Family Secondary Cases from Covid-19 Breakthrough Infections in Vaccinated People

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ABSTRACT

Background: It is not clear whether vaccinating individual people against SARS-CoV-2 protects members of their households.

Objective: To study the prevalence and characteristics of secondary cases in family members after the appearance of a primary case of COVID-19 breakthrough infection

Methodology: An observational, longitudinal, and prospective study of families with one primary case of COVID-19 breakthrough infection was conducted from February 1 to November 30, 2021, in a general medicine office in Toledo, Spain.

Results: 13 primary cases in 13 families (46 people) were included. The crude secondary attack rate (secondary cases / exposed population with complete or incomplete vaccination (15/23) was 45%. The crude secondary attack rate in contacts with complete vaccination (9/17) was 53%. The vaccine effectiveness against transmission among households among contacts (Secondary attack rate in vaccinated / Secondary attack rate in unvaccinated) × 100%= 53/69) was 77%. All secondary cases were mild. Secondary cases were more young women with a lower socio-occupational level.

Conclusion: In the context of general medicine in Toledo (Spain), when the delta variant became dominant, but before the rise of omicron, vaccination reduces but does not eliminate the risk of COVID-19 transmission within homes (crowded indoor environments), which remain important places for transmission. It is suggested to re-evaluate the protocol that vaccinated family contacts do not require isolation.

Keywords: COVID-19; SARS-CoV-2; Household Contact; Secondary Attack Rate; Vaccination; Breakthrough Infection; General Practice.

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Introduction

Real-world evidence from vaccine implementation programs has shown that coronavirus disease (COVID-19) vaccines are highly effective against serious illness, hospitalization, and death.[1] But no vaccine is 100 percent effective and there will be a small percentage of COVID-19 cases among fully vaccinated individuals.[2] In addition, attention has been drawn to the fact that vaccinated people infected with Delta, or other new variants, could more easily transmit it. Some initial findings indicate that virus levels in those who become infected with Delta after being vaccinated may be similar to levels found in unvaccinated people. This can have implications for the infectivity of people, whether they have been vaccinated or not.[3-5]

Homes are the site of most of the global severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission; However, family contagions are not routinely studied, epidemiological evaluation studies of transmissibility and household heterogeneity in the family are not

frequent, so less is known about its effects on transmission between individuals in families.[6,7]

Control of the SARS-CoV-2 pandemic requires targeted interventions, which in turn need precise estimates of quantities that describe transmission. Per-capita transmission rates are influenced by four quantities: (1) the latent period (time from infection to becoming infectious); (2) individual variability in infectiousness (defined by variation in intrinsic transmissibility and contact rate); (3) the incubation period (time from infection to symptom onset); and (4) the serial interval (time between symptom onset of an infector and an infected); These variables can vary depending on disease-mitigating interventions, family size, and population structure, as well as the inherent properties of the SARS-CoV-2 variant.[8]

The majority of people with COVID-19 receive care at home, which increases the probability of exposure of household members. Since vaccination reduces asymptomatic SARS-CoV-2 infection, it is plausible that the vaccine reduces transmission within the home; however, data from clinical trials and observational studies are lacking (1, 9), and it is unclear whether vaccinating individuals against SARS-CoV-2 protects members of their households.[9]

Assessing how well SARS-CoV-2 vaccines can reduce transmission has important epidemiological, social, and policy implications, as ineffective reduction of transmission by vaccines would hamper efforts to achieve herd immunity.[7]

Observational studies are emerging as critical sources of information on vaccine effectiveness outside of the controlled setting of randomized trials, and are being used to generate evidence of effectiveness. These studies can monitor the decline in vaccine effectiveness or measure the performance of vaccines against new variants of SARS-CoV-2 when large randomized controlled trials are not possible.[10]

In this context, the present study aimed to quantify the frequency of secondary home transmission of SARS-CoV-2, from COVID-19 breakthrough infections in vaccinated people to other family members, and to characterize its clinical-epidemiological characteristics.

Material and Methods

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 with at least one other member in the household, was conducted, from February to November 30, 2020 (before beginning with COVID-19 Vaccine Booster), in a general medicine office in Toledo, Spain, which has a list of 2,000 patients> 14 years of age (in Spain, the general practitioners [GPs] care for people > 14 years of age, except for exceptions requested by the child's family, and accepted by the GP). 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.[11]

Outcome of interest

The outcomes of interest were:

1. To assess secondary transmission of SARS-CoV-2 from people vaccinated with the full schedule to other members of the family. For this, secondary attack rate after contact with a primary case of COVID-19. breakthrough infection in fully vaccinated people, in the family, was calculated.
2. Calculate vaccine effectiveness against transmission among household contacts.
3. Describe the clinical-epidemiological characteristics of the primary and secondary cases.

Because the vaccines require about two weeks reaching their maximum effectiveness, a person is not considered fully vaccinated until two weeks after they completed the recommended number

Diagnosis of COVID-19 breakthrough infections in vaccinated people

of doses for the vaccine they received. Therefore, for public health surveillance purposes, a case of COVID-19 vaccine breakthrough is defined as someone who tests positive (reverse transcriptase-polymerase chain reaction -PCR- or antigen) for COVID-19 being fully vaccinated.[2]

To consider a person as fully vaccinated, it was required (12):

1. That they have received 2 doses of vaccine separated by a minimum of 19 days if the first dose was BNT162b2 mRNA vaccine (Comirnaty, Pfizer/BioNTech), 21 days in the case of ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford / AstraZeneca) or 25 days in the case of mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna), and that a minimum period of 7 days has elapsed since the last dose if the last dose was with BNT162b2 mRNA vaccine (Comirnaty), or 14 days if it was with ChAdOx1 nCoV-19 vaccine (Vaxzevria) or mRNA-1273 vaccine (Spikevax). People who received a dose of Janssen vaccine (Johnson & Johnson vaccine) more than 14 days ago were also considered fully vaccinated.

