MedPress
Public Health and Epidemiology

Risk Factors and Incidence Rate of SARS-COV-2 Infection Sequels. A Longitudinal Study in General Medicine

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.

Research Article

***Corresponding author**

Jose Luis Turabian,
Health Center Santa Maria de Benquerencia Toledo, Spain.
E-mail: jturabianf@hotmail.com.

Article Information

Received: 28-12-2022;
Accepted: 14-02-2023;
Published: 20-02-2023.

Abstract

Background

The epidemiological data on the sequels of covid-19 are not well known

Objective

To estimate the incidence rate and the risk factors of sequels of covid-19 in general practitioner consultation.

Methodology

An observational, longitudinal and prospective study of patients with covid-19 to detect sequels of covid-19 in a general practice setting in Toledo, Spain, from March 15, 2020 to October 31, 2022.

Results

687 positive cases of acute covid-19 were diagnosed in the general medicine consultation under study. Of these, 25 cases (32% were women and 28% had >=65 years old) presented sequels of covid-19, which represents a gross incidence rate of 3 % cases x March 15, 2020 to October 31, 2022. The incidence rate of covid-19 sequels with respect to the total population attended in that office (N= 2,000), from March 15, 2020 to October 31, 2022, was 1.25%. The only statistically significant risk factors for sequels of covid-19 were being male [RR= 2.23 (CI 95%: 0.94, 5.26); Moderate risk; X2= 4.1675. p= .041207] and having presented moderate-severe severity of primary infection [RR= 8.9 (95% CI: 4.69, 16.9); Strong risk; Fisher exact < 0.00001]

Conclusion

In the context of general medicine in Toledo (Spain) incidence rate of sequels of covid-19 is moderately high, and having presented moderate-severe severity of primary infection is the main risk factor, followed by being male, for developing they. Although incidence figure found can be considered moderate, but given the number of covid-19 cases, in absolute numbers it can be a significant problem.

Key Words: COVID-19; Coronavirus disease 2019 sequels; Epidemiology; Public Health Practice General Practice

Introduction

Since the publication of the first reported cases in Wuhan, China, in December 2019, the disease caused by SARS-CoV-2 (covid-19) has caused more than 6 million deaths globally to date (1), being one of the most devastating pandemics in recent times (2). Many survivors of serious illnesses suffer lasting physical, cognitive and mental health consequences. Postviral symptoms are not new and have been described after influenza and other pandemics in the past, such as the 1889-1892 influenza pandemic (3). Thus, the number of affected patients with sequels is expected to increase remarkably due to the covid-19 pandemic (4).

On the other hand, many covid-19 survivors receive long-term care from a general practitioner (GP). Therefore, the recognition of the sequels in survivors of covid-19 has made knowledge of its pathogenesis, prognosis, and management an important competitive priority for the GP (4, 5). Prolonged covid-19 follow-up in patients who have survived for at least 30 days after SARS-CoV-2 infection has allowed the identification of incident sequels beyond the respiratory system, including nervous system disorders, neurocognitive disorders, and mental health disorders, metabolic disorders, cardiovascular disorders, gastrointestinal disorders, malaise, fatigue, musculoskeletal pain and anemia.

Therefore, increasing evidence suggests that SARS-CoV-2 is a multisystem infection that produces multiform symptoms and can cause long-term effects (5).

Consequently, it is necessary to investigate the data on the duration of symptoms and the sequels of covid-19 infection. However, the medium- and long-term sequels of SARS-CoV-2 infections have barely been investigated in the general population. Available original research tends to focus on patients who have been admitted to hospital or restrict assessments to a single organ system. So, although studies to date show that persistent sequels of covid-19 are common in people with risk factors (older adults, smokers, and people with underlying comorbidities such as hypertension, obesity, diabetes, cardiovascular disease, chronic lung disease, chronic kidney disease, chronic liver disease, cerebrovascular disease, cancer and immunodeficiency), there are few data in the general population and in previously healthy people (6).

