Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

International Journal of Infectious Diseases 124 (2022) 190–198

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Effect of Inactivated SARS-CoV-2 Vaccines and ChAdOx1 nCoV-19 Vaccination to Prevent COVID-19 in Thai Households (VacPrevent trial)

Marisa Muadchimkaew[1], Taweegrit Siripongboonsitti[1,2,3,*], Saowanee Wongpatcharawarakul[1], Chanyapak Boonsankaew[1], Kriangkrai Tawinprai[1,2], Kamonwan Soonklang[4], Nithi Mahanonda[5]

[1] Infection Control Unit, Chulabhorn Hospital, Chulabhorn Royal Academy, Bangkok, Thailand
[2] Division of Infectious Diseases, Department of Medicine, Chulabhorn Hospital, Chulabhorn Royal Academy, Bangkok, Thailand
[3] Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy, Bangkok, Thailand
[4] Center of Learning and Research in Celebration of HRH Princess Chulabhorn 60th Birthday Anniversary, Chulabhorn Royal Academy, Bangkok, Thailand
[5] Chulabhorn Hospital, Chulabhorn Royal Academy, Bangkok, Thailand

ARTICLE INFO

Article history:
Received 18 March 2022
Revised 16 September 2022
Accepted 22 September 2022

Keywords:
Inactivated vaccine
SARS-CoV-2
COVID-19
ChAdOx1 nCOV-19
Household transmission

ABSTRACT

Objectives: SARS-CoV-2 is primarily transmitted within households, with massive healthcare system burdens. The role of inactivated vaccines and ChAdOx1 nCoV-19 vaccination in the prevention of within-household transmission remains unknown.

Methods: This observational case-control study tracked 408 SARS-CoV-2 polymerase chain reaction–confirmed index cases from April to September 2021. This study aimed to prove the benefit of inactivated and ChAdOx1 nCoV-19 vaccinated index cases in preventing within-household transmissibility.

Results: A total of 1178 household contacts were investigated. A total of 231 index cases were vaccinated with inactivated or ChAdOx1 nCoV-19 vaccine, and 177 were unvaccinated. The vaccinated index cases exhibited a 7.8% risk reduction in household transmission. There was no difference in the secondary attack rate of 50.77% in unvaccinated cases compared with 46.81% in vaccinated index cases (P-value = 0.177). Those who completed the two-dose SARS-CoV-2 vaccination demonstrated a 93% reduction in household transmissibility within 14-90 days. The effectiveness for preventing household transmission was 26.09%. The 87% reduced risk of household transmissibility was observed among those who wore masks.

Conclusion: The completed two-dose SARS-CoV-2 inactivated and ChAdOx1 nCoV-19 vaccination within 14-90 days among index cases demonstrated benefits in preventing within-household transmissibility. Implementing high-efficacy vaccination and an appropriate booster dose can prevent household transmission.

© 2022 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Introduction

COVID-19 is caused by the SARS-CoV-2 infection and caused the pandemic with high mortality. Household transmission is the most common transmission source in the countries with COVID-19 outbreaks (Pollán *et al.*, 2020). In England, the secondary infection rate is 4-6.4 per 100 households (Hall *et al.*, 2021). The secondary attack rate (SAR) in other countries is 16.3-53% (Grijalva *et al.*, 2020; Li *et al.*, 2020; Singanayagam *et al.*, 2022). The systematic review demonstrated an average of 17% secondary infections (4-45%), and the SAR was 31.1% during the B.1.617.2 outbreak, whereas the high transmissibility in Thai households was 56% (Madewell *et al.*, 2020, 2021; Watanapokasin *et al.*, 2021). SARS-CoV-2 vaccination is the best modality to prevent SARS-CoV-2 infection and has been shown to reduce its severity and mortality. A study of index cases vaccinated with ChAdOx1 nCoV-19 or BNT162b2 >21 days found 10% of secondary cases and a 40-50% reduction in infected household contacts. The secondary cases and SAR were 196 (5.7%) and 371 (6.2%) in households with ChAdOx1 nCoV-19 and BNT162b2 vaccinated index cases, respectively (Harris *et al.*, 2021). The effectiveness of BNT162b2 and messenger RNA

* Corresponding author: Taweegrit Siripongboonsitti, Division of Infectious Diseases, Department of Medicine, Chulabhorn Hospital, Chulabhorn Royal Academy, Bangkok, Thailand, Tel: +66816924872
E-mail address: Taweegrit.sir@cra.ac.th (T. Siripongboonsitti).

https://doi.org/10.1016/j.ijid.2022.09.032
1201-9712/© 2022 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

(mRNA)-1273 in households was 8.7% and 42.9% between 2 and 10 weeks after the first dose among vaccinated index cases, and the effectiveness of preventing transmission was 63% among the unvaccinated and 40% in the vaccinated households (Salo *et al.*, 2022). Israeli data showed an 88.5% effectiveness of BNT162b2 against transmission (Prunas *et al.*, 2022). Moreover, a UK study demonstrated that the SAR for the B.1.617.2 variant among vaccinated cases was 25% and 38% in unvaccinated cases (Singanayagam *et al.*, 2022). A community study found a robust negative association between vaccination rates and a two-fold decreased positive test fraction of unvaccinated community members (Milman *et al.*, 2021). This study focused on inactivated SARS-CoV-2 and ChAdOx1 nCoV-19 vaccination in preventing household transmissibility.

Methods

Patients

The electronic medical records of all 793 SARS-CoV-2 polymerase chain reaction-confirmed cases were retrospectively reviewed from April to September 2021 in Chulabhorn Hospital, Bangkok, Thailand, during the B.1.617.2 and B.1.1.7 variant outbreaks (Fig. 1). A total of 408 index cases were identified, excluding non-index cases; index without household members; those who received mRNA or viral vector vaccines; those who previously received antiviral agents or passive antibodies, namely convalescent plasma, monoclonal antibodies, hyperimmune globulin, and hydroxychloroquine/chloroquine prophylaxis within 60 days; residents in nursing care facilities; and those who did not cooperate with the given personnel data (Fig. 2). The close contact households were defined as members who lived less than 6 feet away from index cases for at least 10 minutes in the last 14 days, without any other suspected index case. Secondary household infection was defined by the World Health Organization (2020). The confirmed cases were close contact households who tested positive using the reverse transcriptase-polymerase chain reaction or SARS-CoV-2 antigen rapid diagnosis test, with or without symptoms. The probable cases were household contacts consistent with clinical criteria, including respiratory symptoms or chest roentgenogram compatible with COVID-19, whereas the suspected cases were symptomatic close contact individuals.

