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Household transmission of COVID-19 cases associated with SARS-CoV-2 delta variant (B.1.617.2): national case-control study

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Summary

Background The SARS-CoV-2 Delta variant (B.1.617.2), first detected in India, has rapidly become the dominant variant in England. Early reports suggest this variant has an increased growth rate suggesting increased transmissibility. This study indirectly assessed differences in transmissibility between the emergent Delta variant compared to the previously dominant Alpha variant (B.1.1.7).

Methods A matched case-control study was conducted to estimate the odds of household transmission (≥ 2 cases within 14 days) for Delta variant index cases compared with Alpha cases. Cases were derived from national surveillance data (March to June 2021). One-to-two matching was undertaken on geographical location of residence, time period of testing and property type, and a multivariable conditional logistic regression model was used for analysis.

Findings In total 5,976 genomically sequenced index cases in household clusters were matched to 11,952 sporadic index cases (single case within a household). 43.3% (n=2,586) of cases in household clusters were confirmed Delta variant compared to 40.4% (n=4,824) of sporadic cases. The odds ratio of household transmission was 1.70 among Delta variant cases (95% CI 1.48-1.95, $p < 0.001$) compared to Alpha cases after adjusting for age, sex, ethnicity, index of multiple deprivation (IMD), number of household contacts and vaccination status of index case.

Interpretation We found evidence of increased household transmission of SARS-CoV-2 Delta variant, potentially explaining its success at displacing Alpha variant as the dominant strain in England. With the Delta variant now having been detected in many countries worldwide, the understanding of the transmissibility of this variant is important for informing infection prevention and control policies internationally.

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Introduction

Following detection of the first SARS-CoV-2 cases in England in January 2020, by June 2021, the total number of laboratory confirmed COVID-19 cases in England exceeded four million. Following a dramatic second wave of COVID-19 cases in late 2020, a subsequent national lockdown was implemented alongside an accelerated immunisation programme prioritising older adults and clinically extremely vulnerable individuals.

The number of new COVID-19 infections declined, and from March 2021, had remained stable at low incidence.¹ However, during this time, several emerging SARS-CoV-2 variants were detected in England.²

SARS-CoV-2 variant B.1.617.2, classified by the World Health Organisation (WHO) as the 'Delta' variant,³ was initially detected in India in December 2020 amidst a surge in COVID-19 cases and associated hospitalisations and deaths.⁴ By 1 June 2021, this variant had been detected in 54 countries.⁵ The first genomically confirmed case was detected in England in late March 2021 as part of the national programme for routine sequencing of SARS-CoV-2 cases. The Delta variant was initially declared a variant under investigation by Public Health England and then upgraded to a variant of concern on 6 May 2021.⁶ Initially detected in specific

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Research in context

Evidence before this study

To identify publications on COVID-19 infection due to the Delta variant (B.1.617.2) and associated transmission advantage and household outbreaks, we searched PubMed for articles published with the terms “COVID-19” or “SARS-CoV-2” with “B.1.617.2”, “Delta” or “Indian variant” with no language restrictions. Due to the rapid and recent emergence of the SARS-CoV-2 Delta variant, there were very few publications related to this topic. The few articles available related to local surge testing programmes in response to outbreaks of this variant and the protective effect of the different vaccines to this variant.

Added value of this study

In the absence of studies exploring the transmission advantage of the Delta variant in any setting, and surveillance data showing the rapid spread of this variant internationally, we assessed the impact of this variant on household transmission rates. To assess the emergent SARS-CoV-2 Delta variant and the previously dominant Alpha (B.1.1.7) variant, we conducted a matched case-control study to estimate the likelihood of onward transmission in households with index cases with genomically confirmed Delta variant, compared to genomically confirmed Alpha variant. After adjustment, we found the odds of subsequent transmission from Delta variant cases were 70% higher than from Alpha variant cases.

