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Original Contribution

Impact of BNT162b2 Vaccination and Isolation on SARS-CoV-2 Transmission in Israeli Households: An Observational Study

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Several studies have characterized the effectiveness of vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. However, estimates of their impact on transmissibility remain limited. Here, we evaluated the impact of isolation and vaccination (7 days after the second dose) on SARS-CoV-2 transmission within Israeli households. From December 2020 to April 2021, confirmed cases were identified among health-care workers of the Sheba Medical Centre and their family members. Recruited households were followed up with repeated PCR for at least 10 days after case confirmation. Data were analyzed using a data augmentation Bayesian framework. A total of 210 households with 215 index cases were enrolled; 269 out of 667 (40%) susceptible household contacts developed a SARS-CoV-2 infection. Of those, 170 (63%) developed symptoms. Compared with unvaccinated and unisolated adult/teenager (aged >12 years) contacts, vaccination reduced the risk of infection among unisolated adult/teenager contacts (relative risk (RR) = 0.21, 95% credible interval (CrI): 0.08, 0.44), and isolation reduced the risk of infection among unvaccinated adult/teenager (RR = 0.12, 95% CrI: 0.06, 0.21) and child contacts (RR = 0.17, 95% CrI: 0.08, 0.32). Infectivity was reduced in vaccinated cases (RR = 0.25, 95% CrI: 0.06, 0.77). Within households, vaccination reduces both the risk of infection and of transmission if infected. When contacts were unvaccinated, isolation also led to important reductions in the risk of transmission.

COVID-19; household; infectious disease transmission; physical distancing; SARS-CoV-2; vaccination; vaccine effectiveness

Abbreviations: CrI, credible interval; COVID-19, coronavirus disease 2019; HCW, health-care workers; PCR, polymerase chain reaction; SAR, secondary attack rate; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly transmissible virus that was first detected in Wuhan China in December 2019 (1, 2). It is the cause of coronavirus disease 2019 (COVID-19), which has spread through the world, leading to a pandemic that had infected at least 250 million people and caused more than 5 million deaths worldwide by November 10, 2021 (3). The advent of novel coronavirus disease 2019 (COVID-19) vaccines has been an important breakthrough in the management of the pandemic. To determine how vaccination may modify epidemic dynamics, it is essential to estimate its effectiveness with respect to infection, transmission, and disease severity. Multiple studies have shown that COVID-19 vaccines are effective at reducing both the risk of infection (4–8) and the risk of developing severe symptoms (4, 8–10) in the general population.

Documenting vaccine impact on transmission is more challenging, stemming from the difficulty of thoroughly documenting chains of transmission and accounting for the ways different types of contacts may lead to different risks of transmission (11). Households represent the perfect environment to evaluate factors affecting transmission such as vaccination because the probability of SARS-CoV-2 transmission among household members is high, ranging between 14%

and 32% (12–14). Beyond the evaluation of vaccine effectiveness, understanding how vaccines affect household transmission is also important to determine how recommendations should evolve with vaccines. For example, should isolation precautions be maintained in partially vaccinated households (15)? A number of studies have shown that vaccines provide indirect protection against household transmission (16–20). However, none of these studies evaluated how isolation affected the outcome, and for some of the studies (16–19), the passive nature of surveillance may have led to underestimating household transmission rates.

During the first months of 2021, Israel underwent its third pandemic wave due to the rise of the Alpha variant that quickly accounted for 90% of infections (21). Concomitantly, vaccination was extended to all adults older than age 16 years, making Israel one of the first countries to reach high vaccination coverage in their population, with 60% of the total population being vaccinated by March 22, 2021 (3). During this period, we followed SARS-CoV-2 transmission in the households of 12,518 health-care workers (HCWs) of the Sheba Medical Center, the largest medical center in Israel. Here, we describe dynamics of transmission in these households and evaluate the impact vaccination and isolation measures had on these dynamics.

METHODS

Study design and study population

All HCWs, regardless of their vaccination status, were required to use an electronic questionnaire to report daily any COVID-19 related symptom they, or a member of their household, had. SARS-CoV-2 polymerase chain reaction testing (PCR) was readily available, and HCWs were encouraged to be tested for any mild symptom or suspected exposures. All HCWs were instructed to notify the infection prevention and control unit if one of their household members was SARS-CoV-2 positive. All SARS-CoV-2–detected HCWs as well as those with a positive SARS-CoV-2 household member were immediately contacted as part of the epidemiologic investigation for contact tracing and were provided with instructions regarding isolation precautions. All unvaccinated household members (i.e., those that did not receive the 2 vaccine doses at least 7 days before the detection of the COVID-19 patient) were required to perform 2 PCR tests in the 10 days after the diagnosis of the positive COVID-19 patient. Vaccinated household members were encouraged to perform 2 PCR tests during the 10 days after detection. Household members were not required to test a second time if they had a positive test (Web Table 1 in Web Appendix 1, available at https://doi.org/10.1093/aje/kwac042). Unvaccinated HCW contacts were isolated at home, whereas vaccinated HCWs were instructed to perform a PCR test every day they reported to the hospital for work.

