Impact of SARS-CoV-2 Vaccination and Paediatric Age on Delta Variant Household Transmission

List of Authors and

No.	Name	Highest Degree	Affiliation/ Institution
1	Oon Tek Ng	MRCP	National Centre for Infectious Diseases, Singapore; Tan Tock Seng Hospital, Singapore; Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
2	Vanessa Koh	PhD	National Centre for Infectious Diseases, Singapore; Tan Tock Seng Hospital, Singapore
3	Calvin J Chiew	MPH	Communicable Diseases Division, Ministry of Health, Singapore
4	Kalisvar Marimuthu	MRCP	National Centre for Infectious Diseases, Singapore; Tan Tock Seng Hospital, Singapore Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore;
5	Natascha May Thevasagayam	MSc	National Centre for Infectious Diseases, Singapore; Tan Tock Seng Hospital, Singapore
6	Tze Minn Mak	PhD	National Centre for Infectious Diseases, Singapore
7	Joon Kiat Chua	BSocSci (Hons.)	Ministry of Health, Singapore
8	Shannen Si Hui Ong	MSc	Ministry of Health, Singapore

9	Yong Kai Lim	BEng (Hons.)	Ministry of Health, Singapore
10	Zannatul Ferdous	MBBS	National Centre for Infectious Diseases, Singapore; Tan Tock Seng Hospital, Singapore
11	Alifa Khairunnisa bte Johari	BSc (Hons.)	National Centre for Infectious Diseases, Singapore; Tan Tock Seng Hospital, Singapore
12	Lin Cui	PhD	National Centre for Infectious Diseases, Singapore
13	Raymond Tzer Pin Lin	FRCPA	National Centre for Infectious Diseases, Singapore; Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore
14	Kelvin Bryan Tan	PhD	Ministry of Health, Singapore; Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore; Centre for Regulatory Excellence, Duke-NUS Medical School
15	Alex R Cook	PhD	Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore

16	Prof. Yee-Sin Leo	FRCP	National Centre for Infectious Diseases, Singapore; Tan Tock Seng Hospital, Singapore; Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore; Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore
17	Prof. Vernon JM Lee	PhD	Communicable Diseases Division, Ministry of Health, Singapore; Saw Swee Hock School of Public Health, Singapore

Corresponding Author:

Oon Tek Ng

E-mail: oon_tek_ng@ncid.sg

National Centre for Infectious Diseases

16, Jalan Tan Tock Seng, Singapore 308442

Summary: In this retrospective cohort study of 8470 Delta-exposed household close-contacts, vaccination prevented onward SARS-CoV-2 transmission and there was increased risk of SARS-CoV-2 acquisition and transmission among children compared with young adults. Time after vaccination and vaccine type affected SARS-CoV-2 acquisition.

ABSTRACT

Background

The impact of SARS-CoV-2 vaccination status and paediatric age on transmission of the Delta variant is key to preventing COVID-19 spread. In Singapore, quarantine of all close-contacts, and quarantine-entry and exit PCR testing, enabled evaluation of these factors.

Methods

This retrospective cohort study included all household close-contacts between March 1, 2021 and August 31, 2021. Logistic regression using generalized estimating equations was used to determine risk factors associated with SARS-CoV-2 acquisition and symptomatic disease.

Findings

Among 8470 Delta variant-exposed household close-contacts linked to 2583 indices, full-vaccination of the index with BNT162b2 or mRNA-1273 was associated with significant reduction in SARS-CoV-2 acquisition by contacts (adjusted odds ratio [aOR]:0.56, 95% robust confidence interval [RCI]:0.44–0.71 and aOR:0.51, 95%RCI:0.27–0.96 respectively).

Compared to young adults (18–29y), children (0–11y) were significantly more likely to transmit (aOR:2.37 [95%RCI:1.57–3.60]) and acquire (aOR:1.43 [95%RCI:1.07–1.93]) infection, taking into account vaccination status.

Longer duration from completion of vaccination among contacts was associated with decline in protection against acquisition (first-month aOR:0.42, 95%RCI:0.33–0.55; fifth-month aOR:0.84,

95%RCI:0.55–0.98; p<0.0001 for trend) and symptomatic disease (first-month aOR:0.30, 95%RCI:0.23–0.41; fifth-month aOR;0.62, 95%RCI:0.38–1.02; p<0.0001 for trend). Contacts immunized with mRNA-1273 had significant reduction in acquisition (aOR:0.73, 95%RCI:0.58–0.91) compared to BNT162b2.

Conclusions

Among household close-contacts, vaccination prevented onward SARS-CoV-2 transmission and there was increased risk of SARS-CoV-2 acquisition and transmission among children compared with young adults. Time after completion of vaccination and vaccine type affected SARS-CoV-2 acquisition.

Key Words: SARS-CoV-2, COVID-19, Vaccination, Delta Variant, Transmission

INTRODUCTION

SARS-CoV-2 Delta has spread rapidly even in settings with high vaccine coverage.[1] Initial data suggests that vaccine protection against SARS-CoV-2 acquisition declined steadily after the first month of completing two doses.[2] To understand the role of vaccination on prevention of transmission, it is important to determine the separate and combined impact of index and close-contact vaccination on SARS-CoV-2 transmission.

