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Covid-19 Reinfection Incidence Trend From 2020-2022, 2023 And 2024 In A General Medicine Clinic in Toledo (Spain)

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Abstract:

Background: Long-term evolution of incidence rates of SARS-CoV-2 reinfections cases in community settings are scarce.

Objective: To compare the incidence rates of SARS-CoV-2 reinfections during 2020-2922 period, 2023 and 2024.

Methodology: Comparison of secondary data among covid-19 reinfection cases in 2020-2022 period, 2023 and 2024 years of previous studies, all of them carried out in the same population of patients treated in a general medicine office in Toledo, Spain.

Results: In the period 2000-2022 versus 2023 and 2024, the following were higher: 1) the crude total incidence rate [1.9%, 0.65%, 0.8% respectively (X2 (gl=2)= 18.8815 . p = .000079]; 2) the incidence rate in women [6.3%, 0.6%, 2.1% [X2 (gl=2)= 28.2386. p < 0.00001]; 3) the incidence of cases with more chronic diseases [1.7%, 0.3%, 0.8% (X2 (gl=2)= 16.5945. p= . 000249]; and 4) the rate in people with some type of job specialization [1.8%, 0.1%, 0.4% (X2 (gl=2)= 18.1395. p= .000115.]. However, there is a slight increase in these rates in 2024 compared to 2023.

Conclusions: lincidence rates of covid-19 reinfections both gross and for the different groups tend to decrease in 2023 and 2024 (omicron SARS-CoV-2 variants and 4th and 5th booster doses of vaccine) compared to the period 2020-2022 (alpha, delta and omicron SARS-CoV-2 variants successively, and only 1, 2 or 3 doses of vaccine). However, there is a slight rebound in rates in 2024 compared to 2023. These results should be taken with caution, due to the probable underreporting of cases in 2023 and 2024.

Keywords: COVID-19; SARS-CoV-2; reinfection; covid-19 vaccines; boosters; epidemiological characteristic; secondary analysis; general practice.

Introduction:

Understanding the protection that prior infection provides against repeat infection, disease, and severe disease, in the transition from an epidemic to an endemic state, where a pathogen is stably maintained in a population. is key to projecting the future epidemiology of coronavirus disease 2019 (covid-19), and guiding decisions on vaccination policies [1].

Most people have some degree of protection due to underlying immunity. By the third quarter of 2023 (July–September), 98% had antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with 14% due to vaccination alone, 26% due to infection alone, and 58% due to both (hybrid immunity) [2].

Seroprevalence surveys suggest that more than a third

and possibly more than half of the global population has been infected with SARS-CoV-2 by early 2022. As large numbers of people continue to be infected [6]. However, by 2024, despite the number of covid-19 cases since the start of the pandemic, the prevalence of SARS-CoV-2 estimated in meta-analyses (around 10%) indicates that most of the world's population remains susceptible to SARS-CoV-2 infection [7]. Thus, COVID-19 is now an established and persistent health problem [8].

In this scenario, SARS-CoV-2 reinfections are an important aspect of covid-19 and its potential transition to endemicity [9]. It has been estimated that 4-6 months after a first episode of covid-19 or after being vaccinated (or both -hybrid immunity), a new SARS-CoV-2 infection is expected to be associated with a higher risk of hospitalization and death in the most fragile population [10].

SARS-CoV-2 reinfections were exceptional an unexpected in 2020 [11-13]. They were still rare until the end of 2021, but became common with the arrival of Omicron [14]. A meta-analysis of global SARS-CoV-2 reinfection rate up to March 16, 2023, showed there was a significant increase in the number of SARS-CoV-2 reinfection reports in various countries since the Omicron variant (2022).

However, the trend of reinfection rate over time is not clear [15]. Given the current situation in many places, such as Spain, of not performing diagnostic tests in health services, except for those over 60 years of age and health workers [16], many people with symptoms choose to perform tests at home, the result of which does not appear in statistics, but is generally reported to general practitioner [17].

Previous infection or vaccination may have so far produced a false sense of security against reinfection, which could theoretically increase exposure or relax anti-covid-19 measures. Estimates of the burden of SARS-CoV-2 reinfections remain crucial to assess new SARS-CoV-2 variants with immune escape potential [18]. Ultimately, studying reinfections will help researchers understand what the transition of SARS-CoV-2 to an endemic virus will look like [19].

In this context, we present a comparative study based on previously published data, to evaluate the trend of incidence rates of reinfections covid-19 in the period 2020-2022 (with alpha, delta and omicron SARS-CoV-2 variants; and in 2020 without vaccination, in 2021 with 1 or 2 dose vaccination and in 2022 with first booster), in 2023 (omicron variant and with second booster), and in 2024 (omicron variant with third booster), from the same population attended in a general medicine consultation in these time periods.

Material and Methods:

Design and Emplacement:

This study compares data from previous observational, longitudinal and prospective studies of covid-19 reinfections from March, 2020 to October, 2024, already published [20-24]. All studies were conducted on the same population: patients saw in a general medicine office in Toledo, Spain, which has a list of 2,000 patients > 14 years of age (in Spain, general practitioner (GP) care for people > 14 years of age, except for exceptions). The GPs in Spain work within the National Health System, which is public in nature, and are the gateway for all patients to the system, and each person is assigned a GP. The methodology of all studies has been previously published and here only the main elements will be repeated for the current study.

