designing continuous improvement strategies. The current and unavoidable challenge for our scientific societies is to turn recommendations into action[37].

The Pan-American Health Organization urges the use of scientific evidence to guide decision-making and

Table 1. Description of the questions included in the survey

Questions	Possible responses
Region	North, Central America, and the Caribbean Andean Southern cone
Age Gender	Female Male Transgender Other
What perception do you have of your state of health?	Scale of 1-10 (Unhealthy-very healthy)
Number of inhabitants city/town of residence	< 10,000 population 10,000-100,000 population 100,000-500,000 population > 500,000 population Don't know
Marital relationship	Married Divorced Single United to Widower None of the above
Work relationship	Dependent asset Independent asset Retired/pensioned/retired Independent worker Irregular worker None of the above
Education level	None Primary Secondary University Master's degree
If you are a professional, could you describe your occupation?	Lawyer Business Administration Architect Engineer Entrepreneur Finance Doctor Marketing/Advertising Business Health area personnel Others
Economic Income in US dollars per month	< 499 500-999 1000-1499 1500-1999 2000-2499 2500-2999 > 3000
Access to health services	Private with direct payment Private with medical insurance Social security Public health service None

(Continues)

Table 1. Description of the questions included in the survey *(continued)*

Questions	Possible responses
What chronic diseases do you have?	Cancer Mellitus diabetes Diseases of the immune system Psychiatric mental illness Psychological Chronic lung diseases Renal disease Fatty liver Arterial hypertension Hypothyroidism Polycystic ovary Cholesterol and/or triglyceride problems Overweight/Obesity Smoking None of the above
Have you been diagnosed by a doctor with the following diseases?	Angina pectoris Arrhythmias Disease of the arteries of the lower limbs and/or aorta Stroke Myocardial infarction Heart failure None of the above
Have you had any of the following procedures?	Cardiac catheterization with stent placement in any coronary artery Cardiac surgery for heart valve prostheses Bypass surgery or revascularization of the coronary arteries Lower limb vascular surgery Pacemaker None of the above
For his chronic illnesses, I take my medications	Every day without fail, at the corresponding time Every day without fail, but not at the corresponding time I remember from time to time I forget from time to time I don't take them I don't need medication
How many medications do you take?	1 2 3 4 5 > 5 None I don't like taking medications
Please select your medication scheme	Single-drug pills One pill with two medications One pill with three medications They told me it's called Polypill None of the above
Have you had the flu?	Yes No Don't know
Have you had pneumococcus?	Yes No Don't know
How confident are you in the influenza vaccination?	Scale 1-10 (Not at all confident-very confident)
How confident are you in the pneumococcus vaccination?	Scale 1-10 (Not at all confident-very confident)

(Continues)

Table 1. Description of the questions included in the survey *(continued)*

Questions	Possible responses
How often do you get the influenza vaccine?	Annually in season Every 2 years Every 3 years When I remember From time to time I don't put it on
Have you had a pneumococcus vaccine?	Yes No
Who prescribes the vaccines?	General physician Internal medicine Family medicine Cardiologist Endocrinologist Geriatrician Gynecologist Pulmonologist Neurologist Pediatrician for my children/grandchildren Others (Gastroenterologist, Rheumatologist, etc.) I prescribe myself None of the above
What health service does vaccination provide you?	Public Private Social Security Annual vaccination campaign in my country I buy it at the pharmacy without prescription None of the above
How much do you know about the cardiovascular benefits of vaccination?	Scale 1-10 (I don't know them-I know them)
If you are not a doctor, do you suggest other vaccinations?	Yes No Does not apply
If you are a doctor, do you indicate vaccination for Influenza and Pneumococcus?	Yes No Does not apply
Do you know when the Influenza season is in your country?	Yes No
Are there vaccination campaigns for Influenza and Pneumococcus in your country?	Yes No Don't know
Have you been vaccinated for Covid-19?	Yes No
Number of doses given	1 2 3 4 5 None All necessary
What type of vaccine do you use?	Abdala (Cuban) Moderna J and J/Janssen Oxford/Astra Zeneca Pfizer/BioNTech Sinopharm (China) Sinovac/Biotech (China) Sputnik 5 (Russia) None
How confident are you in the COVID-19 vaccination?	Scale 1-10 (Not at all confident-very confident)

Figure 2. Distribution of participating countries by region. North, Central, and Caribbean region (NCC): Mexico, Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica, Panama, Cuba, Puerto Rico and Dominican Republic. Andean region (AR): Venezuela, Colombia, Ecuador, Bolivia and Peru. Southern Cone region (SCR): Paraguay, Chile, Uruguay, and Argentina.

program implementation to improve immunization rates. In this context, the present study will help advocate for Latin America and enhance vaccination coverage for influenza and pneumococcus, thereby improving the CV prognosis of patients.

