



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Short communication

Relationship between double COVID-19 vaccine uptake and trust in effectiveness and safety of vaccination in general in 23 Member states of the European Union: an ecological study



Àurea Cartanyà-Hueso^{a,b}, Jose M Martínez-Sánchez^a, Juan Carlos Martín-Sánchez^a,
Cristina Lidón-Moyano^a, Hipólito Pérez-Martín^a, Adrián González-Marrón^{a,*}

^a Group of Evaluation of Health Determinants and Health Policies, Department of Basic Sciences, Universitat Internacional de Catalunya, Sant Cugat del Vallès, Spain

^b Group of Perinatal Epidemiology, Environmental Health, and Clinical Research, Department of Medicine, School of Health Sciences, Universitat Jaume I, Av. Vicent Sos Baynat, s/n 12071 Castelló de la Plana, Spain

ARTICLE INFO

Article history:

Received 4 June 2021

Received in revised form 9 June 2022

Accepted 19 June 2022

Available online 23 June 2022

Keywords:

COVID-19

European Union

Vaccination

Vaccine effectiveness

Vaccine safety

ABSTRACT

Introduction: The aim of this study was to assess the relationship between double COVID-19 vaccine uptake and trust in effectiveness and safety of vaccination in general in 23 European Union (EU) countries.

Methods: Ecological study. Data was retrieved from the Flash Eurobarometer 494 and Our World in Data. We estimated Pearson's correlation coefficients and fitted multiple linear regression models.

Results: There is a negative linear correlation between the percentage of people doubly vaccinated and the percentage of low trust in vaccine effectiveness ($r = -0.48$, p -value = 0.021), and the percentage of low trust in vaccine safety ($r = -0.43$, p -value = 0.041). There is a negative adjusted relation between the percentage of low trust in vaccine safety and the percentage of people doubly vaccinated ($\beta_{\% \text{ low trust in vaccine safety}}: -0.25$; 95% CI: $-0.49, -0.01$, p -value = 0.045).

Conclusion: An increase in health literacy of people living in certain countries in the EU may be needed to boost COVID-19 vaccine uptake.

© 2022 Elsevier Ltd. All rights reserved.

1. Introduction

Coronavirus Disease 2019 (COVID-19) is a deadly disorder which has caused over 6.2 million deaths worldwide [1] since its causative agent, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was discovered in late 2019. At the beginning of the pandemic, diverse prophylactic measures, including personal hygiene (e.g., handwashing), social distancing or respiratory etiquette, were recommended to control the transmission of this disease. On a second stage, different organizations, both public and private, quickly tested and developed safe and effective vaccines against the SARS-CoV-2. Subsequently, the corresponding regulatory organizations approved the commercialization and use of these vaccines and as a result, in countries with a high proportion of people vaccinated, COVID-19 incidence and fatality rate, especially among people at highest risk, have greatly declined [2].

In this context, massive vaccination campaigns are being carried out worldwide nowadays. These campaigns, however, are advancing at different velocities [3]. Probably, the main factors associated with the pace of vaccination are structural, mainly the availability of stock of the different types of vaccines. In this sense, while most developed countries have large batches and rates of vaccination are high, developing countries have an important lack of stock and vaccination rates are low, scenario that has led to an unequal access to immunization [4]. Remarkably, immunization is needed globally to fully control the COVID-19 pandemic. Other factors apart from structural, however, should also be considered to understand why countries and territories with even socio-economic development are advancing differently in vaccination.

At the individual level, vaccine acceptance has been proposed to have a fundamental impact on the COVID-19 vaccine uptake [5]. Vaccine acceptance is based on three main pillars, which are vaccination confidence, complacency and convenience [6]. Vaccine confidence is defined as “trust in the effectiveness and safety of vaccines and in the system that delivers them” [6]. Specifically, in the European Union (EU), vaccination rates for different communicable diseases are overall high [7,8]. However, vaccination pro-

* Corresponding author.