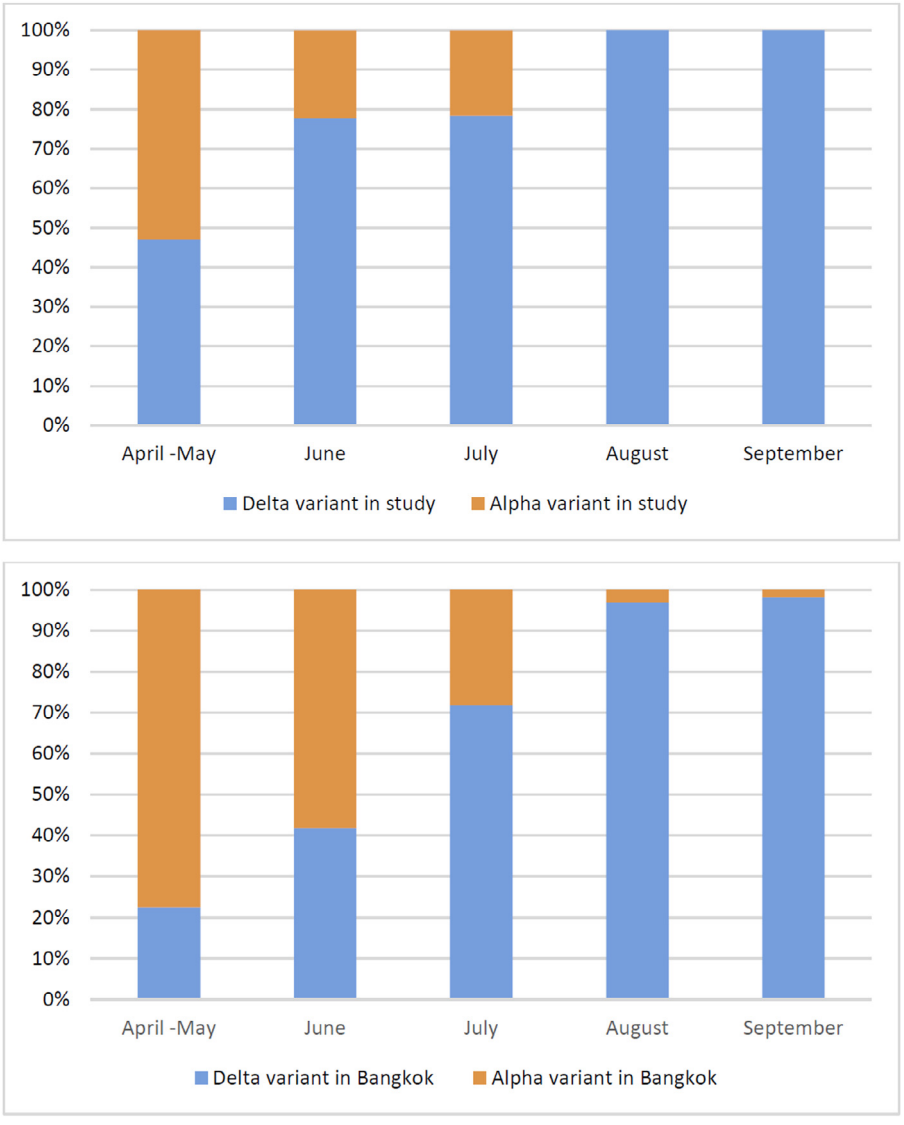

Fig. 1. Percent of SARS-CoV-2 B.1.617.2. variant (Delta) and B.1.1.7 variant (Alpha) distribution of index cases in the study compared with SARS-Cov-2 variants during an outbreak in Bangkok. Thailand from April to September 2021.

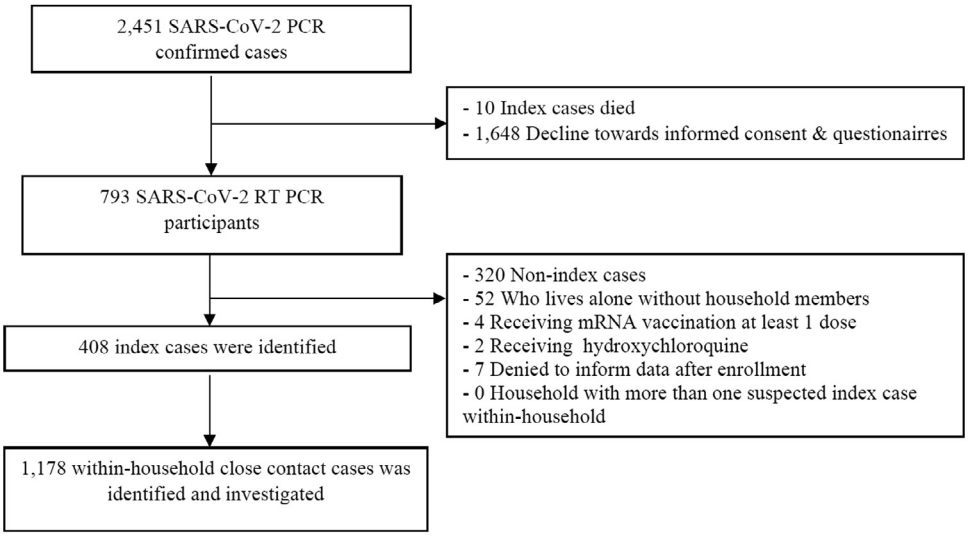

Fig. 2. Flow chart of patients enrollment.

Trial procedure

This retrospective, case-control study compared index cases who received the CoronaVac, BBIBP-CorV, and ChAdOx1 nCoV-19 vaccines, which were authorized for vaccination in Thailand during the study period, and those who did not receive any vaccine. Baseline characteristic data, subvariants, and cycle threshold (Ct) values were collected using contact tracking records and electronic data review. All index cases provided written informed consent and were interviewed about the vaccination and household history by telephone and electronic questionnaires. This clinical trial was registered in the Thai Clinical Trials Registry no. TCTR20211108003.

Statistical analysis

Categorical data and baseline characteristics were analyzed using the chi-square test or Fisher's exact test. Non-normally distributed continuous data were compared using the Mann-Whitney U test for multiple groups. The calculated sample size in this study was 208 to detect the differences in the SAR between vaccinated and unvaccinated index cases, with 80% power and an alpha error of 0.05. Continuous, non-normally distributed data are presented as median (interquartile range) and were analyzed using the Mann-Whitney U test. The adjusted odds ratio (aOR) of any factor between vaccinated and unvaccinated infected households was analyzed using multilevel logistic regression. Statistical significance was defined as a two-sided *P*-value <0.05, and all statistical analyses were performed using STATA, version 16.1 (StataCorp, College Station, TX, USA).