While there is also considerable evidence that children are less susceptible to SARS-CoV-2 infections and the vast majority of infected children are asymptomatic to pauci-symptomatic[3,4], it is unclear if they are less infectious than adults and how much they contribute to onward transmission. Some early household studies suggest that children are less likely to transmit SARS-CoV-2 compared to adults. Studies from Spain and Germany report significantly lower secondary attack rates (SAR) in households with paediatric compared to adult index cases[5,6], and an Israeli study estimated the infectivity of children as 63% (95% CI 37–88%) relative to adults.[7] In contrast, data from two large studies from India and China revealed that although children accounted for fewer overall infections than older age-groups, the former documented the highest rates of transmission from children aged 0–14 years and adults aged ≥65 years[8], and the latter found no statistical evidence of differential transmissibility by age.[9] There is also evidence of efficient SARS-CoV-2 transmission from children to adult household members.[10,11]

Notably, current knowledge on the infectivity of paediatric age groups is limited to data from pre-Delta cohorts. The increase in number of paediatric cases due to global spread of the more infectious Delta variant and significant gains in adult immunization prompt an

updated analysis on the epidemiological role of the unvaccinated paediatric population in potentiating spread of infection.

Determining SARS-CoV-2 acquisition rates is challenging as many settings rely on symptomatic testing of contacts, which would likely miss asymptomatic and mild infections, and underestimate the frequency of milder paediatric cases.[12] This limitation can be overcome in cohorts where routine SARS-CoV-2 testing regardless of symptoms is conducted. Household contacts are ideal for determining the impact of vaccination and age on transmission due to the high transmission-risk setting.

We studied household SARS-CoV-2 transmission in Singapore, where all close-contacts of known SARS-CoV-2 infected persons were contact-traced and quarantined for two weeks. As all close-contacts were tested routinely by PCR upon quarantine entry and exit, this cohort provided the opportunity to determine SARS-CoV-2 acquisition regardless of symptoms. As index-contact pairs are known, risks of onward transmission and acquisition could be estimated.

METHODS

Case and close-contact definitions

All close-contacts of confirmed COVID-19 index cases in Singapore issued quarantine orders by the Ministry of Health (MOH) between March 1, 2021 and August 31, 2021 were included in this retrospective cohort study. Since January 2, 2020, active surveillance for COVID-19 in Singapore has been conducted according to MOH COVID-19 guidelines (Supplementary Appendix), which are updated regularly, and all COVID-19 cases are legally required to be reported to MOH. A confirmed COVID-19 case was defined as positive detection of SARS-CoV-2 nucleic acid by real-time RT-PCR of respiratory specimens.[13]

Contact-tracing was performed by MOH for every diagnosed COVID-19 case.[14] Household close-contacts were defined as persons who shared the same residential address as the index case, regardless of duration or proximity of contact. All identified close-contacts underwent legally-enforced quarantine for 14 days and were not allowed to leave their residence or assigned location. Quarantined individuals were monitored for symptoms daily and transferred to hospital for COVID-19 testing and clinical evaluation if significant symptoms developed. Regardless of symptoms, all quarantined close-contacts were tested for COVID-19 by PCR upon quarantine entry and exit. SAR was defined as the number of PCR-confirmed cases detected among all household close-contacts of the index case. All cases of possible COVID-19 reinfection were independently adjudicated by an expert panel comprising specialists in infectious diseases and laboratory medicine (Supplementary Appendix).

All SARS-CoV-2-positive cases with RT-PCR Ct<30 were subjected to WGS for variant identification (Supplementary Appendix).

Epidemiological analysis

Data on indices and close-contacts were obtained from MOH's contact-tracing database (Supplementary Appendix). Symptom information was collected via phone interview by the MOH contact-tracing team soon after diagnosis, while supplemental oxygen, intensive care requirements and COVID-19-related morbidity were ascertained during the period of inpatient care.

Contacts residing in worker dormitories (where the nature of spread is different from community households[15]), those of overseas or imported cases, and those lacking index case information were excluded. If multiple indices were listed for a close-contact in the national records, the earliest-diagnosed index sharing the same residence as the contact was selected for analysis. It

was assumed that all recorded cases from June 1, 2021 and onwards with missing variant information in the database were infected with the Delta variant (Supplementary Table 1).

MOH investigated every new case for epidemiologically-linked transmission to prior cases and grouped cases into transmission clusters.[16] In this cohort, all cases with individually-assigned variant status in an epidemiologically-linked transmission cluster were found to have identical variant assignment. As such, cases with no individually-assigned variant status were also assigned the transmission cluster variant if available.

Statistical analysis and modelling

Risk-factors for acquisition of infection by household contacts of cases were assessed using logistic regression fitted using generalized estimating equations, to accommodate clustering. Bivariate relationships between the outcome and all epidemiologically relevant and available covariates were assessed first, then all covariates, including those not significant on bivariate analysis, were included in a multivariable model. Significance was taken to be at the 5% level. 24 hypothesis tests were conducted in the multivariable model and another 24 across the bivariate models, so 2–3 false positives might be expected if no relationships existed. We adjusted for the age and gender of both index and contact, the vaccine status of the index, and the duration of exposure from symptom onset or notification of the index to his or her isolation in a healthcare facility as these co-variates have prior data supporting possible effects on SARS-CoV-2 acquisition and morbidity[17–20] (Supplementary Table 2). The small number of cases of severe disease (i.e. need for supplemental oxygen and/or intensive care, and/or death) precluded risk-factor analysis for this endpoint.