E-mail address: agonzalezm@uic.es (A. González-Marrón).

grammes are currently facing challenges due to an erosion of trust in vaccines in some people usually belonging to specific communities or pockets [9]. This situation, which has been relevant for measles lately, is associated to socioeconomic factors, but also more generally to a plethora of other determinants, such as lack of information or access to fake content on vaccination [9]. This erosion of trust in vaccination could also be having an impact on the vaccination against the COVID-19 at the national level, as previous studies have pointed out within specific countries [10]. Knowing if this association occurs in different territories would be of paramount interest to invest for increasing health literacy and for empowering people. Thus, the aim of this study is to explore the relationship between trust in effectiveness and safety of vaccines in general and double COVID-19 vaccine uptake at the national level in 23 EU Member States.

2. Methods

This is an ecological study with country as analysis unit using data from the Flash Eurobarometer 494 about Europeans' attitudes on vaccination against COVID-19 [11] and Our World in Data repository about COVID-19 vaccination [12]. The Flash Eurobarometer 494 aims to obtain input from citizens in the EU regarding their attitudes on vaccination against COVID-19 ($n = 26,106$). It was carried out by Ipsos European Public Affairs at the request of the European Commission, Directorate-General for Communication in the 27 EU Member States (EU-27) between the 21st and 26th of May 2021. Our World in Data repository collects periodically data on COVID-19 vaccination and policies towards COVID-19 vaccination, country by country. Inclusion criteria for our study were: (1) belonging to the EU-27, and (2) having available data on the percentage of people doubly vaccinated against COVID-19 by the 17th of May 2021. In this sense, there were not data available for Ireland, the Netherlands, Portugal and Sweden. After applying inclusion criteria, this study includes data on 23 countries of EU-27.

2.1. Research ethics

The investigation was carried out considering the rules of the Declaration of Helsinki of 2013. We used anonymized secondary data publicly available in the following repositories (https://data.europa.eu/data/datasets/s2512_494_eng?locale=en) and (<https://ourworldindata.org/covid-vaccinations>).

2.2. Variables of study

2.2.1. Trust in effectiveness and safety of vaccines in general

The Flash Eurobarometer 494 collects information about trust in effectiveness of vaccines in general through the item “To what extent do you agree or disagree with the following statements about vaccines in general: Vaccines are effective”, with the options totally agree/tend to agree/tend to disagree/totally disagree/don't know. Respondents were classified according to their trust in effectiveness of vaccines in general into high, for those respondents who answered totally agree or tend to agree; low, for those respondents who answered tend to disagree or totally disagree; and don't know, for those respondents who answered don't know. Trust in safety of vaccines in general was collected through the item “To what extent do you agree or disagree with the following statements about vaccines in general: Vaccines are safe”, with the options totally agree/tend to agree/tend to disagree/totally disagree/don't know. Respondents' trust in safety of vaccines in general was classified as high/low and don't know in the same way as trust in effectiveness.

2.2.2. COVID-19 vaccination and covariates

Our World in Data repository collects and updates periodically COVID-19 vaccination data country by country from official data sources. Also, we collected as covariates those variables that might impact COVID-19 vaccination following the Working Group on Vaccine Hesitancy Determinants Matrix [6] and the nature of the data. We retrieved from each country the percentages of people doubly vaccinated; number of vaccines in the list of vaccines dispensed (e.g., being 3 if a country dispensed Moderna, Oxford/AstraZeneca, and Pfizer/BioNtech); the policy towards COVID-19 vaccination (vaccination available for two of the following three groups: key workers, clinically vulnerable groups or elderly groups; vaccination available for all of the following groups: key workers, clinically vulnerable groups, and elderly groups; availability for all three groups, plus partial additional availability (selected broad group/ages); and universal); total deaths per million attributed to COVID-19; total COVID-19 cases per million; stringency index, which is a composite measure based on 9 response indicators including school closures, workplace closures, and travel bans, rescaled to a value from 0 to 100 (100 = strictest response); gross domestic product (GDP) at purchasing power parity (constant 2011 international dollars) in the most recent year available; median age of the population from the United Nations projection for 2020; and total population by the 17th of May 2021.

