Peertechz

MEDICAL GROUP

ARCHIVES OF
Community Medicine and Public Health OPEN ACCESS JOURNAL

ISSN: 2455-5479 DOI: https://dx.doi.org/10.17352/acmph

Research article

Risk factors for COVID-19 infection in people with 4th dose of bivalent mRNA vaccines in general medicine from October 2022 to February 2023

Jose Luis Turabian*

Specialist in Family and Community Medicine, Health Center Santa Maria de Benquerencia, Regional Health Service of Castilla la Mancha (SESCAM), Toledo, Spain

Received: 17 May, 2023
Accepted: 29 May, 2023
Published: 30 May, 2023

***Corresponding author:** Jose Luis Turabian, Specialist in Family and Community Medicine, Health Center Santa Maria de Benquerencia, Regional Health Service of Castilla la Mancha (SESCAM), Toledo, Spain, Tel: 34925230104; E-mail: jturabianf@hotmail.com; jluist@sescam.jccm.es

ORCiD: https://orcid.org/0000-0002-8463-171X

Keywords: COVID-19; SARS-CoV-2; Vaccine Effectiveness; Bivalent mRNA vaccines; General Practice

https://www.peertechzpublications.com

Check for updates

Abstract

Background: Risk factors of COVID-19 infection in people vaccinated with the 4th dose of mRNA COVID-19 vaccine remain the subject of debate.

Objective: To identify risk and protective factors of COVID-19 in vaccinated people with 4th dose of bivalent mRNA vaccines.

Location: General Practitioner consultation in Toledo (Spain).

Methodology: Longitudinal and prospective study of cases and controls of adult patients with or without COVID-19 infection in vaccinated people with 4th dose of bivalent mRNA vaccines, from October 1, 2022, to February 28, 2023.

Results: Five cases of COVID-19 infections in vaccinated people with 4th dose were included, which were compared with 52 controls (with 4th dose and without COVID-19 after the booster). The risk factors for COVID-19 infection with the 4th dose were: Women (RR = 1.67), Socio-Health Care Workers (RR = 10.39; p = 0.0349), Chronic Diseases of the blood (RR = 6.9. p = 0.0322), Chronic Diseases of Endocrine (RR = 2.72. p = 0.039425), and Chronic Diseases of Circulatory system (RR = 1.87).

Conclusion: In the general practice setting in Toledo, Spain, being a socio-health care worker and having chronic diseases presumably associated with immunosuppression were statistically significant risk factors for COVID-19 infection in people vaccinated with the 4th dose of bivalent mRNA vaccines. The most exposed or immunosuppressed people continue to be at risk of becoming infected with SARS-CoV-2 despite having received the 4th dose of the mRNA COVID-19 vaccine, so other preventive methods in these groups are advisable.

Introduction

Four years after the start of the coronavirus disease 2019 (COVID-19) pandemic, it is important to recognize that we are in a better place than ever. But, it is urgent to face a future in which COVID-19 will remain with us, threatening the health and well-being of millions of people around the world [1].

Vaccination provides substantial protection against both symptomatic and severe COVID-19. However, there has been continued and substantial evolution of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants since the virus emerged, such as Omicron and its sub-variants, posing challenges for the public health response, including ensuring that vaccines continue to provide protection, which has markedly reduced efficacy in regimens based on the ancestral Wuhan variant. Thus, booster vaccination for the prevention of COVID-19 is required to overcome this loss of protection [2-4].

Citation: Turabian JL (2023) Risk factors for COVID-19 infection in people with 4th dose of bivalent mRNA vaccines in general medicine from October 2022 to February 2023. Arch Community Med Public Health 9(2): 027-033. DOI: https://dx.doi.org/10.17352/2455-5479.000198

Since September 2022, Moderna and Pfizer-BioNTech bivalent SARS-CoV-2 vaccines containing equal amounts of spiked mRNA from the ancestral BA.4-BA.5 and omicron subvariants replaced their monovalent counterparts as booster doses for people over 12 years old. It is strongly suggested that a bivalent booster may preserve the safety and serological efficacy of the original monovalent booster while broadening the spectrum of antibody response, helping to restore protection that might have diminished since the last previous dose [5-9].

However, real-world effectiveness monitoring and continued surveillance are needed to determine when the antigenic composition of vaccines should be updated. The release of variant-containing vaccines should be accompanied by systematic collection of data and samples to assess the breadth and magnitude of the immune responses elicited, along with clinical studies, to estimate vaccine efficacy and determination of vulnerable populations to receiving boosts (there is the controversy over whether bivalent boosts against the omicron BA.4 and BA.5 subvariants of SARS-CoV-2, as well as the ancestral strain, should or should not be deployed in the entire population) [2,10-15].

In a scenario of a high level of population immunity, novel approaches are needed for sustained surveillance to assess the epidemiological consequences of new SARS-CoV-2 variants and sublineages, the cost of SARS-CoV-2 infection, and the risk groups to guide rational vaccination policies and decisions. Potential approaches could include, among others, longitudinal studies [16].

