Assessing the effects of SARS-CoV-2 vaccination on the risk of household transmission during delta variant circulation: a population-based data linkage cohort study

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Summary

Background Data on SARS-CoV-2 vaccine effectiveness to reduce transmission of infection in household settings are limited. We examined the effects of SARS-CoV-2 vaccines on Delta variant transmission within households in an infection-naïve population.

Methods This was a population-based data linkage cohort study in the Greater Sydney Metropolitan Area, New South Wales, Australia based on cases observed in June–November 2021. In households with ≥1 confirmed COVID-19 case, we calculated adjusted odds ratios (aOR) and 95% Confidence Intervals (95% CI) for the risk of SARS-CoV-2 transmission, by vaccination status (unvaccinated, partially vaccinated, fully vaccinated, or waning) and type of vaccines (mRNA or vector-based) received by both index cases and household contacts.

Findings In 20,651 households with a single index case, 18,542 of 72,768 (25%) household contacts tested PCR-positive ≤14 days after their respective index case. Household contacts with partial, full, or waning mRNA vaccination had aORs of 0.46 (95% CI 0.40–0.52), 0.36 (95% CI 0.32–0.41) and 0.64 (95% CI 0.51–0.80) compared to unvaccinated contacts, while for vector vaccines the corresponding aORs were 0.77 (95% CI 0.67–0.89), 0.65 (95% CI 0.55–0.76), and 0.64 (95% CI 0.39–1.05). Full mRNA-vaccination in index cases compared to non-vaccination was associated with aORs between 0.09 and 0.21 depending on the vaccination status of household contacts.

Interpretation Full vaccination of household contacts reduced the odds to acquire infection with the SARS-CoV-2 Delta variant in household settings by two thirds for mRNA vaccines and by one third for vector vaccines. For index cases, being fully vaccinated with an mRNA vaccine reduced the odds of onwards transmission by four-fifths compared to unvaccinated index cases. Full vaccination offered stronger protection than partial vaccination, particularly for mRNA vaccines, but with reduced effects when the last vaccination preceded exposure by ≥3 months.

Funding New South Wales Ministry of Health.

Keywords: SARS-CoV-2; COVID-19; Vaccination; Vaccines; Households; Transmission; Infection

Introduction

Vaccines against SARS-CoV-2 have become the most important single public health intervention during the COVID-19 pandemic. A range of vaccines with excellent safety and efficacy profiles have been developed and applied at scale around the world.[1] These vaccines continue to offer high protection against serious illness even as their effectiveness against infection has declined due the emergence of increasingly immune-evasive viral variants, and despite significant declines in antibody levels within a few months of vaccination.[2,3] Important knowledge gaps remain regarding the effects of vaccination status and type of vaccines received on the risk to transmit infection. Households have been identified as

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Research in context

Evidence before this study

The protective effects of SARS-CoV-2 vaccines against severe COVID-19 and death have been comprehensively demonstrated but there are limited data on their effect on transmission of infection in household settings. We searched PubMed, Google Scholar, and MedRxiv until January 09, 2023 for original research articles that reported data on SARS-CoV-2 transmission risks within households, using combinations and variations of the terms 'COVID-19', 'SARS-CoV-2', 'vaccines', 'household', 'transmission', 'infection', 'risk', and 'vaccination status'. We focused on analyses that assessed vaccine effects stratified by vaccination status of both the index case and the household contact, and for different types of vaccines. A pooled analysis from April 2022 based on 6 household transmission studies found reduced risks for household contacts to acquire infection with improved vaccination status, but no change in the risk for index cases to transmit regardless of their vaccination status. No stratified analysis of all possible combinations between index case vaccination status and household contact vaccination status was done, nor were vaccine types considered, nor was adjustment for important confounding factors done. Further, all existing studies were done in settings where high transmission had occurred before or during the observation period, and when uptake of testing was limited. Subsequent to this meta-analysis, two studies from Denmark examined household transmission risks and protective effects of vaccines in relation to Delta and Omicron variant co-circulation and later Omicron BA.1 and BA.2 variant co-circulation. However, these studies were conducted after a substantial time lag between receipt of second dose and exposure, with high background transmission levels, in a context of largely unrestricted population movement, and with much reduced completeness of test and trace capacity. A detailed understanding of the effects of SARS-CoV-2 vaccines on transmission risks in household settings in the absence of these biases therefore remains lacking.

Added value of this study

We conducted a population-based data linkage study among people living in the Greater Sydney Metropolitan Area, New South Wales, Australia between June and November 2021. To our knowledge, this is the first study providing robust estimates of the independent effects of vaccination status (unvaccinated, partially vaccinated, fully vaccinated, or waning) and types of vaccines received (mRNA or vector-based) on SARS-CoV-2 transmission risks at household level. Our analysis confirmed the previously observed reduced risk to acquire infection among susceptible, vaccinated household contacts, with a greater reduction among those fully vaccinated. We further showed similar effects on the risk of onwards transmission from infected, vaccinated index cases, again with a greater reduction among those fully vaccinated. Importantly, we found synergistic protective effects when both the index case and the household contact received an mRNA vaccine. Our study was larger than the pooled sample size of the biggest existing meta-analysis analysis and larger than the subsequent Danish studies comparing Delta and Omicron subvariant transmission. Further, our study setting was characterized by the absence of widespread community transmission prior to our study period, heavily restricted mixing and movement outside households during the study period, high levels of centralised testing of suspected cases, and rigorous contact tracing and testing.