Implications of all the available evidence

This study provides timely real-world evidence of increased transmissibility of the Delta variant, suggesting that it is more strongly associated with onward transmission within household settings compared to Alpha. This evidence highlights the need for a focus on improving strategies to prevent the risk of spread of SARS-CoV-2 within households and to support those in self-isolation to control the COVID-19 pandemic, particularly in the context of emerging and more transmissible variants.

localised outbreaks and in association with travel to India, by 10 June 2021, 16,242 genomically confirmed cases of Delta variant SARS-CoV-2 variant have been detected across England.

Surveillance data suggest the Delta variant quickly became the dominant variant in England, usurping the formerly successful Alpha (B.1.1.7) variant. The Delta variant has by far the highest growth rate of the detected variants, reflecting both the biological properties of this variant and the context in which it is transmitting.⁷

The Delta variant has also been shown to be associated with increased risk of hospital admission compared to the Alpha variant,^{2,8,9} however, evidence has

shown that the available COVID-19 vaccines provide nearly equivalent protection against the Delta variant after two doses as to the Alpha variant.¹⁰ Nevertheless, the observed rapid spread of this variant in England and internationally necessitate investigation into the transmissibility advantage of this variant compared to the previously dominant Alpha variant, to assess its potential impact on the incidence of COVID-19 in England.

Households are high risk settings for transmission of COVID-19¹¹ and are an important factor in wider community spread.¹² By assessing the extent to which the Delta variant results in onward transmission to household members compared to the Alpha variant, we can assess the role of increased transmissibility in the recent rise in COVID-19 infection and provide information vital to the national and international pandemic response.

Methods

Study design

A matched case-control study design was used to estimate the odds of transmission within households, with a focus on assessing the difference in transmissibility between the Delta and Alpha variants. Cases and controls were assigned on the outcome of interest, household clustering, and were matched on fortnight of specimen date, geography (lower tier local authority) and property type. Both case and control groups included Delta and Alpha variant SARS-CoV-2 cases.

Study population

Data on laboratory confirmed COVID-19 cases in England that have been genomically sequenced were extracted on 21st June 2021. The study population consisted of sequenced Delta and Alpha variant SARS-CoV-2-positive cases who: a) had a first positive specimen date between 18th March 2021 and 7th June 2021, to allow for subsequent household cases to be detected; b) resided in a private residential dwelling (terraced, semi-detached or detached house or a flat) and c) had no recorded history of foreign travel within the 14 days preceding the specimen date. Individuals were included in the analysis if they were the first cases within a household, hereby referred to as index cases.

Data sources

In accordance with statutory requirements, positive SARS-CoV-2 tests are notified to Public Health England’s (PHE) Second Generation Surveillance System (SGSS), a laboratory reporting system.

Residential address information for each positive SARS-CoV-2 test was obtained from NHS summary care records, laboratory information management

system (LIMS) or is self-reported at test booking. The LIMS address, supplied by the diagnosing laboratory, was preferentially utilised as this should reflect the address at time of testing, as opposed to the centrally-held NHS address which may not be up to date or include temporary address changes. To facilitate identification of specific residential location and to obtain residential property types, cases were address matched against Ordnance Survey reference databases. These hold all UK addresses and provided a standardised Unique Property Reference Number (UPRN) and Basic Land and Property unit (BLPU) class for each case, facilitating the detection of cases residing at the same property and the identification of property type.

The vaccination status of all index cases included as cases and controls in the analysis was obtained from a national vaccination register (the National Immunisation Management System, NIMS) and linked to case date using patient NHS number. The number of named household contacts for index cases was obtained via NHS test and trace Contact Tracing Advisory Service (CTAS) data. Case data was linked to CTAS data using patient identifying information captured both in SGSS and through contact tracing. Due to incompleteness of commonly held fields within the CTAS dataset, records were linked across a range of identifying factors using an iterative approach, linking on the most reliable identifiers first.

Outcome assessments

In this analysis, a household cluster was defined as two or more subsequent positive SARS-CoV-2 cases at the same private residential dwelling. This includes an initial sequenced laboratory confirmed index case (termed 'case' in our case control study) followed by one or more laboratory confirmed or lateral flow device positive SARS-CoV-2 cases in the same household (based on UPRN) within 14 days of the index cases' positive specimen date. Secondary cases within a household were identified from all case data regardless of whole genome sequencing data availability to optimise case ascertainment.