In addition, given the complexity and heterogeneity of the clinical course of severe covid-19 survivors, GPs play a key role in the management of subsequent sequels, due to their expertise in integrative medicine, coordination of care, encompassing self-care of patients and long-term knowledge of the medical history of patients and their families. Therefore, the covid-19 pandemic emphasizes the need for further research on follow-up care for sequels at the GP level (4).

In this context, we present an observational, longitudinal and prospective study of patients with covid-19 who developed specific sequels, from March 15, 2020 to October 31, 2022 in a general medicine office, with the aim of estimating the prevalence/incidence rate (IR) of the specific sequels of acute covid-19 infection in GP consultation, and to identify risk factors for the specific sequels of acute covid-19 infection.

Material and Methods

Design and emplacement

An observational, longitudinal and prospective study of patients with specific sequels of acute covid-19 infection was carried out from March 15, 2020 to October 31, 2022, in a family medicine office at the Health Center Santa Maria de Benquerencia, 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).

Objectives

1. Estimate the prevalence/incidence rate (IR) of the specific sequels of acute infection by covid-19 in GP consultation. IR was calculated by dividing the number of cases of specific sequels of acute infection by covid-19 by the primoinfections of covid-19 in the follow-up time (from March 15, 2020 to October 31, 2022) (7). Similarly, the data on the incidence of specific sequels of acute covid-19 infection were extrapolated to the entire population attended in the consultation (N=2,000 people) (8).
2. Identify the risk factors for the specific sequels of acute covid-19 infection. In this sense, the variables collected were compared by calculating the relative risk (RR) as the incidence of risk factors in those exposed to specific sequels of acute covid-19 infection / incidence of risk factors in those not exposed to specific sequels of acute covid-19 infection. The RR was interpreted as follows (9): 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.

Inclusion criteria

Basically, specific sequels of acute covid-19 infection were diagnosed, when there were persistent symptoms or pathologies during the acute infection or after an apparent recovery from the acute covid-19 infection, which are not part of the acute covid-19 infection (9). The inclusion and exclusion criteria in this study have already been previously published (10). Criteria for specific sequels of acute infection were:

1. Pathologies that are not part of the acute infection, persistent, and that appear during covid-19 infection
2. Pathologies that are not part of the acute infection, persistent, and with appearance after resolution of the initial symptoms (covid-19 post-infection pathologies)
3. Pathologies that are not part of the acute infection but appear as a consequence of the organic damage produced by the severe infection (true sequels of covid-19).

As examples, these specific sequels of acute covid-19 infection could include: Thromboembolic Disease, Pulmonary Fibrosis, Myopericarditis and Multiple Mononeuritis.

Complications from covid-19 were excluded. Complications are considered health problems that originated as a result of acute covid-19 infection or the treatments performed (11).

Diagnosis of covid-19

The diagnosis was performed with reverse transcriptase polymerase chain reaction (PCR) oropharyngeal swab tests or antigen testing. Spain had not initially devised an intensive testing strategy for suspected cases of covid-19 infections (12); since the beginning of the pandemic in mid-March 2020, PCR tests were only performed in the hospital context until mid-May 2020, date when they began to be performed in general medicine as well. In mid-December 2020, rapid antigen tests began for symptomatic patients with less than 5 days of evolution. The PCR tests were performed both in symptomatic patients and in asymptomatic contacts. A symptomatic confirmed case with active infection was considered to be any person with a clinical picture of sudden onset acute respiratory infection of any severity that occurs, among others, with fever, cough or feeling of shortness of breath. Other symptoms such as odynophagia, anosmia, ageusia, muscle pain, diarrhea, chest pain or headache, among others, were also considered symptoms of suspected SARS-CoV-2 infection according to clinical criteria; plus a positive PCR or rapid antigen test positive.

Definition of cases and controls

Patients with sequels from covid-19 were considered “cases.” "Control" patients were those with acute covid-19 without sequels. Control data were obtained from previous studies in the same consultation, with the same population attended, and carried out by the same researcher (13-16).