Between December 31, 2020, and April 26, 2021, the HCWs who were SARS-CoV-2–positive or reported a positive household member were contacted at least 10 days after detection and were offered enrollment in the study. Those who agreed, and gave their consent, answered a telephone interview.

Data and sample collection

Data collected during the phone interview included the age and gender of the HCW's household members, their vaccination status, information about prior COVID-19 infections, their COVID-19 PCR test dates and results, their symptoms (i.e., fever, cough, myalgia, headache, congestion, diarrhea, vomiting, anosmia, or ageusia), the number of rooms and bathrooms in the household, and the degree to which isolation precautions were adhered to (Web Appendix 2). At the time of the study, only individuals 16 years old or older were eligible for vaccination.

The household member who had the first positive PCR test was defined as the index case. When multiple household members had a positive PCR test on the same day, they were defined as co-index cases. We defined complete isolation as complete separation in sleeping and eating between household contacts and index case(s) (i.e., they did not spend any time in the same room) and whether a separate bathroom was provided for the index case(s). Partial isolation was defined if one of the above was violated, but masks were continuously used, and eating was consistently separate.

For HCWs, nasopharyngeal swabs were collected by trained personnel, and reverse-transcriptase quantitative PCR analysis was performed using the Allplex 2019-nCov RT-qPCR assay (Seegene Inc., Seoul, South Korea) and expressed by cycle threshold (Ct). Other household members reported the results of their COVID-19 test(s) performed by their health-care providers.

Clinical outcome

Confirmed SARS-CoV-2 infections were defined by a positive PCR test (i.e., with a Ct value lower than 40). Symptomatic cases were defined as confirmed cases with the presence of at least 1 symptom from among the following: fever, cough, myalgia, headache, congestion, diarrhea, vomiting, anosmia, or ageusia. Contacts who reported at least 1 of the above-mentioned symptoms but were not confirmed because they performed no PCR test ($n = 6$) or a single test at inclusion ($n = 2$) were also considered as symptomatic cases. Asymptomatic cases were defined as confirmed cases who did not report any symptom over the follow-up period of the household.

Statistical analysis

We evaluated transmission in households using 2 metrics: the secondary attack rate (SAR), defined as the proportion of susceptible household contacts that are infected after the index case is detected (22), and the person-to-person probability of transmission, defined as the per-capita probability that an infected individual transmits to a susceptible household contact. The first metric includes tertiary (i.e., household contacts infected by a household member that is not the index case) and community cases (i.e., household contacts infected in the community) contrary to the second metric. In both cases, we assumed that individuals who reported past infection of SARS-CoV-2 confirmed by PCR over the year preceding the detection of the household index

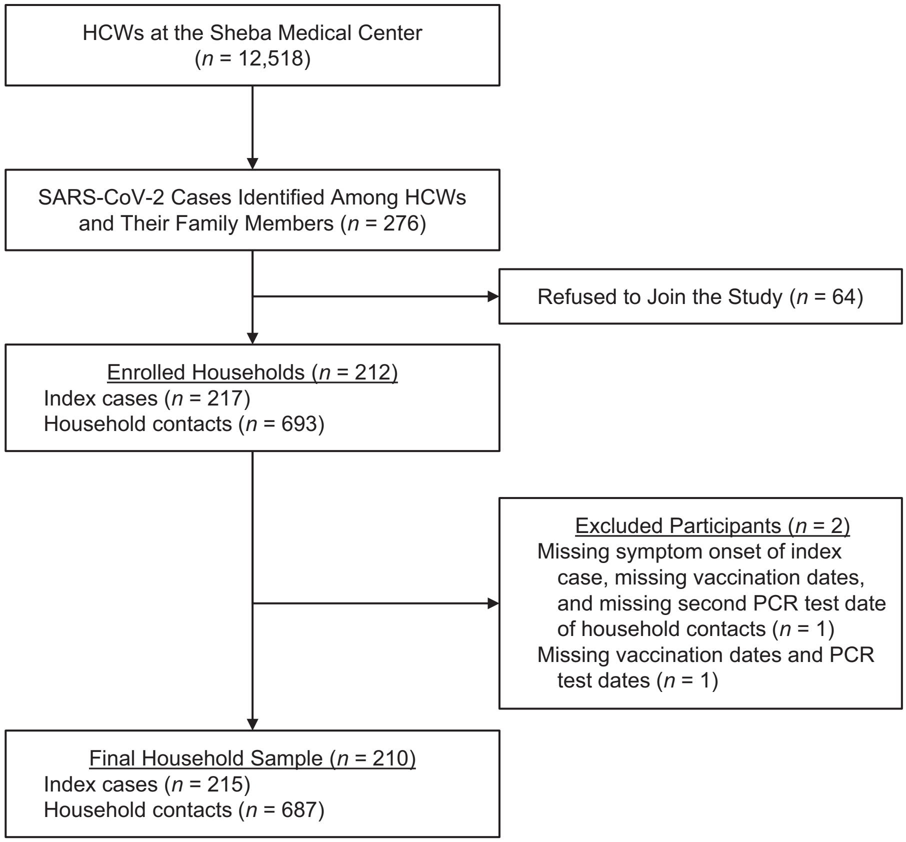

Figure 1. Flow chart of the households included in our analysis, Ramat Gan, Israel, 2020–2021. HCW, health-care worker; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

case (n = 20) were protected from infection and therefore, did not count as susceptible household contacts.