Outcome of interest:

To compare the incidence rates of SARS-CoV-2 reinfections during the period 2020-2022, with those of 2023 and 2024 years in the same population in general medicine.

Calculation of incidence rates:

Cumulative incidence rates were calculated at the GP's office by dividing the number of reinfection events during the study period divided by the individuals that could develop the event at the start of the study (population at risk) [25]. That is, the incidence rate was calculated by dividing the number of cases of covid-19 reinfections by people on the list of patients dependent on the consultation object of the study (N=2,000 people), from the period 2020-2022, with those of 2023 and 2024 years [26, 27].

Calculation of rate denominators:

Data of variables of people in the clinic object of the study were obtained by extrapolating the neighborhood served by the health center to population served in clinic office [28, 29]. Data regarding some variables of interest (as complex family, and chronic diseases) were previously published [30-33]. The denominator data for prevalence of

chronic diseases were taken from previous studies carried out in the same population treated in that general medicine consultation [34-37]. The number of social-health workers was obtained as an extrapolation of the total number for Castilla la Mancha in 2020 for the list of 2000 inhabitants attended in the consultation object of the study [38]. The ethnic minority data was obtained by extrapolating the data of foreigners in the municipality of Toledo to the population attended at the clinic [39]. The data on vaccination with a complete schedule (1, 2 or 3 doses) was obtained by extrapolating the data from Spain to the population of the clinic [40]. Likewise, for 2023 the number of people with the 1st booster dose was extrapolated for the population of the clinic from the data for Spain [41].

Definition of reinfection:

SARS-CoV-2 reinfection was defined as a documented infection occurring at least 90 days after a previous infection [42-44].

Diagnosis of covid-19:

The diagnosis was performed with reverse transcriptase polymerase chain reaction oropharyngeal swab tests or antigen testing [45] performed in health services or at home.

Covid-19 vaccination:

Patients could have received 1, 2 doses of vaccine, first booster for fall-winter 2021, fourth dose (second booster) for fall-winter 2022 [19] and fifth dose (third booster) for fall-winter 2023. In our study, only Pizfer / BioNTech, Spikevax (mRNA-1273- Moderna), Vaxzevria, Oxford / AstraZeneca and Janssen (Johnson & Johnson) vaccines were used for the first and second doses. For the first booster, only messenger RNA (mRNA) was used. And only Moderna and Pfizer-BioNTech's bivalent covid-19 vaccines were used for the second booster. Omicron XBB.1.5 adapted vaccines Pfizer / BioNTech y Spikevax (Moderna) were used for the third booster in autumn-winter 2023-2024 [46-49].

Collected variables:

The following variables were collected:

1. Age and sex.
2. 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" [50].
3. Social-occupancy class (according to the Registrar General's classification of occupations and social status code) [51, 52].
4. If they were Health Care Workers.
5. Problems in the family context 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) [53-56].
6. Ethnic minority (defined as a "human group with cultural, linguistic, racial values and geographical origin, numerically inferior compared to the majority group") [57].
7. Disease severity (classified according to: 1. mild cases: clinical symptoms are mild and no manifestation of pneumonia can be found on images; 2. moderate cases: with symptoms such as fever and respiratory tract symptoms and the manifestation of pneumonia can be seen on the imaging tests; and 3. 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 ≤ 300 mmHg.) [58]; to simplify comparison, moderate and severe cases were counted together.
8. Vaccination status against covid-19 at the date of reinfection: vaccinated with 2 doses of vaccine [45], vaccinated with first booster for fall-winter 2021 [59], vaccinated with fourth dose (second booster) for fall-winter 2022 [60] and vaccinated with fifth dose (third booster) for fall-winter 2023 [61, 62].

Epidemiological analysis:

The calculation of the incidence rates as explained above (subsection "Calculation of incidence rates") was

made by dividing the number of infection events by the person follow-up time (from 2020-2022, 2023 and 2034) [25, 26]. Data on the incidence were extrapolated to the entire population attended in the consultation (N=2,000 people) [27]. The classes that classify the age groups were made taking into account > and < 65 years [31]. The age of 65 years was used as the beginning of old age [63]. Figures with decimals were rounded to facilitate a more intuitive comparison. Similarly, to facilitate understanding of the data, the periods compared were rounded to full years: the period from March 1, 2020 to September 1, 2022 was labeled 2020-2022; from October 1, 2022 to September 30, 2023 was labeled 2023; and from October 1, 2023 to September 30, 2024 was labeled 2024.

Statistical analysis:

The comparisons were performed using the Chi Square test (X2) or test of Kruskal-Wallis when necessary, both with degrees freedom (df)= 2. [df= (number of rows-1) x (number of columns-1)].