Collected variables

The variables collected and their definitions and criteria have been previously published (10). These variables were: Age; sex; acute covid-19 infection date; specific sequels of covid-19,

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" (17), classified according to the International Statistical Classification of Diseases and Health-Related Problems, CD-10 Version: 2019 (18); vaccination status against covid-19 at the date of acute infection; and severity of the disease (mild cases: clinical symptoms are mild and no manifestation of pneumonia can be found on images; moderate cases: with symptoms such as fever and respiratory tract symptoms, and the manifestation of pneumonia can be seen on the imaging tests; and severe cases: respiratory distress, respiratory rate ≥ 30 breaths / min., pulse oxygen saturation ≤ 93% with room air at rest, arterial partial pressure of oxygen / oxygen concentration ration ≤ 300 mmHg.) (19). To simplify comparison, moderate and severe cases were counted together.

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 the expected cell totals) for percentages.

Results

687 positive cases of acute covid-19 were diagnosed in the general medicine consultation under study. Of these, 25 cases (32% were women and 28% had >=65 years old) presented sequels of covid-19, which represents a gross incidence rate of 3 % cases x March 15, 2020 to October 31, 2022. The incidence rate of sequels of covid-19 in the general practitioner consultation with respect to the total population attended in that consultation (N= 2,000) from March 15, 2020 to October 31, 2022 was 1.25% (TABLE 1). The only statistically significant risk factors for sequels of covid-19 were being male [RR= 2.23 (CI 95%: 0.94, 5.26); Moderate risk; X2= 4.1675. p= .041207] and having presented moderate-severe severity of primary infection [RR= 8.9 (95% CI: 4.69, 16.9); Strong risk; Fisher exact test < 0.00001]. Regarding the date of acute covid-19, 9 cases with sequels (36%) were in 2020, 12 (48%) in 2021, and 4 (16%) in 2022. There were more vaccinated covid-19 with 1, 2 or 3 doses at the time of acute covid-19 in patients with sequels vs. in controls without sequels (56% vs. 47%) but the comparison was not statistically significant. Regarding the chronic diseases present at the time of the acute covid-19, the presence of Neoplasms, Mental, Nervous and Senses, and Circulatory system groups were found as risk factors for covid-19 sequels, but all of them without statistical significance (TABLE 2, TABLE 3).

Table 1: Incidence Rates of COVID-19 with Sequels in General Medicine (Toledo, Spain) Regarding Acute COVID-19 Cases from March 15, 2020 TO October 31, 2022

VARIABLES	COVID-19 WITH SEQUELS N=25	ACUTE COVID-19 WITHOUT SEQUELS N= 687	INCIDENCE RATES OF COVID-19 WITH SEQUELS IN GENERAL MEDICINE (TOLEDO, SPAIN) REGARDING ACUTE COVID-19 CASES FROM MARCH 15, 2020 TO OCTOBER 31, 2022
TOTAL	25 (100)	687 (100)	3 % cases x March 15, 2020 to October 31, 2022
> = 65 years	7 (28)	60 (9)`	10 % cases x March 15, 2020 to October 31, 2022
= < 45 years	5 (20)	425 (62)	1 % cases x March 15, 2020 to October 31, 2022
Women	8 (32)	332 (48)	2 % cases x March 15, 2020 to October 31, 2022
Men	17 (68)	355 (52)	5 % cases x March 15, 2020 to October 31, 2022

( ): Denotes percentages

Table 2: Risk Factors of COVID-19 with Sequels

RISK FACTORS	COVID-19 WITH SEQUELS N=25	PRIMARY COVID-19 INFECTIONS WITHOUT SEQUELS N=188	STATISTICAL SIGNIFICANCE	RELATIVE RISK (RR)
> = 65 years	7 (28)	32 (17)	X2 with Yates correction= 1.1199. p= .289942. NS	RR= 1.74 (CI 95%: 0.62, 4.85). Moderate risk
Women	8 (32)	101 (54)	X2= 4.1675. p= .041207. Significant at p < .05.	RR= 0.45 (CI 95%: 1.06, 0.19). Protection factor effectively
Men	17 (68)	87 (46)	X2= 4.1675. p= .041207. Significant at p < .05.	RR= 2.23 (CI 95%: 0.94, 5.26). Moderate risk
Health Care Workers	1 (4)	31 (16)	X2 with Yates correction= 1.8065. p= .178928. NS	RR= 0.24 (CI 95%: 1.94, 0.03). Protection factor effectively
Moderate-severe severity of primary infection	12 (48)	8 (4) pneumoniae]	Fisher exact < 0.00001. Significant at p < .05.	RR= 8.9 (CI 95%: 4.69, 16.9). Strong risk
Chronic diseases presence	14 (56)	108 (57)	X2= 0.07. p= .791386. NS	RR= 1.11 (CI 95%: 0.02, 66.37). Not significant