In this context, we present a longitudinal and prospective study of cases and controls of adult patients with or without COVID-19 infections in vaccinated people with a fourth dose of vaccines bivalent mRNA, in general medicine from October 1, 2022, to February 28, 2023, whose objective was to identify risk factors of COVID-19 of this booster (vaccines bivalent mRNA against the original strain and BA.4/BA.5 variant).

Material and methods

A longitudinal study of cases and controls of adult patients with or without COVID-19 infections in vaccinated people with a fourth dose of vaccines bivalent mRNA, from October 1, 2022, to February 28, 2023, in a general medicine office in Toledo, Spain, which has a list of 2,000 patients > 14 years of age (in Spain, the General Practitioners [GPs] care for people > 14 years of age, except for exceptions requested by the child's family and accepted by the GP) was carried out. The GPs in Spain work within the National Health System, which is public and is the gateway for all patients to the system, and each person is assigned a GP.

Objective of the study

Identify risk and protective factors of COVID-19 in vaccinated 4th dose (vaccines bivalent mRNA against the original strain and BA.4/BA.5 variant) people in a general practitioner consultation. In this sense, the variables collected were compared by calculating the Relative Risk (RR) as the incidence of specific variables in people with a fourth dose of COVID-19 infection/incidence of specific variables in people with a fourth dose without COVID-19 infection. The RR was interpreted as follows [17]: From 0 to 0.5: protection factor effectively; from 0.6 to 0.8: true benefits; from 0.9 to 1.1: not significant; from 1.2 to 1.6: weak risk; from 1.7 to 2.5: moderate risk; more than 2.5: strong risk.

Definition of cases and controls

Patients with acute infection of COVID-19 and 4th dose of vaccine were considered "cases." All the cases seen in the consultation object of the study were included. "Control" patients were those with 4th dose of vaccine and without COVID-19 infection. The controls were chosen by random sampling among the patients who consulted for a reason other than COVID-19, had received the 4th dose of the vaccine, and had not presented COVID-19 since that booster until April 15, 2023.

Booster dose for fall-winter 2022

In the patients included in the study, bivalent Comirnaty, Original/Omicron BA.4 - 5 (COVID-19 mRNA vaccine, Pfizer-BioNTech) [18] was used as a booster dose (4th dose). On August 31, 2022, the Food and Drug Administration licensed Moderna and Pfizer-BioNTech's bivalent COVID-19 vaccines, each containing equal amounts of mRNA encoding the ancestral strain spike protein and the spike protein of BA.4 and variant B.1.1.529 (Omicron) BA.5 strains, for emergency use as a single booster dose at least 2 months after primary or booster vaccination. Since September 1, these two bivalent mRNA vaccines have replaced their monovalent counterparts as booster doses for people 12 years and older in the United States and other countries [19]. In Spain, this vaccination began on September 26, 2022. It was recommended to the population aged 60 and over, to people admitted to nursing homes and other centers for disabilities, those with risk conditions and social and health personnel. But, people under 60 years of age without risk factors that request it could also be vaccinated [20].

Diagnosis of COVID-19

The diagnosis was performed with reverse transcriptase polymerase chain reaction (RT-PCR) oropharyngeal swab tests or antigen testing [21].

Collected variables

The following variables were collected:

- Age and sex
- Chronic diseases (defined as "any alteration or deviation from normal that has one or more of the following characteristics: is permanent, leaves residual impairment, is caused by a non-reversible pathological alteration, requires special training of the patient for rehabilitation, and/or can be expected to require a long period of control, observation or treatment" [22],

Citation: Turabian JL (2023) Risk factors for COVID-19 infection in people with 4th dose of bivalent mRNA vaccines in general medicine from October 2022 to February 2023. Arch Community Med Public Health 9(2): 027-033. DOI: https://dx.doi.org/10.17352/2455-5479.000198

classified according to the International Statistical Classification of Diseases and Health-Related Problems, CD-10 Version: 2019 [23]

- If they were Health Care Workers
- Problems in the family context and low-income households based on the genogram and in the experience of the GP for their continuity of care and knowledge of the family (genogram is a schematic model of the structure and processes of a family, which included the family structure, life cycle, and family relational patterns. It was understood that "complex" genograms present families with psychosocial problems) [24,25]
- Ethnic minority (defined as a "human group with cultural, linguistic, racial values and geographical origin, numerically inferior compared to the majority group") [26].

Sample size

All patients with the 4th dose who met the criteria for COVID-19 infection from October 1, 2022, to February 28, 2023, and who were treated in the general medicine consultation object of the study, were included. For controls, a random sample of patients with the 4th dose and who consulted in the study object of the study until April 15, 2023, and had not had COVID-19 infection criteria from the 4th booster until data collection, was chosen. The size of this sample was calculated for unpaired case-control studies from data on > = 65 years of age, for Comparing Two Means, for a Two-sided Confidence Level (1-alpha) of 95, a Power (% probability of detection) of 80%, a Ratio of 1:10, a hypothetical proportion of exposed controls of 4% and hypothetical proportion of exposed cases of 40%. Thus total Sample Size should be 50; 5 cases and 45 controls [27].