To obtain estimates of waning of protection against infection or symptomatic infection of the contact, by time since the contact's vaccination, and of prevention of transmission by time since

vaccination of the index, we used logistic regression models fit using generalized estimating equations. We counted the months (30 days) since becoming fully-vaccinated, up to five or more months, as beyond six months the small numbers precluded analysis. Statistical analysis was conducted in R.[21]

Ethics

This work was performed as part of outbreak investigations approved under the Infectious Diseases Act of Singapore.[22]

RESULTS

Characteristics of COVID-19 cases and close-contacts

From March 1, 2021 to August 31, 2021, 120,212 close-contacts were quarantined. Contacts residing in dormitories, those linked to overseas or imported cases or those lacking information were excluded, resulting in 81,593 community contacts, of which 8,503 shared the same residence as the linked index and were classified as household contacts (Supplementary Figure 1).

SARS-CoV-2 Delta was first detected in Singapore on April 1, 2021 in an imported case with first detection in a community case on April 27, 2021. From June 1, 2021, all household index cases with known variant assignment were infected with the Delta variant. Prior to June 1, 782 (97.6%) household close-contacts had known variant assignment, of which 768 (98.2%) were exposed to the Delta variant (Supplementary Table 1). None of the 2,583 Delta-infected indices or 8,470 close-contacts analysed were reinfection cases.

The median age of Delta-infected close-contacts was 36 (inter-quartile range [IQR] 26–51) and 4038 (47.7%) were female. Delta-infected indices had median age of 45 (IQR 31–60) and 1002 (38.8%) were female. Of the 8,470 household close-contacts exposed to 2,583 unique Delta-infected indices, 6,403 (75.6%) received at least one dose of the COVID-19 vaccine prior to the start of quarantine, of which 3,955 (61.8%) were fully-vaccinated. The overall household SAR in this cohort was 17.8% (95% bootstrap confidence interval [BCI] 16.5–19.0%). Stratified by vaccination status, SAR was 24.1% (BCI 21.6–26.8%) among the unvaccinated, 16.2% (BCI 14.4–18.1%) among the partially-vaccinated and 15.4% (BCI 14.0–16.8%) among the fully-vaccinated (Table 1). The household symptomatic attack rate among the unvaccinated was 17.8% (BCI 15.5–20.0), partially-vaccinated 11.2% (BCI 9.8–12.7) and fully-vaccinated 8.9% (BCI 7.9–10.0). The prevalence of severe disease among the unvaccinated was 1.8% (BCI 1.1–2.2), partially-vaccinated 0.4% (BCI 0.2–0.6) and fully-vaccinated 0.1% (BCI 0.0–0.3).

Impact of vaccination on Delta variant transmission

After adjusting for age, gender and vaccination status of both contact and index, as well as time exposure of the contact to the index, full-vaccination of the index with BNT162b2 or mRNA-1273 was associated with a significant reduction in contact SARS-CoV-2 acquisition (adjusted odds ratio [aOR] 0.56, 95% robust confidence interval [RCI] 0.44–0.71 and aOR 0.51, 95%RCI 0.27–0.96 respectively) (Table 2). Receipt of at least a single dose of either BNT162b2 (full-vaccination aOR 0.57 [95%RCI 0.47–0.70]) or mRNA-1273 (full-vaccination aOR 0.39 [95%RCI 0.28–0.54]) vaccine had a significant protective effect on contacts against acquisition, independent of other variables (Table 2). Likewise, partial or full-vaccination of contacts with either BNT162b2 (full-vaccination aOR 0.45 [95%RCI 0.36–0.57]) or mRNA-1273 (full-vaccination aOR 0.21 [95%RCI 0.14–0.33]) had a significant protective effect against symptomatic illness (Supplementary Table 3; additional information in Supplementary Tables 4, 5 and 6).

Impact of age in Delta variant transmission

In adults (≥18 years old), infectivity significantly increased with age, evidenced by increasing odds for contact acquisition for indices aged 30–44 years (aOR 1.79 [95%RCI 1.32–2.43]), 45–59 years (aOR 2.43 [95%RCI 1.77–3.33] and 60 years or older (aOR 3.56 [95%RCI 2.59–4.91]), compared with 18–29 year-olds (aOR 1 [ref]). Susceptibility to Delta variant acquisition significantly increases with contact age in adulthood (aOR 1 [ref], aOR 1.46 [95%RCI 1.20–1.78], aOR 1.71 [95%RCI 1.39–2.09], and aOR 2.44 [95%RCI 1.95–3.05] for contacts in the 18–29, 30–44, 45–59, and ≥60 age-groups respectively) (Table 2 and Figure 2). A significant age-related upward trend is similarly observed with regard to contact susceptibility to symptomatic illness (aOR 1 [ref], aOR 1.31 [95%RCI 1.04–1.66], aOR 1.56 [95%RCI 1.23–1.98], and aOR 1.88 [95%RCI 1.45–2.44] for contacts in the 18–29, 30–44, 45–59, and ≥60 age-groups respectively) (Supplementary Table 3; additional information in Supplementary Tables 4, 5 and 7).