2.3. Statistical analysis

We described the percentage of low trust in effectiveness of vaccines in general, the percentage of low trust in safety of vaccines in general, and the percentage of people doubly vaccinated against COVID-19 by the 17th May 2021 in each country included in the analyses. We estimated the Pearson's correlation coefficient between the percentage of people doubly vaccinated against COVID-19 and the percentage of low trust in effectiveness of vaccines in general and in safety of vaccines in general at the national level. Also, we identified the number of vaccines in the list of vaccines dispensed per country against COVID-19, the policy towards COVID-19 vaccination, and the total deaths per million attributed to COVID-19. Further, after checking linear regression model assumptions (linearity, homoscedasticity, normality of the residuals, and independence of residual error terms), we tested the relation between the percentage of people doubly vaccinated against COVID-19 and the percentage of low trust in effectiveness of vaccines in general, percentage of low trust in safety of vaccines in general, and covariates, through simple and multiple linear regression models. In the multiple linear regression model, we adjusted for total deaths per million attributed to COVID-19 after assessing the quality of different models using the Akaike Information Criterion. We weighted simple and multiple regression models according to the population of the country. Significance level was set up to 0.05. The software used was R-4.0.3 and the package used to design the plots was ggplot2 version 3.3.3.

3. Results

The Member State with the highest percentage of people doubly vaccinated against COVID-19 by the 17th of May 2021 was Malta (33.4%), being the percentages of Maltese with low trust in effectiveness and safety of vaccines in general of 3.7% and 6.5%, respectively, while Finland was the country with the lowest percentage of people doubly vaccinated against COVID-19 (5.3%). Latvia, which had the highest percentage of low trust in effectiveness of vaccines (22.9%), and Bulgaria, which had the highest percentage of low trust in safety of vaccines (34.2%) among all the countries included in the analysis, were the countries with the second and third low-

est percentages of people doubly vaccinated against COVID-19 by the 17th of May 2021 (6.1% and 6.8%, respectively) (Table 1).

There is a significant negative linear correlation between the percentage of low trust in effectiveness of vaccines in general and the percentage of people doubly vaccinated against COVID-19 ($r = -0.48$, p -value = 0.021), as well as between the percentage of low trust in safety of vaccines in general and the percentage of people doubly vaccinated against COVID-19 ($r = -0.43$, p -value = 0.041). Further, the policy towards COVID-19 most applied as of 17th of May 2021 was to vaccinate universally (35.7%). Only Spain had a policy towards COVID-19 vaccination of vaccinating two of the following groups: key workers, clinically vulnerable groups, and elderly groups. Moreover, the majority of analyzed countries had four different vaccines available for dispensing (67.9%). Only Slovakia had one type of vaccine available for dispensing (Pfizer/BioNTech), while Hungary was the only country that had five different types of vaccines available for dispensing (Moderna, Oxford/AstraZeneca, Pfizer/BioNTech, Sinopharm/Beijing, Sputnik V) (Fig. 1).

Further, we found a non-significant negative adjusted linear relation between the percentage of low trust in effectiveness of vaccines in general and the percentage of people doubly vaccinated against COVID-19 ($a\beta_{\% \text{ low trust in vaccine effectiveness}}: -0.37$; 95% CI: $-0.76, 0.05$, p -value: 0.103) and a significant negative adjusted linear relation between the percentage of low trust in safety of vaccines in general and the percentage of people doubly vaccinated against COVID-19 ($a\beta_{\% \text{ low trust in vaccine safety}}: -0.25$; 95% CI: $-0.49, -0.01$, p -value: 0.045) (Supplemental Table 1).

4. Discussion

We have found a negative correlation between trust in effectiveness and safety of vaccines in general and double COVID-19 vaccine uptake at the national level in 23 Member states of the EU-27. A significant negative adjusted linear association was also found between double COVID-19 vaccine uptake and trust in safety of vaccines.

These results are in line with previous studies carried out in different countries within the EU, which concluded that the uptake of the COVID-19 vaccine was associated with its acceptance. For instance, in a study carried out in Finland, the main predictor for

COVID-19 vaccination was the perceived safety [13]. In a study based in France, vaccine hesitancy decreased in working-age population when people were informed on the benefits of herd immunity [14]. Also, in an Internet-based study conducted in Spain, reasons obtained from people not getting vaccinated were also similar (e.g., lack of effectiveness, lack of safety) [15]. Besides, when we assessed the relation between high trust in vaccine effectiveness and safety in general, and the percentage of people doubly vaccinated against COVID-19, we found positive linear relations ($r_{\text{effectiveness}} = 0.41$, p -value = 0.051 and $r_{\text{safety}} = 0.35$, p -value = 0.097), results which also support the meaning of our data.