Results

Baseline characteristics

Of the 408 primary cases, 177 (43.38%) were unvaccinated. A total of 231 (56.62%) were vaccinated with ChAdOx1 nCoV-19 and inactivated vaccines, namely CoronaVac and BBIBP-CorV vaccines. All cases were Thai from June to August 2021 and peaked in July to August 2021 during the B.1.617.2 outbreak and the recent CoronaVac and ChAdOx1 nCoV-19 vaccination. The majority of variants of concern (VOCs) consisted of B.1.617.2 (14.9%), followed by B.1.1.7 (5.15%), and 79.66% of unknown variants. Nucleocapsid immunoglobulin G antibodies were higher in the vaccinated index cases (*P*-value = 0.001).

Unvaccinated index cases had more moderate and severe/critical COVID-19 (71.89% and 2.16%, respectively; *P*-value = 0.013). The symptomatic vaccinated index cases had more nasal discharges (*P*-value = 0.006). Most of the index cases were vaccinated <14 days (42.86%) and 14-90 days (55.68%), and the majority were vaccinated using CoronaVac, followed by ChAdOx1 nCoV-19. Half of the vaccinated and unvaccinated index cases shared bedrooms and bathrooms with the household members (Table 1, Supplementary Table 1).

Among 1178 within-household close contact cases, 572 were compatible with the SARS-CoV-2 infection definition: 308 secondary cases from vaccinated index cases and 264 from unvaccinated individuals. Almost all confirmed household contacts were detected by the SARS-CoV-2 antigen rapid diagnostic test. There were high numbers of unvaccinated household contacts, 41.4% and 76.54% in vaccinated and unvaccinated index cases, respectively (Supplementary Table 2). The SAR in those who were fully vaccinated with CoronaVac >14 days was 46% lower than the 53% SAR of those fully vaccinated with ChAdOx1 nCoV-19 >14 days (Supplementary Table 3).

Outcomes

The overall SAR of household contacts was 46.81% in unvaccinated and 50.77% in vaccinated index cases (*P*-value = 0.177). The relative risk reduction of households that contacted the vaccinated index cases was 7.8%. The SARs in household contacts were 64.71%, 40%, and 81.25% in vaccinated index cases who received a completed two-dose vaccination <14 days, 14-90 days, and >90 days, respectively.

Despite the high SAR in each VOC, the study could not demonstrate the difference in SAR between the vaccinated and unvaccinated index cases. The symptomatic index cases had more risk of transmissibility than asymptomatic individuals (odds ratio [OR] 3.19, 95% confidence interval [CI] 1.23, 8.25), which demonstrated decreased transmissibility in individuals without fever and those without cough, with OR 0.44; 95% CI 0.20, 0.95 and OR 0.43; 95% CI 0.20, 0.93, respectively. The SAR peaked 24-48 hours from the onset of symptoms, and the SAR was lower in vaccinated (50.43%) than unvaccinated index cases (65.71%) (*P*-value = 0.042) (Table 2, Supplementary Tables 4, 5).

Table 1
Baseline characteristics of index cases.

Baseline characteristics of index cases	Vaccinated, N (%)	Unvaccinated, N (%)	*P*-value
Primary case (index)	231 (56.62)	177 (43.38)	
Sex			0.369[a]
Male	120 (51.95)	84 (47.46)	
Female	111 (48.05)	93 (52.54)	
Age (years) (median, IQR)	40 (31, 51)	39 (29, 49)	0.178[c]
Age range of index cases (years)			0.328[a]
≤10	0 (0.00)	0 (0.00)	
11-20	1 (0.43)	3 (1.69)	
21-30	53 (22.94)	47 (26.55)	
31-40	63 (27.27)	46 (25.99)	
41-50	53 (22.94)	43 (24.29)	
51-60	25 (10.82)	21 (11.86)	
61-70	18 (7.79)	12 (6.78)	
>70	18 (7.79)	5 (2.82)	
Subvariant			0.183[b]
B.1.617.2	38 (16.45)	23 (12.99)	
B.1.1.7	8 (3.46)	13 (7.34)	
B.1.617.2 and B.1.1.7	1 (0.43)	0 (0.00)	
Unknown	184 (79.65)	141 (79.66)	
Cycle threshold value (N, %)			0.796[a]
<20	106 (46.29)	81 (46.29)	
21-30	92 (40.17)	74 (42.29)	
>30	31 (13.54)	20 (11.43)	
Vaccinated (N, %)			0.000[b]
1st dose of CoronaVac	27 (11.69)	0 (0.00)	
2nd dose of CoronaVac	64 (27.71)	0 (0.00)	
1st dose of ChAdOx1 nCoV-19	115 (49.78)	0 (0.00)	
2nd dose of ChAdOx1 nCoV-19	3 (1.30)	0 (0.00)	
1st dose of BBIBP-CorV	13 (5.63)	0 (0.00)	
2nd dose of BBIBP-CorV	9 (3.90)	0 (0.00)	
Duration from the onset of symptoms			0.889[b]
0-24 hours	88 (38.10)	64 (36.16)	
24-48 hours	35 (15.15)	23 (12.99)	
48-72 hours	72 (31.17)	61 (34.46)	
>72 hours	1 (0.43)	0 (0.00)	
Symptom			0.684[a]
Asymptomatic	42 (18.18)	35 (19.77)	
Symptomatic	189 (81.82)	142 (80.23)	
Severity			0.198[b]
Mild illness	78 (34.82)	44 (26.35)	
Moderate illness	143 (63.84)	120 (71.86)	
Severe/ critical illness	3 (1.34)	3 (1.80)	
Symptoms			
Fever	139 (60.17)	117 (66.10)	0.220[a]
Cough	143 (61.90)	108 (61.02)	0.855[a]
Sore throat	106 (45.89)	74 (41.81)	0.411[a]
Runny nose	119 (51.52)	67 (37.85)	0.006[a]
Diarrhea	52 (22.51)	55 (31.07)	0.051[a]
History of SARS-CoV-2 vaccination			<0.001[b]
Vaccinated <14 days	99 (42.86)	0 (0.00)	
Vaccinated within 14-90 days	124 (53.68)	0 (0.00)	
Vaccinated >90 days	8 (3.46)	0 (0.00)	
Number of household members			0.944[a]
≤2	72 (31.17)	55 (31.07)	
3-4	94 (40.69)	69 (38.98)	
5-6	43 (18.61)	33 (18.64)	
>6	22 (9.52)	20 (11.30)	
Property type			0.751[a]
Condominium	26 (11.26)	15 (8.47)	
Terraced	68 (29.44)	54 (30.51)	
Detached	80 (34.63)	59 (33.33)	
Flat	57 (24.68)	49 (27.68)	

[a] Chi-square test.
[b] Fisher's exact test.
[c] Mann-witney U test, IQR, interquartile range.