Ethical issues:

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

Results:

The crude incidence rate was statistically significantly higher in the period 2000-2022 (alpha, delta and omicron, successively) versus 2023 and 2024 [1.9%, 0.65%, 0.8% respectively; X2 (df = 2) = 18.8815. p = .000079. Significant at p < .05]. In 2020-2022 versus 2023 and 2024, incidence rate in women was statistically significantly higher [6.3%, 0.6%, 2.1% respectively; X2 (df = 2) = 28.2386. p < 0.00001. Significant at p < .05.], also with more chronic diseases [1.7%, 0.3%, 0.8% respectively; X2 (df = 2) = 16.5945. p = .000249. Significant at p < .05.], and the rate in people with some type of labor specialization [1.8%, 0.1%, 0.4% respectively; X2 (df = 2) = 18.1395. p = .000115. Significant at p < .05]. (Table 1, Figure 1, Figure 2).

Variables	Estimated population of gp office N=2.000	Reinfections 2020-2022 (alfa variant en 2020; delta variant en 2021; omicron variant en 2022) N=38	Incidence rates of covid-19 re-infection 2020-2022	Reinfections 2023 (omicron variant en 2023) N=12	Incidence rates of covid-19 re-infection 2023	Reinfections 2024 (omicron variant en 2024) N=15	Incidence rates of covid-19 re-infection 2024	Statistical significance (comparison of 2020-2022, 2023 and 2024
Crude Incident Rate	2.000	38 (100)	1.9%	12 (100)	0.6%	15 (100)	0.8%	X2 (df=2)= 18.8815. p= .000079. Significant at p < .05.
> = 65 years	349 (17)	3 (8)	0.9%	4 (33)	1.1%	4 (27)	1.1%	X2 (df=2)= 0.1837. p= .91222. NS
Women	480 (24)	30 (79)	6.3%	3 (25)	0.6%	10 (67)	2.1%	X2 (df=2)= 28.2386. p) < 0.00001. Significant at p < .05.
Men	1020 (51)	8 (21)	0.8%	9 (75)	0.9%	5 (33)	0.5%	X2 (df=2)= 1.1904. p= .551459. NS
Socio-Health Care Workers	240 (12)	7 (18)	29%	9 (75)	37%	4 (27)	17%	X2 (df=2)= 1.9543. p= .376385. NS

Moderate-severe severity of reinfection	2000 (100)	0	0	3 (25)	0.2%	0	0	Kruskal-Wallis (df=2): 0.25. p= .882 . NS
Chronic diseases	1459 (73)	25 (66)	1.7%	4 (33)	0.3%	12 (80)	0.8%	X2 (df=2)= 16.5945. p= .000249. Significant at p < .05.
People with some type of labor specialization	910 (45)	16 (42)	1.8%	1 (8)	0.1%	4 (27)	0.4%	X2 (df=2)= 18.1395. p= .000115.Significant at p < .05.
Complex family	601 (30)	3 (8)	0.5%	7 (58)	1.2%	2 (13)	0.3%	X2 (df=2)= 3.5235. p= .171748. NS
Ethnic minority	80 (4)	5 (13)	6.2%	1 (8)	1.2%	1 (7)	1.2%	X2 (df=2)= 4.7088. p= .094952. NS
Only 1, 2 ó 3 dosis **	1700 (85)	38 (100)	2.2%	7 (6)	0.4%	10 (67)	0.6%	NR
4 dosis**	1120 (56) en 2023	NR	NR	5 (42)	0.4%	1 (7)	0.1%	NR
5 dosis**	NA	--	--	--	--	4 (27)	NR	NR

Table 1: *Covid-19 reinfection incidence rates in 2020-2022, 2023 and 2024*.*

( ): Denotes percentages; NS: Not significant at p< .05; df= Degrees freedom; NR: Not relevant; NA: Not available; *To facilitate understanding of the data, the periods compared were rounded to full years: the period from March 1, 2020 to September 1, 2022 was labeled 2020-2022; from October 1, 2022 to September 30, 2023 was labeled 2023; and from October 1, 2023 to September 30, 2024 was labeled 2024. ** Statistical comparison is not relevant, as the 4th and 5th doses did not exist in 2000-2022.

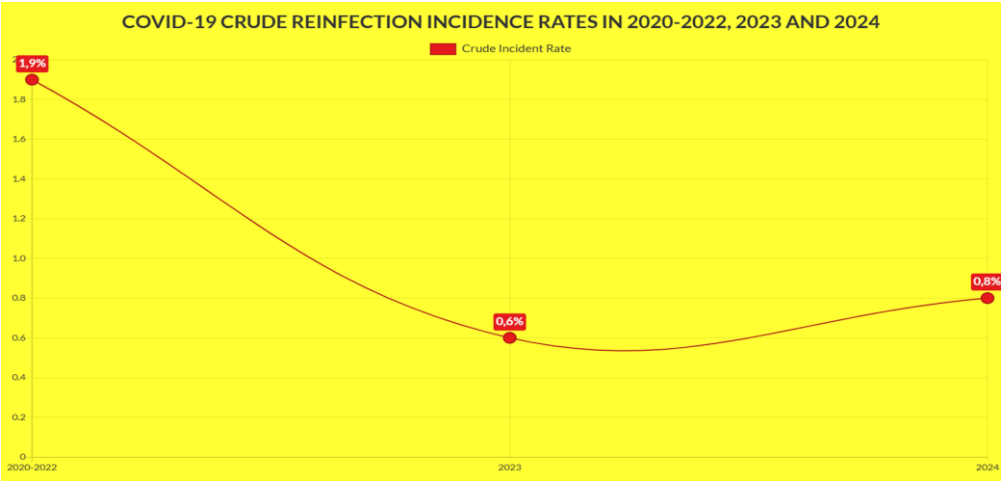

Figure 1: Covid-19 crude reinfection incidence rates in 2020-2022, 2023 and 2024.