Vaccination against the COVID-19 is a key element to accomplish herd immunity globally, which is the objective to control the pandemic. The findings from our exploratory analysis may indicate that Member states achieving higher rates of trust in vaccine effectiveness and safety may have higher acceptance for vaccination against the COVID-19 and be able to reach higher levels of immunization in a short time. On the other hand, countries with a higher proportion of general vaccine hesitancy may face trouble to quickly reach the percentage of population needed to accomplish herd immunity [16].

Vaccine acceptance is a complex decision process in which social and individual determinants play a decisive role [6]. Different actors, such as the media or government policies, may module the decision of vaccine uptake and, for this reason, they should be involved in health literacy of the populations. Also, administrations and governments should identify at the national and local level pockets of people in which vaccine hesitancy is high to allocate resources to improve their health literacy [17].

Our results should be interpreted cautiously in the context of a study that has several limitations. Firstly, the major limitation of this study is that we did not have access to data on vaccine availability; in this sense, by the 17th of May 2021, when the vaccination campaign was starting, this factor was different among Member states, being a determinant factor for the uptake of the COVID-19 vaccine. Secondly, the ecological design of our research hampers drawing conclusions at the individual level. However, our results are in line with previous surveys assessing the association between COVID-19 and diverse determinants of acceptance within the ambit of confidence in research and vaccination in other countries. For example, in a study carried out in the US [18], indi-

Table 1

Percentage of people doubly vaccinated by the 17th of May 2021 and percentages of people with low trust in the effectiveness and safety of vaccines in general in 2021 per country.

Country	ISO Code	% of people doubly vaccinated	% of low trust in effectiveness of vaccines in general	% of low trust in safety of vaccines in general
Finland	FIN	5.3	10.0	12.5
Bulgaria	BGR	6.1	21.7	34.2
Latvia	LVA	6.8	22.9	26.5
Croatia	HRV	7.7	13.4	17.9
Czechia	CZE	10.4	12.3	17.0
Germany	DEU	11.4	7.8	11.5
Austria	AUT	12.3	9.6	14.4
Belgium	BEL	12.3	7.8	25.2
Poland	POL	12.3	8.5	12.0
Slovakia	SVK	12.6	17.6	26.6
Cyprus	CYP	13.1	10.7	15.2
Estonia	EST	13.5	13.8	26.5
France	FRA	13.5	8.2	15.2
Luxembourg	LUX	13.8	8.9	11.8
Slovenia	SVN	14.3	18.0	31.2
Italy	ITA	14.7	7.3	10.9
Romania	ROU	15.1	13.3	16.9
Greece	GRC	15.6	8.1	12.5
Spain	ESP	15.7	3.3	4.1
Lithuania	LTU	16.6	13.9	21.3
Denmark	DNK	18.5	7.6	10.9
Hungary	HUN	28.5	10.9	13.7
Malta	MLT	33.4	3.7	6.5