Vaccine-associated factors were also analyzed. The index cases who completed two doses of any inactivated vaccine and ChAdOx1 nCoV-19 vaccine within 14-90 days had a reduced SARS-CoV-2 transmissibility risk (OR 0.29, 95% CI 0.09, 0.92, *P*-value = 0.035); aOR 0.07, 95% CI 0.01, 0.78), and the SAR was 40% in those who completed the vaccination within 14-90 days and 50.77% in unvaccinated index cases. The ChAdOx1 nCoV-19 vaccinated index cases had reduced transmissibility after the first dose <14 days (aOR 0.002, 95% CI 0.000, 0.295) and <14 days after second dose (aOR 0.042, 95% CI 0.003, 0.638). The SAR in ChAdOx1

Table 2
Secondary attack rate and factors associated with the adjusted odds of infection of household contacts stratified by index cases and household close contacts.

Factors related to SARS-CoV-2 transmissibilityof index cases	Index cases, N (%)	Household contacts, N (%)	Uninfected close contacts, N (%)		Secondary cases, N (%)		The secondary attack rate (%)				Adjusted Odds of infection of household contacts with vaccinated index cases (95%CI)[c]
			Vaccinated index cases	Unvaccinated index cases	Vaccinated index cases	Unvaccinated index cases	All	Vaccinated index cases	Unvaccinated index cases	*P*-value	
Number of cases	408	1178	350 / 658	256 / 520	308 / 658	264 / 520	48.56	46.81	50.77	0.177[a]	-
The age range of household contacts (year-old)											
0-5	0 (0.00)	40 (4.93)	11 (3.85)	10 (5.52)	10 (5.75)	9 (5.26)	47.50	47.62	47.37	0.987[a]	Ref.
6-10	0 (0.00)	48 (5.91)	17 (5.94)	9 (4.97)	11 (6.32)	11 (6.43)	45.83	39.29	55.00	0.281[a]	0.47 (0.06, 3.50)
11-20	4 (0.98)	116 (14.29)	40 (13.99)	17 (9.39)	29 (16.67)	30 (17.54)	50.86	42.03	63.63	0.021[a]	0.35 (0.06, 2.05)
21-30	100 (24.51)	182 (22.41)	59 (20.63)	42 (23.20)	32 (18.39)	49 (28.65)	44.51	35.16	53.85	0.011[a]	0.19 (0.03, 1.08)
31-40	109 (26.72)	143 (17.61)	51 (17.83)	42 (23.20)	35 (20.11)	15 (8.77)	34.97	40.70	26.32	0.077[a]	0.36 (0.07, 1.86)
41-50	96 (23.53)	109 (13.42)	40 (13.99)	29 (16.02)	14 (8.05)	26 (15.20)	36.70	25.93	47.27	0.021[a]	0.16 (0.03, 0.98)
51-60	46 (11.27)	86 (10.59)	33 (11.54)	18 (9.94)	16 (9.20)	19 (11.11)	40.70	32.65	51.35	0.081[a]	0.22 (0.04, 1.29)
61-70	30 (7.35)	42 (5.17)	16 (5.59)	6 (3.31)	16 (9.20)	4 (2.34)	47.62	50.00	40.00	0.580[a]	0.29 (0.04, 2.07)
>70	23 (5.64)	46 (5.67)	19 (6.64)	8 (4.42)	11 (6.32)	8 (4.68)	41.30	36.67	50.00	0.382[a]	0.16 (0.02, 1.16)
The age range of index case (year-old)											
≤20	-	11 (0.93)	4 (1.14)	3 (1.17)	0 (0.00)	4 (1.52)	36.36	0.00	57.14	0.194[b]	-
21-30	-	273 (23.17)	87 (24.86)	63 (24.61)	45 (14.61)	78 (29.55)	45.05	34.09	55.32	<0.001[a]	Ref.
31-40	-	291 (24.70)	97 (27.71)	74 (28.91)	56 (18.18)	64 (24.24)	41.24	36.60	46.38	0.091[a]	0.96 (0.22, 4.13)
41-50	-	274 (23.26)	67 (19.14)	52 (20.31)	86 (27.92)	69 (26.14)	56.57	56.21	57.02	0.892[a]	7.73 (1.01, 22.17)
51-60	-	124 (10.53)	25 (7.14)	27 (10.55)	43 (13.96)	29 (10.98)	58.06	63.24	51.79	0.199[a]	9.94 (1.35, 73.12)
61-70	-	132 (11.21)	42 (12.00)	33 (12.89)	46 (14.94)	11 (4.17)	43.18	52.27	25.00	0.003[a]	5.61 (0.73, 43.03)
>70	-	73 (6.20)	28 (8.00)	4 (1.56)	32 (10.39)	9 (3.41)	56.16	53.33	69.23	0.295[a]	6.80 (0.81, 56.97)
Subvariant											
B.1.617.2	61 (14.95)	167 (14.18)	53 (15.14)	31 (12.11)	44 (14.29)	39 (14.77)	49.70	45.36	55.71	0.187[a]	Ref.
B.1.1.7	21 (5.15)	58 (4.92)	6 (1.71)	28 (10.94)	8 (2.60)	16 (6.06)	41.38	57.14	36.36	0.169[a]	2.65 (0.09, 78.36)
Mixed B.1.617.2 and B.1.1.7	1 (0.25)	2 (0.17)	2 (0.57)	0 (0.00)	0 (0.00)	0 (0.00)	0	0.00	0.00	-	-
Unknown	325 (79.66)	951 (80.73)	289 (82.57)	197 (76.95)	256 (83.12)	209 (79.17)	48.90	46.97	51.48	0.169[a]	0.81 (0.21, 2.98)
Cycle threshold value											
<20	187 (46.29)	495 (42.31)	131 (37.54)	91 (36.40)	152 (49.51)	121 (45.83)	55.15	53.71	57.08	0456[a]	Ref.
21-30	166 (41.09)	516 (44.10)	159 (45.56)	128 (51.20)	109 (35.50)	120 (45.45)	44.38	40.67	48.39	0.078[a]	0.37 (0.12, 1.16)
>30	51 (12.62)	159 (13.59)	59 (16.91)	31 (12.40)	46 (14.98)	23 (8.71)	43.40	43.81	42.59	0.883[a]	0.38 (0.08, 1.79)
Duration from the onset of symptoms											
0-24 hours	152 (37.25)	432 (36.67)	129(36.86)	93(36.33)	113 (36.69)	97 (36.74)	48.61	46.69	51.05	0.368[a]	Ref.
24-48 hours	58 (14.22)	185 (15.70)	57(16.29)	24(9.38)	58 (18.83)	46 (17.42)	56.22	50.43	65.71	0.042[a]	1.13 (0.26, 6.07)
48-72 hours	133 (32.60)	384 (32.60)	110(31.43)	90(35.16)	95 (30.84)	89 (37.71)	47.92	46.34	49.72	0.508[a]	1.15 (0.32, 4.11)
>72 hours	1 (0.25)	1 (0.08)	0(0.00)	0(0.00)	1 (0.32)	0 (0.00)	100	100.00	0.00	-	-