2. Or, that having passed the disease they have received a dose of any of the vaccines, after the minimum period equal to that established for the second doses.

3. In the heterologous regimen in which Vaxzevria (Oxford/AstraZeneca) is used in the first dose and mRNA vaccines in the second, 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.

The diagnosis of COVID-19

The diagnosis was performed with reverse transcriptase-polymerase chain reaction (PCR) oropharyngeal swab tests or antigen testing. Rapid antigen tests began to be carried out for symptomatic patients with less than 5 days of evolution. The PCR tests were performed both in symptomatic patients and in asymptomatic contacts. The cases included confirmed cases and asymptomatic carriers. Information on COVID-19 patients and their contacts was obtained from the registry systems used by general medical services in the consultation. Asymptomatic 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; and a positive PCR or rapid antigen test positive.[13]

Secondary attack rate

Secondary attack rate was defined as the number of new cases divided by the number of people exposed to a primary case. The existence of second or third-generation cases was not assessed. The cases for the determination of the attack rate included confirmed symptomatic cases and asymptomatic cases.

Household contacts

Household contacts were defined as people who shared a residence with the COVID-19 index case. We defined family members as those who had lived with primary cases in a house 14 days before and for more than 24 hours after the primary cases developed illness related to COVID-19. The presumed domiciliary transmission from an index case in the homes was cataloged using the time definition of secondary transmission from 1 to 14 days.[14] The onset date of a confirmed case was defined as the date of the first appearance of self-reported clinical symptoms.(15) The onset date for an asymptomatic carrier was defined as the date a positive COVID-19 PCR test was obtained.[15] Household contacts (not vaccinated or not fully vaccinated and people with full vaccination schedule) with no COVID-19 symptoms were screened 5 to 7 days after close contact with a person with confirmed COVID-19.[16] Every person with suspected infection underwent a diagnostic

test for active SARS-CoV-2 infection in the first 24 hours.[13]

Isolation measures at home

In the cases of COVID-19, isolation was maintained until three days after the resolution of the fever and the clinical picture, with a minimum of 10 days from the onset of symptoms. After the diagnosis of a primary case of COVID-19 breakthrough infection in a vaccinated family member, isolation for 10 days was advised only to family members who were not vaccinated or with an incomplete schedule; Family members with a complete vaccination schedule were not isolated; In these last cases, it was advised only to avoid contact with vulnerable people, to wear a mask in their social interactions, not to attend mass events, and to monitor the possible appearance of compatible symptoms.[13]

Calculation of vaccine effectiveness against transmission among household contacts

We calculated the vaccine effectiveness against transmission via the secondary attack rate among close contacts of confirmed index cases (17, 18), as follows:

(Secondary attack rate in vaccinated/secondary attack rate in unvaccinated) × 100.

Collected variables

Data on the index case and close contacts were extracted from the medical records of the general medicine practice under study. The following variables were collected:

1. Primary case or secondary case

2. Age and sex

3. Symptoms

4. 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" (19), classified according to the International Statistical Classification of Diseases and Health-Related Problems, CD-10 Version: 2019.[20]

5. Duration of symptoms in days.

6. Social-occupancy class (according to the Registrar General's classification of occupations and social status code).[21,22]

7. If they were Health Care Workers.

8. Problems in the family context and low income household, both based on the genogram and in the experience of the general practitioner (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).[23-26]

9. Number of family members

10. Ethnic minority

11. Symptomatic / asymptomatic COVID-19

12. Time in days since the last vaccine dose

13. the 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 ≤ 300 mmHg).[15] To simplify the comparison, moderate and severe cases were counted together.

14. Vaccine type: Comirnaty (Pfizer-BioNTech-BNT162b2 mRNA; Pfizer / BioNTech), Moderna-mRNA-1273 mRNA, Vaxzevria (AstraZeneca), and Janssen / Johnson & Johnson vaccine (Currently, the European Commission has licensed four vaccines: Comirnaty, Pfizer / BioNTech, licensed December 21, 2020; Moderna vaccine, licensed January 6; AstraZeneca vaccine, licensed 29 December and the Janssen / Johnson & Johnson vaccine, authorized on March 11. In Spain, these four vaccines are currently available, all of which have been approved by the European Medicines Agency).[27]

Sample

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

Statistic analysis

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

Results

Thirteen primary cases (10 men and 3 women) were included in 13 families with at least other family members in addition to the primary case of COVID-19 breakthrough infection, representing a total of 46 people. The average size (arithmetic mean + - standard deviation) of family was 3.5 + - 2.2 members. The exposed population in these 13 families was 33 people, of which 20 were secondary positive cases positive cases (10 men and 10 women); of those 20 secondary cases and therefore positive, 15 were vaccinated (9 fully vaccinated and 6 vaccinated with a single dose or without meeting adequate time from the last dose to positive test). Of the 33 people exposed, there were 5 people who were not vaccinated, and these were negative.**(Figure 1)**