Implications of all the available evidence

This study provides new quantitative estimates of the extent to which both viral vector and mRNA vaccines were able to reduce SARS-CoV-2 transmission risks in the context of the Delta variant, without significant levels of prior infection. In addition to direct protection of household contacts from both types of vaccines, breakthrough cases were less infectious in this context, even after a single dose. Despite large changes in circulating variants and near ubiquitous exposure to infection since our observation period, there is still potential for vaccines to prevent transmission besides providing protection against severe disease. This would appear most likely with Omicron-containing vaccines that are well-matched to circulating sub-lineages, given recent evidence of improved protection from bivalent BA.4/5-containing vaccines.

important settings of SARS-CoV-2 transmission,[4] and given suitable epidemiological conditions such as good vaccination data, high testing rates, strong contact tracing, and low population immunity levels, allow to measure these effects in detail.

During 2020, Australia had been highly effective at controlling the spread of SARS-CoV-2 through a combination of international and domestic border closures, movement and mixing restrictions, and contact tracing and testing.[5] However, an outbreak of the Delta variant in Sydney, New South Wales (NSW) beginning 16 June 2021 continued to grow despite a combination of strict movement restriction and comprehensive contact tracing, testing and isolation.[6] Until then there had been very limited community transmission of SARS-CoV-2 in NSW, with a cumulative case count of locally acquired infections of only 2095 in a population of 8.1 million since the start of the pandemic, and with the last recorded cluster of locally acquired infection at the start of 2021.[7] Coverage with ≥1 vaccine doses in NSW was just over 20% at that time, and nearly all administered vaccines in Australia were either AstraZeneca or Pfizer.[8] Vaccine uptake as of June 2021 was geographically heterogeneous, and coverage was strongly associated

with income levels across local government areas (LGAs).[9] Concerted efforts to improve uptake, including targeted campaigns to interrupt transmission in LGAs with higher incidence, led to first and second dose coverage in NSW in those aged 16 years and above rising to 68% and 37% by 31 August 2021,[10] and to 94% and 88% by 31 October 2021.[11] Over this period, the epidemic in NSW, which was concentrated within Sydney LGAs, peaked and declined, and strict movement restrictions were largely removed by the middle of October (Fig. 1 Panel A and B).[12] At the same time, a very high level of testing coverage using polymerase chain reaction (PCR) assays at central testing facilities was maintained, as well as extensive contact tracing.[13–15] This provided the opportunity to closely observe a large-scale SARS-CoV-2 outbreak in an infection-naïve population with concurrent vaccine rollout.

In this context we conducted a data-linkage study with the aim to estimate SARS-CoV-2 transmission risks within households by vaccination status and type of vaccines received for both index cases and household contacts.

Methods

Study design

This was a population-based person-level record linkage cohort study using routinely collected data from people living in the Greater Sydney Metropolitan Area, New South Wales, Australia between June and November 2021.

Data sources

We received a dataset from the NSW Ministry of Health (NSW Health) that contained individual records from the Australian Immunisation Register (AIR)[16] and the NSW Health Notifiable Conditions Information Management System (NCIMS),[17] linked by the NSW government's Centre for Health Record Linkage (CheReL) system.[18] ChrRel is the official health record linkage system in NSW and as such used frequently for health data linkage studies in Australia.[19] It uses a combined deterministic and probabilistic matching algorithm from the Choicemaker software package,[20] with all unclear or undetermined matching results being verified individually by trained staff using established decision-making algorithm.[21] AIR is a national register that records data on vaccines provided in Australia under national immunisation programs and for other purposes such as international travel. AIR contains geocoded address data that are largely based on data from Medicare, Australia's public health insurance scheme. For our analysis, we assumed that the address data in AIR defined place of residence, and that people with the same address resided in the same household. NCIMS is a NSW Health owned state-level data system managing the surveillance and reporting of notifiable diseases and conditions, which has been extensively modified to support detailed case and contact investigations for COVID-19. Demographic and vaccination-related information for our analysis was obtained from AIR, while symptom status was obtained from NCIMS.

We used data from the 2016 Australian Census[22] to determine the socio-economic status (SES) of each household.

Participants

We established COVID-19 vaccination and SARS-CoV-2 infection status for all people residing in the same household based on recorded address data. We designated the earliest recorded case of COVID-19 among members of each household as the index case for the household.

Among all records with geocoded Medicare addresses in the LGAs that constitute the Greater Sydney Metropolitan Area,[23] see Fig. 1 Panel C, we excluded people with geographically unspecified addresses on AIR, such as PO Boxes. We also excluded people whose address was not shared by any other person as they could not have household contacts to investigate. We further excluded people who shared an address with at least 9 others, as these were more likely to represent institutional group living arrangements (e.g., aged care facilities, prisons) which would be likely to differ from domestic households in regard to their transmission characteristics. We also excluded cases whose infection was determined to have been acquired overseas, as these individuals were placed in mandatory hotel quarantine upon arrival and hotel isolation for the entire duration of their infectious period. We further excluded households in which no recorded resident was aged above 19 years.

