

Assessing the risk between vaccination status and infections within families with COVID-19 cases in Spain

Jose Luis Turabian

Health Center Santa Maria Benquerencia. Regional Health Service of Castilla la Mancha (SESCAM). Toledo, Spain.

*. **Corresponding author:** Turabian, J.L. Health Center Santa Maria Benquerencia. Toledo, Spain. E-mail: jturabianf@hotmail.com.

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Abstract

Background: It's unclear whether vaccination individuals against SARS-CoV-2 protects family members in the same way.

Objective: The assessment of risk factors for SARS-CoV-2 transmission from index cases with COVID-19 breakthrough infection in completely vaccinated patients to fully vaccinated family members.

Methods: From February 1 to November 30, 2021, an observational, longitudinal, and prospective research of families with one primary case of COVID-19 breakthrough infection was done in a general medicine practice in Toledo, Spain.

Results: Thirteen primary cases of COVID-19 breakthrough infection in 13 families with at least one other family member were included, of which 9 were positive secondary cases (sick) and 8 were negative partners (healthy) properly vaccinated. Being a woman, being over 45 years old, being a social-health professional, being an ethnic minority, and having chronic conditions all increased the likelihood of developing COVID-19 in fully vaccinated contacts and main cases. Although vaccination 2ChAdOx1 nCoV-19 had a higher effectiveness than BNT162b2 mRNA, none of these risk or protective factors were statistically significant.

Conclusion: Young women, social health workers, ethnic minority groups, and people with chronic diseases are the completely vaccinated contacts with the highest risk of having COVID-19, after primary cases also vaccinated in the family, in Toledo (Spain), when the delta variant became dominant but before the rise of omicron.

Keywords: COVID-19; SARS-CoV-2; Household contact; Vaccination; Breakthrough Infection; Relative Risks; General Practice; Spain

Introduction

COVID-19 vaccinations are effective and will be crucial in ending the pandemic. Vaccines that are currently available appear to restrict infection and viral replication, lowering viral loads below the threshold for transmission and preventing symptoms (1). However, no vaccination is 100 percent effective, and even among completely vaccinated people, there will be a small number of COVID-19 infections, hospitalizations, and deaths (2). Furthermore, it has been noted that, unlike prior versions, vaccinated patients infected with Delta and other future forms may be able to transmit it more easily (3, 4).

The global immunization campaign is expected to

control the pandemic caused by the severe acute respiratory syndrome coronavirus 2. (SARS-CoV-2). However, there are still questions concerning the virus's long-term relationship with humans, as well as which coronavirus disease types will be prevalent in the future (COVID-19) (5).

It's possible that the vaccine minimizes transmission because it reduces asymptomatic SARS-CoV-2 infection. However, there is a scarcity of data from clinical trials and observational investigations (6). In this context, houses are the primary locations of SARS-CoV-2 transmission worldwide (7), and it is unknown if individual SARS-CoV-2 vaccination protects family members at home (6).

Furthermore, epidemiological evaluation studies of transmissibility in most viral infectious diseases (the probability that a pathogen spreads from an infected individual to an uninfected individual) and family heterogeneity are uncommon; thus, risk factors for transmission in a household, given an index case, are unknown. Many respiratory viruses are dependent on time and proximity (8 – 10), even though the standard depiction of "transmission chains" helps to break out some of the parameters that affect transmission. However, the pathogen has received all the attention, and it is not only about the variation, but also about the host and the environment (11).

The majority of COVID-19 patients are cared for at home, which raises the risk of exposure for family members. Family members and others who care for people with COVID-19 in the community, on the other hand, have received less attention (12). Transmission at home before to vaccination was, predictably, prevalent (13, 14). In this context, the current study sought to determine potential risk factors for SARS-CoV-2 transmission from people who had received all of their vaccines to other family members who had received all of their vaccines.

Materials and methods

From February 1 to November 30, 2021 (before the COVID-19 Vaccine Booster was introduced), an observational, longitudinal, and prospective study of all families in which at least one case of COVID-19 breakthrough infection was diagnosed in vaccinated people with a full vaccination schedule and at least one other member in the household was conducted in a general medicine office in Toledo, Spain, with a list of 2,000 patients > 14 years of age (in Spain, general practitioners (GP) is referred to as "GPs" GPs in Spain work under the public National Health System and serve as the system's entry point for all patients. Each person is allocated to a GP (15). The study's general methodology has already been published (16).