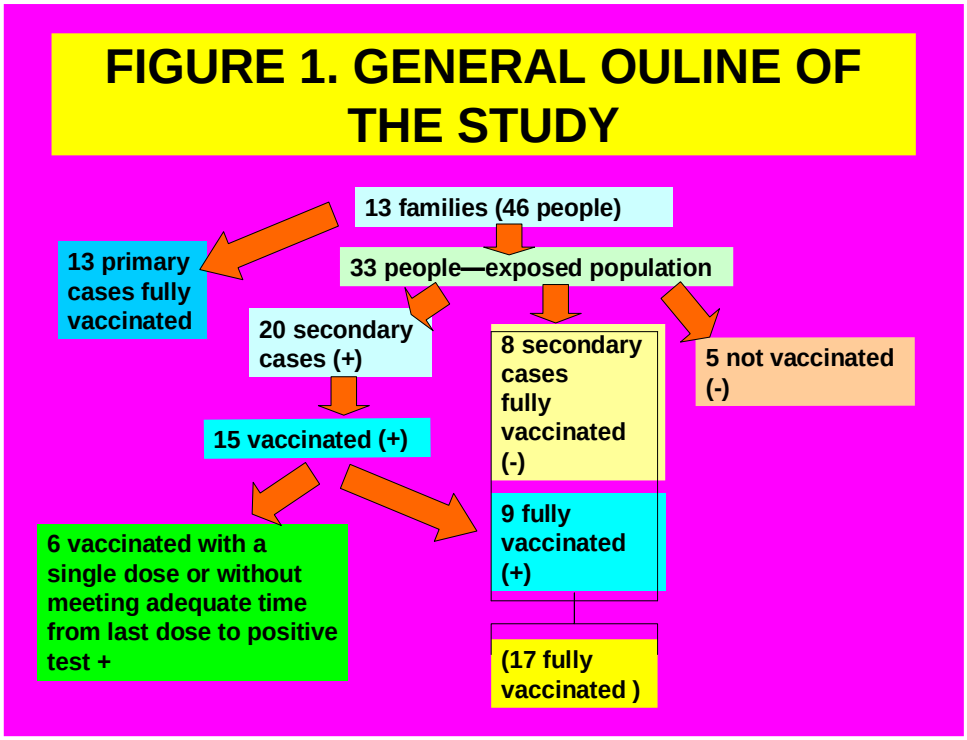

Figure 1: General Outline of the Study

The secondary attack rate (secondary cases/population exposed with complete or incomplete vaccination = 15/23) was 45%. The secondary attack rate in fully vaccinated contacts was 9/17 (53%). Vaccine effectiveness against transmission among household among contacts [(Secondary attack rate in vaccinated / Secondary attack rate in unvaccinated) × 100%] (53/69) was 77%.

All secondary cases were mild, and 80% were symptomatic. The only statistically significant differences found between primary cases and secondary cases were that the secondary cases of primary cases of COVID-19 breakthrough infections in fully vaccinated people were more young women, with a lower socio-occupational level and with fewer chronic genitourinary diseases. There were no differences between the symptoms of primary and secondary cases. There were significantly more primary cases vaccinated with Janssen (Johnson & Johnson vaccine). **(Table 1, Table 2, Table 3, Table 4, Table 5, and Table 6).**

Variables	Primary Cases N=13	Secondary Cases N=20	Statistical Significance
Men	10 (77)	10 (50)	X2= 2.392. p= .121957. NS
Men-Age (Arithmetic mean + - Standard deviation)	58.1 +- 10.3	36.1 +- 25.6	t= 2.51298. p-value= .010857. The result is significant at p < .05.
Women	3 (23)	10 (50)	X2= 2.392. p= .121957. NS
Women — Age (Arithmetic mean + - Standard deviation)	70.3 +- 15.3	52.7 +- 13.3	t= 1.95422. p= .038282. The result is significant at p < .05.
>= 65 years	5 (38)	4 (20)	X2 with Yates correction= 0.5831. p= .445118. NS
Children and adolescents <= 22 years	0	4 (20)	Fisher exact test= 0.1359. NS
Age in years (Arithmetic mean and Standard deviation)	60.9 +- 12.2	44.4 +- 21.6	t= 2.49781. p= .009006. The result is significant at p < .05.
Socio-health workers	2 (15)	4 (20)	Fisher exact test= 1. NS
Social-occupancy class of patients (people with some type of labor specialization)	5 (38)	1 (5)	Fisher exact test= 0.0248. The result is significant at p < .05.
Complex family	0	0	Fisher exact test= 1. NS
-Ethnic minority	1 (8)	4 (20)	Fisher exact test= .6253. NS
-Low income household	0	0	Fisher exact test= 1. NS
-Asymptomatic	0 (only symptomatic primary cases were chosen)	4 (20)	NR
-Symptomatic	13 (100)	16 (80)	NR
-Moderate-severe severity	3 (23) (3 pneumonia)	0	Fisher exact test= 0.0524. NS
-Duration of symptoms (Arithmetic mean and Standard deviation)	7.3 +- 5.7	(N=16) 5.1 +- 2.1	t= 1.45536. p= .078549. NS
-Incubation period (Arithmetic	NA	(n=16)	NR

mean and Standard deviation) (Arithmetic mean and standard deviation)		2.8 +- 1.4	
-Chronic diseases presence	10 (77)	12 (60)	X2 with Yates correction= 0.3966. p= .528832. NS