Ethical issues

No personal data of the patients were used, but only group results, which were taken from the clinical history.

Statistical analysis

The bivariate comparisons were performed using the Chi-Square test (X2) with Yates correction or Fisher Exact Test when necessary, (according to the number of the expected cell totals) for percentages, and the Student test for the mean.

Results

From October 1, 2022, to February 28, 2023, 5 cases of COVID-19 infections in vaccinated people with fourth a dose were included, which were compared with 52 controls (with a fourth dose and without COVID-19 after the booster). Mean age (Arithmetic mean ± Standard deviation; Range) in COVID-19 infection in people with the fourth dose was 65.6 ± 22.42 (38 - 95 years) and in people with the fourth dose and without COVID-19 infections 69.21 ± 9.48 (38 - 91 years) (t - value = -0.70392. p = .242226. NS).

Risk factors for COVID-19 infection with 4th dose were: Women (RR = 1.67; Weak risk: not statistically significant); Socio-Health Care Workers (RR = 10.39; Strong risk; Fisher exact test = 0.0349); Chronic Diseases of the blood (RR = 6.9. Strong risk; Fisher exact test = 0.0322. Significant at $p < .05$); Chronic Diseases of Endocrine (RR = 2.72. Strong risk; X2 with Yates correction= 4.2425. p = .039425); Chronic Diseases of Circulatory system (RR = 1.87. Moderate risk; not statistically significant).

They were Protection factor effectively for COVID-19 infection with 4th dose: > = 65 years (RR = 0.28; Complex family/ Problems in the family context (RR = 0); Low-income household (RR = 0); Ethnic minority (RR = 0); Presence of Chronic diseases (RR = 0.07); Chronic diseases of Neoplasms (RR = 0); Chronic diseases of Nervous and Senses (RR = 0); Chronic diseases of Respiratory system (RR = 0); Chronic diseases of Digestive system (RR = 0); Chronic diseases of Musculoskeletal (RR = 0.5), and Chronic diseases of Genitourinary (RR = 0.56), but all of them were not statistically significant (Tables 1,2).

Table 1: Risk factors in COVID-19 infection with fourth dose of vaccines bivalent mRNA.

Risk factors	People with a fourth dose and with COVID-19 infections N = 5	People with a fourth dose and without COVID-19 infections* N = 52	Statistical significance	Relative risk (CI 95%)
> = 65 years	2 (40)	38 (73)	Fisher exact test = 0.1509. NS	RR = 0.28 (CI 95%: 3.16, 0.02). Protection factor effectively
Women	3 (60)	24 (46)	Fisher exact test = 0.6597. NS	RR = 1.67 (CI 95%: 0, 7251.35). Weak risk
Socio-Health Care Workers	2 (40)	2 (4)	Fisher exact test = 0.0349. Significant at $p < .05$.	RR = 10.39 (CI 95%: 1.18, 91.4). Strong risk
Complex family/ Problems in the family context	0	7(13)	Fisher exact test = 1. NS	RR = 0 (CI 95%: Infinity, 0). Protection factor effectively
Low-income household	0	1 (2)	Fisher exact test = 1. NS	RR = 0 (CI 95%: Infinity, 0). Protection factor effectively
Ethnic minority	0	1 (2)	Fisher exact test = 1. NS	RR = 0 (CI 95%: Infinity, 0). Protection factor effectively
Chronic diseases	4 (80)	52 (100)	Fisher exact test = 0.0877. NS	RR = 0.07 (CI 95%: 2.43, 0). Protection factor effectively

*Taken from a covid-19 sample in the same general medicine consultation object of the current study; ( ): Denotes percentages; RR: Relative risk; NS: Not significant.

Citation: Turabian JL (2023) Risk factors for COVID-19 infection in people with 4th dose of bivalent mRNA vaccines in general medicine from October 2022 to February 2023. Arch Community Med Public Health 9(2): 027-033. DOI: https://dx.doi.org/10.17352/2455-5479.000198

Table 2: Chronic diseases risk factors in COVID-19 infection with fourth dose of vaccines bivalent mRNA.