Children aged 0–11 years were significantly more likely to transmit (aOR 2.37 [95%RCI 1.57–3.60]) and acquire (aOR 1.43 [95%RCI 1.07–1.93]) infection compared to older children (12–17 years old) and young adults (18–29 years old; aOR 1), even when vaccination status (immunization was not yet available to this age-group) was taken into account (Table 2 and Figure 2). Contacts 0–11 years of age had comparable odds of developing symptomatic disease as older children and young adults (aOR 1.14 [95%RCI 0.81–1.91], p=0.45), and indices 0–11 years of age were significantly more likely to be linked to symptomatic secondary cases (aOR 2.47 [95%RCI 1.57–3.88]) (Supplementary Table 3; additional information in Supplementary Tables 4, 8 and 9).

Impact of vaccine type on Delta variant transmission

After adjusting for age, gender, and vaccine status of both contact and index (including duration since being fully-vaccinated), and time exposure of the contact to symptomatic index, immunization of the contact with mRNA-1273 was associated with significant reduction in SARS-CoV-2 acquisition (aOR 0.75, 95%RCI 0.59–0.94) as well as susceptibility to symptomatic illness (aOR 0.69, 95%RCI 0.52–0.92) compared to immunization with BNT162b2 (Table 3; additional information in Supplementary Tables 10 and 11).

Effect of duration from completion of vaccination on Delta variant acquisition and symptomatic disease

After adjusting for for age-group and gender of both the contact and index, and duration of exposure to the index, duration from vaccination completion of the contact was associated with a decline in protection against SARS-CoV-2 acquisition (first-month aOR 0.42, 95%RCI 0.33–0.55; fifth-month aOR 0.84, 95%RCI 0.55–0.98; p<0.0001 for trend) and symptomatic disease (first-month aOR 0.30, 95%RCI 0.23–0.41; fifth-month aOR 0.62, 95%RCI 0.38–1.02; p<0.0001 for trend), compared to the unvaccinated state (Figure 1). There was no statistically significant association determined for time since completion of vaccination of the index with decline of protection against close-contact SARS-CoV-2 acquisition (p=0.20 for trend).

DISCUSSION

This study examined the impact of household SARS-CoV-2 vaccination and paediatric age on transmission. Vaccination of contacts and indices were independently associated with reduced SARS-

CoV-2 Delta acquisition and COVID-19 disease among household contacts. Our analysis suggested that mRNA-1273 was associated with reduced risk of SARS-CoV-2 Delta acquisition among vaccinated contacts compared with BNT162b2. The effect of full-vaccination of contacts on reducing SARS-CoV-2 Delta disease acquisition and symptomatic disease declined over time. In adults, infectivity and susceptibility to Delta variant acquisition significantly increased with age; however, children (0–11 years) were significantly more likely to transmit and acquire infection compared to young adults (18–29 years old), regardless of vaccination status. Infected paediatric contacts (0–11 years) were just as likely as young adults to present with symptomatic disease.

While reduction of SARS-CoV-2 acquisition following vaccination is well-described[23], there is limited evidence of the effect of vaccination on onward transmission. Viral dynamics studies have measured comparable peak viral loads in fully-vaccinated individuals with breakthrough infections and unvaccinated cases, although viral load decline occurred at a faster rate in the former.[24] Vaccination of healthcare workers was associated with a reduction in reported cases of COVID-19 among their household members.[25] However, the study predated the emergence of the more infectious Delta variant in India and its subsequent global predominance.[1] Our findings from this Delta-infected cohort underscore the importance of vaccination that extends beyond individual protection to protection of household contacts and suggests that vaccination would also help prevent transmission in the community.

Our results also affirm previous reports on waning immunity post-vaccination with mRNA vaccines[2,26,27] and support the need for booster doses in order to maintain initial high levels of protection against acquisition. As our analysis focuses on an exclusively Delta-infected cohort, we are able to show that the association with increased risk of SARS-CoV-2 infection is indeed dependent on time from full-vaccination and not simply inherent to the Delta variant.

Data from the United States CDC have suggested that there may be variation in vaccine-induced protection depending on vaccine type, with vaccine effectiveness against hospitalization

reportedly higher for the mRNA-1273 vaccine (93%) than the BNT162b2 vaccine (88%).[28] The CDC did not evaluate cases that did not result in hospitalization and did not stratify vaccine effectiveness by variant. Doing so in this study, we have similarly found that mRNA-1273 was associated with reduced risk of SARS-CoV-2 acquisition compared with BNT162b2, taking into account time since full-vaccination.