(*continued on next page*)

Table 2 (*continued*)

Factors related to SARS-CoV-2 transmissibilityof index cases	Index cases, N (%)	Household contacts, N (%)	Uninfected close contacts, N (%)		Secondary cases, N (%)		The secondary attack rate (%)				Adjusted Odds of infection of household contacts with vaccinated index cases (95%CI)[c]
			Vaccinated index cases	Unvaccinated index cases	Vaccinated index cases	Unvaccinated index cases	All	Vaccinated index cases	Unvaccinated index cases	*P*-value	
Household size											
2	127 (31.13)	129 (10.95)	36(10.29)	27(9.77)	36 (11.69)	30 (11.36)	51.16	50.00	52.63	0.767[a]	Ref.
3-4	163 (39.95)	406 (34.47)	138(39.43)	86(33.59)	96 (31.17)	86 (32.58)	44.83	41.03	50	0.072[a]	0.39 (0.08, 1.82)
5-6	76 (18.63)	320 (27.16)	93(26.57)	66(25.27)	91 (29.55)	70 (26.52)	50.31	49.46	51.47	0.722[a]	1.07 (0.20, 5.66)
>6	42 (10.29)	323 (27.42)	83(23.71)	77(30.08)	85 (27.60)	78 (29.55)	50.46	50.60	50.32	0.961[a]	0.91 (0.14, 6.07)
Clinical severity of index case											
Mild illness	122 (31.20)	327 (29.12)	117 (34.11)	58 (25.55)	89(29.67)	63 (24.90)	46.48	43.20	52.07	0.121[a]	Ref.
Moderate illness	263 (67.26)	774 (68.92)	219 (63.85)	167 (73.57)	208(69.33)	180 (71.15)	50.13	48.71	51.87	0.382[a]	1.73 (0.56, 5.35)
Severe/ critical illness	6 (1.53)	22 (1.96)	7 (2.04)	2 (0.88)	3(1.00)	10 (3.95)	59.0	30.00	83.33	0.027[b]	0.99 (0.01, 76.68)
Index case											
Complete vaccination < 14 days (2-dose)	18 (4.17)	34 (2.89)	12 (3.43)	0 (0.00)	22 (7.14)	0 (0.00)	64.71	64.71	0	-	Ref.
Complete vaccination within 14-90 days (2-dose)	54 (13.24)	160 (13.58)	96 (27.43)	0 (0.00)	64 (20.78)	0 (0.00)	40.00	40.00	0	-	0.07 (0.01, 0.78)
Complete vaccination >90 days (2-dose)	4 (0.98)	16 (1.36)	3 (0.86)	0 (0.00)	13 (4.22)	0 (0.00)	81.25	81.25	0	-	2.57 (0.04, 172.44)
Incomplete vaccination	155 (37.99)	448 (38.03)	239 (68.29)	0 (0.00)	209 (67.86)	0 (0.00)	46.65	46.65	0	-	0.20 (0.02, 1.77)
Using face mask											
Non-wearing face mask	238 (58.33)	684 (58.06)	197 (56.29)	108 (42.19)	231 (75.00)	148 (56.06)	55.41	53.97	57.81	0.328[a]	Ref.
Wearing face mask	170 (41.67)	494 (41.94)	153 (43.71)	148 (57.81)	77 (25.00)	116 (43.94)	39.07	33.48	43.94	0.017[a]	0.13 (0.04, 0.43)
Living behavior after COVID-19 diagnosis											
Shared bedrooms and bathrooms	47 (11.52)	110 (9.34)	20 (5.71)	18 (7.03)	41 (13.31)	31 (11.74)	65.45	67.21	63.27	0.665[a]	Ref.
Separated bedrooms and bathrooms	122 (29.90)	403 (34.21)	155 (44.29)	75 (29.30)	116 (37.66)	57 (21.59)	42.93	42.80	43.18	0.943[a]	0.56 (0.01 0.38)
Separated bedrooms/ Shared bathrooms	49 (12.01)	150 (12.73)	31 (8.86)	30 (11.72)	42 (13.64)	47 (17.80)	59.33	57.53	61.04	0.662[a]	0.17 (0.02, 1.65)
Shared bedrooms/ Separated bathrooms	9 (2.21)	27 (2.29)	2 (0.57)	4 (1.56)	12 (3.90)	9 (3.41)	77.78	85.71	69.23	0.303[a]	1.77 (0.05, 61.80)
Quarantine in isolation facilities	181 (44.36)	488 (41.43)	142 (40.57)	129 (50.39)	97 (31.49)	120 (45.45)	44.47	40.59	48.19	0.091[a]	0.05 (0.01, 0.35)

[a] Chi-square test
[b] Fisher's exact
[c] Multi-level logistic regression

nCoV-19 vaccinated index case was 56.1% after the first dose <14 days, but SAR after the second dose had a sample size that was too small (Table 2, Supplementary Table 5).

The completed two-dose CoronaVac vaccination within 14-90 days demonstrated significantly reduced household transmissibility of 69% (OR 0.31, 95% CI 0.10, 0.97, *P*-value = 0.045). In contrast, the completed two-dose CoronaVac vaccination <14 days demonstrated an increased risk of transmissibility (OR 77.82, 95% CI 2.22, 2728.76, *P*-value = 0.016) (Supplementary Table 6).

The SAR was lower in the vaccinated index cases who presented 24-48 hours after the onset of symptoms of index cases (*P*-value = 0.042). In severe and critical illnesses, vaccinated index cases showed lower SAR (30%) than unvaccinated cases (83.33%) (*P*-value = 0.027). The asymptomatic vaccinated index cases did not demonstrate decreased within-household transmissibility. The SARs for Ct values ≤20, 21-30, and >30 were 55.15%, 44.38%, and 43.40%, respectively, without affecting the risk of transmissibility in the different Ct values of the index cases.

The lower SAR of household contacts in vaccinated index cases aged 11-20, 21-30, and 41-50 years than unvaccinated individuals and those aged 41-50 years showed that vaccinated index cases had reduced transmissibility (aOR 0.16, 95% CI 0.03, 0.98). Vaccinated index cases aged 21-30 years had a lower SAR (*P* <0.001), whereas vaccinated index cases aged 61-70 years had a higher SAR (*P*-value = 0.003). Transmissibility was increased among vaccinated index cases aged 41-50 and 51-60 years (aOR 7.73, 95% CI 1.01, 22.17; aOR 9.94 1.35, 73.12) (Table 2).