Criteria for inclusion and exclusion of participants

All families in which a case of COVID-19 was diagnosed in a fully vaccinated person throughout the study period, had at least one member of the family exposed to infection transmission, were attending the same consultation, and their medical information was accessible were included.

1. Diagnosis of COVID-19 breakthrough infections in vaccinated people:

Because vaccines take roughly two weeks to gain

maximum effectiveness, a person is not considered fully vaccinated until two weeks after receiving the recommended number of doses for the vaccine. As a result, a case of COVID-19 vaccination breakthrough is defined as someone who tests positive (reverse transcriptase polymerase chain reaction-PCR-or antigen) for COVID-19 after being completely vaccinated for public health purposes (2). To be considered fully vaccinated, a person had to:

A. That they received two vaccine doses separated by at least 19 days if the first dose was BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech), 21 days if the first dose was ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford / AstraZeneca), or 25 days if the first dose was mRNA-1273 vaccine (Spikevax, formerly COVID-19 (Spikevax). Those who had the Janssen vaccine (Johnson & Johnson vaccine) more than 14 days ago were also regarded completely immunized.

B. Or, that they have received a dosage of any of the vaccinations after having passed the sickness, following a minimum period of time equal to that established for the second doses.

C. It was considered fully vaccinated after 7 days if the second dose was with Comirnaty, or after 14 days if it was with the Moderna vaccine, in the heterologous regimen in which Vaxzevria (Oxford/AstraZeneca) was used in the first dose and mRNA vaccines in the second (17).

2. Diagnosis of COVID-19:

Antigen testing or reverse transcriptase polymerase chain reaction (PCR) oropharyngeal swab tests were used to make the diagnosis. For symptomatic individuals with fewer than 5 days of evolution, rapid antigen tests were started. Both symptomatic patients and asymptomatic contacts were tested with PCR. Asymptomatic carriers and confirmed cases were among the cases. The registration systems used by general medical services in the consultation were utilized to acquire information on COVID-19 patients and their contacts. Any person with a clinical picture of rapid onset acute respiratory infection of any severity, including fever, cough, or shortness of breath, was classified as a symptomatic confirmed case with active infection. According to clinical criteria, other symptoms such as odynophagia, anosmia, ageusia, muscle pain, diarrhea, chest discomfort, or headache were also deemed signs of suspected SARS-CoV-2 infection, and a positive PCR or fast antigen test was positive (17).

3. Household contacts:

People who lived in the same house as the COVID-19 index case were considered household contacts. We classified family members as people who lived in the same residence as the major cases for 14 days before and for more than 24 hours after they experienced COVID-19-related sickness. The time definition of transmission from 1 to 14 days was used to catalog the supposed domiciliary transmission from an index case in the residences (18, 19). The initial appearance of self-reported clinical symptoms was designated as the onset date of a verified case (20). The date a positive COVID-19 PCR test was acquired was used to determine the onset date for an asymptomatic carrier (20). Five to seven days following close contact with a person with confirmed COVID-19, household contacts (people with full immunization schedule included) with no COVID-19 symptoms were screened (21). In the first 24 hours after a person suspected of having SARS-CoV-2 infection, they were all tested for active SARS-CoV-2 infection (17).

4. Isolation measures at home:

In the cases of COVID-19, isolation was maintained for at least 10 days after the beginning of symptoms, and for at least three days following the remission of the fever and clinical picture. Following the discovery of a primary case of COVID-19 breakthrough infection in a vaccinated family member, family members who were not vaccinated or had an incomplete vaccination schedule were advised to be isolated for 10 days; family members who had completed their vaccination schedule were not isolated. Only avoiding contact with vulnerable persons, wearing a mask in social interactions, not attending mass gatherings, and monitoring the likely appearance of similar symptoms were recommended in these circumstances (20).

Outcomes of interest:

1. The characteristics obtained were examined as predictors (potential risk factors) of SARS-CoV-2 transmission from those who had received a full vaccination schedule to other members of the family who had also received a full vaccination schedule. In this way, the variables were compared by calculating the relative risk (RR) as the incidence among the exposed population divided by the incidence among the population not exposed to potential risk factors. The RR informs clinicians of a patient's increased risk

of being exposed to a risk factor and also helps to identify persons who are at high risk, but it does not indicate the likelihood that someone with the risk factors would develop the disease. The following is how the RR was read (22):

- 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

2. The efficacy of each particular type of vaccine (VE) used in secondary cases, which was estimated as a percentage: $[1 - RR (\text{Incidence of COVID-19 among the exposed population to a given type of vaccine} / \text{Incidence of COVID-19 among the population not exposed to that particular type of vaccine}) * 100]$ (23).