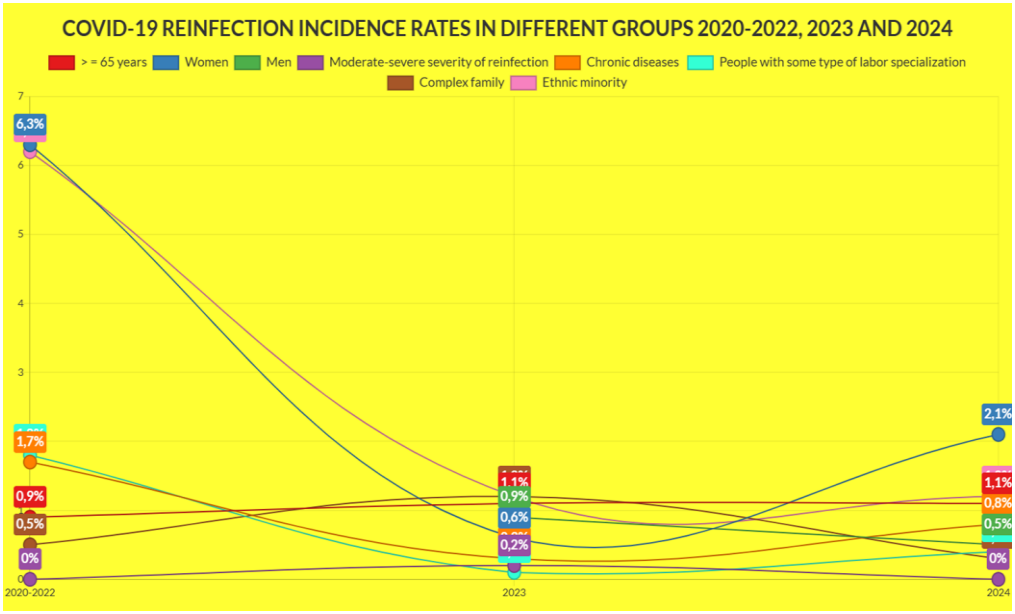

Figure 2: Covid-19 reinfection incidence rates in different groups 2020-2022, 2023 and 2024.

Discussion:

1. Main findings:

Our main findings were that the incidence rates of reinfections by covid-19 both crude and for the different groups tend to decrease in 2023 and 2024 (omicron SARS-CoV-2 variants and 4th and 5th booster doses of vaccine) compared to the period 2020-2022 (alpha, delta and omicron SARS-CoV-2 variants successively, and only 1, 2 or 3 doses of vaccine). Although the lowest point is in 2023, and a slight increase in rates is observed in 2024 compared to 2023.

3 fundamental factors must be taken into account to correctly evaluate our data: the local evolution of SARS-CoV variants, local degree of vaccination, and degree of diagnostic testing when there are symptoms.

a. Since 2020 SARS-CoV variants spectrum covers alpha, beta, gamma, delta and omicron. In Spain, the Alpha variant was dominant during 2020. By June 2021, only sporadic cases and outbreaks in various communities of the beta and gamma variants were detected in Spain [64]. In Aug. 2021, the Delta variant accounted for 90% of total cases in Spain [65]. In May 2022, the Omicron variant was the dominant one in Spain after having displaced the Delta variant [66]. The omicron variant was the dominant one in Spain November, 2022 [49]. The XBB.1.5 lineage became the dominant in March de 2023 in Spain [67]. The predominant variants in Spain during 2023 were those of the XBB family [62, 67-71]. In January 2024 in Spain, XBB.1.5-like + F456L accounted for 42% and BA.2.86 for 44% of positive cases [23]. In July and August 2024, the KP.3 lineage was detected in 84% of cases [72]. In September 2024, the incidence of the XEC variant of the coronavirus, a new Omicron subvariant was increasing markedly in Spain. At that time, it was the second most common strain in cases recorded in September, although still far behind the main KP.3.3, with an incidence of 13% [73, 74].

b. On the other hand, in Spain, in April 2022, the population vaccinated with the complete regimen (2 or 3 doses) was 85.27% (40). In November 2022, more than 60% of people over 80 years of age, and 37% of people over 60 years of age, already had the second booster dose of the covid-19 vaccine [75, 76]. By June 2023, the number of people with the 1st booster dose was 56% of the population (41). And 60% of the population over 80 years of age has already received the vaccine adapted against the covid-19 subvariants of the 2023/2024 campaign [77].

c. In any case, the results must be evaluated with caution. In Spain, since April 28, 2022 there was a new "Surveillance and Control Strategy Against Covid-19" that include the non-performance of

diagnostic tests, except on over 60 years of age [16]. This means that positive cases have been counted with tests carried out in health services and with tests carried out at home and later reported to the GP. Thus, there is probably an underreporting.