A 'case' was an individual recorded on NCIMS as having tested PCR-positive for SARS-CoV-2 between 16 June and 18 November 2021. Each household with at least one case was assigned an 'index case', defined as the person recorded as having tested positive first ('index onset date'). We defined onset dates for index and contact cases as symptom onset, if available, or the specimen collection date of the first positive PCR test otherwise. Rapid antigen tests were not available for community use until 1 November 2021 and uptake was very low until rise of the Omicron variant after our observation period.[24] All other members of that household were considered 'household contacts'. Households in which there were no cases, and those in which more than one person had the same, earliest onset date were excluded from further analysis. Household contacts recorded as having tested positive within 14 days of the index onset date, as defined by the contact onset date, were classified as 'positive contacts', while household contacts without onset dates during that period were classified as 'negative contacts'.

Variables

The primary outcome variable was the SARS-CoV-2 infection status (positive or negative) of household

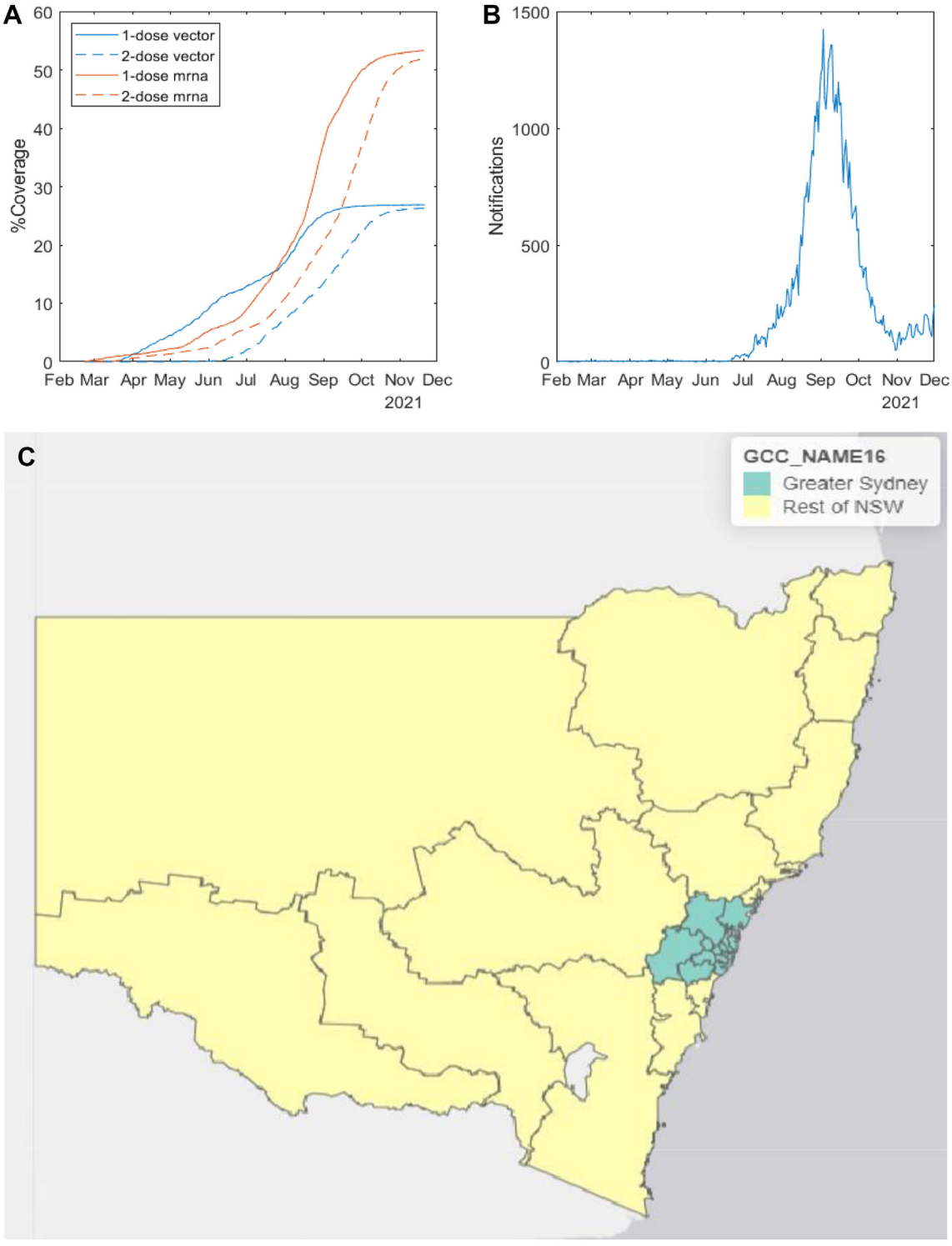

Fig. 1: Incidence (Panel A), vaccination coverage (Panel B) in the Greater Sydney Metropolitan Area (Panel C) during 2021.

contacts. Available individual-level variables of contacts were vaccination status, type of vaccine received, and age. Available individual-level variables of index cases were vaccination status, type of vaccine received, age, sex, and symptom status. Available household-level variables were SES, household size, household type as per age composition defined above, and LGA. The variables symptom status of index case and LGA of household did not meet the definition of confounding variables as per directed acyclic graph (DAG) analysis and were hence excluded (see Supplementary Material 1 for details), while all other variables were retained.

We classified the vaccination status of household contacts by the number of doses received and the most recent date of vaccination prior to the index onset date as follows: (a) 'unvaccinated' if they had received no vaccine or their first dose was less than 21 days prior to the index onset date; (b) 'partially vaccinated' if they received one dose or their second dose less than 14 days before the index onset date; (c) 'fully vaccinated' if they received their second dose 14 or more days before the index onset date; and (c) 'waning' if they received their second dose three or more months before the index onset date. Third doses (boosters) had not been made available widely at this stage in Australia.[25] The vaccination status of index cases used the same classification system. Vaccines were grouped by type into: (a) 'vector' (AstraZeneca); or (b) 'mRNA' (Pfizer or Moderna).