Conclusion

This study will provide insight into the impact of influenza and pneumococcus vaccinations in Latin American populations and the barriers preventing the immunization targets from being actualized. Hopefully, this will help to facilitate the development of targeted and focused health prevention strategies.

Funding

This study received an unrestricted grant from Sanofi-Pasteur.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality, informed consent and ethical approval. The authors have followed the confidentiality protocols of their institution, have obtained informed consent from the patients, and have the approval of the Ethics Committee. The recommendations of the SAGER guidelines have been followed, according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence for the writing of this manuscript.

References

1. Joseph P, Leong D, McKee M, Anand SS, Schwalm JD, Teo K, et al. Reducing the global burden of cardiovascular disease, part 1: the epidemiology and risk factors. Circ Res. 2017;121:677-94.
2. Warren-Gash C, Smeeth L, Hayward AC. Influenza as a trigger for acute myocardial infarction or death from cardiovascular disease: a systematic review. Lancet Infect Dis. 2009;9:601-10.
3. Clayton TC, Thompson M, Meade TW. Recent respiratory infection and risk of cardiovascular disease: Case-control study through a general practice database. Eur Heart J. 2008;29:96-103.
4. Kwok CS, Aslam S, Kontopantelis E, Myint PK, Zaman MJ, Buchan I, et al. Influenza, influenza-like symptoms and their association with cardiovascular risks: a systematic review and meta-analysis of observational studies. Int J Clin Pract. 2015;69:928-37.
5. Madjid M, Miller CC, Zarubaev VV, Marinich IG, Kiselev OI, Lobzin YV, et al. Influenza epidemics and acute respiratory disease activity are associated with a surge in autopsy-confirmed coronary heart disease death: Results from 8 years of autopsies in 34,892 subjects. Eur Heart J. 2007;28:1205-1210.
6. Kwong JC, Schwartz KL, Campitelli MA, Chung H, Crowcroft NS, Karnauchow T, et al. Acute myocardial infarction after laboratory-confirmed influenza infection. N Engl J Med. 2018;378:345-53.
7. Hung IF, Leung AY, Chu DW, Leung D, Cheung T, Chan CK, et al. Prevention of acute myocardial infarction and stroke among elderly persons by dual pneumococcal and influenza vaccination: a prospective cohort study. Clin Infect Dis Off Publ Infect Dis. Soc Am. 2010;51:10071016.
8. Nichol KL. Influenza vaccination in the elderly: impact on hospitalisation and mortality. Drugs Aging. 2005;22:495-515.
9. Nichol KL, Margolis KL, Wuorenma J, Von Sternberg T. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. N Engl J Med. 1994;331:778-84.
10. Nichol KL, Nordin J, Mullooly J, Lask R, Fillbrandt K, Iwane M. Influenza vaccination and reduction in hospitalizations for cardiac disease and stroke among the elderly. N Engl J Med. 2003;348:1322-32.
11. Bridges CB, Fukuda K, Uyeki TM, Cox NJ, Singleton JA, Centers for Disease Control and Prevention, Advisory Committee on Immunization Practices. Prevention and control of influenza: recommendations of the advisory committee on immunization practices (ACIP). Mmwr Recomm Rep. 2002;51:1-40.
12. Udell JA, Zawi R, Bhatt DL, Keshtkar-Jahromi M, Gaughran F, Phrommintikul A, et al. Association between influenza vaccination and cardiovascular outcomes in high-risk patients: a meta-analysis. JAMA. 2013;310:1711-20.
13. Clar C, Oseni Z, Flowers N, Keshtkar-Jahromi M, Rees K. Influenza vaccines for preventing cardiovascular disease. Cochrane Database Syst Rev. 2015;2015:CD005050.
14. LeBras MH, Barry AR. Influenza vaccination for secondary prevention of cardiovascular events: a systematic review. Can J Hosp Pharm. 2017;70:27-34.
15. Lamontagne F, Garant MP, Carvalho JC, Lanthier L, Smieja M, Pilon D. Pneumococcal vaccination and risk of myocardial infarction. CMAJ. 2008;179:773-7.
16. Vila-Corcoles A, Ochoa-Gondar O, Rodriguez-Blanco T, Gutierrez-Perez A, Vila-Rovira A, Gomez F, et al. Clinical effectiveness of pneumococcal vaccination against acute myocardial infarction and stroke in people over 60 years: the CAPAMIS study, one-year follow-up. BMC Public Health. 2012;12:222.