2. Comparison with other studies:

One of the key questions in predicting the course of covid-19 is how well and for how long immune responses protect the host from reinfection [78]. Whether reinfection occurs in an individual is not only determined by the magnitude and duration of specific immunity, but also by the various circumstances of their risk of exposure to the virus [79].

There is a significant increase in the number of reports of SARS-CoV-2 reinfection in several countries. However, the trend of the reinfection rate over time is unclear. In a meta-analysis of 55 studies including 111,846 cases of SARS-CoV-2 reinfection up to 16 March 2023, the pooled SARS-CoV-2 reinfection rate was 0.94% [15]. In a population-based observational study, residents of Vojvodina registered and laboratory-confirmed with SARS-CoV-2 were followed up between 6 March 2020 and 31 October 2021 for reinfections, the overall incidence rate of reinfections was 0.599 per 100 person-months [80]. Reinfections before the omicron variant were very rare, around 0.5%, but as new subvariants appeared, immune escape is greater. Not only from vaccines, but also from natural immunity [81-83]. From 28 September to 27 December 2020 (alpha variant) in 36920 users of the COVID Symptom Study app in the UK, 0.7% of reinfections were identified [84]. For 2020 in Italy, approximately 17% of covid-19 survivors were reported to test positive again in a longitudinal study [85]. In the UK, reinfections accounted for 1% of cases in April 2021. With the introduction of Omicron, reinfection rates increased to 11% of all infections. In 2022, reinfections accounted for 25-27% of cases in the UK [14].

A study in Qatar reported that as of April 2021, the incidence rates of reinfection with the beta variant were estimated at 4.34 cases per 10,000 person-weeks. Regarding the alpha variant, the incidence rates were 0.53 cases per 10,000 person-weeks [86]. In an Israeli cohort study (August and September 2021, when delta variant was predominant), the longer the time after vaccination, infection, or both, the higher the likelihood of infection with the Delta variant. The adjusted reinfection rate in the recovered and unvaccinated cohort increased from 10.5 per 100,000 person-days at 4–6 months to 30.2 at ≥12 months after initial recovery. In recovered and vaccinated individuals, these rates were 3.7 and 11.6 at 2 months and 6–8 months after vaccination, respectively. In those who had received two doses of vaccine, infection rates increased from 21.1 (2 months after vaccination) to 88.9 (6–8 months after vaccination). The three-dose cohort only had data up to 2 months after vaccination, at which time the infection rate was 8.2 [5]. A cohort study of healthcare workers from June 2021 showed a low probability of reinfection after a previous SARS-CoV-2 infection (2.2%) and higher post-vaccination infections among women and those without previous infection [87].

Probably related to current situation in many places, such as Spain, of not performing diagnostic tests in health services, except for those over 60 years of age and health workers (16), current trends in reported cases of covid-19 are underestimates of the true number of infections and reinfectionin [8]. So, in our study, we found that the rates of reinfections are higher in social-health workers.

In summary, the crude incidence rate of reinfection in our study was higher in the period 2000-2022 versus 2023 and 2024, which is consistent with other studies, where they report a rate of 0.5-0.6% for 2020, 0.6-1% for 2021, and 11%-17% for 2022 with the arrival of omicron, which makes the figures higher in that period 2020-2022 when studied as a group. In addition, the lower incidence figures in 2023-2024 suggest a protective effect of hybrid immunity against omicron. Although there is also a tendency to increase the incidence in 2024. In any case figures for 2023 and 2024 have a bias due to underreporting.

Study limitations and strengths:

1. The sample was small, so some data may cause misinterpretation.
2. Asymptomatic cases were missing because they did not attend in GP consultation, as no surveillance or systematic screening was done.
3. There may be an underreporting of infections to GP of patients with a positive test at home.
4. The great accessibility of patients to the GP, and the fact of the continuity of care that characterizes family medicine, have important epidemiological connotations, presenting a unique opportunity to

study incidence rates of diseases in small geographical bases.

Conclusión:

In the context of general medicine in Toledo (Spain), the incidence rates of reinfections by covid-19, both crude and for the different groups, tend to decrease in 2023 and 2024 (omicron SARS-CoV-2 variant and 4th and 5th booster doses of vaccine) compared to the period 2020-2022 (successively alpha, delta and omicron SARS-CoV-2 variants, and only 1, 2 or 3 doses of vaccine). However, there is a slight increase in the rates in 2024 compared to 2023. Data suggest that booster doses appear to decrease risk of reinfection. These results should be taken with caution due to the probable underreporting of cases in 2023 and 2024.