Baseline characteristics of the index cases and household contacts were described according to their vaccination status. All individuals older than 12 years were considered as adults/teenagers. We calculated the SAR for different categories of household contacts: unisolated and unvaccinated adults/teenagers, unisolated and vaccinated adults/teenagers, isolated and unvaccinated adults/teenagers, vaccinated and isolated adults/teenagers, unisolated children, and isolated children. Here, isolation corresponds to complete or partial isolation between household contacts and the index case. We also defined the SAR of vaccinated and unvaccinated index cases as the proportion of infected household contacts in households with vaccinated or unvaccinated index cases, respectively. In a sensitivity analysis, the SAR calculation was restricted to households in which a single index case was identified (Web Table 2 in Web Appendix 3). We also report the 95% confidence interval of the SAR.

We developed a statistical model to evaluate the effect of age, isolation precautions, BNT162b2 vaccination, and household size on SARS-CoV-2 transmission dynamics in households (Web Appendix 4). The model uses the sequence of symptom onset dates and positive molecular test dates to estimate the person-to-person risk of transmission within the household while accounting for the community hazard of infection (i.e., household contacts infected outside the household) and the possibility of tertiary transmissions (i.e., household contacts infected by a member of the household that is not the index case) (23). The person-to-person risk of transmission is decomposed into the baseline person-to-person risk of infection depending on household size, the relative infectivity of the infector depending on their vaccination status (reference group: unvaccinated cases), and the relative susceptibility of the infectee depending on their age, isolation behavior, and vaccination status. The relative susceptibility is estimated separately for unisolated children, isolated children, isolated and unvaccinated adults/teenagers, unisolated and vaccinated adults/teenagers, and adults/teenagers that are both isolated and vaccinated, considering the group of adults/teenagers that are unisolated and unvaccinated as the reference group. None of the children were vaccinated at the time of the study. This formulation accommodates the potential confounding effects between the 3 variables characterizing household contacts (i.e., being vaccinated, being isolated, or being a child). We assumed that individuals whose isolation behavior was missing ($n = 6$) did not comply with isolation precautions.

Model parameters were estimated using Bayesian Markov chain Monte Carlo sampling with data augmentation (23)

Table 1. Characteristics of the Index Cases According to Age, Ramat Gan, Israel, 2020–2021

Characteristic	Adult/Teenager Index Cases[a] (*n* = 191)			Child Index Cases (*n* = 24)			All Index Cases (*n* = 215)		
	No.	%	Median (IQR)	No.	%	Median (IQR)	No.	%	Median (IQR)
Male sex	76	40		14	58		90	42	
Age, years[b]	36 (14)			6 (4)			32 (16)		
Cluster size[c]			2 (1–3)			2 (1–3)			2 (1–3)
Symptom status									
Symptomatic	172	90		10	42		182	85	
Asymptomatic	19	10		14	58		33	15	
Vaccination									
Vaccinated	15	8		N/A	N/A		15	7	
Days from second dose to detection			44 (13–59)			N/A			44 (13–59)

Abbreviation: IQR, interquartile range; N/A, not applicable.
[a] Individuals aged >12 years were considered adults/teenagers.
[b] Values are expressed as mean (standard deviation).
[c] Number of secondary cases among the susceptible contacts of the index case(s).

(Web Appendix 5). Data were augmented with the probable date of infection of confirmed cases. For symptomatic cases, the date of infection was reconstructed from the date of symptom onset, using the probabilistic distribution of the incubation period (24). For asymptomatic cases, we assumed that the date of infection could occur up to 10 days prior to their molecular detection based on a meta-analysis (25).

Since the study was conducted during the vaccine rollout, participants were enrolled at varying stages of their vaccination process. We assumed that vaccines reach their full effect 7 days after receiving a second dose (4, 9, 10). Cases were therefore considered vaccinated if their symptom onset (or if unknown, the date of their first positive PCR test) occurred ≥7 days after the second dose. Similarly, household contacts were considered vaccinated if their exposure to the index case (starting with symptom onset or, in its absence, from the date of first positive PCR of the index case) occurred ≥7 days after the second dose. In a sensitivity analysis, we investigated how parameter estimates changed under the assumption that vaccination is effective ≥15 days after the first dose. We also assessed how estimates changed when the analysis was restricted to households in which all negative contacts had performed at least 1 or 2 PCR tests in the 10 days following the detection of the index case. In the baseline scenario, we assumed that asymptomatic cases are 40% less infectious than symptomatic cases based on a meta-analysis (26), and we investigated whether assuming the same level of infectivity in asymptomatic and symptomatic cases modified our estimates. Finally, in our baseline analysis, we chose a log-normal with log-mean = 0 and log-standard deviation = 1 prior distribution for the relative infectivity and relative susceptibility parameters and explored smaller and larger values (log-standard deviation = 0.7 or 2) in a sensitivity analysis.