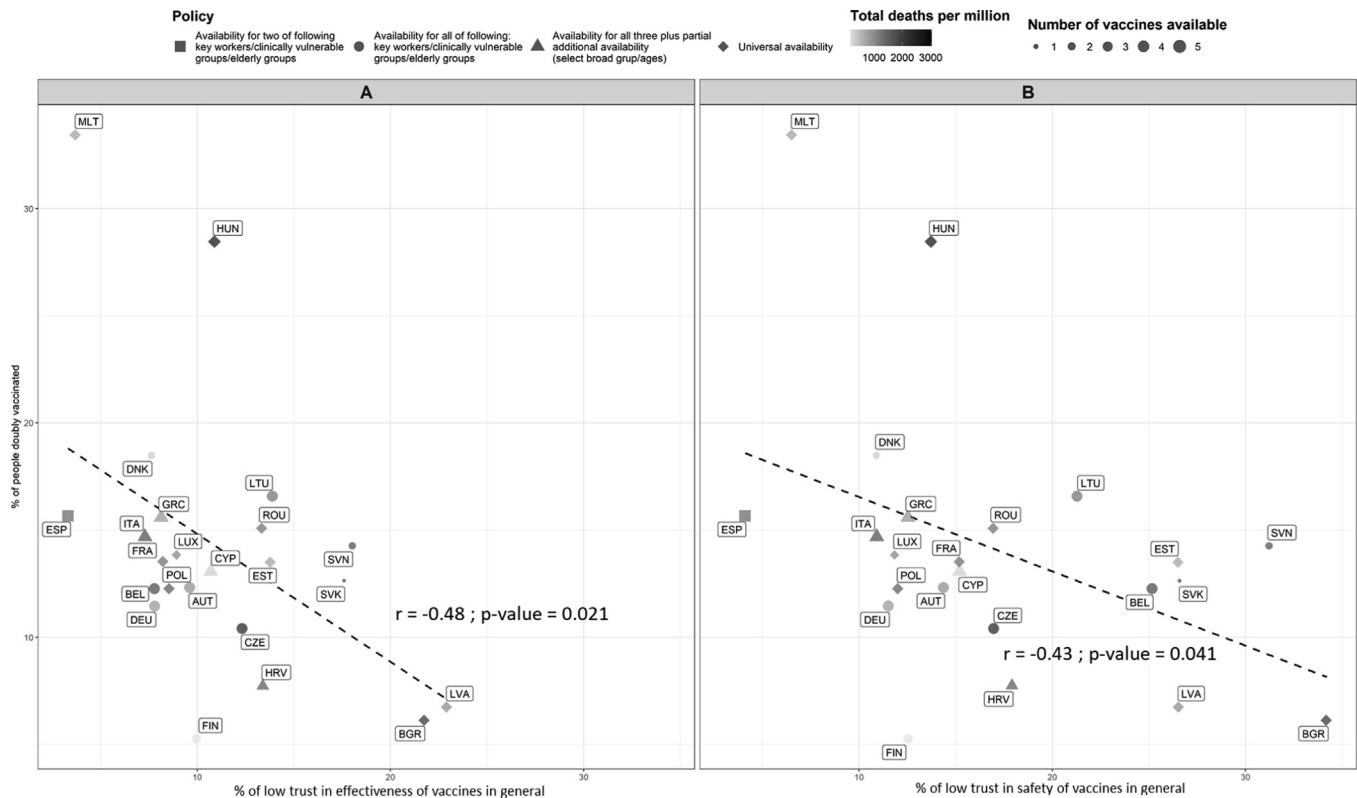


Fig. 1. Scatterplots representing the correlation at the national level between percentage of people doubly vaccinated by the 17th of May 2021 and percentage of low trust in effectiveness of vaccines in general in 2021 (A), and between percentage of people doubly vaccinated by the 17th of May 2021 and percentage of low trust in safety of vaccines in general in 2021 (B).

viduals who had greater confidence in scientists and researchers were more than three times as likely to vaccinate against COVID-19 than individuals with hardly any confidence. Also, results arising from a survey in Russia, showed that the most common reasons for not taking the vaccine were concerns on vaccine’s effectiveness, safety and side effects [19]. Also, there are probably many other factors apart from the trust in vaccine effectiveness and vaccine safety, both individual and structural, associated with vaccine uptake, which have not been taken into account in our adjusted analysis due to the nature of the data used, such as sex. These factors may be confounding the association explored. Further, since we used already available and public data, we could not use a variable of specific knowledge about the COVID-19 vaccine.

In conclusion, we have found a negative association between trust in vaccine effectiveness and safety in general, and double COVID-19 vaccine uptake, in 23 countries in the EU. Our results may indicate the need to increase health literacy of people living in certain countries in the EU, with regards to knowledge of vaccination, to boost COVID-19 vaccine uptake.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. À.C.-H., J.M.M.-S., J.C.M.-S., C.L.-M., H.P.-M, and A.G.-M. are supported by the Departament de Universitats i Recerca de la Generalitat de Catalunya (2017SGR608).

Declaration of Competing Interest

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

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2022.06.049>.