Households were classified according to the age composition of their members as follows: (a) 'working age only' if all members were aged 19–64 years; (b) 'retirement age only' if all members were aged ≥65 years; (c) 'working age with school age' if all members were ≤64 years but at least one was ≤18; (d) 'working age with retirement age' if no member was ≤18 years but at least one was ≥65 years; and (e) 'multigenerational' if all age groups (under 19, 19–64 and over 64) were present.

We calculated households' SES using the Socio-Economic Indexes for Areas (SEIFA), a geographical classification system of relative socio-economic disadvantage provided by the census,[26] based on the Statistical Area Level 1 (SA-1) and represented using quintiles. SA-1 is the smallest geographical unit for which census data are routinely released, generally with a population of 200–800.[27]

Statistical methods

We used percentages, medians and inter-quartile ranges (IQR) to describe the distribution of characteristics among index cases and household contacts. We calculated crude odds ratios (cOR) with 95% confidence intervals (95% CI) of the risk of infection for household contacts in relation to specific categorical variables using a logistic regression model with a random intercept for household. We then built a multivariable logistic regression model, again with a random household factor, adjusting for all pre-identified potential confounders, to calculate the adjusted odds ratios (aOR) and 95% CIs of the effects of vaccination status and type of vaccine received on the risk of infection for household contacts.

We then explored possible interaction effects between the vaccination status of the household contacts and the index cases by log-likelihood ratio testing (LRT) of the multivariable model with and without a term for interaction between these two variables, and by plotting the odds ratios of infection for varying levels of vaccination status for household contacts and index cases. We then fitted a multivariable regression model, again with a random household factor, to estimate aORs and 95% CIs for all possible combinations between vaccination status of index cases and household contacts (unvaccinated, partially vaccinated, fully vaccinated), and stratified by type of vaccine (mRNA or vector vaccine). We also conducted sensitivity analyses to explore the effects of not presenting contacts with waning immunity separately in the multivariable analysis, and of the effects of presenting merged results from households where not all household members receiving the same type of vaccines. All models were fitted using the 'lme4' package in R 4.0.2.

Role of funding source

This study was supported by funding from NSW Health. NSW Health facilitated data access and conducted the data linkage, provided funding support for the analysis, provided feedback on draft results, and supported the decision to submit for publication.

Results

Over the study period 16 June to 18 November 2021, there were 62,942 SARS-CoV-2 cases in the Greater Sydney Metropolitan Area recorded in NCIMS. Of these, 58,144 (92.4%) were linked to records in AIR by CheReL, resulting in a dataset with a total of 29,091 unique addresses with at least one SARS-CoV-2 case, and 82,021 people registered at these addresses who were not recorded as having become a case during the study period. We excluded 1122 cases with an incomplete or unreliable geocoded addresses, 111 recorded as being in quarantine upon arrival from outside Australia, and 3797 with no household contacts in our data set. We further excluded all people registered at 1830 addresses shared by 10 or more people, and all people from 128 addresses in which only individuals aged 19 or younger were listed as resident. We also excluded all members of 143 households associated with cases with multiple addresses, and 1758 households with multiple cases sharing the same earliest diagnosis date. A further 33 households for which a SEIFA rank could not be identified, and 4 households for which the sex of the index case could not be determined were excluded. The resulting study

population consisted of 72,768 household contacts in 20,651 households with one index case each, of whom 18,542 (25%) became positive in the two weeks following the index onset date (Supplementary Material 2).

As shown in Table 1, 57% of index cases were male, with a median age of 21 (IQR 31,46), and largely (74%) unvaccinated. Coverage with a vector vaccine (AstraZeneca) and mRNA vaccine (Pfizer or Moderna) was similar (11% and 14%, respectively). Nearly half of the households included working-aged and school-aged members (49%); had between 5 and 9 members (45%); and were classified as being in the lowest SES category (46%).

As shown in Table 2, the characteristics of household contacts resembled those of index cases. Compared to unvaccinated household contacts, the cORs of acquiring infection for partially vaccinated, fully vaccinated, and household contacts with waning immunity were 0.43 (95% CI 0.39–0.48), 0.31 (95% CI 0.28–0.34), and 0.40 (95% CI 0.33–0.49), respectively. Household contacts whose associated index cases were partially vaccinated, fully vaccinated, or whose immunity was waning, had cORs of infection of 0.45 (95% CI 0.38–0.52), 0.24 (95% CI 0.20–0.29), and 0.30 (95% CI 0.23–0.4), respectively.