( ): Denotes percentages; NA: No disponible; NR: Not relevant; NS: Not significant

Table 1: Comparison of Selected Variables in Index Cases and Secondary Cases

SYMPTOMS * According to Who, ICD-10 Groups	Primary Cases N=13	Secondary Cases N=20	Statistical Significance
General (discomfort, asthenia, myalgia, fever, artralgias)	17 (44)	14 (32)	X2= 1.2243. p= .268513. NS
Respiratory (cough, dyspnea, chest pain)	10 (26)	8 (18)	X2= 0.6773. p= .410511. NS
ENT (Anosmia / ageusia, odynophagia, rhinorrhea, pharyngeal dryness-mucus, epixtasis)	7 (18)	15 (34)	X2= 2.7655. p= .096319. NS
Digestive (anorexia, nausea / vomiting, diarrhea, abdominal pain)	3 (7)	0	Fisher exact test= 0.0995. NS
Neurological (headache, dizziness, mental confusion -brain fog)	2 (5)	6 (14)	X2 with Yates correction= 0.8803. p= .348113
Psychiatric (Anxiety, insomnia)	0	1 (2)	Fisher exact test= 1. NS
Skin (chilblains, flictenas, rash)	0	0	Fisher exact test= 1. NS
Total symptoms*	39 (100)	44 (100)	---

( ): Denotes percentages; NS: Not significant; * Patients could have more than one symptom. The percentages are over the total of symptoms.

Table 2: Comparison of Symptoms between Primary and Secondary Cases

Chronic Diseases According to Who ICD-10 Groups*	Primary Cases N=13	Secondary Cases N=20	Statistical Significance
-I Infectious	0	0	Fisher exact test= 1. NS
-II Neoplasms	1 (3)	0	Fisher exact test= 1. NS
-III Diseases of the blood	1 (3)	1 (4)	Fisher exact test= 1. NS
-IV Endocrine	7 (17)	7 (27)	X2= 1.0332. p= .309399
-V Mental	2 (5)	2 (8)	Fisher exact test= 0.6335. NS
-VI-VIII Nervous and Senses	4 (9)	2 (8)	Fisher exact test= 1. NS
-IX Circulatory system	6 (14)	5 (19)	X2 with Yates correction = 0.0397. p= .842017. NS
-X Respiratory system	2 (5)	0	Fisher exact test= 0.5206. NS

-XI Digestive system	9 (21)	3 (11)	X2 with Yates correction= 0.5074. p= .476251
-XII Diseases of the skin	0	0	Fisher exact test= 1. NS
-XIII Musculo-skeletal	6 (14)	6 (23)	X2 with Yates correction= 0.3562. The p= .550621. NS
-XIV Genitourinary	4 (9)	0	Fisher exact test= 0.0104. The result is significant at p < .05.
TOTAL chronic diseases*	42 (100)	26 (100)	---

( ): Denotes percentages; NS: Not significant;* Patients could have more than one chronic disease. The percentages are over the total of chronic diseases.

Table 3: Comparison of the Prevalence of Chronic Diseases between Primary and Secondary Cases

Variables Related to Covid-19 Vaccination	Primary Cases N=13	Secondary Cases N=20	Statistical Significance
Fully vaccinated	13 (100) (sólo se incluyeron casos primarios vacunados completamente)	9/20 (45)	NR
Vaccinated one dose or without meeting adequate time from last dose to positive test	0	6/20 (30)	NR
Fully vaccinated, or with a dose, or without meeting adequate time from last dose to positive test	13 (100)	15/20 (75)	NR
Not vaccinated	---	5/20 (25)	NR
Time in days from last dose of vaccine to positive COVID test (Arithmetic mean + - standard deviation; range)	84.7+- 54.7 (Range; 14-157 días)	(N=15 Fully vaccinated + vaccinated one dose or without meeting adequate time from last dose to positive test) 94.4 +- 59.4 (Range: 11-180 días)	t= -0.44649. p= .329472. NS
VACCINE TYPES	N=13	N=15 Fully vaccinated + vaccinated one dose or without meeting adequate time from last dose to positive test	----
BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech)	6 (46)	11 (73)	X2= 2.1569. p= .141929. NS
mRNA-1273 vaccine	0	0	Fisher exact test= 1.

(Spikevax, formerly COVID-19 Vaccine Moderna)			NS
2ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford /AstraZeneca)	2 (15)	4 (27)	X2 with Yates correction= 0.0696. p= .791892. NS
Janssen (Johnson & Johnson vaccine)	5 (39)	0	Fisher exact test= 0.0131. The result is significant at p < .05.
TOTAL	13 (100)	15 (100)	---

( ): Denotes percentages; NR: Not relevant; NR: Not significant

Table 4: Comparison of Variables Related to Covid-19 Vaccination between Primary and Secondary Cases

Covid-19 Vaccination Status in Population Exposed to Primary Cases	Covid-19 Positive N=20	Coved-19 Negative N=13	Total (exposed population) N = 33	Statistical Significance
Fully vaccinated	9 (45)	8 (61)	17 (52)	X2= 0.8628. p= .352957. NS
Incomplete vaccinated	6 (30)	0	6 (18)	Fisher exact test= 0.0598. NS
Not vaccinated	5 (25)	5 (38)	10 (30)	X2 with Yates correction= 0.1889. p= .663861. NS
TOTAL	20 (100)	13 (100)	33 (100)	---

( ): Denotes percentages; NS: Not significant

Table 5: Vaccination and Covid-19 Status in the 13 Families

Secondary Cases of Covid-19 Breakthrough Infections in Fully Vaccinated People After Index Cases of Covid-19 Breakthrough Infections in Vaccinated People within the Family	Gross Secondary Attack Rate	Secondary Cases of Covid-19 Breakthrough Infections in Partially Vaccinated People or No Vaccinated After Index Cases of Covid-19 Breakthrough Infections in Vaccinated People within the Family	Gross Secondary Attack Rate
9/17	53%	11/16	69%

Vaccine effectiveness against transmission among household among contacts = (Secondary attack rate in complete vaccinated / Secondary attack rate in incomplete or unvaccinated vaccinees) × 100 = 53 / 69=77%.