We compared the observed and expected distributions of the number of cases per household size to assess the goodness-of-fit of the model (Web Table 3 in Web Appendix 6). We report the posterior median and the 95% credible interval (CrI) of estimated parameters. We also report the posterior probability that isolated and vaccinated adult/teenager contacts are less susceptible than vaccinated adult/teenager contacts that do not isolate. To measure the strength of evidence of a reduced susceptibility in isolated contacts among vaccinated ones, we report the associated Bayes factor. Here, it directly corresponds to the posterior odds of a reduced susceptibility in isolated contacts among vaccinated ones. Additional details are available in Web Appendix 1–6.

Ethics

The study was approved by the Sheba Medical Center institutional review board committee (approval #8130-21).

RESULTS

All 12,518 HCWs employed by the Sheba Medical Center were eligible to join the study. Between December 19 and April 28, 2021, 91% of the Sheba Medical Center personnel received both doses of the BNT162b2 vaccine, and a rapid and significant decrease in newly detected cases was observed among HCWs.

From December 31, 2020, to April 26, 2021, 276 SARS-CoV-2 cases were identified among HCWs of the Sheba Medical Center and their household members (Figure 1). Of these, 212 agreed to participate, gave their consent, and were enrolled in the study with their household members. Two households were excluded due to missing vaccination

Table 2. Characteristics of the Household Contacts According to Age, Ramat Gan, Israel, 2020–2021

Characteristic	Adult/Teenager Household Contacts[a] (n = 494)			Child Household Contacts (n = 193)			All Household Contacts (n = 687)		
	No.	%	Median (IQR)	No.	%	Median (IQR)	No.	%	Median (IQR)
Male sex	242	49		109	56		351	51	
Age, years[b]	36 (17)[c]			6 (4)			27 (20)		
Infection and symptom status									
Past infection	16	3		4	2		20	3	
Not infected	304	62		94	49		398	58	
Symptomatic	127	26		41	21		168	24	
Asymptomatic	46	9		53	27		99	14	
Symptomatic (missing onset)	1	0		1	1		2	0	
Vaccination									
Vaccinated	125	25		N/A	N/A		125	18	
Days from second dose to exposure			23 (14–36)			N/A			23 (14–36)
Isolation									
Partial	115	23		32	17		147	21	
Complete	227	46		58	30		285	41	
Missing	5	1		1	1		6	1	

Abbreviation: IQR, interquartile range; N/A, not applicable
[a] Individuals aged >12 years were considered adults/teenagers.
[b] Values are expressed as mean (standard deviation).
[c] Missing age for 5 adult/teenager contacts.

status, dates of PCR test, and/or symptom onset. In total, we analyzed data from 210 households with 215 index cases, including 4 co-index cases, and their 687 household contacts. The median household size was 4 (interquartile range, 3–5). Mean age was 32 years among index cases (Table 1) and 27 years among household contacts (Table 2). Age was missing for 5 adult/teenager contacts, and isolation behavior was missing for 6 contacts. There was a slight over-representation of females among index cases (58%), and 191 index cases (89%) were adults/teenagers, of whom 15 (8%) were vaccinated. None of the 24 child index cases were vaccinated. Among the 494 adult/teenager household contacts, 125 (25%) were vaccinated. Of these, 83 (17%) also complied with isolation precautions. Among the 369 unvaccinated adult/teenager contacts, 259 (70%) isolated during the study. None of the 193 child household contacts were vaccinated and 47% of them (n = 90) isolated during the study period (Table 2). In the following, we refer to susceptible contacts (i.e., contacts that did not report SARS-CoV-2 infection over the preceding year) as contacts.

A total of 269 out of 667 (40%) household contacts developed a SARS-CoV-2 infection. Of those, 170 (63%) developed symptoms (Table 2). The SAR varied with the characteristics of the contacts. Among the 105 adult/teenager contacts who were unisolated and unvaccinated, 80 (76%) were infected by SARS-CoV-2 (Table 3). This proportion dropped to 28% (11 out of 40) among those who were unisolated and vaccinated, 29% (71 out of 245) among those who were isolated but unvaccinated, and 11% (9 out of 83) among those who were isolated and vaccinated; 65% (66 out of 101) of child contacts who were unisolated got infected by SARS-CoV-2. This proportion declined to 33% (29 out of 87) for isolated child contacts. The proportion of asymptomatic cases varied from 26% (46 out of 174) among adult/teenager contact cases to 56% (53 out of 95) among child contact cases (Table 2).