Collected variables:

From the medical records of the general medicine practice under investigation, data on the index case and close connections were collected. The variables that were gathered were:

- Primary case or secondary case
- Age and sex
- "Any change or deviation from normal that has one or more of the following characteristics" is defined as Chronic disease; it is permanent, results in residual impairment, is caused by a pathological alteration (non-reversible), needs special training of the patient for rehabilitation, and/or can be expected to require a long period of control, observation, or treatment" (24), and is classified using the International Statistical Classification of Diseases and Health-Related Conditions (25)
- Social-occupancy class (according to the Registrar General's classification of occupations and social status code) (26, 27)
- If they were Health Care Workers
- Problems in the family context and low-income households based on the genogram and the GP's experience for continuity of care and family knowledge (a genogram is a schematic model of the structure and processes of a family that includes the family structure, life cycle, and family relational patterns). Families with "complex" genograms were thought to have psychosocial issues. (28-31)
- Number of family members
- Ethnic minority
- Comirnaty (Pfizer-BioNTech-BNT162b2 mRNA; Pfizer / BioNTech), Vaxzevria (AstraZeneca), and

Janssen / Johnson & Johnson vaccine (The European Commission has currently approved four vaccines: Comirnaty, Pfizer / BioNTech, which was approved on December 21, 2020; Moderna, which was approved on January 6; AstraZeneca, which was approved on December 29; and Janssen / Johnson & Johnson, which was approved on March 11. These four vaccinations, all of which have been approved by the European Medicines Agency, are currently available in Spain. (32)

Statistical analysis:

The Chi Square test (X^2), X^2 with Yates correction, or Fisher Exact Test (according to the predicted cell totals) for percentages, and the Student's t-test for the mean, were used for bivariate comparisons.

Results

In addition to the primary case of COVID-19 breakthrough infection, thirteen primary cases in 13 families with at least one other family member were included, totaling 46 people. The study's overall findings have already been published (16). In these 13 families, a total of 33 people were exposed, with 9 positive secondary cases (sick) in fully vaccinated people and 8 negative partners (healthy) in fully vaccinated people (Figure 1). Being a woman, being >45 years old, being a social health professional, being an ethnic minority, and presenting any chronic disease were all risk factors for having COVID-19 in completely vaccinated contacts, of main cases also fully vaccinated in the family (within these, blood and nervous and senses groups). Being male, being > 65 years old, and having chronic disorders of the mental and genitourinary groups were all protective factors for not developing COVID-19 in entirely vaccinated contacts, of main cases also completely vaccinated in the family. The BNT162b2 mRNA vaccine (Comirnaty, Pfizer/BioNTech) and the 2ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford/AstraZeneca) were the only vaccines used. Vaccine efficacy was higher in individuals who received 2ChAdOx1 nCoV-19 than in those who received BNT162-2 mRNA. However, statistically, none of these risk or protective factors were significant (Table 1, Table 2, and Table 3).

Discussion

COVID-19 vaccinations lower the risk of infection and infectivity associated with it (33–35). However, it has become obvious that some persons can contract COVID-19 despite receiving a complete vaccine,

particularly if they are older or immunocompromised, or if longer intervals have passed since the second dose. Those who contract COVID-19 despite being completely vaccinated are far less contagious to their contacts, who are protected from infection if they are also fully vaccinated (36). A person who has been vaccinated may become infected again if their defenses have not responded well to the vaccines; second, if the vaccines have lost potency after several months, which can happen in people with a weak immune system; and third, if they have risk factors such as diabetes, obesity, or asthma (37).

Vaccine-induced immunity has four important properties that can minimize transmission, and vaccines can theoretically suppress SARS-CoV-2 at all phases to prevent transmission: 1. Infection: When the virus infects the target cells at the exposure site, it causes infection. As a result, even if vaccinations are as successful in preventing Delta infections as they were with earlier variations, if Delta is more infectious, household transmission may increase (38, 39). 2. Viral replication: If a virus replicates at a high enough level within its host, it can spread from host to host. According to research, only a small percentage of those who have been vaccinated have significant virus loads (40). The most potent immunizations appear to significantly reduce viral replication and thereby transmission (39); 3. 4. Degree of symptomatology: vaccinations can trigger immune responses that limit the infectivity of the virus released; and 5. Threshold for transfer from host to host: vaccines can further reduce the degree of transmissibility by reducing symptoms (e.g., coughing and sneezing); and (1). Transmission is determined not only by the susceptibility of the contacts, but also by the infectivity of the cases, and while vaccination lowered susceptibility, it did not appear to reduce infectivity (41, 42).