The SAR was increased in unvaccinated index cases aged >70 years (69.23%), household members aged 11-20 years (63.63%), severe or critical illness (83.33%), and those who shared bedrooms after being diagnosed with either a shared bathroom or not. In the vaccinated index case, increased SAR was found in those who received one dose of CoronaVac <14 days (60%), those who completed two doses of the vaccine >90 days (81.25%), and those who received two doses of the CoronaVac <14 days (93.75%) and >90 days (81.25%), and those who shared bedrooms, with separated bathrooms or not (85.71%) (Table 2, Supplementary Table 5).

The overall vaccine effectiveness in preventing household transmission was 26.09%, 95% CI 21.57-30.61. The effectiveness of a two-dose vaccination was 23.59%, 95% CI 14.04-33.14 and 5.72%, 95% CI 0.00-13.64 in <14 days, ≥14 days after the second dose, respectively (Supplementary Table 7).

The SAR of the vaccinated index cases who wore a face mask was 33.48% compared to 43.94% of unvaccinated individuals. The observation among those who were vaccinated and wore face masks showed an 87% reduced transmissibility (aOR 0.13, 95% CI 0.04, 0.43), whereas those who did not wear masks were at risk of transmissibility 7.56 times (aOR 7.56, 95% CI 2.35, 24.34). After primary cases were diagnosed, prompt separation of bedrooms and bathrooms demonstrated reduced transmissibility (aOR 0.56, 95% CI 0.01, 0.38). Quarantine in facilities reduced transmissibility (aOR, 0.05; 95% CI 0.01, 0.35) (Table 2, Supplementary Table 5).

Discussion

During the SARS-CoV-2 outbreak that attacked Bangkok, B.1.617.2 rapidly increased and predominated in July 2021, resulting in enormous healthcare burdens (Medical Genomics Centre, 2021). Recent studies demonstrated the efficacy of BNT162b2 and mRNA-1273 in reducing household transmission among vaccinated index cases, with a 55% risk reduction (Ng et al., 2021). Our novel data demonstrated a completed two-dose inactivated or ChAdOx1 nCoV-19 vaccination within 14-90 days reduced within-household transmissibility. The risk reduction was 7.8% that was less than the previous study (Ng *et al.*, 2021). However, there were more unvaccinated household contacts among unvaccinated index cases than vaccinated index cases, resulting in a high SAR without demonstrating the difference between vaccinated and unvaccinated index cases, which is consistent with a UK study (Singanayagam *et al.*, 2022).

In addition to vaccination issues, Thai households were crowded, with extended families, multigeneration members, a culture wherein a family eats meals together, low socioeconomic status, and with more than half sharing bedrooms and bathrooms. Despite no different property types and the number of household members indicating increased transmissibility, recent studies have shown that households with high inoculum with limited living spaces have increased transmissibility (Cerami *et al.*, 2022). These constituent effects might explain the rapid, extensive household transmissibility and widespread transmission with SAR above 50% in Thai households.

Our results showed that the vaccine effectiveness in preventing within-household transmission after the first dose of mostly ChAdOx1 nCoV-19 and CoronaVac vaccine <14 days and >14 days was 35.56% and 13.33%, respectively. Although the very low vaccine effectiveness after the second dose, mostly CoronaVac, <14 days and >14 days were 5.72% and 23.59%, respectively. Only a full dose of CoronaVac within 14-90 days diminished the risk of household transmissibility among close contacts, in the same with the effect after the first dose of ChAdOx1 nCoV-19. The increased risk of transmission of CoronaVac vaccinated index cases demonstrated the relatively low effectiveness of CoronaVac after the second dose <14 days. Recent studies showed that one dose of ChAdOx1 nCoV-19 might have a 30% effectiveness among the B.1.617.2 variant and 48.7% among the Alpha variant. The effectiveness of the two doses of the ChAdOx1 nCoV-19 vaccine was 74.5% among the B.1.1.7 variant and 67% among the B.1.617.2 variant (Lopez Bernal et al., 2021a). However, the SAR in unvaccinated contacts exposed to the Delta variant was 25.8%, and the effectiveness in complete vaccination was 56.4%. A previous study could not demonstrate an association between vaccinated index cases and SARS-CoV-2 acquisition among contact cases (Ng *et al.*, 2021). Our study implied that SARS-CoV-2 acquisition by household contacts depended on the duration after vaccination and the efficacy and type of vaccines.

The very high SAR in those who received one dose of CoronaVac <14 days and two doses of CoronaVac >90 days was 93.75% and 81.25%, respectively, which might be from the waning immunity. Although the neutralizing antibodies might be persistent 6 months after the second dose, the geometric mean plaque reduction neutralization test 50 and plaque reduction neutralization test 90 were relatively low after the first and second doses of CoronaVac compared with BNT162b2, implying substantially lower effectiveness of CoronaVac for the prevention of symptomatic cases and protection of transmission. Therefore, a study recommended a third dose of CoronaVac 2 months after the second dose to achieve a protective immunity level. (Lim *et al.*, 2021; Zeng *et al.*, 2022). Encouraging awareness and implementing basic infection prevention measures after complete vaccination should be a concern.

However, having no significant difference in the SAR and reduced transmissibility among BBIBP-CorV and the second dose ChAdOx1 nCoV-19 vaccines might be a limitation from a small population due to the early period of vaccines implemented in Thailand. The ChAdOx1 nCoV-19 vaccine showed a 99% reduced transmissibility after the first dose <14 days, corresponding with the UK data that found 5.7% secondary cases and 48% transmissibility reduction (aOR 0.52, 95% CI 0.43-0.62) in households vaccinated with the ChAdOx1 nCoV-19 vaccine ≥21 days compared with 10.1% secondary cases in the unvaccinated group (Harris *et al.*, 2021). These findings correlated with immunogenicity studies and proved that ChAdOx1 nCoV-19 demonstrated substantial vaccine effectiveness early at 0-3 and 10-13 days after the first dose vaccination (Lopez Bernal et al., 2021b).

The nucleocapsid immunoglobulin G antibodies were higher in the vaccinated index cases than in the unvaccinated index cases, implying a possible longer duration of transmissibility in the vaccinated index cases. Although more natural antibodies were produced in vaccinated index cases, there was no difference in SAR between seropositive and seronegative index cases. Our data suggested that the high SAR was found within 0-72 hours and peaked 24-48 hours after the onset of symptoms. However, vaccinated index cases had milder and less severe illnesses than unvaccinated index cases, which was not demonstrated in the Household Transmission Evaluation Dataset (HOSTED) study (Hall *et al.*, 2021; Li *et al.*, 2021). Severe and critical COVID-19 also had more transmissibility, implying that severe illness might have more symptoms, less immunity, and possibly delayed viral clearance. Transmissibility evidence shows that infectiousness depends on local immunity rather than the quantitative virus (Luo *et al.*, 2021). Vaccinated recipients with breakthrough infections may have a more rapid viral clearance than unvaccinated individuals (Chia *et al.*, 2022; Kissler *et al.*, 2021).