'Controls' were cases where no further SARS-CoV-2 cases were reported in the household in the subsequent 14 days. Cases and controls were matched on a 1:2 ratio on the fortnight of specimen date, geography (lower tier local authority) and property type i.e. terraced, semi-detached or detached house or flat. Matching was undertaken as a way to address potential inter-relationships between time, geography of residence and property type, and to minimise potential for confounding related to household size and regional variation in incidence rates, and local interventions.

Exposure assessment

Delta and Alpha variant cases were identified from sequencing information nationally co-ordinated by the

COG-UK (COVID-19 Genomics UK) consortium and uploaded to the CLIMB (Cloud Infrastructure for Big Data Microbial Bioinformatics) database. PCR confirmed cases were sampled for whole genome sequencing (WGS) with over 50% of laboratory confirmed cases in England sequenced during the study period.¹³ Sequences were assigned according to Public Health England's single nucleotide and multinucleotide polymorphisms based variant definitions.¹⁴

Exclusions

Cases and controls who did not have a full 14 days of follow-up time were excluded from the analysis. Additionally, any households that had laboratory confirmed cases in the preceding 90 days from the index case were excluded under the assumption that this would independently reduce the number of susceptible persons in a household and potential observed effects on transmission. Co-primary case households, defined as more than one case having the same earliest positive specimen date, were also excluded.

Targeted testing was undertaken for close contacts of cases with a variant of concern, apart from the Alpha variant. As such, using the available case-level data provided by the National COVID-19 operations team, we identified and excluded households that were targeted for testing prior to 21 May 2021 as this would bias case-finding (and therefore cluster detection) for Delta variant cases.

To minimise the impact of potential bias introduced through different isolation guidance for travellers and non-travellers, including quarantine guidance and compulsory hotel quarantine for returning travellers, cases with history of traveling outside the UK in the 14 days preceding diagnosis were excluded from analysis. Data on recent travel history for sequenced cases was collected via passenger locator forms, Contact Tracing Advisory Service (CTAS) dataset and enhanced follow up of cases with genomically confirmed variants of concern through local health protection teams.

There are two main testing routes for COVID-19 in the UK: tests carried out by hospital and public health laboratories, which can include testing of those presenting to healthcare services (referred to as Pillar 1) and wider population testing (referred to as Pillar 2), which includes both community testing sites and postal tests. While not exclusively hospitalised patients, cases identified through Pillar 1 were omitted to minimise bias in terms of household transmission for those identified as SARS-CoV-2 positive while hospitalised, which would not contribute to household transmission and therefore dilute the estimated difference in transmission risk between variants.

The number of household contacts for each case was counted from the CTAS dataset; named contacts are recorded and linked to index cases as part of the contact

tracing process. Cases with no named contacts were excluded from the analysis. Cases which could not be uniquely linked in to the CTAS dataset were also excluded.

Statistical analysis

A conditional logistic regression model was used to account for the matched design, matching on geographical location of residence, time period of testing and property type. A multivariable conditional logistic regression model was used for analysis to assess the association between the variant and household transmission. This model was adjusted for potential confounding by age group, sex, ethnicity, index of multiple deprivation (IMD) (quintiles), number of household contacts and vaccination status of index case.

To assess the impact of using a limited number of cases and controls in the matched design, an additional sensitivity analysis was carried out fitting a logistic regression model using all index cases during the study period that met the inclusion criteria, without applying case control matching.

Results

During the study period (18th March – 7th June), of the genomically sequenced cases in England, there were 50,213 and 67,375 cases identified as Delta and Alpha variants respectively, representing 98.1% of all sequenced cases in total in England during this period.