Chronic diseases** (classified according to the ICD-10 Version: 2019)	People with a fourth dose and without COVID-19 infections N = 5	People with a fourth dose and without COVID-19 infections* N = 52	Statistical significance	Relative risk (CI 95%)
-II Neoplasms	0	12 (5)	Fisher exact test = 0.6078. NS	RR = 0 (IC 95%: Infinity, 0). Protection factor effectively
-III Diseases of the blood	2 (9)	2 (1)	Fisher exact test = 0.0322. Significant at $p < .05$.	RR = 6.9 (IC 95%: 1.25, 37.97). Strong risk
-IV Endocrine	7 (32)	34 (13)	X2 with Yates correction = 4.2425. $p = .039425$. Significant at $p < .05$.	RR = 2.72 (IC 95%: 1.05, 7.05). Strong risk
-V Mental	2 (9)	22 (8)	Fisher exact test = 1. NS	RR = 1.07 (IC 95%: 0.7, 1.64). Not significant
-VI-VIII Nervous and Senses	0	20 (8)	Fisher exact test = 0.3825. NS	RR = 0 (IC 95%: Infinity, 0). Protection factor effectively
-IX Circulatory system	7 (32)	49 (19)	X2 with Yates correction = 1.3597. $p = .243594$. NS	RR = 1.87 (IC 95%: 0.66, 5.34). Moderate risk
-X Respiratory system	0	15 (6)	Fisher exact test = 0.6166. NS	RR = 0 (IC 95%: Infinity, 0). Protection factor effectively
-XI Digestive system	1 (4)	33 (13)	Fisher exact test = 0.4921. NS	RR = 0.34 (IC 95%: 4.78, 0.02). Protection factor effectively
-XII Diseases of the skin	0	5 (2)	Fisher exact test = 1. NS	RR = 0 (IC 95%: Infinity, 0). Protection factor effectively
-XIII Musculoskeletal	2 (9)	45 (17)	X2 with Yates correction = 0.5025. $p = .478394$. NS	RR = 0.5 (IC 95%: 3.39, 0.07). Protection factor effectively
-XIV Genitourinary	1 (4)	21 (8)	Fisher exact test = 1. NS	RR = 0.56 (IC 95%: 221.73, 0). Protection factor effectively
TOTAL chronic diseases**	22 (100)	258 (100)	---	---

( ): Denotes percentages; RR: Relative risk; NS: Not significant; *Taken from a covid-19 sample in the same general medicine consultation object of the current study; **Patients could have more than one chronic disease; the percentages of chronic diseases are over the total of chronic diseases.

Discussion

Main findings

There were statistically significant risk factors for COVID-19 infection with the 4th dose for 1. Being Socio-Health Care Workers; 2. Presenting Chronic Diseases of the blood; and 3. Presenting chronic Diseases of Endocrine.

It must be taken into account that in Spain, from November 21 to 27, 2022, the Omicron percentage stood at 100%. Lineages BQ.1 and its derivatives of it, including BQ.1.1, accounted for 78.4%; For the BA.4 and BA.5 lineages, the percentages ranged between 87% and 96.3%, and for the BA.2 lineage, between 0% and 39.9% [20]. On the other hand, In Spain, since April 28, 2022, there was a new "Surveillance and Control Strategy Against COVID-19" that included the non-performance of diagnostic tests, which were focused only on those over 60 years of age, immunosuppressed and pregnant women, socio-health workers and serious cases [28]. The fourth dose began to be given to the elderly and socio-health workers [7,20,29]. In practice, this meant that patients with symptoms of viral infections in the community were not tested (and cases were lost) and that those who were tested were more likely older patients and socio-health workers.

Comparison with other studies

Throughout the months of September and October 2022, four vaccines adapted to the new circulating Omicron variants were authorized in the European Union. These adapted vaccines are bivalent mRNA vaccines against the parent strain and BA.1 variant and against the parent strain and BA.4/BA.5 variant of the Comirnaty and Spikevax vaccines [20]. These updated boosters can help restore protection that has diminished since previous vaccination and provide broader protection against newer variants [30].

Numerous reports indicate that the bivalent booster vaccine against COVID-19 has greater efficacy than monovalent boosters, reduces the risk of symptomatic infection, provides substantial additional protection against severe omicron infections, and elicits higher neutralizing responses, suggesting that it is more immunogenic than the vaccine original [15,19,31-33].

Data suggest that protection from COVID-19 vaccines could wane within about six months and even more rapidly for clinically vulnerable groups, such as cancer patients [34]. But the durability of immunity is complex. How long the immune system can fend off SARS-CoV-2 infection depends not only on how much immunity wanes over time but also on how well the immune cells recognize their target. And that has more to do with the virus and how much it mutates. It also depends on how many people have immunity against a recent infection, ie the existing levels of immunity in a population [35,36].

Although immunocompromised people account for much of the decreased protection against severe disease [37], the bivalent vaccine appears to protect immunocompetent patients well, and the immunocompromised as well, providing greater protection against hospital admission for COVID-19 [38-40]. We found that the presence of Chronic Diseases of the blood and Endocrine, which can be interpreted as an indicator of immunocompromise, were significant risk factors for COVID-19 in people with bivalent vaccines.

Citation: Turabian JL (2023) Risk factors for COVID-19 infection in people with 4th dose of bivalent mRNA vaccines in general medicine from October 2022 to February 2023. Arch Community Med Public Health 9(2): 027-033. DOI: https://dx.doi.org/10.17352/2455-5479.000198

On the other hand, it has been reported that the magnitude of protection with bivalent boosters was greater among older adults [41]. Up to 70 days after its application, the bivalent or Omicron-adapted booster of the vaccine reduces hospitalizations and mortality in patients older than 65 years [42]. In our study, we found that being older than 65 years was a protection factor, although not statistically significant, for presenting COVID-19 infection with the 4th dose.