Main findings:

Our study's main finding is that current vaccines appear to have only moderate efficacy in preventing COVID-19 transmission in fully vaccinated contacts of primary cases who are also fully vaccinated in their family, with women, those 45 years or older, socio-health workers, and those with chronic diseases being at higher risk.

Table 1. Comparison of the variables studied between positive secondary cases and negative partners in fully vaccinated people (healthy)

Risk factors	Positive secondary cases (sick) in fully vaccinated people (N=9)	Negative partners (healthy) in fully vaccinated people (N=8)	Statistical significance	Relative risk (RR)
-Woman	5 (56%)	3 (37%)	X ² with Yates correction= 0.0664. p= .796643. NS	RR= 1.41 (CI 95%: 0.11, 18.8). <i>Weak risk</i>
> = 65 years	2 (22%)	3 (37%)	Fisher exact test= 0.6199. NS	RR= 0.69 (CI 95%: 65.01, 0.01). <i>True benefits</i>
< = 45 years	5 (56%)	1 (12%)	Fisher exact test= 0.1312. NS	RR= 2.29 (CI 95%: 0.69, 7.63). <i>Moderate risk</i>
-Workers with some type of specialization	2 (22%)	2 (25%)	Fisher exact test= 1. NS	RR= 0.93 (CI 95%: 1.28, 0.67). NS
-Socio-health workers	3 (33%)	0	Fisher exact test= 0.2059. NS	RR= 2.33 (CI 95%: 0.56, 9.73). <i>Moderate risk</i>
-Ethnic minority	1 (11%)	0	Fisher exact test= 1. NS	RR= 2 (CI 95%: 0, 13635671207.68). <i>Moderate risk</i>
-Low income household	0	0	Fisher exact test= 1. NS	NaN
-Complex family	0	0	Fisher exact test= 1. NS	NaN
-Family with > = 4 members	6 (67%)	5 (62%)	Fisher exact test= 1. NS	RR= 1.09 (CI 95%: 0.65, 1.82). NS
-Presence of chronic diseases	8 (89%)	5 (62%)	Fisher exact test= 0.2941. NS	RR= 2.46 (CI 95%: 0.2, 29.52). <i>Moderate risk</i>

(): Denotes percentages of total in patients (positive PCR) and in healthy (negative PCR and asymptomatic); NS: Not significant at p< .05; CI: Confidence interval; NaN: "It is not a Number" (it is a value that is usually returned as the result of an operation with invalid input operands); RR: Relative risk

Table 2. Comparison of chronic diseases between positive secondary cases and negative partners in fully vaccinated people (healthy)

Chronic diseases according to WHO, ICD-10 Groups	Positive secondary cases (sick) in fully vaccinated people (N=9)	Negative partners (healthy) in fully vaccinated people (N=8)	Statistical significance	Relative risk (RR)
-II Neoplasms	0	0	Fisher exact test= 1. NS	NaN
-III Diseases of the blood	1 (4%)	0	Fisher exact test= 1. NS	RR= 1.77 (CI 95%: 0, 3077.21). Moderate risk
-IV Endocrine	6 (26%)	5 (29%)	X ² with Yates correction= 0.0157. p= .900242. NS	RR= 0.93 (CI 95%: 2.78, 0.31). NS
-V Mental	1 (4%)	1 (6%)	Fisher exact test= 1. NS	RR= 0.86 (CI 95%: 1.54, 0.48). True benefits
-VI-VIII Nervous and Senses	1 (4%)	0	Fisher exact test= 1. NS	RR= 1.77 (CI 95%: 0.31, 7.21). Moderate risk
-IX Circulatory system	4 (18%)	3 (18%)	X ² with Yates correction= 0.1599. p= .689272. NS	RR= 0.99 (CI 95%: 1.04, 0.94). NS
-X Respiratory system	2 (9%)	1 (6%)	Fisher exact test= 1. NS	RR= 1.17 (CI 95%: 0.37, 3.66). NS
-XI Digestive system	3 (13%)	2 (12%)	Fisher exact test= 1. NS	RR= 1.05 (CI 95%: 0.81, 1.37). NS
-XII Diseases of the skin	0	0	Fisher exact test= 1. NS	NaN
-XIII Musculo-skeletal	5 (22%)	4 (23%)	X ² with Yates correction= 0.062. p= .803412. NS	RR= 0.96 (CI 95%: 1.32, 0.7). NS
-XIV Genitourinary	0	1 (6%)	Fisher exact test= 0.425. NS	RR= 0 (CI 95%: Infinity, 0). Protection factor effectively
Total*= Total	23 (100%)	17 (100)	---	---