We excluded index cases with confirmed Delta or Alpha variant with specimen dates between 18th March – 7th June 2021 that did not meet the inclusion and matching criteria (Supplementary Table 1). 5,772 (40.2%) Delta variant index cases and 8,586 (59.8%) Alpha variant index cases were excluded as they did not specifically meet the inclusion criteria, namely they were tests carried out via Pillar 1 (primarily conducted as part of hospital and travel associated testing), they had recently travelled, or were co-primary cases (multiple index cases) and had no household contacts. A further 8,915 Delta variant index cases and 13,621 Alpha variant index cases were excluded as they could not be matched to a case/control. A total of 7,410 confirmed Delta variant cases were included in the matched case-control analysis (Table 1).

After applying eligibility and matching criteria, we obtained a sample of 17,928 individual index cases. This included 5,976 index cases in household clusters (hereafter referred to as 'cases' in the case-control study) and 11,952 sporadic cases ('controls') (Table 1).

The index cases excluded from the analysis ($n=54,822$) differed from those included in terms of variant, PHE centre of residence, age, sex, ethnicity, IMD and vaccination status (Supplementary Table 2). A higher proportion of included cases were 10-19 years old

compared to excluded cases (28.2%, 21.1%, respectively) and a lower proportion were over 70 (0.9% v 2.7%). A lower proportion of included cases were of Asian ethnicity (13.3% vs 16.4%). A higher proportion of included cases were resident in London, North West and Yorkshire and Humber compared to excluded cases.

Study population

Females made up 49.3% (2,945) of cases and 51.1% (6,130) of controls. There was a slightly higher proportion of cases aged between 30-59 compared to controls (Table 1). The majority of the study population were of White ethnicity (78.9%, 14,140) with a higher proportion of Asian ethnicity among cases (15.2%, 911) compared to controls (12.3%, 1,468). A large proportion of the study population resided in the North West (36.1%, 6,468) and the Yorkshire and Humber (26.3%, 4,722), reflecting the geographical spread of COVID-19 cases in England during the study period. The most common residential setting for both cases and controls was terraced houses (37.0%, 6,633), followed by semi-detached (38.8%, 6,957). A higher proportion of cases were also unvaccinated compared to controls (68.6% vs 66.7%).

A higher proportion of cases had confirmed Delta variant (43.3%, 2,586), compared to controls (40.4%, 4,824).

Household Transmission

In the univariable analysis, the odds of household transmission were 1.71 among those with Delta variant (95%CI 1.49-1.96, $p < 0.001$) compared to those with Alpha variant. After adjusting for age, sex, ethnicity, IMD, number of household contacts and vaccination status of index case, evidence of this association remained with the adjusted odds ratio of household transmission of 1.70 among those with Delta variant (95%CI 1.48-1.95, $p < 0.001$).

Differences in the odds of household transmission were also seen between age and ethnic groups (Table 2). Prior to adjustment for potential confounders, the odds of transmission were increased among index cases aged between 40-49, 50-59 and over 70 compared to those aged 30-39. After adjustment, this trend remained. There was also evidence of decreased odds of household transmission among those aged under 29 compared to those aged 30-39.

The odds of household transmission were increased when an index case was of Asian ethnicity (aOR 1.12, 95%CI 1.01-1.25) and less likely when an index case was of Black ethnicity (aOR 0.80, 95%CI 0.65-0.98), compared with index cases of White ethnicity.

In the sensitivity analysis without restriction to matching criteria (Supplementary Table 3), logistic regression models including all eligible index cases found the crude odds of transmission was 1.20 among those with the Delta variant compared to those with the