Vaccinated covid-19 with 1, 2 or 3 doses at the time of acute covid-19	14 (56)	88 (47)	X2= 0.747. p= .387425. NS	RR= 1.39 (CI 95%: 0.51, 3.75). Weak risk
Not vaccinated at the time of acute covid-19	11 (44)	100 (53)	X2= 0.747. p= .387425. NS	RR= 0.72 (CI 95%: 1.94, 0.27). True benefits

( ): Denotes percentages; NS: Not significant

Table 3: Chronic Diseases Risk Factors in COVID-19 with Sequels

CHRONIC DISEASES	COVID-19 WITH SEQUELS N=25	COVID-19 WITHOUT SEQUELS N=188	STATISTICAL SIGNIFICANCE	RELATIVE RISK (RR)
-I Infectious	0	0	Fisher exact test= 1. NS	RR= NaN
-II Neoplasms	2 (6)	9 (3)	Fisher exact test= 0.2593. NS	RR= 2.08 (CI 95%: 0.15, 28.28). Moderate risk
-III Diseases of the blood	0	5 (1)	Fisher exact test= 1. NS	RR= 0 (CI 95%: Infinity, 0). Protection factor effectively
-IV Endocrine	6 (18)	65 (19)	X2 0.0316. p= .858896. NS	RR= 0.93 (CI 95%: 15.99, 0.05). Not significant
-V Mental	5 (15)	24 (7)	Fisher exact test= 0.1639. NS	RR= 2.07 (CI 95%: 0.68, 6.31). Moderate risk
-VI-VIII Nervous and Senses	5 (15)	34 (10)	X2 with Yates correction= 0.3438. p= .557668. NS	RR= 1.5 (CI 95%: 0.39, 5.77). Weak risk
-IX Circulatory system	7 (20)	44 (13)	X2 with Yates correction is 1.013. p= .314183. NS	RR= 1.66 (CI 95%: 0.62, 4.44). Moderate risk
-X Respiratory system	1 (3)	23 (7)	Fisher exact test= 0.7107. NS	RR= 0.45 (CI 95%: 10.97, 0.02). Protection factor effectively
-XI Digestive system	2 (6)	43 (12)	X2 with Yates correction= 0.7381. p= .390273. NS	RR= 0.46 (CI 95%: 2.7, 0.08). Protection factor effectively
-XII Diseases of the skin	0	11 (3)	Fisher exact test= 0.6087. NS	RR= 0 (CI 95%: Infinity, 0). Protection factor effectively
-XIII Musculo-skeletal	3 (9)	46 (13)	X2 with Yates correction= 0.2359. p= .627214. NS	RR= 0.65 (CI 95%: 3.64, 0.12). True benefits
-XIV Genitourinary	3 (9)	40 (12)	X2 with Yates correction= 0.0433. p= .835071. NS	RR= 0.75 (CI 95%: 10.99, 0.05). True benefits
TOTAL chronic diseases**	34 (100)	344 (100)	---	---

Discussion

Main findings

The two main findings of our study are:

1. Gross incidence rate of covid-19 sequels was 3% cases x March 15, 2020 to October 31, 2022. This figure can be considered moderate, but given the number of covid-19 cases, in absolute numbers, it may represent a significant issue. However, it must be taken into account that the "denominator" of the IR [the total number of covid-19 cases in the consultation (687 positive cases)] is probably underestimated. 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, that focused only on those over 60 years of age, immunosuppressed and pregnant women, vulnerable areas (socio-health wokers) and serious cases, and the elimination of contact tracing. Therefore, since that date, patients carried out self-diagnosis with antigen tests purchased at a pharmacy, although they usually informed the GP of their result if it was positive. In contrast, the IR "numerator" (cases with sequels) are probably valid, due to the characteristics of the sequels itself, which requires assistance from the GP.
2. The only statistically significant risk factors for sequels of covid-19 were being male [RR= 2.23 (CI 95%: 0.94, 5.26) and having presented moderate-severe severity of primary infection [RR= 8.9 (CI 95%: 4.69), 16.9)].

Comparison with other studies

Although most infected people recover, a significant proportion experience sequels after their acute illness (20). However, there are two major problems for comparing data from different studies: 1) the lack of homogeneity of the criteria used in the different studies. Thus, the confusion and overlapping of the definitions of "long covid", "complications" and "sequels" often makes it difficult to draw clear conclusions; and 2) the different time dates for conducting the studies, which implies different variants of SARS-CoV-2, which may give rise to different frequencies of sequels.

Our study maintains a clear definition of "specific sequels of covid-19" (persistent symptoms or pathologies during acute

infection or after an apparent recovery from acute covid-19 infection, which are not part of acute covid-19 infection) (9), and complications of covid-19 (health problems that originated as a result of acute covid-19 infection or the treatments performed) (11) were excluded, which we believe gives greater reliability to the results.

On the other hand, our study includes everything in the period of evolution of the covid-19 pandemic, from March 15, 2020 to October 31, 2022. In the period from March to April, 2020, in Spain the A lineage of the coronavirus predominated, especially the SEC7 and SEC8, and from summer to December, 2020, the 20E (EU1) variant (21, 22). In the period from January 2021 the alpha variant predominated, and from the summer-autumn of 2021 the delta variant (23, 24). From January 2022 to October 2022, the omicron variant predominated (25-27). It has been reported that the cases of covid-19 that required hospitalization during the first wave of the pandemic developed a significant range of sequels (28). In our study, 36% of the cases of covid-19 with sequels presented the acute phase in 2020 and 48% in 2021, dates that correspond to the predominance of alpha and delta variant.

Regarding the IR of the sequels of covid-19, in general they are very diverse: It has been communicated figures between 10% and 15% of patients recovered from acute covid-19 (29); other authors reported figures of 37% for fatigue and 31% for neurocognitive impairment (30); Dyslipidemia and decreased physical resistance have also been reported as sequels (6). In addition, there is increasing evidence that patients who recover after a SARS-CoV-2 infection may have the sequels of newly diagnosed diabetes. It has been reported that overall, the incidence of diabetes after covid-19 was 15.53 per 1000 person-years, and the relative risk of diabetes after covid-19 infection was high (RR 1.62 [1.45–1.80]) (31). Likewise, respiratory sequels from covid-19 have been described, especially after adult respiratory distress syndrome, such as pulmonary fibrosis, induced pulmonary thrombotic events, and consequences such as pulmonary hypertension and effort limitation (32). Similarly, covid-19 appears to increase the risk of mental sequels, but with wide variation in prevalence estimates (9-90% for anxiety, 5-65% for depression), and with an overestimation of mental disorders common when using screening measures compared to diagnostic interviews (33-35). In any case, due to the global proliferation of covid-19 infection, the burden of sequels is expected to be immense (36, 37).

It is a fact repeated that young, previously healthy and non-hospitalized people recover to a large extent from a mild infection and the multisystem effect of covid-19 is less than that observed in older or hospitalized patients (36). In a systematic review that included 57 studies with 250,351 covid-19 survivors, where 79% were hospitalized during the acute phase of covid-19, half experienced post-acute sequels of covid-19 six months later of recovery (31, 38). Our study repeats this sequels risk in acute covid-19 with gravity.