Table 6: Secondary Attack Rate among Contacts in the Family of Confirmed Index Cases with Covid-19 Breakthrough Infections in Vaccinated People and Vaccine Effectiveness Again Infection

Discussion

How is transmissibility measured?

It is measured by measuring the number of cases in the cohabitants of those who have been vaccinated, comparing them against the number of cases in the cohabitants of unvaccinated people. The domestic secondary attack rate characterizes the transmissibility of the virus. It should be noted that families/homes are closed spaces, where family members can huddle together and be in close contact with the conversation; also there may be reduced use of

personal protective equipment compared to other environments.[28] In this sense, outbreaks of COVID-19 cases have been described where vaccinated people become infected with SARS-CoV-2 and spread the virus to dozens of places,[29-31], and it is admitted that most of the transmission of the SARS-CoV-2 occurs in homes, but transmission between fully vaccinated people in this setting is unclear to date.[32]

Will COVID-19 breakthrough infections in vaccinated people transmit the disease to others? Do vaccines decrease contagion?

In none of the clinical trials did this figure as an outcome. But, despite the fact that the vaccines that are currently available initially were not designed to prevent infection, we now know that they all have this capacity to some extent after the full regimen.[33] In one study, researchers estimated that unvaccinated people would have a 12-fold higher risk of transmitting the virus than those who have been vaccinated.[34] Other research carried out to analyze the effectiveness of the vaccine in preventing transmission between vaccinated persons and close household contacts concluded that these showed effectiveness against transmission of around 70%.[18] That is, people who are fully vaccinated are probably less contagious than those who are not vaccinated.[35] In another study of post-vaccination SARS-CoV-2 infections in healthcare workers, although no documented secondary cases were identified, it is notable that samples from 43% of cases had low PCR cycle thresholds and positive antigen assay results, suggesting potential infectivity, a consideration of greater concern today with the emergence of the Delta variant.[36]

Our study, it found vaccine effectiveness against transmission among households among contacts with primary cases of COVID-19 breakthrough infections in fully vaccinated people, (calculated as Secondary attack rate in vaccinated / Secondary attack rate in unvaccinated) × 100%) of the 77%, which is in line with what was previously published. Our study runs from February to November 2021, so it includes the predominant presence of the delta variant in recent months. It has been reported that in the rare cases where fully vaccinated people were infected with the Delta variant, they were less likely to transmit it than unvaccinated people; but a person vaccinated with a Delta infection was almost twice as likely to transmit the virus as a person infected with Alpha.[37] However, another study conducted since March 2021, identified 4 major infections among 8678 fully vaccinated healthcare workers; based on epidemiological investigation and contact tracing, investigators determined that three of the workers had been infected by exposure to unvaccinated household members, and the remaining worker had been infected by another vaccinated health worker, who in turn Once, she had contracted a breakthrough infection from her unvaccinated spouse. Therefore, the transmission of SARS-CoV-2 between vaccinated people is possible.[38]

In another carefully designed cohort study in the UK, secondary attack rates in household contacts exposed to the delta variant were 25% in vaccinated contacts and 38% in unvaccinated ones.[32,39,40] Likewise, in a population study in Cologne, Germany, between December 2020 (date of the first vaccination) and August, 2021, the ratio of infected contacts to total contacts per index patient in the vaccinated group and the unvaccinated group were 0.13 and 0.37, respectively; contact persons had a 79% lower risk of infection if the index patient was vaccinated.[41]

In our study, the crude rate of secondary attack in fully vaccinated contacts with primary cases of COVID-19 breakthrough infections in fully vaccinated people was 53% vs. a crude rate of secondary attack in contacts without complete vaccination or not vaccinated, of 69%. This finding indicates that COVID-19 breakthrough infections in fully vaccinated people can transmit the infection to fully vaccinated contacts, to a lesser extent than to partially or unvaccinated contacts, but in any case efficiently at home, even to fully vaccinated contacts. In any case, in the

same population, in a study carried out from March 15 to December 31, 2020, before starting vaccination, the secondary attack rate in families was clearly higher, 76% (42), which indicates that cases of COVID-19 in vaccinated people are less infectious than cases in unvaccinated people (7), and points to the effectiveness of the vaccine. But, on the other hand, In the real world, individuals with symptomatic infection will be more likely than those with asymptomatic infection to self-isolate, which could reduce the degree of transmission of them, despite the greater potential for transmissibility of these individuals.[7] It should be remembered that in our study, fully vaccinated family contacts were not self-isolated.