Paediatric household transmission is relatively understudied, with evidence limited to the pre-Delta era. The role of this age-group in driving onward transmission particularly during Delta predominance and in the context of varying rates of adult immunization is important. Results from early household studies have differing results, with some suggesting that children are less likely to transmit SARS-CoV-2 compared to adults[5–7,29], and others documenting comparable rates of transmission.[8],[9] Our findings suggest that young children (0–11 years) are important drivers of onward transmission to their household contacts, and support paediatric vaccination where available[30], especially in multi-generational households with high-risk elderly or immunocompromised family members. Children are known to shed infectious SARS-CoV-2[31], and a few studies have detected higher or similar nasopharyngeal viral loads in children compared to adults[32,33]. Increasing use of physical-distancing and masks at home was associated with older age of indices ≤18 years old, suggesting that younger children may be less capable of adhering to strict hygiene practices[10], and/or are less able to self-isolate from caregivers when they are ill.

Since the completion of our study, the Omicron variant has largely replaced the Delta variant as the predominant strain. Preliminary findings from Denmark reported a higher household SAR for the Omicron variant than the Delta variant[34]. Reassuringly, vaccination appears to remain effective against the Omicron variant[34,35].

The risk of household contacts acquiring infections outside of the household prior to quarantine cannot be excluded, but this would be minimized by the low number of community cases in Singapore during the study period (0.56 cases per 100,000 population per day over the study duration) and short lag-time between case notification and quarantine of household contacts. There is a possibility that the index (i.e. the first COVID-19-diagnosed person in the household) may not be the true primary case. However this scenario would likely be minimized by aggressive contact-tracing and establishment of transmission chains in Singapore since the first diagnosed case, and where possible assignment of the index would be dependent on the earliest symptom onset or likely transmission source outside of the household.[36,37] Contacts' symptom data was based on interview by MOH contact-tracers soon after index diagnosis and may have resulted in the misclassification of pre-symptomatic individuals (who were asymptomatic at time of interview) as asymptomatic, which could affect risk estimates of symptomatic infection. Chronic disease data is not routinely captured in the MOH contact-tracing database and hence chronic disease was not adjusted for in our analyses. As chronic diseases tend to be more common in older age, this could have been reflected by the increased risk estimates in older age-groups.

As the number of paediatric cases increases worldwide due to the spread of more infectious variants, the role of children in onward transmission will grow. Household members especially those who are primary caregivers of infected children recuperating at home should be aware of the potential risks and take necessary precautions. While breakthrough infections occur in fully-vaccinated individuals, our findings support both adult and paediatric vaccination in mitigating the risks of onward transmission. The increase in SARS-CoV-2 acquisition with longer time since complete vaccination suggests that booster doses would help reduce household transmission. Vaccine type is a factor to consider in efforts to prevent SARS-CoV-2 transmission.

NOTES

CONTRIBUTORS

OTN and KM conceived of and led the study. CJC, TMM, JKC, SSHO, YKL, KBT were involved in data collection. OTN, VK, NMT, ZF and AKJ have accessed and verified the data. OTN, VK, NMT, ARC and VJML were involved in data analysis, data interpretation and writing of the manuscript in consultation with CJC, KM, TMM, JKC, SSHO, YKL, ZF, AKJ, SM-S, LC, RTPL, KBT, ARC and YSL.

DATA SHARING STATEMENT

Individual-level participant data that underlie the results reported in this article, after de-identification (text, tables, figures, and appendices), is regarded as sensitive and will not be shared. The study methods and statistical analyses are described in detail in the manuscript.

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The sponsor(s) of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors were not precluded from accessing data in the study, and they accepted responsibility to submit for publication.

DECLARATION OF INTERESTS

We declare no competing interests.

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1 **TABLES**

2

3 **Table 1. Secondary attack rate among household close-contacts (n=8470) of Delta variant-positive index cases, by vaccination status**

	Vaccination[a] status of contact			
	All	**Unvaccinated**	**Partially-vaccinated[b]**	**Fully-vaccinated[c]**
Number of contacts	8470	2067	2448	3955
Median age of contacts, in years (IQR)	36[d] (26—51)	26[e] (7—39)	33 (26—40)	46 (32—59)
Number of female contacts (%)	4038[f] (47.7)	1072[g] (51.9)	1169 (47.8)	1797 (45.4)
Number of unique index cases linked to all contacts[h]	2583	1061	1352	1940
Median age of unique index cases linked to all contacts, in years (IQR)	45 (31—60)	39 (30—54)	43 (31—58)	46 (32—61)
Number of females among unique index cases linked to all contacts (%)	1002 (38.8)	426 (40.2)	524 (38.8)	729 (37.6)
Unvaccinated individuals among unique index cases (%)	612 (23.7)	415 (39.1)	306 (22.6)	340 (17.5)
Partially-vaccinated individuals among unique index cases (%)	602 (23.3)	268 (25.3)	437 (32.3)	396 (20.4)
Fully-vaccinated individuals among unique index cases (%)	1369 (53.0)	378 (35.6)	609 (45.0)	1204 (62.1)
Number of unique contact groups[i,j]	2583	1061	1352	1940
1 contact (%)	474 (18.4)	545 (51.4)	743 (55.0)	866 (44.6)
2 contacts (%)	517 (20.0)	269 (25.4)	341 (25.2)	517 (26.6)
3 to 5 contacts (%)	1342 (52.0)	229 (21.6)	251 (18.6)	536 (27.6)
≥6 contacts (%)	250 (9.7)	18 (1.7)	17 (1.3)	21 (1.1)
Median number of contacts in each contact group (IQR)[i]	3 (2—4)	1 (1—2)	1 (1—2)	2 (1—3)
Mean number of contacts in each contact	3 (2)	2 (1)	2 (1)	2 (1)