We found that being a socio-health care worker was a strong risk to present COVID-19 with the fourth dose of mRNA vaccine. Healthcare workers can be considered at risk due to their increased exposure to SARS-CoV-2. Low vaccine efficacy against infections in HCWs has been reported, as well as relatively high viral loads suggesting that those infected were infectious, so a fourth dose in healthy young HCWs may have marginal benefits [43-45]. Furthermore, we found that being a woman implies a weak risk. Possibly in relation to their frequent role as family caregivers of older adults with chronic diseases [46-49].

Finally, it is evident that COVID-19 vaccine boosters are proving a useful tool against omicron, but endless boosting might not be a practical or sustainable strategy. However, from the current perspective of booster results, it is inevitable that further adaptations of the composition of COVID-19 vaccines will be made to address existing and future circulating variants. Variant-specific reinforcement may be required as new variants evolve [50,51].

Study limitations

1. Infections were not genetically sequenced
2. The small number of COVID-19 cases may mask the statistical significance between variables.
3. Follow-up was short-term and does not allow evaluation of the duration of the immune response

Conclusion

In the general practice setting in Toledo, Spain, being a socio-health care worker and having chronic diseases presumably associated with immunosuppression were statistically significant risk factors for COVID-19 infection in people vaccinated with the 4th dose of bivalent mRNA vaccines. In a time marked by uncertainty about the risks versus the benefits of repeated booster doses of the COVID-19 vaccine (immune system overload vs. efficacy against new variants), the marginal efficacy of the fourth dose of vaccine increases protection against infection, symptomatic infection, and severe outcomes. But the most exposed or immunosuppressed people continue to be at risk of becoming infected with SARS-CoV-2 despite having received the 4th dose of the mRNA COVID-19 vaccine, so other preventive methods in these groups are advisable.

References

1. El-Sadr WM, Vasan A, El-Mohandes A. Facing the New Covid-19 Reality. N Engl J Med. 2023 Feb 2;388(5):385-387. doi: 10.1056/NEJMp2213920. Epub 2023 Jan 28. PMID: 36724378.
2. Grant R, Sacks JA, Abraham P, Chunsuttiwat S, Cohen C, Figueroa JP, Fleming T, Fine P, Goldblatt D, Hasegawa H, MacIntrye CR, Memish ZA, Miller E, Nishioka S, Sall AA, Sow S, Tomori O, Wang Y, Van Kerkhove MD, Wambo MA, Cohen HA, Mesfin S, Otieno JR, Subissi L, Briand S, Wentworth DE, Subbarao K. When to update COVID-19 vaccine composition. Nat Med. 2023 Apr;29(4):776-780. doi: 10.1038/s41591-023-02220-y. PMID: 36807683.
3. Callaway E. COVID 'variant soup' is making winter surges hard to predict. Nature. 2022 Nov;611(7935):213-214. doi: 10.1038/d41586-022-03445-6. PMID: 36307585.
4. Khoury DS, Docken SS, Subbarao K, Kent SJ, Davenport MP, Cromer D. Predicting the efficacy of variant-modified COVID-19 vaccine boosters. Nat Med. 2023 Mar;29(3):574-578. doi: 10.1038/s41591-023-02228-4. Epub 2023 Mar 2. PMID: 36864253.
5. Lin DY, Xu Y, Gu Y, Zeng D, Sunny SK, Moore Z. Durability of Bivalent Boosters against Omicron Subvariants. N Engl J Med. 2023 May 11;388(19):1818-1820. doi: 10.1056/NEJMc2302462. Epub 2023 Apr 12. PMID: 37043647; PMCID: PMC10120009.
6. European Medicines Agency (2022) ECDC-EMA statement on booster vaccination with Omicron adapted bivalent COVID-19 vaccines. News 06/09/2022. https://www.ema.europa.eu/en/news/ecdc-ema-statement-booster-vaccination-omicron-adapted-bivalent-covid-19-vaccines
7. Jiménez AL. Portfolio of omicron-adapted vaccines expands: how does each one work? The EMA has already recommended the authorization of the vaccines against COVID-19 adapted from Comirnaty Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.1 and Comirnaty Original/Omicron BA.4-5. 2022; https://www.consalud.es/pacientes/especial-coronavirus/como-funcionan-vacunas-adaptadas_120131_102.html
8. Kingsley T. UK 'blind' to new immune-evasive Covid variants creating 'perfect storm' for devastating wave. The Independent; 2022; https://webcache.googleusercontent.com/search?q=cache:kZEI2MAHtYQJ:https://www.independent.co.uk/news/health/uk-covid-variant-omicron-new-wave-b2183934.html&cd=2&hl=es&ct=clnk&gl=es
9. Chalkias S, Harper C, Vrbicky K, Walsh SR, Essink B, Brosz A, McGhee N, Tomassini JE, Chen X, Chang Y, Sutherland A, Montefiori DC, Girard B, Edwards DK, Feng J, Zhou H, Baden LR, Miller JM, Das R. A Bivalent Omicron-Containing Booster Vaccine against Covid-19. N Engl J Med. 2022 Oct 6;387(14):1279-1291. doi: 10.1056/NEJMoa2208343. Epub 2022 Sep 16. PMID: 36112399; PMCID: PMC9511634.
10. Loewy MA. COVID-19: the weekly summary (September 30 to October 6, 2022). Medscape. (2022) https://espanol.medscape.com/verarticulo/5909795?src=mkm_ret_221009_mscpmrk-ES_ExcNews&uac=327178AR&implD=4719707&faf=1
11. Wang Q, Bowen A, Valdez R, Gherasim C, Gordon A, Liu L, Ho DD. Antibody Response to Omicron BA.4-BA.5 Bivalent Booster. N Engl J Med. 2023 Feb 9;388(6):567-569. doi: 10.1056/NEJMc2213907. Epub 2023 Jan 11. PMID: 36630643; PMCID: PMC9847504.
12. Collier AY, Miller J, Hachmann NP, McMahan K, Liu J, Bondzie EA, Gallup L, Rowe M, Schonberg E, Thai S, Barrett J, Borducchi EN, Bouffard E, Jacob-Dolan C, Mazurek CR, Mutoni A, Powers O, Sciacca M, Surve N, VanWyk H, Wu C, Barouch DH. Immunogenicity of BA.5 Bivalent mRNA Vaccine Boosters. N Engl J Med. 2023 Feb 9;388(6):565-567. doi: 10.1056/NEJMc2213948. Epub 2023 Jan 11. PMID: 36630611; PMCID: PMC9847505.
13. Marks PW, Califf RM. Bivalent Covid-19 Vaccines. N Engl J Med. 2023 Mar 23;388(12):1151. doi: 10.1056/NEJMc2301323. Epub 2023 Mar 1. PMID: 36856582.
14. Offit PA. Bivalent Covid-19 Vaccines - A Cautionary Tale. N Engl J Med. 2023 Feb 9;388(6):481-483. doi: 10.1056/NEJMp2215780. Epub 2023 Jan 11. PMID: 36630616.
15. Zou J, Kurhade C, Patel S, Kitchin N, Tompkins K, Cutler M, Cooper D, Yang Q, Cai H, Muik A, Zhang Y, Lee DY, Şahin U, Anderson AS, Gruber WC, Xie X,