*Patients could have more than one chronic disease. The percentages are over the total of chronic disease; NS: Not significant at p< .05; CI: Confidence interval; NaN: "It is not a Number" (it is a value that is usually returned as the result of an operation with invalid input operands); RR: Relative risk

Table 3. Comparison of vaccine types between positive secondary cases and negative partners in fully vaccinated people (healthy)

Vaccine types	Positive secondary cases (sick) in fully vaccinated people (N=9)	Negative partners (healthy) in fully vaccinated people (N=8)	Statistical significance	Relative risk (RR)	Vaccine Effectiveness [VE= (1 – RR) * 100]
BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech)	6 (67%)	5 (62%)	Fisher exact test= 1. NS	RR= 1.09 (CI 95%: 0.65, 1.82). NS	VE= (1-1.09) * 100= -9% (The incidence rate of COVID-19 in those vaccinated with BNT162b2 mRNA is greater than the number of COVID-19 cases in subjects not vaccinated with said vaccine, but vaccinated with 2ChAdOx1 nCoV-19)
2ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford /AstraZeneca)	3 (33%)	3 (38%)	Fisher exact test= 1. NS	RR= 0.92 (CI 95%: 1.51, 0.56). NS	VE= (1-0.92) * 100= 8% (The incidence rate of COVID-19 in those vaccinated with 2ChAdOx1 nCoV-19 is less than the number of COVID-19 cases in subjects not vaccinated with said vaccine, but vaccinated with BNT162-2 mRNA)
TOTAL	9 (100%)	8 (100%)	---	---	---

NS: Not significant at p< .05; CI: Confidence interval; VE: Vaccine effectiveness; RR: Relative risk

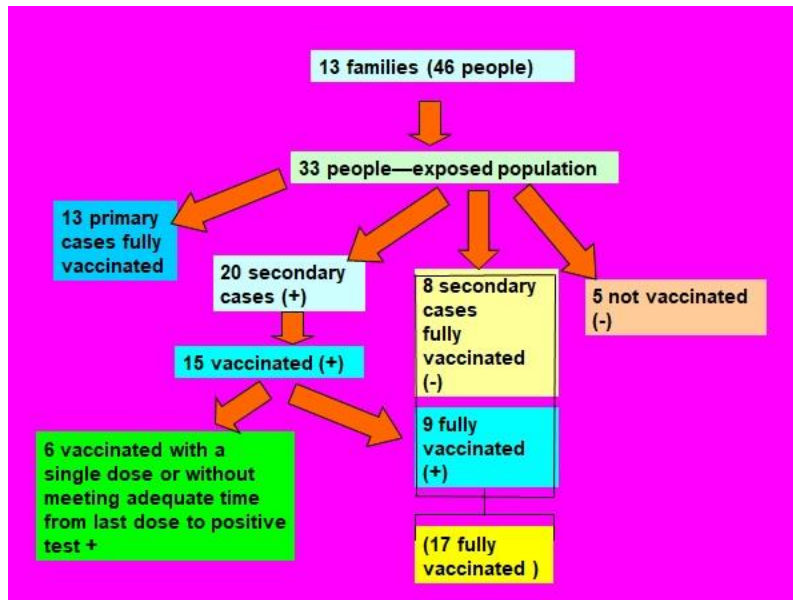


Figure 1. General outline of the study

Similar and different studies:

To calculate it, the risk of something happening (in this case, getting sick with COVID-19 inside the family despite having been vaccinated) when exposed to something (in this case, COVID-19 Breakthrough Infection in a fully vaccinated family member) must be estimated (22). Individual risk of contracting COVID-19 after vaccination is determined by a number of factors that differ from person to person, including general health, where they live and with whom they live, local conditions, precautions taken, and the frequency with which people are exposed to other people who may be carriers of the virus (43). Patient features (for example, age), circumstances (for example, time from vaccination), and virus characteristics (for example, lineage) can all influence the chance of infection following a vaccine (1).