References

- [1] Johns Hopkins - University of Medicine. Coronavirus Resource Center 2021. <https://coronavirus.jhu.edu/> (accessed April 29, 2022).
- [2] Leshem E, Wilder-Smith A. COVID-19 vaccine impact in Israel and a way out of the pandemic. *Lancet* (London, England) 2021;397:1783–5. [https://doi.org/10.1016/S0140-6736\(21\)01018-7](https://doi.org/10.1016/S0140-6736(21)01018-7).
- [3] Our World in Data. COVID-19 Dqata Explorer 2020. <https://ourworldindata.org/explorers/coronavirus-data-explorer> (accessed October 14, 2021).
- [4] Sheikh AB, Pal S, Javed N, Shekhar R. COVID-19 vaccination in developing nations: challenges and opportunities for innovation. *Infect Dis Rep* 2021;13:429–36. <https://doi.org/10.3390/idr13020041>.
- [5] Sallam M. COVID-19 vaccine hesitancy worldwide: a concise systematic review of vaccine acceptance rates. *Vaccines* 2021;9(2):160.
- [6] MacDonald NE, Eskola J, Liang X, Chaudhuri M, Dube E, Gellin B, et al. Vaccine hesitancy: definition, scope and determinants. *Vaccine* 2015;33:4161–4. <https://doi.org/10.1016/j.vaccine.2015.04.036>.
- [7] Statista. Share of children immunized against Diphtheria, Tetanus and Pertussis (DPT) in selected European countries in 2018 2020. <https://www.statista.com/statistics/1122303/dpt-immunization-in-europe/> (accessed October 14, 2021).
- [8] World Health Organization (WHO). Measles in Europe: record number of both sick and immunized 2019.
- [9] Ammon A, Prats MX. Vaccines, trust and European public health. *Euro Surveill* 2018;23. <https://doi.org/10.2807/1560-7917.ES.2018.23.17.18-00210>.
- [10] Paul E, Steptoe A, Fancourt D. Attitudes towards vaccines and intention to vaccinate against COVID-19: implications for public health communications. *Lancet Reg Heal - Eur* 2021;1:. <https://doi.org/10.1016/j.lanepe.2020.100012>.
- [11] European Union. Attitudes on vaccination against Covid-19. Eurobarom Surv 2021. <https://europa.eu/eurobarometer/surveys/detail/2512> (accessed October 11, 2021).
- [12] Ritchie H, Ortiz-Ospina E, Beltekian D, Mathieu E, Hasell J, Macdonald B, et al. Coronavirus (COVID-19) Vaccinations. OurWorldInDataOrg 2019. <https://ourworldindata.org/covid-vaccinations#source-information-country-by-country> (accessed May 26, 2021).

- [13] Karlsson LC, Soveri A, Lewandowsky S, Karlsson L, Karlsson H, Nolvi S, et al. Fearing the disease or the vaccine: the case of COVID-19. *Pers Individ Dif* 2021;172. <https://doi.org/10.1016/j.paid.2020.110590>.
- [14] Schwarzinger M, Watson V, Arwidson P, Alla F, Luchini S. COVID-19 vaccine hesitancy in a representative working-age population in France: a survey experiment based on vaccine characteristics. *Lancet Public Heal* 2021;6: e210–21. [https://doi.org/10.1016/S2468-2667\(21\)00012-8](https://doi.org/10.1016/S2468-2667(21)00012-8).
- [15] Eguia H, Vinciarelli F, Bosque-Prous M, Kristensen T, Saigí-Rubió F. Spain's hesitation at the gates of a COVID-19 vaccine. *Vaccines* 2021;9(2):170.
- [16] Randolph HE, Barreiro LB. Herd immunity: understanding COVID-19. *Immunity* 2020;52:737–41. <https://doi.org/10.1016/j.immuni.2020.04.012>.
- [17] González-Marrón A, Martínez-Sánchez JM. Measles in Europe: necessity of global and local action to achieve its eradication. *Gac Sanit* 2018;32:590–1. <https://doi.org/10.1016/j.gaceta.2017.06.010>.
- [18] Malik AA, McFadden SAM, Elharake J, Omer SB. Determinants of COVID-19 vaccine acceptance in the US. *EClinicalMedicine* 2020;26: <https://doi.org/10.1016/j.eclim.2020.100495>100495.
- [19] Tran VD, Pak TV, Gribkova EI, Galkina GA, Loskutova EE, Dorofeeva VV, et al. Determinants of COVID-19 vaccine acceptance in a high infection-rate country: a cross-sectional study in Russia. *Pharm Pract (Granada)* 2021:19. <https://doi.org/10.18549/PHARMPRACT.2021.1.2276>.