Finally, having Cancer, Chronic Kidney Disease, Chronic Liver Disease, Chronic Lung Disease, Cystic Fibrosis, Dementia or other neurological conditions, Diabetes, Disabilities, Heart Conditions, HIV, and Immunosuppression put at increased risk of severe illness from covid-19, and consequently of presenting sequels (39). We found the presence of chronic diseases of the Neoplasms, Mental, Nervous and Senses, and Circulatory system groups as risk factors for sequels of covid-19, but all of them without statistical significance.

Study limitations and strengths

1. Our study maintains a clear definition of “specific sequels of covid-19, which we believe gives greater reliability to the results.
2. The number of cases was relatively small, despite the fact that our study includes everything in the evolution period of the covid-19 pandemic, from March 15, 2020 to October 31, 2022, which allows assigning complications to variants predominant

Conclusions

In the context of general medicine in Toledo (Spain), the incidence rate of sequels of covid-19 is moderately high (3% of acute covid-19 cases and 1.25% of the general population). Having presented moderate-severe severity of primary infection is the main risk factor, followed by being male. Although IR found can be considered moderate, given the number of covid-19 cases, in absolute numbers it can pose a significant problem. In addition, the consequences of covid-19 are multiple and encompass different physical, emotional, organizational and economic aspects, which will require a multidisciplinary, transversal and collaborative approach, which is the essence of the GP's work. Therefore, the management of the consequences of covid-19 will fall on this level of care.

References:

1. Johns Hopkins Coronavirus Resource Center (2022) Global Deaths. Johns Hopkins University & Medicine. https://coronavirus.jhu.edu/
2. Silva-Ayarza I, Bachelet VC (2021) What we know and don’t know on SARS-CoV-2 and COVID-19. Medwave; 21(4): e8198. https://www.medwave.cl/link.cgi/English/Reviews/Clinical/8199.act
3. Honigsbaum M, Krishnan L (2020) Taking pandemic sequels seriously: from the Russian influenza to COVID-19 long-haulers. Lancet; 396(10260):1389-91. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7550169/
4. Schmidt K, Gensichen J, Gehrke-Beck S, et al. (2021) Management of COVID-19 ICU-survivors in primary care: - a narrative review. BMC Fam Pract; 22: 160. https://doi.org/10.1186/s12875-021-01464-2
5. Beasley R, Kearns N, Hills T (2021) Charting a course for the management of long COVID. Lancet Infect Dis; 12: 1358-60. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00314-3/fulltext
6. Deuel JW, Lauria E, Lovey T, et al. (2022) Persistence, prevalence, and polymorphism of sequels after COVID-19 in unvaccinated, young adults of the Swiss Armed Forces: a longitudinal, cohort study (LoCoMo). Lancet Infect Dis; 22(12): 1694-702. https://doi.org/10.1016/S1473-3099(22)00449-2
7. Nandí-Lozano E, Espinosa LE, Viñas-Flores L, Avila-Figueroa C (2002) [Acute respiratory infection in children who go to a child development center.]. Salud Publica Mex; 44:201-6. https://www.scielosp.org/article/spm/2002.v44n3/201-206/es/
8. Cauthen DB (1994) Family practice incidence rates. JABFP; 7: 303-9. https://www.ncbi.nlm.nih.gov/pubmed/7942099