17. Rodrigues BS, David C, Costa J, Ferreira JJ, Pinto FJ, Caldeira D. Influenza vaccination in patients with heart failure: a systematic review and meta-analysis of observational studies. Heart. 2020;106:350-7.

18. Davis BM, Black D. Identifying the challenges to adult influenza vaccination in latin America. Value Health. 2017;20:PA934.

19. Zimmerman RK, Santibanez TA, Fine MJ, Janosky JE, Nowalk MP, Bardella IJ, et al. Barriers and facilitators of pneumococcal vaccination among the elderly. Vaccine. 2003;21:1510-7.

20. Centers for Disease Control and Prevention (CDC). Reasons reported by medicare beneficiaries for not receiving influenza and pneumococcal vaccinations-United States, 1996. Mmwr Morb Mortal. 1999;48:886-90.

21. Centers for Disease Control. Adult immunization: knowledge, attitudes, and practices--DeKalb and Fulton Counties, Georgia, 1988. JAMA. 1988;260:3253-5.

22. Bovier PA, Chamot E, Bouvier Gallacchi M, Loutan L. Importance of patients' perceptions and general practitioners' recommendations in understanding missed opportunities for immunisations in Swiss adults. Vaccine. 2001;19:4760-7.

23. Schmid P, Rauber D, Betsch C, Lidolt G, Denker ML. Barriers of influenza vaccination intention and behavior-a systematic review of influenza vaccine hesitancy, 2005-2016. PLoS One. 2017;12:e0170550.

24. Burki TK. Vaccine misinformation and social media. Lancet Digit Health. 2019;1:E258-9.

25. Hill JA, Agewall S, Baranchuk A, Booz GW, Borer JS, Camici PG, et al. Medical misinformation: vet the message! Int J Cardiol. 2019;277:1-2.

26. Hill JA, Agewall S, Baranchuk A, Booz GW, Borer JS, Camici PG, et al. Medical Misinformation: Vet the Message! Int J Cardiol. 2019 Feb 15;277:1-2. doi: 10.1016/j.ijcard.2018.12.071. PMID: 30661544; PMCID: PMC6380668.

27. Chan MS, Jamieson KH, Albarracin D. Prospective associations of regional social media messages with attitudes and actual vaccination: a big data and survey study of the influenza vaccine in the United States. Vaccine. 2020;38:6236-47.

28. Sosa Liprandi Á, Zaidel EJ, Lopez Santi R, Araujo JJ, Baños González MA, Busso JM, et al. 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. Vaccines (Basel). 2021;9:123.

29. Liprandi AS, Liprandi MI, Zaidel EJ, Aisenberg GM, Baranchuk A, Barbosa EC, et al. Influenza vaccination for the prevention of cardiovascular disease in the Americas: consensus document of the inter-American society of cardiology and the word heart federation. Global Heart. 2021;16:55.

30. Li S, Peng Y, Wang X, Qian Y, Xiang P, Wade SW, et al. Cardiovascular events and death after myocardial infarction or ischemic stroke in an older Medicare population. Clin Cardiol. 2019;42:391-9.

31. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005;353:487-97.

32. Tamargo J, Castellano JM, Fuster V. The Fuster-CNIC-Ferrer cardiovascular polypill: a polypill for secondary cardiovascular prevention. Int J Cardiol. 2015;201:S15-22.

33. Modin D, Claggett B, Køber L, Schou M, Jensen JUS, Solomon SD, et al. Influenza vaccination is associated with reduced cardiovascular mortality in adults with diabetes: a nationwide cohort study. Diabetes Care. 2020;43:2226-33.

34. Santi RL, Márquez MF, Piskorz D, Saldarriaga C, Lorenzatti A, Wyss F, et al. Ambulatory patients with cardiometabolic disease and without evidence of COVID-19 during the pandemic. The CorCOVID LATAM study. Glob Heart. 2021;16:15.

35. Saldarriaga-Giraldo CI, Ramírez-Ramos CF, Lopez-Santi R, Lanas F, Valdés Martín A, Sotomayor Perales JL, et al. Gender-related differences in the impact of COVID-19 pandemic in cardiometabolic patients in Latin America: the CorCOVID latam gender sub-study. Curr Probl Cardiol. 2022;47:101075.

36. Camilletti J, Renna NF, López-Santi R, Erriest J, García-Bello E, Araujo J, et al. Impact of COVID-19 pandemic on cardiometabolic patients without SARS-CoV-2 infection in Latin America. Arch Cardiol Mex. 2023;93:1-9.

37. Rosengren A, Smyth A, Rangarajan S, Ramasundarahettige C, Bangdiwala SI, AlHabib KF, et al. Socioeconomic status, and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the prospective Urban Rural Epidemiologic (PURE) study. Lancet Glob Health. 2019;7:e74860.