References:

1. Cohen C, Pulliam J (2023) COVID-19 infection, reinfection, and the transition to endemicity. Lancet; 401(10379): 798-800.
2. Bobrovitz N, Ware H, Ma X, et al. (2023) Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression. Lancet Infect Dis; 23(5): 556-67.
3. Srivastava K, Carreño JM, Gleason C, et al. (2024) SARS-CoV-2-infection- and vaccine-induced antibody responses are long lasting with an initial waning phase followed by a stabilization phase. Immunity; 57(3): 587-99.e4.
4. Link-Gelles R, Weber ZA, Reese SE, et al. (2023) Estimates of Bivalent mRNA Vaccine Durability in Preventing COVID-19–Associated Hospitalization and Critical Illness Among Adults with and Without Immunocompromising Conditions — VISION Network, September 2022–April 2023. MMWR Morb Mortal Wkly Rep; 72: 579–88.
5. Goldberg Y, Mandel M, Bar-On YM, et al (2022) Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2. N Engl J Med.
6. Pilz S, Theiler-Schwetz V, Trummer C, Krause R, Ioannidis JPA (2022) SARS-CoV-2 reinfections: Overview of efficacy and duration of natural and hybrid immunity. Environ Res; 209: 112911.
7. Ukwishaka J, Mela CF, Aseneh JBN, et al. (2024) Seroprevalence of SARS-CoV-2 antibodies among healthy blood donors: a systematic review and meta-analysis. BMC Public Health; 24.
8. OPS (2023 [COVID-19 is now an established and persistent health problem]; 8 Mayo.
9. Rustom A, Halloran ME (2021) Transition to endemicity: Understanding COVID-19. Immunity; 54(10): 2172-6.
10. Soriano V (2022) COVID de repetición: ¿peor que la primera vez? Blog; 14/11.
11. Mandavilli A (2020) First Documented Coronavirus Reinfection Reported in Hong Kong. The patient did mount an immune response to the new infection, however, and did not experience symptoms. The New York Times; Published Aug. 24.
12. Bowen T (2020) Nevada State Public Health Lab-led team studying COVID-19 reinfection. Fighting the pandemic: University of Nevada, Reno research effort continues with early, genomics-based evidence of reinfection. University of Nevada, Reno. School of Medicine; August 27.
13. Yeager A (2020) More SARS-CoV-2 Reinfections Reported, But Still a Rare Event. Repeat COVID-19 cases could offer clues about people's immunity to the novel coronavirus and how to vaccinate against it. The Scientist; Oct 26.
14. Zoco M, Jetelina K (2022) [Epidemiology of reinfections]. Su Epidemiólogo Local; Jul 08.
15. Chen Y, Zhu W, Han X, et al. (2024) How does the SARS-CoV-2 reinfection rate change over time? The global evidence from systematic review and meta-analysis. BMC Infect Dis; 24(1): 339.
16. Turabian JL (2022) An ostrich strategy for covid-19 is too risky. BMJ; 377: o1112.
17. Turabian JL (2024) Covid-19 Infections with Positive Test at Home Versus in Health Services, In the Period from October 2022 to October 2023, In the General Medicine Office, In Toledo (Spain). J General Medicine and Clinical Practice; 7(8).
18. Planas D, Saunders N, Maes P, et al.(2022) Considerable escape of SARS-CoV-2 Omicron to antibody neutralization. Nature; 602: 671-5.
19. Mallapaty S (2022) COVID reinfections surge during Omicron onslaught. Immunity acquired through previous infection is less effective against Omicron than against other variants, but the risk of severe COVID-19 remains low. Nature; 16 February.
20. Turabian JL (2024) Covid-19 reinfections clinical-epidemiological characteristics trend between 2020-2022, 2023 and 2024 in a general medicine clinic in Toledo (Spain). International Journal of Clinical Epidemiology. In Press.
21. Turabian JL (2022) Does the Booster Vaccination