The SAR also varied with the vaccination status of the index case regardless of the contacts' characteristics. Among the 622 household contacts whose index case was unvaccinated, 261 (42%) developed a SARS-CoV-2 infection (Table 3). This proportion dropped to 19% (8 out of 42) among household contacts whose index case was vaccinated. Finally, the SAR was relatively invariant with household size: 31%, 40%, 32%, and 32% for households of size 2, 3, 4, and 5, respectively (Web Figure 1 in Web Appendix 6).

Our statistical model makes it possible to perform a multivariate analysis of the drivers of SARS-CoV-2 transmission in households. We estimate that, relative to adult/teenager

Table 3. Observed Secondary Attack Rates According to the Type of Contact, Ramat Gan, Israel, 2020–2021

Type	No. of Infected Contacts	No. of Susceptible Contacts	SAR	
			%	95% CI
Contacts[a]				
Unisolated and unvaccinated adult/teenager	80	105	76	67, 84
Isolated and unvaccinated adult/teenager	71	245	29	23, 35
Unisolated but vaccinated adult/teenager	11	40	28	15, 44
Isolated and vaccinated adult/teenager	9	83	11	5, 20
Unisolated child	66	101	65	55,75
Isolated child	29	87	33	24, 44
Index[b]				
Vaccinated	8	42	19	9, 34
Unvaccinated	261	622	42	38, 46

Abbreviations: CI, confidence interval; SAR, secondary attack rate.

[a] Isolation is missing for 1 child contact and for 5 adult contacts.

[b] The last 2 rows correspond to the SAR among the household contacts of vaccinated (n = 14 households) and unvaccinated index cases (n = 195 households). One household was excluded from this analysis because its co-index cases did not have the same vaccination status.

contacts who were unisolated and unvaccinated, the relative risk of being infected was 0.21 (95% CrI: 0.08, 0.44) among adult/teenager household contacts who were vaccinated but unisolated (Figure 2A, Web Table 4 in Web Appendix 7). It was 0.12 (95% CrI: 0.06, 0.21) among household contacts who did isolate and were unvaccinated, and 0.07 (95% CrI: 0.03, 0.16) among household contacts who were both isolated and vaccinated. Isolation might reduce the risk of infection among vaccinated contacts (96% posterior probability, Bayes factor = 23) with a relative risk of 0.34 (95% CrI: 0.11, 1.14). Relative to adult/teenager contacts who were unisolated and unvaccinated, the relative risk of infection was 0.50 (95% CrI: 0.32, 0.77) for child contacts that did not isolate, and 0.17 (95% CrI: 0.08, 0.31) for those that did. We estimate that the risk of transmission from vaccinated cases was 0.25 (95% CrI: 0.06, 0.77) times that of unvaccinated cases (Figure 2B, Web Table 4 in Web Appendix 7).

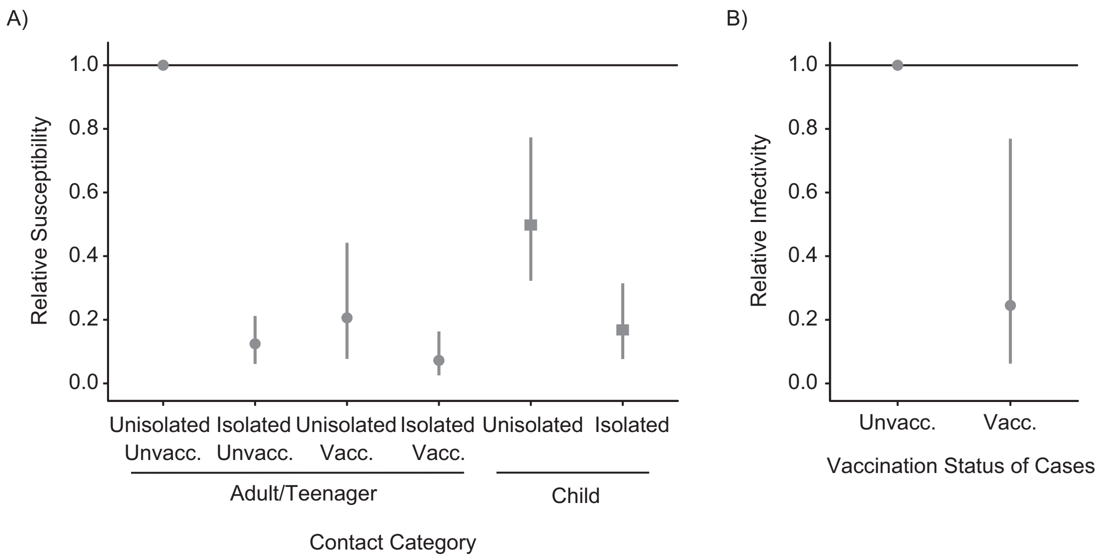

Figure 2. Estimates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission parameters within households, Ramat Gan, Israel, 2020–2021. A) Estimated relative susceptibility of isolated and unvaccinated adults/teenagers, unisolated but vaccinated adults/teenagers, isolated and vaccinated adults/teenagers, unisolated children, and isolated children. The reference group is the group of adults/teenagers that were unisolated and unvaccinated. B) Estimated relative infectivity of vaccinated cases compared with unvaccinated cases. The posterior median and its associated 95% Bayesian credible interval are reported.