However, only 0.4% of symptomatic vaccinated index cases had a duration from onset of symptoms >72 hours. A possible hypothesis is that asymptomatic index cases had a low risk of transmission owing to the lack of fever, the absence of cough, or negligible risk of silent transmission, which might be an advantage of vaccination, despite the prolonged duration of living in households before patients seek medical help.

The study failed to show that lower Ct values or different VOCs affected the increasing within-household transmissibility, in contrast with NHS data, which demonstrated that the B.1.617.2 caused an increased transmissibility within-household contacts compared with the B.1.1.7 variant (OR 1.7, 95% CI 1.48-1.95) (Allen *et al.*, 2022; Ng *et al.*, 2021; Singanayagam *et al.*, 2022). Although, the SAR of the B.1.617.2 variant was 49.7% in our study. According to the Department of Medical Sciences Ministry of Public Health data in Thailand, the B.1.617.2 has infected more than 95% of cases since July (Department of Medical Sciences, Ministry of Public Health, 2021).

The very high SAR in unvaccinated index cases aged >70 years, severe illness may be associated with dependent functional status and comorbidities. The high SAR in households aged 11-20 years was affected by in-school transmission (Giardina *et al.*, 2021). Although vaccinated index cases had a higher SAR among those aged 61-70 years, this might be due to the immunosenescence effect (Ranzani *et al.*, 2021). Transmissibility was increased among vaccinated index cases aged 41-50 and 51-60 years (aOR 7.73, 95% CI 1.01, 22.17; aOR 9.94 1.35, 73.12), although no association was found and differed from the previous result that revealed less susceptibility and more infectiousness in children and adolescents (Chu *et al.*, 2021; Li *et al.*, 2021).

Index cases who did not wear masks had a potential sevenfold risk of transmission, whereas, those who wearing face masks, especially within 0-72 hours from onset of symptoms, reduced household transmissibility by 87% and might be considered an adjunctive measure. In index cases with very high SAR who shared bedrooms and either shared bathrooms or not, a prompt separation of bedroom and bathroom when COVID-19 was diagnosed was essential to minimize transmissibility in addition to awaiting individuals' immunity effects (Eikenberry *et al.*, 2020; Pratt *et al.*, 2021). If home isolation is impossible, providing isolated facilities might be necessary to control household transmission and reduce reproductive numbers in the household (Li *et al.*, 2021).

The limitations of this study, we cannot stratify the effectiveness of each vaccine type. The lack of characteristics of SARS-CoV-2 acquisition and infection control elements in contact cases should be cautiously interpreted. The study period was the recent implementation of inactivated and ChAdOx1 nCoV-19 vaccines in Bangkok and did not include mRNA vaccines. The number of BBIBP-CorV-vaccinated cases was too small to be described. Comparing to the previous report, we could not evaluate the individual's household contacts with comorbidities, which had a high SAR (Madewell *et al.*, 2021). Most households were diagnosed using rapid antigen tests, which may have misled lower than the actual SAR.

Our results confirmed that individuals who received two doses of inactivated or ChAdOx1 nCoV-19 vaccines and were vaccinated within 14-90 days demonstrated the most significant advantage in preventing household transmission. The SAR was very high in index cases vaccinated with the CoronaVac within <14 days and >90 days, indicating that CoronaVac had the most effectiveness 14-90 days after the second dose and needed an early booster dose before 90 days after the second dose. However, the effectiveness of inactivated and ChAdOx1 nCoV-19 vaccines was relatively low compared with recent reports, and mRNA vaccines or high-efficacy vaccines should be implemented in countries with a high SAR for the highest benefit to prevent within-household transmission. SARS-CoV-2 vaccination and appropriate booster should be implemented nationwide, especially in unvaccinated and vaccinated individuals with waning immunity. The effect of preventing household transmissibility depends on the period of highest effectiveness of the vaccine and supports the concept of herd immunity (Aschwanden, 2021). The effect of a heterologous booster vaccination with high-efficacy vaccines after the first and second doses of inactivated vaccination to decrease within-household transmissibility is very important to interrupt the spreading of the virus. Vaccination in index cases could be a primary measure to prevent within-household transmission, which is a deserving, controllable strategy independent of socioeconomic and emotional factors. Post-exposure prophylaxis with novel agents to prevent household transmission needs to be proven in a clinical trial to eradicate the COVID-19 pandemic.

Funding

This study was supported by the Chulabhorn Royal Academy in Bangkok, Thailand.

Ethics approval

This study was approved by the Ethics Committee for Human Research, Chulabhorn Research Institute (EC No. 132/2564).

Authors contributions

M.M. and T.S. had full access to all of the data in this study and took responsibility for the data's integrity and accuracy. M.M.–first authors. T.S.- Corresponding author, K.T., S.W., C.B., K.S., N.M.. contributed equally to the study. Conceptualization, data curation, formal analysis: M.M., T.S., K.T., funding acquisition: N.M., investigation, methodology: M.M., T.S., K.T., S.W., C.B. project administration: T.S., M.M., resources, supervision: N.M., T.S., validation, visualization: T.S., writing – original draft: M.M., T.S., and writing – review & editing: T.S.

Declaration of competing interests

The authors have no competing interests to declare.

Acknowledgments

The authors thank all healthcare providers who worked in the frontline at the Acute Respiratory Tract Infection Clinic, COVID-19

Outpatient Clinic, and the cohort wards for supporting and providing clinical data for this study. The authors thank the Center of Learning and Research in Celebration of HRH Princess Chulabhorn's 60th Birthday Anniversary, Chulabhorn Royal Academy, Bangkok, Thailand for supporting the research process, with special thanks to Dr. Chirayu Auewarakul and Dr. Teerapat Ungtrakul. All authors extend their deepest sympathies and condolences to patients and their families.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.09.032.

References

Allen H, Vusirikala A, Flannagan J, Twohig KA, Zaidi A, Chudasama D, et al. Household transmission of COVID-19 cases associated with SARS-CoV-2 delta variant (B.1.617.2): national case-control study. Lancet Reg Health Eur 2022;12.

Aschwanden C. Five reasons why COVID herd immunity is probably impossible. Nature 2021;591:520–2.