Symptoms

Although data shows that the virus can thrive in the respiratory tract of vaccinated people.[43] since vaccination reduces the incidence of symptomatic infection, the fraction of time in which the vaccinated individual is infectious, even if a similar peak viral load is reached, could decrease.[35] While an unvaccinated person remains infected, and therefore is contagious, for several days, the vaccinated person has little time (1-2, maximum 3 days) to transmit the infection. In those vaccinated, the viral load of the first days after infection may be equal to that of the unvaccinated, but then the vaccinated tends to reduce the viral load more quickly compared to the others.[44] In our study, we did not find differences in symptoms, neither in their duration nor in their severity, between primary and secondary cases (although regarding moderate-severe severity, it was 23% -3 pneumonias- in primary cases vs. 0% in secondary cases; "almost" statistically significant -Fisher exact test = 0.0524).

Time since the last vaccination dose

Immunity to the COVID-19 vaccine appears to be declining. The reduction in protection could be due to a number of factors, including the now widespread Delta that can cause more infections than previous variants, or the possibility that immunity is waning as more time passes since participants received their vaccinations.[45,46] In one study, the median time since vaccination was 101 days among vaccinated infected contacts, compared with 64 days for uninfected, suggesting that protection begins to decline earlier than expected.[32] In our study, we did not find statistically significant differences in the time since the last dose of vaccine in primary cases of COVID-19 breakthrough infections in fully vaccinated people vs. secondary cases of COVID-19 breakthrough infections in complete and incomplete vaccinates.

Can the transmission of the virus be prevented with vaccines?

In short, people who develop COVID-19 despite being fully vaccinated are considerably less infectious to contact persons, and similarly vaccinated contact persons have a lower risk of contracting the infection.[41] But our study, in line with others, suggests that total interruption of transmission with available vaccines does not occur; although this transmission can be reduced. It should be noted that if basic prevention measures such as hygiene, a mask, and distancing, if necessary, are added to them, transmission drops considerably.[47]

Study limitations

- The sample studied was small.
- It must be taken into account that changes in community transmission during the study period, with an improved general situation in community transmission, may also imply changes in one sense or another of cautious and personal protection behaviors, which could be an element of confusion to interpret the results of the risk of secondary infection in the family observed during that period.
- Asymptomatic primary cases may have been missed, as no surveillance or systematic screening was done. It must be remembered that there is a limited percentage of fully immunized people who can become infected, almost always

without developing the disease, and infect.[44]

- There is the possibility of misclassifying transmission in the home if the infection in the secondary case was actually acquired outside the home or if the true index case in the home was not evaluated.
- Epidemiological contact tracing data have not been combined with genomic data to estimate the rates of secondary attacks in the family environment, so the secondary attack rates found may have errors due to the high heterogeneity in the circulation of the lineage of the SARS-CoV-2.[8]

Conclusion

In the context of general medicine in Toledo (Spain), (when the delta variant became dominant, but before the rise of omicron), vaccine effectiveness against transmission among households among contacts was moderately high. (77%) Complete vaccination of primary cases, and /or family contacts (who did not isolate), was associated with a reduction in the number of secondary cases in the family vs. incomplete vaccinated and unvaccinated household contacts. However, the secondary attack rate in fully vaccinated contacts from fully vaccinated primary cases was relatively high.(53%) These results support the key message that vaccinated contacts are better protected than unvaccinated ones. But, vaccination reduces but does not eliminate the risk of COVID-19 transmission within homes. Our findings indicate a risk of infection in household contacts despite full vaccination. These data suggest that with current vaccines, households (crowded indoor environments) are high-risk settings for the transmission of SARS-CoV-2. In addition to increasing the complete vaccination rate, it is suggested to re-evaluate the protocol that vaccinated family contacts do not require isolation, implementing a comprehensive preventive intervention that could include (in addition to detection tests, the use of medical masks, and optimized ventilation), the isolation of household contacts fully vaccinated, at least in the current situation.

References

1. Feng S, Phillips,DJ, White T, et al. (2021) Correlates of protection against symptomatic and asymptomatic SARS-CoV-2 infection. Nat Med; 27: 2032–40. https://doi.org/10.1038/s41591-021-01540-1
2. South Carolina Department of Health and Environmental Control (2021) Breakthrough cases: Tracking disease infection after vaccination. https://scdhec.gov/covid19/covid-19-vaccine/breakthrough-cases-tracking-disease-infection-after-vaccination
3. Reuters Staff (2021) Early Signs COVID-19 Vaccines May Not Stop Delta Transmission, England Says.Medscape;August09.https://www.medscape.com/viewarticle/956134?src=WNL_mdpls_210813_mscpedit_fmed&uac=327178AR&spon=34&impID=3566304&faf=1
4. Subbaraman N (2021) How do vaccinated people spread Delta? What the science says. Emerging data suggest that Delta could spread more readily than other coronavirus variants among people vaccinated against COVID-19. But key questions remain. Nature; 596: 327-8. https://www.nature.com/articles/d41586-021-02187-1?utm_source=Nature+Briefing&utm_campaign=13115e4795-briefing-dy-20210816&utm_medium=email&utm_term=0_c9dfd39373-13115e4795-42937943
5. Reuters Staff (2021) Lambda Variant Shows Vaccine Resistance. Medscape; August 03. https://www.medscape.com/viewarticle/955883?src=mkm_ret_210826_mscpmr