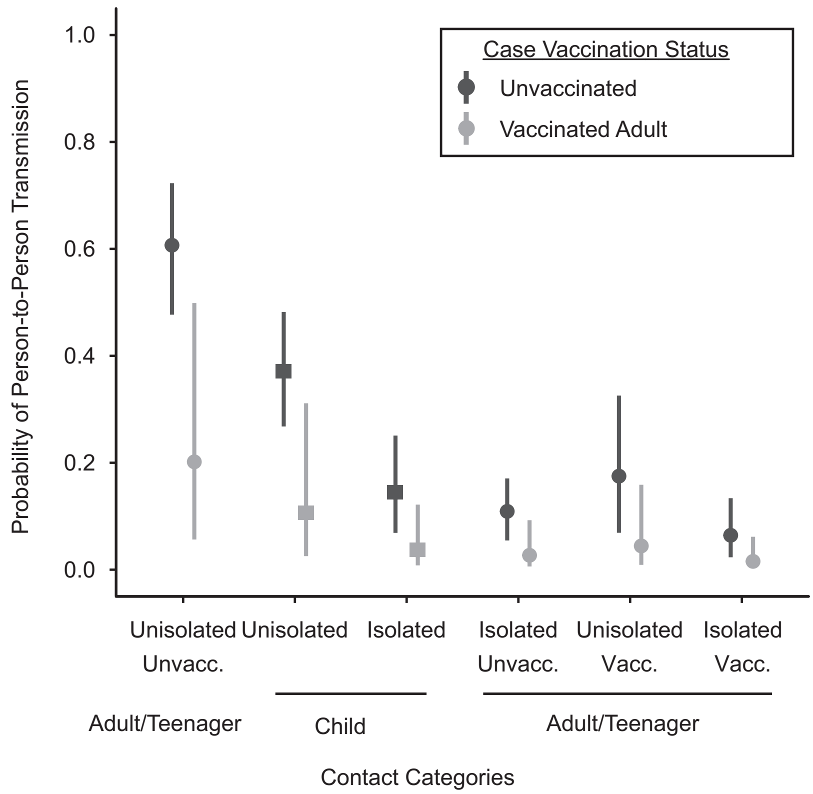

Figure 3. Person-to-person probability of transmission within households according to the characteristics of the case and of the contact, Ramat Gan, Israel, 2020–2021. Estimated person-to-person probability of transmission within households of size 4, decomposed by the age, isolation behavior, and vaccination status of the contact as well as the vaccination status of the case. The posterior median and its associated 95% Bayesian credible interval are reported.

Overall, we estimate that, in a household of size 4, the person-to-person probability of SARS-CoV-2 transmission is 61% (95% CrI: 48, 72) between an unvaccinated case and an unvaccinated and unisolated adult/teenager. This probability drops to 4% (95% CrI: 1, 16) between 2 vaccinated adults/teenagers who do not follow isolation rules (Figure 3, Web Table 5 in Web Appendix 7). The person-to-person probability of transmission from an unvaccinated case to a child who does not isolate is 37% (95% CrI: 27, 48). This probability drops to 11% (95% CrI: 3, 31) if the case is vaccinated and to 14% (95% CrI: 7, 25) if the child contact is isolated.

In general, our estimates of relative susceptibility and relative infectivity were robust to model assumptions (Figure 4). When the analysis was restricted to households in which all contacts performed at least 1 or 3 PCR tests in the 10 days following the recruitment of the index case, the relative susceptibility of vaccinated adult/teenager contacts who did not isolate was slightly higher compared with the baseline scenario. It increased from 0.21 (95% CrI: 0.08, 0.44) in the baseline scenario to 0.28 (95% CrI: 0.09, 0.66) in the analysis with at least 1 PCR and 0.32 (95% CrI: 0.09, 0.83) with at least 2 PCR tests (Web Table 4 in Web Appendix 7). In the alternative scenarios, the number of individuals included was substantially lower, increasing CrIs (Web Figures 2 and 3, Web Tables 6–9 in Web Appendix 8). Similarly, the relative susceptibility of vaccinated adult/teenager contacts who did isolate increased from 0.07 (95% CrI: 0.03, 0.16) in the baseline scenario to 0.12 (95% CrI: 0.04, 0.28) in the analysis with at least 1 PCR, and 0.13 (95% CrI: 0.04, 0.32) in the one with at least 2 PCR tests. Consequently, the posterior probability that isolated and vaccinated adult/teenager contacts were less susceptible than vaccinated adult/teenager contacts that did not isolate dropped from 96% to 88% with 1 PCR and 89% with 2 PCR tests. Still, the statistical support was high with a Bayes factor equal to 7 and 8, respectively. Relative infectivity and relative susceptibility were slightly sensitive to their prior distribution (Web Table 10 in Web Appendix 8). When the log-standard deviation increased, estimates were pulled towards lower values.