[1-RR (Incidence of COVID-19 among the exposed population to a specific kind of vaccine/Incidence among the population not exposed to that specific type of vaccine) x 100] was used to calculate the VE of each type of vaccination employed in our investigation. (23). In this regard, it was revealed that the contagion rate at home between two vaccinated people was 27 percent in an inquiry conducted between April and October 2021 with the analysis of more than 30,000 cases of contagion between close contacts, both domiciliary and non-domiciliary (23, 44).

The presence of comorbidities has been shown to reduce vaccination efficacy (23). Immunosuppression, diabetes, obesity, and asthma would all be risk factors for COVID-19 infections in patients who had been vaccinated (37, 45). Chronic illnesses were observed to increase the probability of COVID-19 infection in completely vaccinated contacts (RR = 2.46; Moderate risk). Being 45 years old was discovered to be a risk factor (RR = 2.29; moderate risk). However, persons over the age of 60 are at a larger risk since immunizations have a reduced protective impact (18). Being a woman (RR = 1.41; weak risk) and being a socio-health worker (RR = 2.33; moderate risk) were revealed to be risk factors for having COVID-19 in completely vaccinated contacts of primary cases who were also fully vaccinated in the family. In the COVID-19 pandemic, it was already noted that women experience more psychosocial consequences in regard to job, family, intra-family transmission and childcare, quarantine, and other factors, which is exacerbated by the fact that the majority of health workers are women (46). In our culture, women are more eager to care for the home and children, which includes activities such as grocery shopping. Other research on household infections in the immunized suggest that women are at a higher risk than men (23). In contrast, we discovered in our study that being an ethnic minority increased the probability of presenting COVID-19 in fully vaccinated contacts of a primary

case (RR = 2.00; moderate risk). This information could be connected to unsafe conduct. The variation of risk attitudes among poor households in wealthy nations is little understood. Heads of families with lower risk aversion may be willing to take on more risk, and there has been evidence of a negative association between household size and risk aversion (47).

Furthermore, it should be noted that in our study, the index case's fully vaccinated family members did not perform isolation, despite being urged to wear masks and prevent close contact. The contagion rate at home is lower (15%) when the infected individual is not vaccinated and their contact is vaccinated than when two vaccinated people are together (27%) and also when the index case is vaccinated but their spouse is not vaccinated (41 percent). To explain why this percentage is lower than when both parents are vaccinated, it is thought that when both parents are vaccinated, there are fewer preventative measures in place at home (23, 44).

COVID-19 vaccines are not all created equal. The two mRNA vaccines are clearly highly successful at preventing illnesses caused by early variations (before Delta and Omicron) (48). At 24 weeks, the chance of COVID-19 outcomes was reported to be lower with mRNA-1273 than with BNT162b2; this pattern was similar during the periods when the alpha and delta variants predominated (49). Among completely vaccinated secondary cases, we found no statistically significant changes in risk based on vaccine type. Vaccine efficacy was higher in individuals who received 2ChAdOx1 nCoV-19 than in those who received BNT162-2 mRNA. Due to the small number of participants included, these findings should be interpreted with caution.

Study limitations:

1. It should be noted that changes in community transmission throughout the study period may imply changes in personal protective actions in some way, which could cause confusion when interpreting the results of the risk of infection secondary in the family.
2. If the virus in the secondary case was truly obtained outside the home, it's possible that transmission at home was misclassified. Genomic data has not been integrated with epidemiological contact tracing data.
3. Because our selection of families is opportunistic rather than probabilistic, sample bias is a possibility. Because GPs in Spain constitute the gateway to the health system, the vast majority of COVID-19 breakthrough infections among vaccinated family members were likely included (15).
4. Finally, the sample size is modest, which may

restrict the statistical significance of the findings.

Conclusion

Most COVID-19 patients are cared for at home, increasing the risk of exposure for family members. These vaccines appear to have only moderate efficacy in preventing the transmission of COVID-19 in fully vaccinated contacts of primary cases also fully vaccinated in the family in the context of general medicine in Toledo (Spain) on the dates the study was carried out (with an increase in the prevalence of the Delta variant, but before the introduction of microns, and before starting the third dose of the vaccines), assuming greater risk in women, people aged 45, and people in their 50s. Vaccines prevent transmission, but easing restrictions can negate their effectiveness.

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