Provide Advantages to Prevent Reinfection Over 1 or 2 Doses of COVID–19 Vaccine? Medp Public Health Epidemiol. 2022; 1(1): mpphe–202209003.
22. Turabian JL (2024) Reinfections of Covid-19 with and Without Fourth Dose of Bivalent mRNA Vaccine in the Period from October 2022 to October 2023 in a General Medicine Office in Toledo (Spain). J Dise Dis Tre; SRC/JDDT-129.
23. Turabian JL (2024) What are the risk factors of covid-19 reinfection in people with 4th dose of bivalent mrna vaccines? A study in general medicine from october 2022 to october 2023. International Journal of Clinical Epidemiology; 3(3).
24. Turabian JL (2024) What are the Clinical-Epidemiological Differences between Initial Infection and Reinfection Covid-19 with Fourth Dose of Bivalent mRNA Vaccine? A Study in the Period from October 2022 to October 2023, In a General Medicine Office (Toledo, Spain). J Inf Dis Trav Med; 8(1): 000183.
25. Slater MR (2003) Veterinary epidemiology. St. Louis, Missouri (USA): Butterworth Heinemann.
26. 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.
27. Cauthen DB (1994) Family practice incidence rates. JABFP; 7: 303-9.
28. Demografia de Polígono Santa María de Benquerencia (Toledo) (2023) Foro-Ciudad.com; 24/01.
29. Toledo (2023). Wikipedia.
30. Turabian JL, Minier-Rodriguez LE, Cucho-Jove R, Rodriguez-Almonte FE, Villarin-Castro A (2016) The Patient Companion in the Consultation of Family Medical Practice is an Indicator of Hidden Family Problems. Arch Fam Med Gen Pract; 1:001.
31. Turabian JL (2017) Prevalence of Chronic Diseases: in Defence of Epidemiological Craftsmanship in Family Medicine. CP Epidemiology; 1[1]: 005.
32. 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.
33. Turabian JL (2023) What is the Frequency with which Sars-COV-2 Reinfection Occurs in People with Fourth Dose of Vaccines Bivalent mRNA? Incidence Rate of Covid-19 Re-Infection from October 2022 to October 2023 in A General Medicine Office in Toledo (Spain). J of Clin Case Stu Reviews & Reports; 2(1), 1-8.
34. Turabian JL (2017) Secular Trend throughout 30 Years of Chronic Diseases in a Family Medicine Office in Toledo, Spain: 1985-1995-2016. J Gen Pract (Los Angel) 5: 329.
35. Turabian JL, Gutiérrez V. (1996) [Variation in the frequency of chronic diseases and risk factors in primary care: 1985-1995]. Aten Primaria; 18(2): 65-9.
36. Turabian JL (2022) Frequency and Variation of Chronic Diseases of Covid-19 Cases from 2020 to 2022 in General Medicine and Comparison with Baseline Data from the Same Population in 2017, in Toledo (Spain). J Community Prev Med; 5(2): 01-07.
37. Turabian JL (2024) Endemic Period COVID-19 Risk Evolution Between 2023 and 2024 Years in a General Medicine Office in Toledo, Spain. Incidence Rate and Other Risk Measures are Declining or Stable. Journal of Family Medicine and Preventive Medicine; SRC/JFMPM-101.
38. [Statistics on specialized care health centers. Centers with internment 2020]. Consejería de sanidad dirección general de planificación, ordenación e inspección sanitaria. Servicio de planificación.
39. Toledo (2022) [Population: immigrants, emigrants and other data on the inhabitants of each municipality. Data updated on January 17, 2022]. Epdata.
40. Datadista (2022) Evaluation of Covid-19 vaccination in Spain]. 22 abr.
41. GIV COVID-19 (2023) [COVID-19 Vaccination Executive Report]. Ministerio de Sanidad. Gobierno de España; 30 jun 2023.
42. Slezak J, Bruxvoort K, Fischer H, Broder B, Ackerson B, Tartof S (2021) Rate and severity of suspected SARS-Cov-2 reinfection in a cohort of PCR-positive COVID-19 patients. Clin Microbiol Infect; 27(12): 1860.E7-E10.
43. Altarawneh HN, Chemaitelly H, Ayoub Hh, et al. (2022) Effects of Previous Infection and Vaccination on Symptomatic Omicron Infections. N Engl J Med; 387: 21-34.
44. Ayoub HH, Tomy M, Chemaitelly H, et al. (2023) Estimating protection afforded by prior infection in preventing reinfection: applying the test-negative study. Am J Epidemiol; kwad239.
45. Ministerio de Sanidad (2021) [COVID-19 early detection, surveillance and control strategy. Updated December 1].