Citation: Turabian JL (2023) Risk factors for COVID-19 infection in people with 4th dose of bivalent mRNA vaccines in general medicine from October 2022 to February 2023. Arch Community Med Public Health 9(2): 027-033. DOI: https://dx.doi.org/10.17352/2455-5479.000198

Swanson KA, Shi PY. Neutralization of BA.4-BA.5, BA.4.6, BA.2.75.2, BQ.1.1, and XBB.1 with Bivalent Vaccine. N Engl J Med. 2023 Mar 2;388(9):854-857. doi: 10.1056/NEJMc2214916. Epub 2023 Jan 25. PMID: 36734885; PMCID: PMC9891359.

16. Cohen C, Pulliam J. COVID-19 infection, reinfection, and the transition to endemicity. Lancet. 2023 Mar 11;401(10379):798-800. doi: 10.1016/S0140-6736(22)02634-4. Epub 2023 Feb 16. PMID: 36930672; PMCID: PMC9934854.

17. Rey Calero J. Epidemiological method and community health. Madrid: Interamericana. McGraw-Hill. 1989.

18. Consejo interterritorial de salud. (2022) Comirnaty Bivalente, Original/Omicron BA.4-5 (COVID-19 mRNA Vaccine, Pfizer-BioNTech) Technical Guide. https://www.sanidad.gob.es/profesionales/saludPublica/prevPromocion/vacunaciones/covid19/Guias_Tecnicas/docs/Guia_Tecnica_COMIRNATY_bivalente.pdf

19. Lin DY, Xu Y, Gu Y, Zeng D, Wheeler B, Young H, Sunny SK, Moore Z. Effectiveness of Bivalent Boosters against Severe Omicron Infection. N Engl J Med. 2023 Feb 23;388(8):764-766. doi: 10.1056/NEJMc2215471. Epub 2023 Jan 25. PMID: 36734847; PMCID: PMC9933929.

20. Consejo Interterritorial. Update of the vaccination recommendations against COVID-19 for autumn-winter in Spain Approved by the Public Health Commission on December 15, 2022. Prepared by the Report on the Vaccination Program and Registry. 2022. https://www.sanidad.gob.es/profesionales/saludPublica/prevPromocion/vacunaciones/covid19/docs/Recomendaciones_vacunacion_Otono_Invierno_Covid.pdf

21. Ministerio de Sanidad. COVID-19 early detection, surveillance and control strategy. 2021; https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/COVID19_Estrategia_vigilancia_y_control_e_indicadores.pdf

22. Strauss AL. Chronic illness and the quality of life. St Louis: The C.V. Mosby Company. 1984.

23. WHO. International Statistical Classification of Diseases and Health-Related Problems. ICD-10 Version: 2019. https://icd.who.int/browse10/2019/en

24. Turabian JL. Family Genogram in General Medicine: A Soft Technology that can be Strong. An Update. Res Med Eng Sci. 2017; 3(1). http://crimsonpublishers.com/rmes/pdf/RMES.000551.pdf

25. Russell LT. Capturing Family Complexity in Family Nursing Research and Practice. J Fam Nurs. 2020; 26(4):287-93. https://journals.sagepub.com/doi/10.1177/1074840720965396

26. Pan-Hispanic Dictionary of Legal Spanish (2022) [Ethnic minority]. https://dpej.rae.es/lema/minor%C3%ADa-%C3%A9tnica

27. Open Source Epidemiologic Statistics for Public Health. http://www.openepi.com/SampleSize/SSCC.htm

28. Turabian JL. An ostrich strategy for covid-19 is too risky. BMJ. 2022 May 3;377:o1112. doi: 10.1136/bmj.o1112. PMID: 35504630.