9. Rey Calero J (1989) [Epidemiological method and community health]. Madrid: Interamericana. McGraw-Hill.
10. Huang Y, Pinto MD, Borelli JL, et al. (2022) COVID Symptoms, Symptom Clusters, and Predictors for Becoming a Long-Hauler Looking for Clarity in the Haze of the Pandemic. Clin Nurs Res; 31(8):1390-8. https://journals.sagepub.com/doi/10.1177/10547738221125632
11. Turabian JL (2023) SARS-CcV-2 infection post-acute specific sequels case series in general medicine from March 15, 2020 to October 31, 2022, in Toledo, Spain. MedPress Public Health and Epidemiology. In Press.
12. Pacheco Campos L, Dávila Aliaga C, Espinola Sánchez M (2022) Factors associated with complications from COVID-19 in hospital workers: A retrospective cohort study. Medwave. http://doi.org/10.5867/medwave.2022.09.2536
13. Montenegro P, Brotons C, Serrano J, et al. (2021) Community seroprevalence of COVID-19 in probable and possible cases at primary health care centres in Spain. Family Practice; 38(2): 154–9. https://doi.org/10.1093/fampra/cmaa096
14. Turabian JL (2022) Covid-19 Breakthrough Infections In Vaccinated People With Vaccine Booster In 2022 Versus Covid-19 Cases In Unvaccinated People In 2020: A New Disease Whose Clinic We Should Know Or Another Cause Of The Old Symptoms Of The Common Cold? J General medicine and Clinical Practice; 5(2). https://www.auctoresonline.org/uploads/articles/1655371786Covid__1_.pdf
15. Turabian JL (2022) Secondary infections in the family from primary cases of covid-19 breakthrough infections in fully vaccinated or not fully vaccinated people. Two doses modestly reduce family transmission but does not eliminate it. Journal of SARS-CoV-2 Research; 2: 12-24. https://doi.org/10.36013/sarc-cov-2.v2i.85
16. Turabian JL (2022) Risk Factors and Incidence Rates of Covid-19 Breakthrough Infections in Vaccinated People in General Medicine Practice in Toledo (Spain). Arch Fam Med Gen Pract; 7(1):183-92. https://scholars.direct/Articles/family-medicine/afmgp-7-033.pdf?jid=family-medicine
17. Turabian JL (2022) Incidence Rates and Risk Factors of Covid-19 Reinfections from March 1, 2020 To July 1, 2022 in A General Medicine office in Toledo, Spain. Ann Community Med Prim Health Care; 1(1): 1006. https://meddocsonline.org/annals-of-community-medicine-and-primary-health-care/incidence-rates-and-risk-factors-of-covid-19-reinfections-from-March-1-2020-to-july-1-2022-in-a-general-medicine-office-in-toledo-spain.pdf
18. Strauss AL (1984) Chronic illness and the quality of life. St Louis: The C.V. Mosby Company.
19. WHO (2019) International Statistical Classification of Diseases and Health-Related Problems. ICD-10 Version: 2019. https://icd.who.int/browse10/2019/en
20. Mao S, Huang T, Yuan H, et al. (2020) Epidemiological analysis of 67 local COVID-19 clusters in Sichuan Province, China. BMC Public Health; 20: 1525. https://doi.org/10.1186/s12889-020-09606-4
21. Aiyegbusi OL, Hughes SE, Turner G, et al. (2021) Symptoms, complications and management of long COVID: a review. J R Soc Med; 114(9):428-42. https://journals.sagepub.com/doi/10.1177/01410768211032850
22. López MG, Chiner-Oms Á, García de Viedma D, et al. (2021) The first wave of the COVID-19 epidemic in Spain was associated with early introductions and fast spread of a dominating genetic variant. Nat Genet; 53: 1405–14. https://www.nature.com/articles/s41588-021-00936-6.pdf
23. Hodcroft EB, Zuber M, Nadeau S, et al. (2020) Spread of a SARS-CoV-2 variant through Europe in the summer of 2020, Nature; 595: 707. https://www.nature.com/articles/s41586-021-03677-y.pdf
24. Centro de Coordinación de Alertas y Emergencias Sanitarias (2021) [Update on the epidemiological situation of variant B.1.1.7 of SARS-CoV-2 and other variants of interest]. Ministerio de sanidad. Gobierno de España. https://www.sanidad.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/20210208_Variantes_de_SARS-CoV-2_en_Espana.pdf
25. García Marín AM, Chiner Oms A, González Candelas F, Comas Espadas I, López MG, Coscolla Devis M (2021) [What genomic epidemiology teaches us about the waves of COVID-19 in Spain (and how to avoid a new wave)]. The Conversation; 11 de Julio. https://theconversation.com/lo-que-nos-ensena-la-epidemiologia-genomica-sobre-las-olas-de-covid-19-en-espana-y-como-evitar-una-nueva-ola-155401
26. Evaluación rápida de riesgo (2022) [SARS-CoV-2 variants in Spain: Ómicron lineages BA.2.12.1, BA.4 and BA.5 11th update, June 28, 2022]. Centro de Coordinación de Alertas y Emergencias Sanitarias. Ministerio de sanidad. España. https://www.sanidad.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/20220628-ERR.pdf
27. Centro de Coordinación de Alertas y Emergencias Sanitarias (2022).[Update of the epidemiological situation of SARS-CoV-2 variants in Spain. May 17, 2022]. Ministerio de Sanidad. España. https://www.sanidad.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/COVID19_Actualizacion_variantes_20220517.pdf
28. Centro de Coordinación de Alertas y Emergencias Sanitarias (2022) [October 17, 2022 Update on the epidemiological situation of SARS-CoV-2 variants in Spain]. Ministerio de Sanidad. España. https://www.sanidad.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/COVID19_Actualizacion_variantes_20221017.pdf
29. Romero-Duarte Á, Rivera-Izquierdo M, Guerrero-Fernández de Alba I, et al. (2021) Sequels, persistent symptomatology and outcomes after COVID-19 hospitalization: the ANCOHVID multicentre 6-month follow-up study. BMC Med; 19: 129. https://doi.org/10.1186/s12916-021-02003-7
30. Pérez Miguel A (2022) [They reveal the most frequent sequels after passing the covid. The WHO identifies several conditions derived from having passed the