DISCUSSION

We evaluated the impact of BNT162b2 vaccination on case infectivity and the mitigating effect of age, isolation from the index case, and BNT162b2 vaccination on susceptibility to infection in household settings. Our approach accounts for infections in the community, potential tertiary infections within the households, the reduced infectivity of asymptomatic cases, potential misidentification of

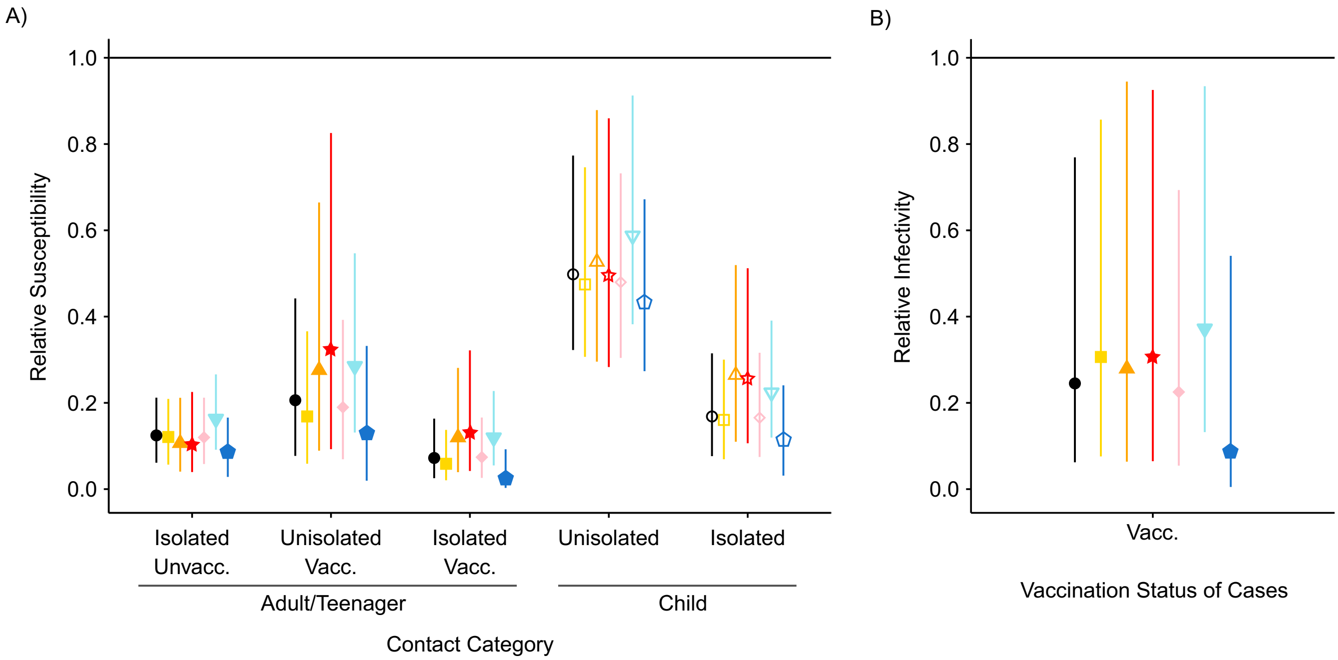

Figure 4. Impact of model assumptions on the estimation of the relative susceptibility and relative infectivity parameters, Ramat Gan, Israel, 2020–2021. A) Estimates of the relative susceptibility of household contacts for the baseline and sensitivity analysis scenarios. B) Estimates of the relative infectivity of vaccinated cases compared with unvaccinated ones for the baseline and sensitivity analysis scenarios. In the baseline scenario (black circle), we assumed that vaccination was effective from 7 days after the second dose, the relative infectivity of asymptomatic cases compared with symptomatic cases was equal to 60%, and the log-standard deviation of the relative infectivity and relative susceptibility prior distributions was equal to 1. Sensitivity analysis scenarios: yellow square, vaccination is effective ≥15 days after the dose; orange triangle, 1 polymerase chain reaction (PCR) test for all negative contacts; red star, 2 PCR tests for all negative contacts; pink diamond, 100% infectivity of asymptomatic cases; blue inverted triangle, relative parameter prior with log-standard deviation = 0.7; blue pentagon, relative parameter prior with log-standard deviation = 2. The posterior median and its associated 95% Bayesian credible interval are reported.

the index case(s), and varying follow-up periods between households.

In our analysis, the SAR in unvaccinated adult/teenager contacts who did not isolate was estimated at around 76%, which is substantially higher than previous estimates obtained in household settings (12–14, 18, 27, 28). In meta-analyses (12–14), the average SAR ranged between 14% and 32%; however, in some studies, it could be as high as 90% (13). Most of these studies date back to the time when historical lineages were still dominant. In contrast, our study took place when the Alpha variant represented up to 90% of infections in Israel (21). Our higher estimate could be at least partly explained by the fact that the Alpha variant is substantially more transmissible than historical lineages (21, 29–31).