Table 3 shows estimates of the protective effects of vaccination for household contacts to acquire infection, adjusted for index-case vaccination status and other pre-identified potentially confounding co-variates. Household contacts who were partially or fully vaccinated with a vector vaccine, had aORs of infection of 0.77 (95% CI 0.67–0.89) and 0.65 (95% CI 0.55–0.76), respectively, compared to unvaccinated household contacts. The respective aORs for mRNA vaccinated household

	Unvaccinated		Partially vaccinated		Fully vaccinated		Waning vaccination		Total	
	Count	Row %	Count	Row %	Count	Row %	Count	Row %	Count	Column %
Total	15,358	74	2476	12	2093	10	724	4	20,651	100
Type of vaccine received by index case										
Unvaccinated	15,358	100	0	0	0	0	0	0	15,358	74
Vector	0	0	1257	54	958	41	130	6	2345	11
mRNA	0	0	1219	41	1135	39	594	20	2948	14
Age group of index case, years										
0–18	3262	96	86	3	55	2	3	0	3406	16
19–29	4490	79	622	11	464	8	120	2	5696	28
30–39	3229	74	578	13	411	9	152	3	4370	21
40–64	3744	65	923	16	842	15	261	5	5770	28
65+	633	45	267	19	321	23	188	13	1409	7
Sex of index case										
Male	8478	73	1562	13	1254	11	392	3	11,686	57
Female	6876	77	914	10	839	9	332	4	8961	43
Missing	4	100	0	0	0	0	0	0	4	<0.1
Household size, n										
2	2231	66	481	14	450	13	196	6	3358	16
3–4	5746	72	1019	13	898	11	290	4	7953	39
5–9	7381	79	976	10	745	8	238	3	9340	45
Household type										
Working age with school age	8206	81	950	9	699	7	233	2	10,088	49
Working age only	3634	68	821	15	687	13	211	4	5353	26
Working age with retirement age	1810	64	424	15	414	15	159	6	2807	14
Retirement age only	122	35	71	20	94	27	64	18	351	2
Multi-generational	1586	77	210	10	199	10	57	3	2052	10
Socio-economic status of household										
1 (most disadvantaged)	7642	80	1047	11	672	7	152	2	9513	46
2	3655	73	644	13	527	11	170	3	4996	24
3	2088	71	390	13	339	12	128	4	2945	14
4	1284	65	245	12	308	16	142	7	1979	10
5 (least disadvantaged)	666	56	144	12	245	21	130	11	1185	6
Missing	23	70	6	18	2	6	2	6	33	0.1

Table 1: **Index case/household-level characteristics by vaccination status.**

	Positive contacts		Negative contacts		Total		Crude odds-ratio[a]
	Count	Column %	Count	Column %	Count	Column %	OR (95% CI)
Total	18,542	100	54,226	100	72,768	100	
Vaccination status of household contact							
Unvaccinated	15,610	84	37,461	69	53,071	73	1
Partially vaccinated	1394	8	6860	13	8254	11	0.43 (0.39–0.48)
Fully vaccinated	1254	7	8283	15	9537	13	0.31 (0.28–0.34)
Waning vaccination	284	2	1622	3	1906	3	0.40 (0.33–0.49)
Type of vaccine received by household contact							
Unvaccinated	15,610	84	37,461	69	53,071	73	1
Vector	1208	7	6189	11	7397	10	0.46 (0.42–0.51)
mRNA	1724	9	10,576	20	12,300	17	0.32 (0.29–0.35)
Vaccination status of household contact type by vaccine type							
Unvaccinated	15,610	84	37,461	69	53,071	73	1
Partially vaccinated—Vector	678	4	2941	5	3619	5	0.54 (0.47–0.62)
Partially vaccinated—mRNA	716	4	3919	7	4635	6	0.36 (0.32–0.41)
Fully vaccinated—Vector	488	3	2923	5	3411	5	0.39 (0.33–0.45)
Fully vaccinated—mRNA	766	4	5360	10	6126	8	0.26 (0.23–0.3)
Waning vaccination—Vector	42	0.2	325	0.6	367	0.5	0.32 (0.20–0.51)
Waning vaccination—mRNA	242	1	1297	2	1539	2	0.42 (0.34–0.52)
Vaccination status of index case							
Unvaccinated	15,593	84	40,470	75	56,063	77	1
Partially vaccinated	1661	9	6456	12	8117	11	0.45 (0.38–0.52)
Fully vaccinated	950	5	5529	10	6479	9	0.24 (0.20–0.29)
Waning vaccination	338	2	1771	3	2109	3	0.30 (0.23–0.4)
Type of vaccine received by index case							
Unvaccinated	15,593	84	40,470	75	56,063	77	1
Vector	1342	7	5615	10	6957	10	0.43 (0.36–0.5)
mRNA	1607	9	8141	15	9748	13	0.27 (0.24–0.32)
Vaccination status of index case by vaccine type							
Unvaccinated	15,593	84	40,470	75	56,063	77	1
Partially vaccinated—Vector	813	4	3041	6	3854	5	0.50 (0.41–0.62)
Partially vaccinated—mRNA	848	5	3415	6	4263	6	0.40 (0.32–0.49)
Fully vaccinated—Vector	477	3	2278	4	2755	4	0.36 (0.28–0.46)
Fully vaccinated—mRNA	473	3	3251	6	3724	5	0.16 (0.13–0.21)
Waning vaccination—Vector	52	0.3	296	0.5	348	0.5	0.28 (0.14–0.56)
Waning vaccination—mRNA	286	2	1475	3	1761	2	0.31 (0.22–0.42)
Age group of household contact, years							
0–18	8034	43	14,922	28	22,956	32	1
19–29	2857	15	11,069	20	13,926	19	0.41 (0.37–0.44)
30–39	2288	12	7821	14	10,109	14	0.47 (0.43–0.51)
40–64	4334	23	15,622	29	19,956	27	0.50 (0.47–0.54)
65+	1029	6	4792	9	5821	8	0.32 (0.29–0.36)
Age group of index case, years							
0–18	4372	24	9321	17	13,693	19	1
19–29	4004	22	17,027	31	21,031	29	0.25 (0.22–0.3)
30–39	3890	21	11,255	21	15,145	21	0.51 (0.44–0.59)
40–64	5387	29	13,808	25	19,195	26	0.63 (0.54–0.72)
65+	889	5	2815	5	3704	5	0.55 (0.44–0.69)
Sex of index case							
Male	9988	54	31,226	58	41,214	56	1
Female	8554	46	22,984	42	31,538	43	1.46 (1.33–1.61)
Missing	0	0	16	<0.1	16	<0.1	–