k_eumonthly_int&uac=327178AR&impID=3590043&faf=1

6. Thompson HA, Mousa A, Dighe A, et al. (2021) Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) setting-specific transmission rates: a systematic review and meta-analysis. Clin Infect Dis; 73(3):e754-e764. https://pubmed.ncbi.nlm.nih.gov/33560412/
7. Mostaghimi D, Valdez CN, Larson HT, Kalinich CC, Iwasaki A (2021) Prevention of host-to-host transmission by SARS-CoV-2 vaccines. Lancet Infect Dis. https://doi.org/10.1016/S1473-3099(21)00472-2
8. Kraemer MUG, Pybus OG, Fraser C, et al. (2021) Monitoring key epidemiological parameters of SARS-CoV-2 transmission. Nat Med; 27: 1854–55. https://doi.org/10.1038/s41591-021-01545-w
9. Shah ASV, Gribben C, Bishop J, et al. (2021) Effect of Vaccination on Transmission of SARS-CoV-2.N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMc2106757?query=TOC&cid=NEJM%20eToc,%20September%209,%202021%20DM277747_NEJM_Non_Subscriber&bid=607481677
10. Natalie E. Dean, Joseph W. Hogan, Mireille E. Schnitzer (2021) Covid-19 Vaccine Effectiveness and the Test-Negative Design. N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMe2113151?query=TOC&cid=NEJM%20eToc,%20September%209,%202021%20DM277747_NEJM_Non_Subscriber&bid=607481677
11. Turabian JL (1995) Cuadernos de Medicina de Familia y Comunitaria. Una introducción a los principios de Medicina de Familia. [Notebooks of Family and Community Medicine. An introduction to the principles of Family Medicine]. Madrid: Díaz de Santos. http://www.amazon.co.uk/Cuadernos-medicina-familia-y-comunitaria/dp/8479781920
12. Ministerio de Sanidad (2021) [COVID-19 early detection, surveillance and control strategy]. Actualizado a 23 de julio de 2021. https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/COVID19_Estrategia_vigilancia_y_control_e_indicadores.pdf
13. Instituto de Salud Carlos III (2020) [Strategy for early detection, surveillance and control of COVID-19. Updated December 1, 2020]. Ministerio de Sanidad. España. https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/COVID19_Estrategia_vigilancia_y_control_e_indicadores.pdf
14. Paul LA, Daneman N, Schwartz KL, et al.(2021) Association of Age and Pediatric Household Transmission of SARS-CoV-2 Infection. JAMA Pediatr. https://jamanetwork.com/journals/jamapediatrics/fullarticle/2783022
15. 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
16. National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases (2021) Interim Public Health Recommendations for Fully Vaccinated People. Updated Nov. 19, 2021. CDC. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html
17. Snijders BEP, van Lier A, van de Kassteele J, et al. (2012) Mumps vaccine effectiveness in primary schools and households, the Netherlands, 2008. Vaccine; 30(19):2999-3002.

https://doi.org/10.1016/j.vaccine.2012.02.035 PMID: 22381073

18. de Gier B, Andeweg S, Joosten R, et al. (2021) Vaccine effectiveness against SARS-CoV-2 transmission and infections among household and other close contacts of confirmed cases, the Netherlands, February to May 2021. Euro Surveill; 26(31):pii=2100640. https://doi.org/10.2807/1560-7917.ES.2021.26.31.2100640
19. Strauss AL (1984) Chronic illness and the quality of life. St Louis: The C.V. Mosby Company.
20. WHO. International Statistical Classification of Diseases and Health-Related Problems. ICD-10 Version: 2019. https://icd.who.int/browse10/2019/en
21. Royal Collage of General Practitioners (1986) The Classification and Analisis of General Practice Data. Ocasional Paper 26.
22. Donaldson RJ, Donaldson LJ (1983) Essential Comunity Medicine. Lancaster: MTP Press.
23. Turabian JL (2017) Family Genogram in General Medicine: A Soft Technology that can be Strong. An Update. Res Med Eng Sci; 3(1). http://crimsonpublishers.com/rmes/pdf/RMES.000551.pdf
24. Russell LT (2020) Capturing Family Complexity in Family Nursing Research and Practice. J Fam Nurs; 26(4):287-93. https://journals.sagepub.com/doi/full/10.1177/1074840720965396
25. 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. https://academic.oup.com/heapol/article/13/4/459/596227
26. McIlvain H, Crabtree B, Medder J, et al. (1998) Using practice genograms to understand and describe practice configurations. Fam Med; 30: 490-6. https://pubmed.ncbi.nlm.nih.gov/9669161/
27. Consejería de Sanidad Castilla La Mancha (2021). [Vaccination campaign against COVID-19]. https://sanidad.castillalamancha.es/ciudadanos/enfermedades-infecciosas/coronavirus/preguntas-frecuentes-sobre-el-coronavirus-covid-19/campa%C3%B1a-vacunacion
28. Madewell ZJ, Yang Y, Longini IM, Halloran ME, Dean NE (2020) Household Transmission of SARS-CoV-2: A Systematic Review and Meta-analysis. JAMA Netw Open; 3(12):e2031756. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774102
29. Mandavilli A (2021) Why Vaccinated People Are Getting 'Breakthrough' Infections. The vaccines are effective at preventing serious illness and death, but they are not a golden shield against the coronavirus. The New York Times; Updated July 23.
30. Wallace-Wells B (2021) My Family Was a COVID Cluster. Four vaccinated adults and two unvaccinated children had mild symptoms. Is this what the end of the pandemic looks like? The New Yorker; September 23. https://www.newyorker.com/news/annals-of-inquiry/my-family-was-a-covid-cluster?utm_source=nl&utm_brand=tny&utm_mailing=TNY_Daily_092321&utm_campaign=aud-dev&utm_medium=email&bxid=5bd674a024c17c104800ee41&cndid=36284699&hasha=c5ce033f231235ecb64f4a6525782d31&hashb=81cbb2130141176d41ef1200276f33a8c1521fc2&hashc=b5e42f15a090694cfdf25e243a360eecd5a0020f81a88bd2b9a0a95a592fcf62&esrc=footer-unit&mbid=CRMNYR012019&utm_term=TNY_Daily
31. Farinholt T, Doddapaneni H, Qin X, et al. (2021) Transmission event of SARS-CoV-