46. Consejo Interterritorial de Salud (2022) [COMIRNATY BIVALENTE, Original/Omicron BA.4-5 (COVID-19 mRNA Vaccine, Pfizer-BioNTech) Technical Guide December 27, 2022].
47. Consejo Interterritorial de Salud (2023) [BIVALENT SPIKEVAX, Original/Omicron BA.1 and Original/Omicron BA.4-5 (Modern COVID-19 mRNA Vaccine) Technical Guide January 23, 2023].
48. Lin D-Y, Xu Y, Gu Y, et al. (2023) Effectiveness of Bivalent Boosters against Severe Omicron Infection. N Engl J Med 2023; 388: 764-6.
49. Consejo Interterritorial (2022) [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]. Sistema Nacional de Salud. España.
50. Strauss AL (1984) Chronic illness and the quality of life. St Louis: The C.V. Mosby Company.
51. Royal Collage of General Practitioners (1986) The Classification and Analysis of General Practice Data. Occasional Paper 26.
52. Donaldson RJ, Donaldson LJ (1983) Essential Community Medicine. Lancaster: MTP Press.
53. Turabian JL (2017) Family Genogram in General Medicine: A Soft Technology that can be Strong. An Update. Res Med Eng Sci; 3(1).
54. Russell LT (2020) Capturing Family Complexity in Family Nursing Research and Practice. J Fam Nurs; 26(4):287-93.
55. Watts C, Shrader E (1998) How to do (or not to do)... The genogram: a new research tool to document patterns of decision-making, conflict and vulnerability within households. Health Policy Plan; 13: 459-64.
56. McIlvain H, Crabtree B, Medder J, Stange KC, Miller WL (1998) Using practice genograms to understand and describe practice configurations. Fam Med; 30: 490-6.
57. Diccionario panhispánico del español jurídico (2022) [Ethnic minority].
58. 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.
59. [Update 10 Vaccination strategy against COVID-19 in Spain. Recommendations agreed upon in the Public Health Commission after review and proposal made by the Vaccination Program and Registry Report together with the COVID-19 Vaccination Technical Working Group and the COVID-19 Vaccination Working Group in the Child Population December 2021].
60. Consejo Interterritorial (2022) [COVID-19 vaccination recommendations for autumn in Spain. Approved by the Public Health Commission on 22 September 2022. Prepared by the Vaccination Programme and Registry Committee]. Sistema Nacional de Salud. España.
61. Grupo de Trabajo sobre Vacunaciones de la Sociedad Española de Epidemiología (2023) [COVID-19 AND FLU VACCINATION GUIDE, AUTUMN 2023]. Sociedad Española de Epidemiología.
62. Rodríguez-Artalejo FJ, Ruiz-Galiana J, Cantón R, et al. (2023) COVID-19: On the threshold of the fifth year. The situation in Spain. Rev Esp Quimioter; 37(1): 17-28.
63. Reijneveld SA, Gunning-Schepers LJ (1994) Age, socioeconomic status, and mortality at the aggregate level. J Epidemiol Community Health; 48: 146-50.
64. Pulido S (2021) [COVID variants by country: a comprehensive analysis and experiences in the UK and US with genetic testing]. Revista Española de Economía de la Salud; 21 junio.
65. Punzano D (2021) [The Delta variant of Covid-19 accounts for almost 90% of total cases in Spain]. Redacción Médica; ago. 2021.
66. Centro de Coordinación de Alertas y Emergencias Sanitarias (2022) [Update on the epidemiological situation of SARS-CoV-2 variants in Spain. May 23, 2022]. Ministerio de Sanidad, Gobierno de España.
67. Centro de Coordinación de Alertas y Emergencias Sanitarias (2023). [May 22, 2023 Update on the epidemiological situation of SARS-CoV-2 variants in Spain]. Ministerio de Sanidad. España.
68. Viciosa M (2023) [If you have covid today, the new variant O EG.5 or 'Eris' may have something to do with it (and it is not more serious)]. Newtral; 11 agosto.
69. Pérez B (2023) [The new eris variant, more contagious, already alerts doctors to the rebound in covid]. El Periódico; 10 de agosto.
70. Looi M (2023) Covid-19: Hospital admissions rise in England amid fears of new variant and waning immunity. BMJ; 382: p1833.
71. Smith DG (2023) What to Know About the New Dominant Covid Variant. EG.5 is spreading quickly, but experts say it's no more dangerous than

previous versions. Another new variant, called BA.2.86, is being closely watched because of its mutations. The New York Times; Aug. 11.
72. [WEEKLY EPIDEMIOLOGICAL REPORT COMMUNITY OF MADRID. Week 40] (2024). SG de Vigilancia en Salud Pública. Dirección General de Salud Pública CONSEJERÍA DE SANIDAD – COMUNIDAD DE MADRID. 8 de Octubre.
73. AM (2024) [XEC Covid variant: this is the new strain that is spreading across Europe and what its symptoms are]. Onda Cero; Madrid; 09.10.
74. Córdoba Jiménez P (2024) [XEC: New COVID variant threatens Europe, leaving 1,115 cases worldwide]. Gaceta Médica; 10 octubre.
75. Vacuna Covid-19 (2021) [Covid-19 vaccination strategy in Spain]. Ministerio de sanidad.
76. Notas de Prensa (2022) [More than 60% of people over 80 years of age now have a second booster dose against COVID-19]. Ministerio de Sanidad. España; 11.11.
77. Noticias (2023) [60% of the population over 80 years old has already been vaccinated against Covid 19 in 2023]. Ministerio de Sanidad, Gobierno de España; 15 de diciembre.
78. Iwasaki A (2020) What reinfections mean for COVID-19. Lancet Infect Dis; 21(1): 3 - 5.
79. Ju Zhang, Nan Ding, Lili Ren, et al. (2021) COVID-19 reinfection in the presence of neutralizing antibodies, Natl Sci Rev; 8(4): nwab006.
80. Medić S, Anastassopoulou C, Lozanov-Crvenković Z, et al. (2022) Risk and severity of SARS-CoV-2 reinfections during 2020–2022 in Vojvodina, Serbia: A population-level observational study. Lancet Regional Health – Europe; 20.
81. Roa R (2022) [Covid: increased risk of complications with reinfections]. La biblioteca de Springfield: 29 de junio.
82. Wise J (2022) Covid-19: Omicron infection is poor booster to immunity, study finds. BMJ; 377: o1474.
83. Pulliam JRC, van Schalkwyk C, Govender N, et al. (2022) Increased risk of SARS-CoV-2 reinfection associated with emergence of Omicron in South Africa. Science; 376(6593):eabn4947.
84. Graham NS, Sudre mCH, May A, et al. (2021) Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study. Lancet Public Health.
85. McNamara D (2020) [Approximately 17% of COVID-19 survivors test positive again in longitudinal study]. Medscape; 12 de nov.
86. Chemaitelly H, Bertollini R, Abu-Raddad LJ (2021) Efficacy of Natural Immunity against SARS-CoV-2 Reinfection with the Beta Variant. N Engl J Med;385:2585-6.
87. Dhumal S, Patil A, More A, et al. (2022) SARS-CoV-2 reinfection after previous infection and vaccine breakthrough infection through the second wave of pandemic in India: An observational study. Int J Infect Dis:118: 95-103.