(Table 2 continues on next page)

	Positive contacts		Negative contacts		Total		Crude odds-ratio[a]
	Count	Column %	Count	Column %	Count	Column %	OR (95% CI)
(Continued from previous page)							
Household size, n							
2	873	5	2486	5	3359	5	1
3–4	5327	29	14,765	27	20,092	28	1.04 (0.88–1.23)
5–9	12,342	67	36,975	68	49,317	68	0.93 (0.79–1.1)
Household type							
Working age with school age	12,401	67	28,443	52	40,844	56	1
Working age only	2235	12	10,419	19	12,654	17	0.27 (0.24–0.31)
Working age with retirement age	1318	7	6660	12	7978	11	0.24 (0.21–0.28)
Retirement age only	135	0.7	241	0.4	376	0.5	1.60 (1.04–2.45)
Multi-generational	2453	13	8463	16	10,916	15	0.44 (0.37–0.51)
Socio-economic status							
1 (most disadvantaged)	10,009	54	25,884	48	35,893	49	1
2	4213	23	12,423	23	16,636	23	0.80 (0.70–0.9)
3	2460	13	7571	14	10,031	14	0.72 (0.62–0.84)
4	1170	6	5044	9	6214	9	0.40 (0.33–0.48)
5 (most advantaged)	661	4	3251	6	3912	5	0.33 (0.26–0.42)
Missing	29	0.2	53	<0.1	82	0.1	–

[a]Based on a logistic regression model with a random intercept at 'household' level.

Table 2: **Household contact characteristics and unadjusted estimates for the risk of infection for household contacts.**

contacts were 0.46 (95% CI 0.40–0.52) for partially vaccinated and 0.36 (95% CI 0.32–0.41) for fully vaccinated. Similar levels of protection regardless of type of vaccine were found among household contacts with waning immunity (aOR 0.64 for both).

As shown in Supplementary Material 3, there was a consistent and substantial reduction in the cORs for household contacts with improving vaccination status (unvaccinated, partially vaccinated, fully vaccinated) of both the household contact and the index case. Log-likelihood ratio testing between the multivariable model and the multivariable model with interaction term indicated that the association between the risk of infection and vaccination status of household contacts varied significantly by vaccination status of their index case (LRT p-value < 0.001), with improvements in vaccination status of both having positive synergetic effects. These synergistic effects seemed to be more pronounced for mRNA vaccines than for vector vaccines, and only for fully mRNA-vaccinated index cases did changes in household contact vaccination status not alter the risk to transmit (see Fig. 2 and Supplementary Material 4). This pattern held true overall in a multivariable model with type of vaccine taken into account: The protective effects of vaccination against transmission were generally strongest when both the index case as well has the household contact were fully vaccinated and when at least one of them had received an mRNA vaccine. Full vaccination status of the index with an mRNA vaccine was associated with a reduction in the adjusted odds of onwards transmission in the range 0.09–0.21, depending on the vaccination status of the household contact (see Fig. 2 and Supplementary Material 4).

Sensitivity analyses with separate category for waning immunity (Supplementary Material 5) and excluding vector vaccines (Supplementary Material 6) did not change overall trends in risk estimates by vaccination status substantially compared to the main analysis, indicating our analysis decisions to be appropriate.

	Adjusted odds-ratio[a]	95% CI
Unvaccinated	1	
Partially vaccinated—Vector	0.77	0.67–0.89
Partially vaccinated—mRNA	0.46	0.40–0.52
Fully vaccinated—Vector	0.65	0.55–0.76
Fully vaccinated—mRNA	0.36	0.32–0.41
Waning vaccination—Vector	0.64	0.39–1.05
Waning vaccination—mRNA	0.64	0.51–0.80

[a]Based on a logistic regression model with a random intercept at 'household' level, and adjusted for: vaccination status of the index case, age of index case, sex of index case, age of household contact, socio-economic status of household, household size, household type.

Table 3: **Adjusted estimates for the risk of infection for household contacts.**

Discussion

We provide new quantitative estimates of the extent to which viral vector and mRNA vaccines were able to reduce the risk of SARS-CoV-2 transmission in the context of the Delta variant. To our knowledge, this is