group, rounded (SD)[i]				
Median days from symptom onset or notification of diagnosis (if asymptomatic) to hospital admission of index case (IQR)	1 (0—2)	1 (0—2)	1 (0—2)	1 (0—2)
Number of contact groups with no cases among contacts (%)	1707 (66.1)	735 (69.3)	1051 (77.7)	1469 (75.7)
Number of contact groups with cases among contacts (%)	876 (33.9)	326 (30.7)	301 (22.3)	471 (24.3)
1 case	523	218	233	373
2 cases	194	69	46	71
3 cases	81	21	16	19
≥4 cases	78	18	6	8
Type of vaccine administered[k]				
BNT162b2 (% of vaccinated)	5140 (80.3)	NA	1865 (76.2)	3275 (82.8)
mRNA-1273 (% of vaccinated)	977 (15.3)	NA	373 (15.2)	604 (15.3)
Others/mixed[l] (% of vaccinated)	285 (4.5)	NA	210 (8.6)	75 (1.9)
Number of cases among contacts	1504	499	397	608
Secondary attack rate (%) (95% BCI)	17.8 (16.5–19.0)	24.1 (21.6–26.8)	16.2 (14.4–18.1)	15.4 (14.0–16.8)
Number of symptomatic cases among contacts	995	367	275	353
Attack rate (%) (95% BCI)	11.7 (10.8–12.7)	17.8 (15.5–20.0)	11.2 (9.8–12.7)	8.9 (7.9–10.0)
Number of severe cases[m] among contacts	51	37	9	5
Attack rate (%) (95%BCI)	0.6 (0.4–0.7)	1.8 (1.1–2.2)	0.4 (0.2–0.6)	0.1 (0.0–0.3)

Abbreviations: BCI, bootstrap confidence interval; IQR, inter-quartile range; SD, standard deviation

[a] Vaccination is defined as having received at least one dose of vaccine before the start date of quarantine.

[b] Partially-vaccinated is defined to mean having received one vaccine dose or to be within 14 days of the second vaccine dose on the start date of quarantine.

[c] Fully-vaccinated is defined to mean having received both doses of vaccine more than 14 days prior to the start date of quarantine.

[d] Of 8470 contacts, age information was not available for one (0.01%).

[e] Of 2067 contacts, age information was not available for one (0.05%).

[f] Of 8470 contacts, gender information was not available for one (0.01%).

[g] Of 2067 contacts, gender information was not available for one (0.05%).

[h] Note that a unique index case may be linked to multiple contacts with different vaccination statuses.

[i] Contact group refers to a group consisting of an index case and their close-contacts. Note that a unique index case may be linked to multiple contacts with different vaccination statuses.

[j] Refers to the number of contacts, excluding the linked index case(s).

[k] Refers to vaccine administered to contacts. Of 6403 partially/fully-vaccinated contacts, vaccine brand information was not available for one fully-vaccinated contact (0.02%).

[l] This category includes those who were administered the CoronaVac and BBIBP–CorV vaccines, or two-dose combinations of different brands.

[m] Severe cases refer to those requiring oxygen supplementation, resulting in ICU admission, or resulting in death

Table 2. Multivariable logistic regression of risk factors associated with SARS–CoV–2 acquisition by household contacts of index cases infected with the Delta variant (n=8470). Features of both contact and index are considered. Models are fit with generalized estimating equations to account for clustering at the household level.