29. Atlas España. The new vaccination campaign for the fourth dose of Covid19 starts throughout Spain. 2022; ABC; 25/09. https://www.abc.es/espana/arranca-espana-nueva-campana-vacunacion-cuarta-dosis-20220925183607-vi.html

30. CDC. Stay Up to Date with COVID-19 Vaccines Including Boosters. 2022. Updated Sept. 8, 2022. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvaccines%2Fbooster-shot.html

31. Davis-Gardner ME, Lai L, Wali B, Samaha H, Solis D, Lee M, Porter-Morrison A, Hentenaar IT, Yamamoto F, Godbole S, Liu Y, Douek DC, Lee FE, Rouphael N, Moreno A, Pinsky BA, Suthar MS. Neutralization against BA.2.75.2, BQ.1.1, and XBB from mRNA Bivalent Booster. N Engl J Med. 2023 Jan 12;388(2):183-185. doi: 10.1056/NEJMc2214293. Epub 2022 Dec 21. PMID: 36546661; PMCID: PMC9812288.

32. Doheny K. What's Next for COVID? Here's What to Know. Medscape. 2023. Jan 03. https://www.medscape.com/viewarticle/986429?src=wnl_recnlnew1_ous_230105_MSCPEDIT_&uac=327178AR&impID=5062591#vp_%3Cfont%20style=%22vertical-align:%20inherit;%22%3E%3Cfont%20style=%22vertical-align:%20inherit;%22%3E1%20%3C/font%3E%3C/font%3E

33. Winokur P, Gayed J, Fitz-Patrick D, Thomas SJ, Diya O, Lockhart S, Xu X, Zhang Y, Bangad V, Schwartz HI, Denham D, Cardona JF, Usdan L, Ginis J, Mensa FJ, Zou J, Xie X, Shi PY, Lu C, Buitrago S, Scully IL, Cooper D, Koury K, Jansen KU, Türeci Ö, Şahin U, Swanson KA, Gruber WC, Kitchin N; C4591031 Clinical Trial Group. Bivalent Omicron BA.1-Adapted BNT162b2 Booster in Adults Older than 55 Years. N Engl J Med. 2023 Jan 19;388(3):214-227. doi: 10.1056/NEJMoa2213082. PMID: 36652353; PMCID: PMC9933930.

34. Mahase E. Covid-19: Booster vaccines rolled out as hospital admissions rise. BMJ. 2022 Oct 14;379:o2484. doi: 10.1136/bmj.o2484. PMID: 36241204.

35. Vogel G. Omicron booster shots are coming—with lots of questions. COVID-19 vaccines get their first update since the pandemic began. Here's what you need to know about them. Science. 2022. https://www.science.org/content/article/omicron-booster-shots-are-coming-lots-questions

36. Willyard C (2023) How quickly does COVID immunity fade? What scientists know. Vaccination, infection with SARS-CoV-2 and a combination of both provide varying degrees of protection. Nature; 02 February. https://doi.org/10.1038/d41586-023-00124-y

37. Sahly ElH, Glück T, Sakoulas G. Vaccine Effectiveness Against SARS-CoV-2 Variants, Revisited. NEJM Journal Watch; November 2. 2022. https://www.jwatch.org/na55378/2022/11/02/vaccine-effectiveness-against-sars-cov-2-variants?query=etoc_jwid&jwd=000012293400&jspc=GP&cid=DM1624666_Non_Subscriber&bid=1243657113

38. Roa R. The second booster dose protects well at 6 months. La biblioteca de Springfield. 2022. https://rubenroa.blogspot.com/2022/11/la-segunda-dosis-de-refuerzo-protege.html

39. Roa R. Fourth dose of Covid-19 vaccine. La biblioteca de Springfield. 2022. https://rubenroa.blogspot.com/2022/09/cuarta-dosis-de-vacuna-covid-19.html

40. Adams K, Rhoads JP, Surie D, Gaglani M, Ginde AA, McNeal T, Talbot HK, Casey JD, Zepeski A, Shapiro NI, Gibbs KW, Files DC, Hager DN, Frosch AE, Exline MC, Mohamed A, Johnson NJ, Steingrub JS, Peltan ID, Brown SM, Martin ET, Lauring AS, Khan A, Busse LW, Duggal A, Wilson JG, Chang SY, Mallow C, Kwon JH, Chappell JD, Halasa N, Grijalva CG, Lindsell CJ, Lester SN, Thornburg NJ, Park S, McMorrow ML, Patel MM, Tenforde MW, Self WH; Influenza and other Viruses in the AcutelY ill (IVY) Network. Vaccine effectiveness of primary series and booster doses against covid-19 associated hospital admissions in the United States: living test negative design study. BMJ. 2022 Oct 11;379:e072065. doi: 10.1136/bmj-2022-072065. PMID: 36220174; PMCID: PMC9551237.