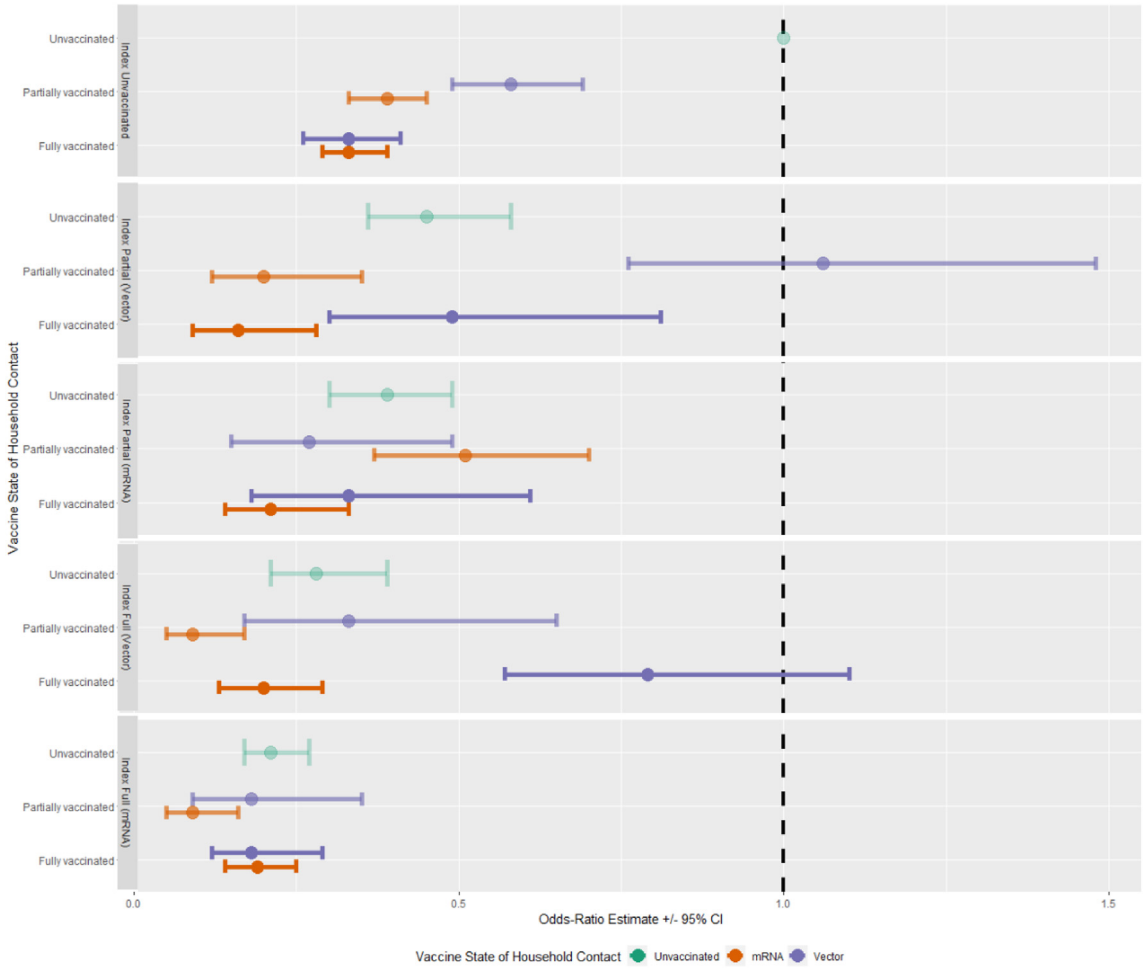

Fig. 2: **Adjusted estimates for the risk of transmission between household contacts and index case by vaccination status and type of vaccine.**

the first study presenting robust, adjusted estimates for the effects of the vaccination status and types of vaccines on the transmission risks within households. We found strong evidence that vaccination reduced the odds of infection for household contacts by one third for vector vaccines and by nearly two thirds for mRNA vaccines, and that being fully vaccinated with an mRNA vaccine reduced the odds of onwards transmission to their household contacts by at least four fifths. Being fully vaccinated offered stronger protection than partial vaccination, and protection was consistently stronger for mRNA than for vector vaccines. However, protective effects were lower in those whose last vaccination was three months or longer prior to exposure. Vaccination of cases and contacts appeared to have synergistic protective effects, in particular when both the household contact and the index case were fully vaccinated and if one of them had received an mRNA vaccine.

Pooled analyses of Delta variant data from the Netherlands,[28] Norway,[29] Denmark,[30] Singapore,[31] Israel,[32] Spain,[33] and the UK[34] showed reduced risks for household contacts to acquire infection with better vaccination status, but low pooled risks for index cases to transmit regardless of their vaccination status, which the authors attribute to the heterogeneity of included studies and study populations.[35] While our study also found a reduced risk to acquire infection for vaccinated household contacts, our analysis suggests that improved vaccination status of index cases may have had even stronger effects on their risk to transmit, and that there were synergistic effects between both factors. Ours is the first study to differentiate this by vaccine type, and we found these synergistic effects for both vector and mRNA-based vaccines.

We acknowledge several limitations. First, we had to rely on constructed household entities through record linkage. It is therefore possible that not all of the entities

were real households. Our exclusion of addresses shared by 10 or more people or where only people below the age of 19 were registered aimed at excluding institutional living arrangements from our analysis, however we cannot guarantee that all were excluded, potentially underestimating observed vaccine effects. Second, no data were available on behavioural adaptations within households such as self-isolation, which may have operated in a manner correlated with vaccination status, potentially overestimating observed vaccine effects. Third, address information on AIR was primarily drawn from Medicare, which might have led to an underrepresentation of people without public health care coverage, and also potentially not reflected the actual place of residence for some people who were temporarily not living at their registered address (e.g., university students). This might have biased our sample towards smaller-sized households with higher SES, potentially overestimating observed vaccine effects. Fourth, vaccination for children below 12 years of age was only made available after our study period, and partway during our study period for those aged 12–15 years, which might have led to an association between age and vaccination status in these age groups as found in other studies.[36] Despite having adjusted for age in our multivariable analysis, we cannot rule out residual confounding potentially leading to an underestimation of observed effect sizes. Fifth, data from 4798 (7.6%) unlinked and hence excluded cases was not available to us for comparison with included records, which makes the presence and extent of any selection bias difficult to ascertain in our study. Lastly, no validation of the database linkage quality was possible due to unavailability of external data sources.