Variables		Case	Control	Univariable Analysis		Multivariable Analysis	
Person	**Risk factor**	**n=1504**	**n=6966**	**OR (95%RCI)**	**P Value**	**aOR (95%RCI)**	**P Value**
Contact	Unvaccinated (ref)	499	1568	1 (ref)	ref	1 (ref)	ref
"	BNT162b2						
	Partially-vaccinated[a]	317	1548	0.64 (0.54–0.77)	<0.0001	0.73 (0.59–0.90)	0.0033
	Fully-vaccinated[b,c]	538	2737	0.62 (0.52–0.73)	<0.0001	0.57 (0.47–0.70)	<0.0001
"	mRNA–1273						
	Partially-vaccinated[a]	45	328	0.43 (0.30–0.61)	<0.0001	0.49 (0.34–0.71)	0.0002
	Fully-vaccinated[b,c]	62	542	0.36 (0.27–0.49)	<0.0001	0.39 (0.28–0.54)	<0.0001
"	Others/mixed[d]						
	Partially-vaccinated[a]	35	175	0.63 (0.39–1.00)	0.051	0.88 (0.55–1.41)	0.59
	Fully-vaccinated[b,c]	8	68	0.37 (0.16–0.84)	0.018	0.47 (0.20–1.11)	0.084
"	Female (ref)	775	3263[f]	1 (ref)	ref	1 (ref)	ref
"	Male	729	3703[f]	0.83 (0.74–0.93)	0.0018	0.95 (0.84–1.06)	0.36
"	Age group (years):						
	0–11	173	584	2.17 (1.67–2.82)	<0.0001	1.43 (1.07–1.93)	0.017
	12–17	49	330	1.09 (0.74–1.59)	0.66	0.97 (0.66–1.42)	0.87
	18–29	212	1553	1 (ref)	ref	1 (ref)	ref
	30–44	444	2185	1.49 (1.23–1.81)	<0.0001	1.46 (1.20–1.78)	0.0002
	45–59	289	1354	1.56 (1.29–1.90)	<0.0001	1.71 (1.39–2.09)	<0.0001
	≥60	337	960	2.57 (2.09–3.16)	<0.0001	2.44 (1.95–3.05)	<0.0001
"	Exposure to symptomatic index[e] (per day)	–	–	1.00 (0.98–1.02)	0.85	0.99 (0.97–1.01)	0.41
Index	Unvaccinated (ref)	483	1525	1 (ref)	ref	1 (ref)	ref
"	BNT162b2						
	Partially-vaccinated[a]	273	1323	0.65 (0.51–0.83)	0.0005	0.78 (0.60–1.02)	0.072
	Fully-vaccinated[b]	629	3234	0.61 (0.51–0.74)	<0.0001	0.56 (0.44–0.71)	<0.0001
"	mRNA–1273						
	Partially-vaccinated[a]	28	241	0.37 (0.19–0.69)	0.0019	0.45 (0.23–0.87)	0.017
	Fully-vaccinated[b]	45	303	0.47 (0.25–0.89)	0.021	0.51 (0.27–0.96)	0.037
"	Others/mixed[d]						
	Partially-vaccinated[a]	36	279	0.41 (0.24–0.70)	0.0012	0.52 (0.30–0.91)	0.023

	Fully-vaccinated[b]	10	61	0.52 (0.23–1.15)	0.11	0.64 (0.28–1.46)	0.29
"	Female (ref)	524	2610	1 (ref)	ref	1 (ref)	ref
"	Male	980	4356	1.12 (0.95–1.32)	0.18	1.23 (1.04–1.46)	0.016
"	Age group (years):						
	0–11	88	261	3.22 (2.20–4.72)	<0.0001	2.37 (1.57–3.60)	<0.0001
	12–17	22	101	2.08 (1.03–4.21)	0.041	1.81 (0.91–3.60)	0.089
	18–29 (ref)	138	1319	1 (ref)	ref	1 (ref)	ref
	30–44	450	2290	1.88 (1.40–2.53)	<0.0001	1.79 (1.32–2.43)	0.0002
	45–59	379	1753	2.07 (1.54–2.78)	<0.0001	2.43 (1.77–3.33)	<0.0001
	≥60	427	1242	3.29 (2.45–4.41)	<0.0001	3.56 (2.59–4.91)	<0.0001

Abbreviations: aOR, adjusted odds ratio; RCI, robust confidence interval; ref, reference level

[a] Partially-vaccinated is defined to mean having received one vaccine dose or to be within 14 days of the second vaccine dose on the start date of quarantine.

[b] Fully-vaccinated is defined to mean having received both doses of vaccine more than 14 days prior to the start date of quarantine.

[c] One of 3955 (total) fully-vaccinated individuals was excluded as vaccine type information was not available.

[d] This category includes those who were administered the CoronaVac and BBIBP–CorV vaccines, or two-dose combinations of different brands.

[e] Refers to the time interval between symptom onset or notification (if asymptomatic) and hospitalization of the index case.

[f] One of 6966 individuals (controls) was excluded as gender information was not available.

Table 3. Multivariable logistic regression of risk factors associated with SARS-CoV-2 acquisition and symptomatic illness by household contacts of index cases infected with the Delta variant, comparing BNT162b2 with mRNA-1273. Features of both contact and index are considered. Models are fit with generalized estimating equations to account for clustering at the household level.

Variables		Multivariable Analysis[a] (Acquisition)		Multivariable Analysis[a] (Symptomatic Infection)	
Person	**Vaccine type**	**aOR (95%RCI)**	**P Value**	**aOR (95%RCI)**	**P Value**
Contact	BNT162b2	1 (ref)	ref	1 (ref)	ref
"	mRNA–1273	0.75 (0.59–0.94)	0.013	0.69 (0.52–0.92)	0.012
"	Others/mixed[b]	1.16 (0.77–1.73)	0.47	1.45 (0.91–2.33)	0.12
Index	BNT162b2	1 (ref)	ref	1 (ref)	ref
"	mRNA–1273	0.71 (0.46–1.08)	0.11	0.68 (0.40–1.14)	0.14
"	Others/mixed[b]	0.75 (0.48–1.18)	0.22	0.81 (0.49–1.33)	0.41

Abbreviations: aOR, adjusted odds ratio; RCI, robust confidence interval; ref, reference level

[a] Models are adjusted for both contact and index age and gender, duration of exposure of contact to symptomatic index (i.e. time interval between symptom onset or notification [if asymptomatic] and hospitalization of the index case) and both contact and index vaccine status (i.e. unvaccinated, partially-vaccinated or fully-vaccinated) including duration since being fully-vaccinated