41. Loewy MA. COVID-19: the weekly roundup. February 10-16, 2023. Medscape 17 de feb. 2023. https://espanol.medscape.com/verarticulo/5910436?ecd=mkm_ret_230218_mscpmrk-ES_ExcNews&uac=327178AR&impID=5173986&faf=1

42. Loewy MA. COVID-19: the weekly summary (January 6-12, 2023). Medscape 13 de enero. 2023. https://espanol.medscape.com/verarticulo/5910270?src=mkm_ret_230116_mscpmrk-ES_ExcNews&uac=327178AR&impID=5089349&faf=1

43. Regev-Yochay G, Gonen T, Gilboa M, Mandelboim M, Indenbaum V, Amit S, Meltzer L, Asraf K, Cohen C, Fluss R, Biber A, Nemet I, Kliker L, Joseph G, Doolman R, Mendelson E, Freedman LS, Harats D, Kreiss Y, Lustig Y. Efficacy of a Fourth Dose of Covid-19 mRNA Vaccine against Omicron. N Engl J Med. 2022 Apr 7;386(14):1377-1380. doi: 10.1056/NEJMc2202542. Epub 2022 Mar 16. PMID: 35297591; PMCID: PMC9006792.

44. Mallapaty S. Fourth dose of COVID vaccine offers only slight boost against Omicron infection. Nature. 2022 Feb 23. doi: 10.1038/d41586-022-00486-9. Epub ahead of print. PMID: 35197600.

Citation: Turabian JL (2023) Risk factors for COVID-19 infection in people with 4th dose of bivalent mRNA vaccines in general medicine from October 2022 to February 2023. Arch Community Med Public Health 9(2): 027-033. DOI: https://dx.doi.org/10.17352/2455-5479.000198

45. Jiménez AL. Is a fourth dose of the vaccine necessary in healthcare professionals?. Consalud.es; 21.03. 2022. https://www.consalud.es/pacientes/especial-coronavirus/es-necesaria-cuarta-dosis-vacuna-profesionales-sanitarios_111849_102.html

46. Bueno MV, Chase JD. Gender Differences in Adverse Psychosocial Outcomes among Family Caregivers: A Systematic Review. West J Nurs Res. 2023 Jan;45(1):78-92. doi: 10.1177/01939459221099672. Epub 2022 May 25. PMID: 35614567.

47 Turabian JL. Sex and Gender Bio-psychosocial Differences in Coronavirus Disease 2019 (Covid-19): Men have more Biological Problems, but Women Suffer more Long-Term Serious Psychosocial Consequences and with more Implications for Population. J Women's Health Care. 2020. 9:487. https://www.longdom.org/open-access/sex-and-gender-biopsychosocial-differences-in-coronavirus-disease-2019-covid19-men-have-more-biological-problems-but-wom.pdf

48. Wenham C, Smith J, Davies SE, Feng H, Grépin KA, Harman S, Herten-Crabb A, Morgan R. Women are most affected by pandemics - lessons from past outbreaks. Nature. 2020 Jul;583(7815):194-198. doi: 10.1038/d41586-020-02006-z. PMID: 32641809.

49. Loewy MA. Pan American Health Organization: COVID-19 disproportionately affects women. Medscape; 19 de mayo. 2020. https://espanol.medscape.com/verarticulo/5905441?src=mkm_latmkt_200521_mscmrk_escoronavirus_nl&uac=327178AR&impID=2388598&faf=1

50. Guidry CA, Beyene RT, Watson CM, Sawyer RG, Chollet-Hinton L, Simpson SQ, Atchison L, Derickson M, Cooper LC, Pennington GP 2nd, VandenBerg S, Halimeh BN, O'Dell JC. Trial of antibiotic restraint in presumed pneumonia: A Surgical Infection Society multicenter pilot. J Trauma Acute Care Surg. 2023 Feb 1;94(2):232-240. doi: 10.1097/TA.0000000000003839. Epub 2022 Nov 18. PMID: 36534474.

51. Qu P, Faraone JN, Evans JP, Zheng YM, Yu L, Ma Q, Carlin C, Lozanski G, Saif LJ, Oltz EM, Gumina RJ, Liu SL. Durability of Booster mRNA Vaccine against SARS-CoV-2 BA.2.12.1, BA.4, and BA.5 Subvariants. N Engl J Med. 2022 Oct 6;387(14):1329-1331. doi: 10.1056/NEJMc2210546. Epub 2022 Sep 7. PMID: 36069925; PMCID: PMC9511629.

Citation: Turabian JL (2023) Risk factors for COVID-19 infection in people with 4th dose of bivalent mRNA vaccines in general medicine from October 2022 to February 2023. Arch Community Med Public Health 9(2): 027-033. DOI: https://dx.doi.org/10.17352/2455-5479.000198