The most notable strength of our study in comparison to others was a combination of epidemiological and contextual factors that were conducive for high data quality and scientific validity of our findings, namely: very low prior exposure to SARS-CoV-2 among the study population; strict movement restrictions for the majority of the observation period; and intensive case-finding, contact tracing and testing. There was no widespread community transmission in the months preceding our study period. The first COVID-19 wave in NSW occurred in March and April 2020, was limited in size (total around 3000 confirmed cases), and was dominated by imported cases from overseas travellers that only resulted in sporadic transmission in the local population.[37] Population-level seroprevalence after this first wave was well below 1% in Greater Sydney.[38] The following year until the beginning of our study period was characterized by occasional small, well-traced outbreaks,[7] and strict lockdowns; the latter extended well into our study period. While the absence of circulating infection in a largely infection-naïve population at the start of our study period makes us confident that our data closely captured the true evolution of this outbreak, the restrictions on population movement and social mixing during our study period mean that household exposure was the most likely source of infection for household contacts in this setting. The very strong public health capacity in NSW during 2021 and the use of NCIMS as a centralized case database make it likely that a very high proportion of all cases in our study population were detected. High levels of centralised testing and contact tracing, coupled with high levels of compliance with public health recommendations to seek a SARS-CoV-2 PCR test for any respiratory symptoms resulted in PCR-positivity rates of at most 1–2% during our study period, strongly suggestive of high testing coverage.[39] A further strength of our study was its sample size, which was larger than the largest existing meta-analysis for the Delta variant (n = 71,504 contacts),[35] as well as subsequent, pivotal epidemiological studies on the Omicron variant with n = 61,002 and n = 50,588 contacts, respectively.[40,41] Lastly, we are confident about the accuracy and completeness of vaccine data in our study since AIR constitutes a well-established, central immunisation register where all routine and SARS-CoV-2 immunizations administered by any health care provider in Australia are automatically recorded. Similarly, NCIMS functions as a central SARS-CoV-2 register capturing all PCR-confirmed cases from any test provider in NSW, thereby making substantial underreporting highly unlikely.

Together with the availability of information on important confounding factors, this allowed us to calculate precise, adjusted estimates rather than crude measures like household attack rates that other studies have presented. It also enabled us, for the first time, to investigate different combinations, including synergistic effects, of vaccination status and type of vaccine for both index cases and household contacts in the same study population.

While our data originate from the Delta variant, there is still potential in the current pandemic state for vaccines to prevent transmission in addition to providing additional protection against severe disease, despite large changes in circulating variants and near ubiquitous exposure to infection. Although current Omicron subvariants exhibit substantially more immune escape than the Delta variant, the results reported here are encouraging for continued protection against transmission within three months of vaccination. High coverage with bivalent vaccines that are well-matched to circulating Omicron sub-lineages may still be important during the current epidemic period, as evidenced by recent neutralization studies[42,43] as well as vaccine effectiveness studies from the US[44] and Europe.[45] Linkage between the routine, population level data collections provided an efficient study design for estimating vaccine effects. In the context of Denmark, this approach has been applied to study differences in transmission and vaccine protection between BA.1 and

BA.2 Omicron subvariants,[31,32] raising the potential for more routine surveillance of the effectiveness of variant-specific vaccines on SARS-CoV-2 transmission.

In conclusion, vector vaccines and mRNA vaccines reduced the odds to acquire infection with the SARS-CoV-2 Delta variant for household contacts by about one third and by two thirds, respectively. Being fully vaccinated with an mRNA vaccine reduced the odds of index cases to transmit infection to their household contacts by four-fifths compared to unvaccinated index cases. Full vaccination offered stronger protection than partial vaccination, in particular for mRNA vaccines, but was reduced if the last vaccination preceded exposure by three or more months.

Contributors

Conceptualization: JK, JW. Data curation: NR. Formal Analysis: FV, NR, JW. Funding acquisition: JK, JW. Investigation: FV, NR, MC, BL, KM, JK, JW. Methodology: FV, NR, JW. Project administration: MC, JW. Resources: JW, JK. Software: NR. Supervision: JK, JW. Validation: NR, JW. Visualization: FV, NR, JW. Writing—original draft: FV. Writing—review & editing: FV, NR, MC, BL, KM, JK, JW.

Data sharing statement

Contingent on approval from the owner on the data (NSW Health) de-identified line listed data that allow replication of the presented analysis can be made available upon reasonable individual request by other researchers following publication.

Ethics statement

This was a secondary data analysis without prospective data collection or interaction with study subjects. The study resulted from work undertaken to inform urgent COVID-19 responses in NSW as part of wider public health surveillance efforts carried out under the NSW *Public Health Act 2010*.[33] Data were supplied to the researchers by the NSW Ministry of Health, with all records de-identified and securely managed to ensure privacy and the study's compliance with the Ethical Considerations in Quality Assurance and Evaluation Activities of Australia's National Health and Medical Research Council. The NSW *Public Health Act* allows for such release of data, and, following review, the NSW Ministry of Health approved this study. The project oversight and approval for publication was provided by the NSW Ministry of Health.

Editor note

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Declaration of interests

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2023.100930.

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