[b] This category includes those who were administered the CoronaVac and BBIBP–CorV vaccines, or two-dose combinations of different brands

FIGURE LEGENDS

Figure 1. Adjusted odds ratios (aOR) of SARS-CoV-2 acquisition or symptomatic infection of the contact by vaccine status. (a) Acquisition, by vaccine status of the contact. (b) Symptomatic infection, by vaccine status of the contact. (c) Acquisition, by vaccine status of the index case. aOR are relative to unvaccinated contact (a and b) or index (c). Partially-vaccinated (PV) is defined to mean having received one vaccine dose or to be within 14 days of the second vaccine dose on the start date of quarantine. Thereafter, time is aggregated to 30-day intervals ("months") since being fully-vaccinated (15 days or more from the second dose). Estimates are adjusted for age-group and gender of both contact and index, and duration of exposure to the index. The p for trend for (a) and (b) were <0.0001 and the p for trend for (c) was 0.20. Clustering at the household level is accommodated using generalized estimating equations. Whiskers are 95% confidence intervals.

Figure 2. Adjusted risks of infection of the contact, based on (a) the contact's age and vaccine status, and (b) the index's age and vaccine status. Risks are derived from bootstrapped logistic regression models with interactions on vaccine status of index and contact, adjusting for age (of the other individual) and sex (of both). For (a), a mixture distribution of vaccine status and age of the index was used to match the overall distribution, while for (b) the same was done but for contacts. The risks for fully-vaccinated and partially-vaccinated children under 12 were not calculated as they were not part of the vaccine programme at the time. Note the non-linear spacing on the x-axes.

63 Figure 1

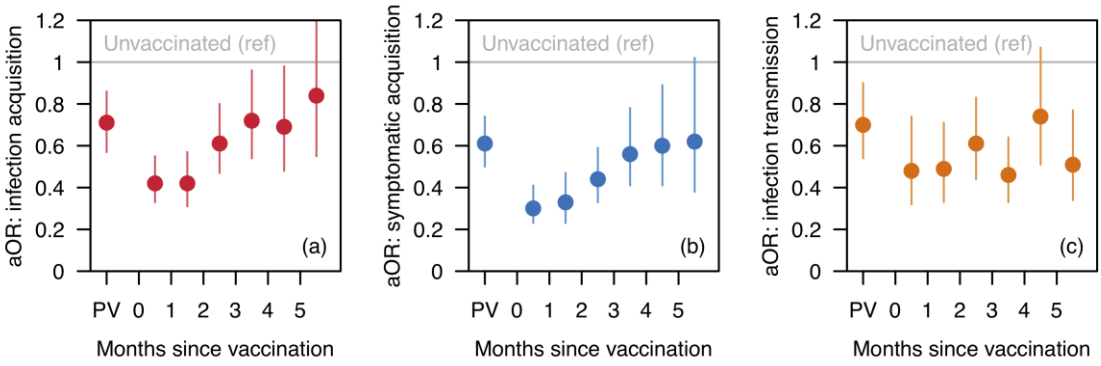

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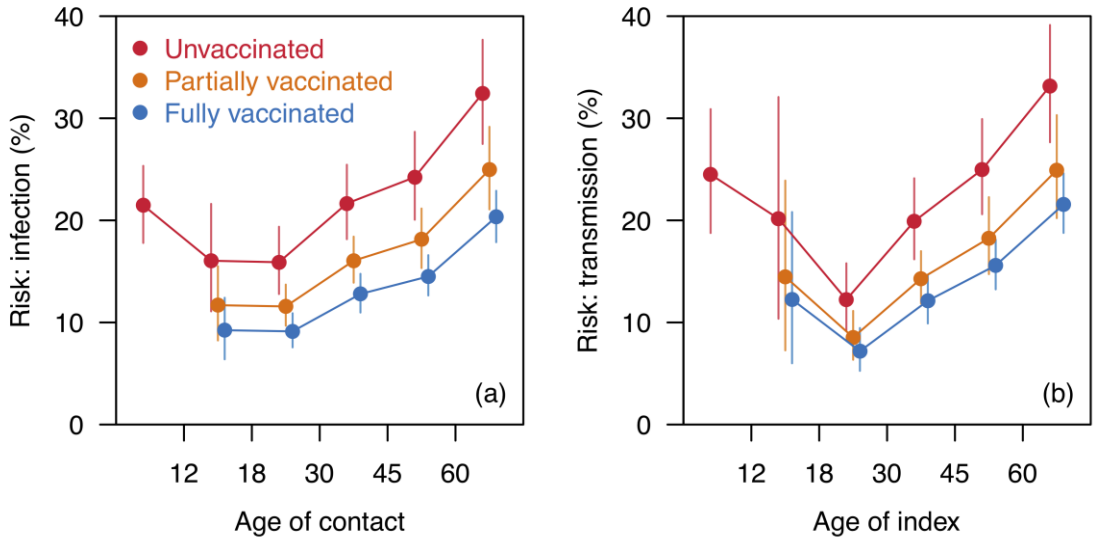
Figure 2



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