Cerami C, Rapp T, Lin FC, Tompkins K, Basham C, Muller MS, et al. Household transmission of severe acute respiratory syndrome coronavirus 2 in the United States: living density, viral load, and disproportionate impact on communities of color. Clin Infect Dis 2022;74:1776–85.

Chia PY, Ong SWX, Chiew CJ, Ang LW, Chavatte JM, Mak TM, et al. Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine breakthrough infections: a multicentre cohort study. Clin Microbiol Infect 2022;28:612 .e1–7.

Chu VT, Yousaf AR, Chang K, Schwartz NG, McDaniel CJ, Lee SH, et al. Household transmission of SARS-CoV-2 from children and adolescents. N Engl J Med 2021;385:954–6.

Eikenberry SE, Mancuso M, Iboi E, Phan T, Eikenberry K, Kuang Y, et al. To mask or not to mask: modeling the potential for face mask use by the general public to curtail the COVID-19 pandemic. Infect Dis Modell 2020;5:293–308.

Giardina J, Bilinski A, Fitzpatrick MC, Kendall EA, Linas BP, Salomon J, et al. Model-estimated relationship between elementary school-related SARS-CoV-2 transmission, mitigation interventions, and vaccination coverage across community incidence levels. medRxiv; 2021 16 November https://www.medrxiv.org/content/10.1101/2021.08.04.21261576v2.

Grijalva CG, Rolfes MA, Zhu Y, McLean HQ, Hanson KE, Belongia EA, et al. Transmission of SARS-COV-2 infections in households - Tennessee and Wisconsin. April–September 2020. MMWR Morb Mortal Wkly Rep 2020;69:1631–4.

Hall JA, Harris RJ, Zaidi A, Woodhall SC, Dabrera G, Dunbar JK. HOSTED-England's Household Transmission Evaluation Dataset: preliminary findings from a novel passive surveillance system of COVID-19. Int J Epidemiol 2021;50:743–52.

Harris RJ, Hall JA, Zaidi A, Andrews NJ, Dunbar JK, Dabrera G. Effect of vaccination on household transmission of SARS-CoV-2 in England. N Engl J Med 2021;385:759–60.

Kissler SM, Fauver JR, Mack C, Tai CG, Breban MI, Watkins AE, et al. Viral dynamics of SARS-CoV-2 variants in vaccinated and unvaccinated persons. N Engl J Med 2021;385:2489–91.

Li F, Li YY, Liu MJ, Fang LQ, Dean NE, Wong GWK, et al. Household transmission of SARS-CoV-2 and risk factors for susceptibility and infectivity in Wuhan: a retrospective observational study. Lancet Infect Dis 2021;21:617–28.

Li W, Zhang B, Lu J, Liu S, Chang Z, Peng C, et al. Characteristics of household transmission of COVID-19. Clin Infect Dis 2020;71:1943–6.

Lim WW, Mak L, Leung GM, Cowling BJ, Peiris M. Comparative immunogenicity of mRNA and inactivated vaccines against COVID-19. Lancet Microbe 2021;2:e423.

Lopez Bernal J, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (delta) variant. N Engl J Med 2021a;385:585–94.

Lopez Bernal J, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ 2021b;373.

Luo CH, Morris CP, Sachithanandham J, Amadi A, Gaston D, Li M, et al. Infection with the SARS-CoV-2 delta variant is associated with higher infectious virus loads compared to the alpha variant in both unvaccinated and vaccinated individuals. medRxiv; 2021.

Madewell ZJ, Yang Y, Longini IM, Jr Halloran ME, Dean NE. Household transmission of SARS-CoV-2: a systematic review and meta-analysis. JAMA Netw Open 2020;3.

Jr Madewell ZJ, Yang Y, Longini IM, Halloran ME, Dean NE. Factors associated with household transmission of SARS-CoV-2: an updated systematic review and meta-analysis. JAMA Netw Open 2021;4.

Medical Genomics Centre. Variant of Concern Surveillance. Department of Medical Sciences, Ministry of Public Health; 2021 https://www3.dmsc.moph.go.th/post-view/1328. [Accessed 27 November 2021.].

Milman O, Yelin I, Aharony N, Katz R, Herzel E, Ben-Tov A, et al. Community-level evidence for SARS-CoV-2 vaccine protection of unvaccinated individuals. Nat Med 2021;27:1367–9.

Ng OT, Koh V, Chiew CJ, Marimuthu K, Thevasagayam NM, Mak TM, et al. Impact of delta variant and vaccination on SARS-CoV-2 secondary attack rate among household close contacts. Lancet Reg Health West Pac 2021;17.

Pollán M, Pérez-Gómez B, Pastor-Barriuso R, Oteo J, Hernán MA, Pérez-Olmeda M, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet 2020;396:535–44.

Pratt CQ, Chard AN, LaPine R, Galbreath KW, Crawford C, Plant A, et al. Use of stay-at-home orders and mask mandates to control COVID-19 transmission - blackfeet tribal reservation. Montana, June–December 2020. MMWR Morb Mortal Wkly Rep 2021;70:514–18.

Prunas O, Warren JL, Crawford FW, Gazit S, Patalon T, Weinberger DM, et al. Vaccination with BNT162b2 reduces transmission of SARS-CoV-2 to household contacts in Israel. Science 2022;375:1151–4.

Ranzani OT, Hitchings MDT, Dorion M, D'Agostini TL, de Paula RC, de Paula OFP, et al. Effectiveness of the CoronaVac vaccine in older adults during a gamma variant associated epidemic of covid-19 in Brazil: test negative case-control study. BMJ 2021;374:n2015.

Salo J, Hägg M, Kortelainen M, Leino T, Saxell T, Siikanen M, et al. The indirect effect of mRNA-based Covid-19 vaccination on unvaccinated household members. Nat Commun 2022;13:1162.

Singanayagam A, Hakki S, Dunning J, Madon KJ, Crone MA, Koycheva A, et al. Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. Lancet Infect Dis 2022;22:183–95.

Watanapokasin N, Siripongboonsitti T, Ungtrakul T, Muadchimkaew M, Wongpatcharawarakul S, Auewarakul C, et al. Transmissibility of SARS-CoV-2 variants as a secondary attack in Thai households: a retrospective study. IJID Reg 2021;1:1–2.

World Health Organization. *Household transmission investigation protocol for coronavirus disease 2019 (COVID-19).* No. WHO/2019-nCoV/HHtransmission/2020.4.. WHO; 23 March 2020.

Zeng G, Wu Q, Pan H, Li M, Yang J, Wang L, et al. Immunogenicity and safety of a third dose of CoronaVac, and immune persistence of a two–dose schedule, in healthy adults: interim results from two single-centre, double-blind, randomised, placebo-controlled phase 2 clinical trials. Lancet Infect Dis 2022;22:483–95.