coronavirus infection]. Burgosconecta; Martes, 30 agosto. https://www.burgosconecta.es/sociedad/salud/desvelan-secuelas-frecuentes-20220830131259-nt.html

31. Peter RS, Nieters A, Kräusslich H, et al. (2022) Post-acute sequels of covid-19 six to 12 months after infection: population based study. BMJ; 379: e071050. https://www.bmj.com/content/379/bmj-2022-071050
32. Zhang T, Mei Q, Zhang Z, et al. (2022) Risk for newly diagnosed diabetes after COVID-19: a systematic review and meta-analysis.BMC Med; 20: 444. https://doi.org/10.1186/s12916-022-02656-y
33. Molina-Molina M (2020) [Sequels and consequences of COVID-19]. Medicina respiratoria; 13 (2): 71-7. https://www.neumologiaysalud.es/descargas/R13/R132-8.pdf
34. Scott HR, Stevelink SAM, Gafoor R, et al. (2023) Prevalence of post-traumatic stress disorder and common mental disorders in health-care workers in England during the COVID-19 pandemic: a two-phase cross-sectional study. Lancet Psychiatry; 10(1): 40-9. https://doi.org/10.1016/S2215-0366(22)00375-3
35. Glock C (2022) [Epidemiological and social consequences of the pandemic for Brazilian youth]. Medscape; 13 de dezembro. https://portugues.medscape.com/verartigo/6508950
36. van den Heuvel M (2022) [More flu, less corona; COVID-19 as a risk factor for depression; Corona tsunami in China? Prone is not a lifesaver]. Medscape; 12 de diciembre. https://deutsch.medscape.com/artikelansicht/4911923#vp$_2$
37. Deuel JW, Schlagenhauf P (2021) In for the long-haul? Seropositivity and sequelae 1 year post COVID-19. BMC Med; 19: 200. https://doi.org/10.1186/s12916-021-02084-4
38. FAQS COVID-19 (2022) [What are the most common sequels after having passed the Covid?]. Redacción Médica. https://www.redaccionmedica.com/recursos-salud/faqs-covid19/cuales-son-las-secuelas-mas-comunes-por-covid
39. Groff D, Sun A, Ssentongo AE, et al. (2021) Short-term and Long-term Rates of Postacute Sequels of SARS-CoV-2 Infection: A Systematic Review. JAMA Netw Open; 4(10): e2128568. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2784918
40. CDC (2022) People with Certain Medical Conditions. Updated Dec. 6, 2022. National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Citation: Turabian JL. Risk Factors and Incidence Rate of SARS-COV-2 Infection Sequels. A Longitudinal Study in General Medicine. Medp Public Health Epidemiol. 2022; 2(1): mpphe–202212007.