In agreement with previous reports, we found that children are less susceptible to SARS-CoV-2 infections than adults/teenagers (12–14, 32). We further estimated that, 7 days after their second dose, vaccinated adults/teenagers benefit from a 79% reduction in the risk of infection compared with unvaccinated adults/teenagers. We show, consistent with previous studies (21, 33), that BNT162b2 vaccination is highly effective against infection by the Alpha variant. In general population studies, vaccine effectiveness for symptomatic infections ranged from 57% 14 days after the first dose (4) to 89% (4), and 97% 7 days after the second dose (9). For asymptomatic infections, vaccine effectiveness against infection was 79% 10 days after the first dose (5) and 94% 14 days after the second dose (7). Our estimate of vaccine effectiveness in household settings is lower than those obtained in the general population. This is consistent with estimates obtained in households (19, 20, 33) and might in part be explained by the elevated contact rates in households that may favor transmission. Additionally, studies in the general population are less suitable to detect all asymptomatic cases compared with the household setting. This might lead general population studies to overestimate vaccine effectiveness against asymptomatic infections if vaccinated contacts are less often tested than unvaccinated ones. On another note, we estimate a vaccine effectiveness against transmission of 75% (95% CrI: 23, 94), which is in line with other studies in household settings (18–20).

To our knowledge, this is the first study estimating the effect of isolation on SARS-CoV-2 transmission in households that are partially vaccinated. We showed that isolation precautions markedly reduce the overall infection risk in both adult/teenager and child contacts even when considering partial physical distancing measures. We estimated a similar reduction of infection in adult/teenager contacts that were vaccinated but did not isolate. There was a signal in the data that isolation also benefited vaccinated individuals, although credible intervals were larger, and further investigations are required to confirm this finding.

Our study has several limitations. First, household studies such as ours may be affected by multiple sources of bias. On the one hand, we may overestimate the SAR if we are more likely to detect households with multiple cases. On the other hand, we might underestimate it if some asymptomatic, or paucisymptomatic, cases are missed during follow-up. Second, we estimated an important reduction of infectivity in vaccinated cases with 2 doses compared with unvaccinated cases as previously shown (18–20, 34). However, this is associated with important uncertainty due to the small number of cases (15 vaccinated index cases and 21 vaccinated secondary cases). Thus, more data are needed to reduce the size of credible intervals. Third, we assumed that vaccination was effective from 7 days after the second dose (or 15 days after the first dose in our sensitivity analysis; see Web Table 11 in Web Appendix 8). In practice, the effect of the vaccine is likely to be progressive, which might push down estimates of effectiveness since individuals with early partial protection would be considered to be unvaccinated. However, excluding households with the early-vaccinated index cases did not affect our estimates (Web Figure 4 and Web Table 12 in Web Appendix 8). The limited number of households does not make it possible to dissociate early vs. full protection conferred by the vaccine nor to investigate the infectivity of children relative to adults/teenagers. Fourth, testing instructions were different for vaccinated and unvaccinated household contacts, as well as HCWs and non-HCWs. Most vaccinated contacts were HCWs at the Sheba Medical Center who complied with testing instructions to go back to work, leading to high testing rates in vaccinated individuals, with 67% having at least 2 PCR tests and 70% having 1 positive PCR or at least 2 PCR tests in the 10 days following case detection (Web Table 1 in Web Appendix 1). Among unvaccinated contacts, 49% had at least 2 PCR tests and 79% had 1 positive PCR or at least 2 PCR tests in the 10 days following case detection. This higher testing rate is notably due to the high proportion of single positive tests (30%). These differential testing behaviors and positivity rates between vaccinated, unvaccinated, HCW, and non-HCW contacts make it difficult to anticipate the directionality of a potential bias. When restricting our evaluation to households where all negative contacts were tested at least once or twice, estimates remained relatively similar to the baseline values. In the analysis with at least 2 tests for all negative contacts, we observed a slight reduction in the point estimate for vaccine effectiveness against infection that remained difficult to interpret given the very broad credible intervals (17%–91%). Fifth, the measurement of isolation precautions may be subject to recall bias and/or overreporting, as they represent a socially desirable behavior. The timing and evolution of isolation precautions were not measured, and thus not integrated in our model. Nevertheless, our estimate of isolation effectiveness is consistent with a 10-day period of quarantine in modeling studies (35). Finally, we estimate vaccine effectiveness against infection and transmission in a context where the Alpha variant was dominant. These estimates are very likely to be different for the Delta variant (36) that was first reported in October 2020 and rapidly became dominant worldwide (37).

To conclude, vaccination with 2 doses substantially reduces the risk of transmission and the risk of infection in households. Isolation from the index case while sleeping and eating provides a high level of protection to unvaccinated household members, whether they are adults/teenagers or children. Household contacts of COVID-19 patients should ideally isolate, or at least refrain from significant contact, with household cases. This may also be the case for vaccinated household members, although larger studies are required to confirm this finding.

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Data and code are available online at https://github.com/mlayan/VaccineEffectivenessSheba.

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