2 delta variant reveals multiple vaccine breakthrough infections. BMC Med; 19: 255. https://doi.org/10.1186/s12916-021-02103-4

32. Torjesen I (2021) Covid-19: One in four vaccinated people living in households with a covid-19 case become infected, study finds. BMJ; 375: n2638. https://www.bmj.com/content/375/bmj.n2638?utm_source=etoc&utm_medium=email&utm_campaign=tbmj&utm_content=weekly&utm_term=20211105
33. Ruben Roa (2021) [Vaccines decrease contagion?]. La biblioteca de Springfield;19 de noviembre. https://rubenroa.blogspot.com/2021/11/las-vacunas-disminuyen-el-contagio.html
34. Institut Pasteur (2021) [Epidemiology of SARS-CoV-2 in a vaccinated population and implications for the control of a fall rebound]. https://modelisation-covid19.pasteur.fr/evaluate-control-measures/impact-partially-vaccinated-population/
35. Chia PY, Ong SWX, Chiew CJ, et al. (2021) Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine-breakthrough infections: a multi-center cohort study. Clin Microbiol Infect. https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00638-8/fulltext
36. Bergwerk M, Gonen T, Lustig Y, et al. (2021) Covid-19 Breakthrough Infections in Vaccinated Health Care Workers. N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMoa2109072?query=TOC&cid=NEJM%20eToc.%20July%2029,%202021%20B%20DM177922_NEJM_Non_Subscriber&bid=567294879
37. Mallapaty S (2021) COVID vaccines cut the risk of transmitting Delta — but not for long. Nature; 05 October. https://www.nature.com/articles/d41586-021-02689-y?utm_source=Nature+Briefing&utm_campaign=7be0a7791d-briefing-dy-20211005&utm_medium=email&utm_term=0_c9dfd39373-7be0a7791d-42937943
38. Jung J, Sung H, Kim S-H (2021) Covid-19 Breakthrough Infections in Vaccinated Health Care Workers. N Engl J Med; 385:1629-31. https://www.nejm.org/doi/full/10.1056/NEJMc2113497
39. Wilder-Smith A (2021) What is the vaccine effect on reducing transmission in the context of the SARS-CoV-2 delta variant? Lancet Infect Dis. https://doi.org/10.1016/S1473-3099(21)00690-3
40. Singanayagam A, Hakki S, Dunning J, et al. (2021) Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. Lancet Infect Dis. https://doi.org/10.1016/S1473-3099(21)00648-4
41. Hsu L, Grüne B, Buess M, et al. (2021) COVID-19 Breakthrough Infections and Transmission Risk: Real-World Data Analyses from Germany's Largest Public Health Department (Cologne). Vaccines. 2021; 9(11):1267. https://doi.org/10.3390/vaccines9111267
42. Turabian JL (2021) SARS-COV-2 infection prevalence and characteristics in domestic contacts: Study of 39 families and 132 people in a general medicine clinic in Toledo (Spain): Implications for the general practitioners. Int J Epidemiol Health Sci 2021;2(1): e02. http://www.ijehs.com/article_241686_87096153ff166d3db0d393bb6d249939.pdf
43. Mandavilli A (2021) Behind the Masks, a Mystery: How Often Do the Vaccinated Spread the Virus? The Ney York Times;

Friday, July 30. https://www.nytimes.com/2021/07/29/health/cdc-masks-vaccinated-transmission.html?campaign_id=2&emc=edit_th_20210730&instance_id=36616&nl=todaysheadlines&regi_id=16392743&segment_id=64850&user_id=c5ce033f231235ecb64f4a6525782d31

44. Cuppini L (2021) CORONAVIRUS. Variante Delta. [What happens when you get Covid being vaccinated? In vaccinated people, the coronavirus stays in the nose and for a few days]. El Mundo; Martes, 3 agosto. https://www.elmundo.es/ciencia-y-salud/salud/2021/08/03/6108cf92fc6c83ee208b459b.html
45. Melchor A (2021) Study Reveals Declining COVID-19 Vaccine Efficacy Against Infection. The vaccines remain protective against serious disease and death. The Scientist; Aug 25.
46. Shrotri M, Navaratnam AMD, Nguyen V, et al. (2021) Spike-antibody waning after second dose of BNT162b2 or ChAdOx1. Lancet. https://doi.org/10.1016/S0140-6736(21)01642-1
47. Domínguez N (2021) [Why the covid vaccine does not prevent the transmission of the virus. The rebound in infections among those vaccinated is to be expected, but it will not cause complications in the vast majority of cases.]. El País; 19 NOV. https://elpais.com/ciencia/2021-11-19/por-que-la-vacuna-contra-la-covid-no-impide-la-transmision-del-virus.html

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