	Controls		Cases	
	Count	Percent	Count	Percent
Total	11,952		5,976	
Variant				
Delta (B.1.617.2)	4,824	40.36	2,586	43.27
Alpha (B.1.1.7)	7,128	59.64	3,390	56.73
Household type				
Terraced	4,422	37.00	2,211	37.00
Semi-detached	4,638	38.81	2,319	38.81
Detached	1,984	16.60	992	16.60
Flat	908	7.60	454	7.60
Specimen date (2 week period)				
w/c 14th March 2021	2,008	16.80	1,004	16.80
w/c 28th March 2021	1,844	15.43	922	15.43
w/c 11th April 2021	1,058	8.85	529	8.85
w/c 25th April 2021	1,044	8.73	522	8.73
w/c 9th May 2021	1,054	8.82	527	8.82
w/c 23rd May 2021	4,326	36.19	2,163	36.19
w/c 6th June 2021	618	5.17	309	5.17
PHE Centre				
East Midlands	1,146	9.59	573	9.59
East of England	584	4.89	292	4.89
London	818	6.84	409	6.84
North East	542	4.53	271	4.53
North West	4,312	36.08	2,156	36.08
South East	532	4.45	266	4.45
South West	118	0.99	59	0.99
West Midlands	752	6.29	376	6.29
Yorkshire and Humber	3,148	26.34	1,574	26.34
Age				
<10	658	5.51	414	6.93
10-19	3,494	29.23	1,564	26.17
20-29	2,921	24.44	1,047	17.52
30-39	2,287	19.13	1,270	21.25
40-49	1,304	10.91	908	15.19
50-59	852	7.13	561	9.39
60-69	339	2.84	149	2.49
70+	97	0.81	63	1.05
Sex				
Female	6,130	51.29	2,945	49.28
Male	5,822	48.71	3,031	50.72
Ethnicity				
Asian	1,468	12.28	911	15.24
Black	339	2.84	147	2.46
Mixed	392	3.28	152	2.54
Other	233	1.95	146	2.44
White	9,520	79.65	4,620	77.31
IMD (quintile)				
1	3,859	32.29	2,052	34.34
2	2,474	20.70	1,250	20.92
3	2,023	16.93	934	15.63
4	1,920	16.06	906	15.16
5	1,676	14.02	834	13.96
No. of household contacts				
1	3,537	29.59	1,284	21.49

(continued)

Table 1 (Continued)

	Controls		Cases	
2	3,137	26.25	1,431	23.95
3	3,210	26.86	1,887	31.58
≥4	2,068	17.30	1,374	22.99
Vaccination status				
Unvaccinated	8,198	68.59	3,990	66.77
<21 days post dose 1	853	7.14	454	7.60
>= 21 days post dose 1	1,581	13.23	913	15.28
>= 14 days post dose 2	344	2.88	156	2.61
Unknown	976	8.17	463	7.75

Table 1: Characteristics of genomically sequenced confirmed SARS-CoV-2 cases and controls in England 18 March – 7 June 2021.

IMD = Index of Multiple Deprivation (1= least deprived, 5 = most deprived).

Alpha variant (95% CI 1.15-1.26, $p < 0.001$). With adjustment for property type, fortnight of specimen date, lower tier local authority of residence, age, sex, ethnicity, IMD, number of household contacts and vaccination

status of index case, the adjusted odds of transmission were similar to the matched analysis at 1.80 for the Delta compared to the Alpha variant (95% CI 1.67-1.96, $p < 0.001$) (Supplementary Table 3).

	Household Transmission			
	OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Variant				
Delta (B.1.617.2)	1.71(1.49-1.96)	<0.001	1.70(1.48-1.95)	<0.001
Alpha (B.1.1.7)	1.00	-	1.00	-
Sex				
Female	1.00	-	1.00	-
Male	1.08(1.02-1.15)	0.01	1.07(1.01-1.14)	0.03
Age group				
<10	1.14(0.98-1.31)	<0.001	0.98(0.85-1.14)	<0.001
10-19	0.8(0.73-0.88)		0.71(0.64-0.79)	
20-29	0.64(0.58-0.71)		0.67(0.6-0.74)	
30-39	1.00		1.00	
40-49	1.27(1.13-1.41)		1.24(1.11-1.39)	
50-59	1.19(1.05-1.36)		1.42(1.23-1.63)	
60-69	0.8(0.65-0.98)		1.07(0.86-1.34)	
70+	1.18(0.85-1.63)		1.74(1.23-2.47)	
Ethnicity				
Mixed	0.81(0.67-0.98)	<0.001	0.84(0.69-1.02)	0.003
Asian	1.34(1.22-1.48)		1.12(1.01-1.25)	
Black	0.92(0.76-1.13)		0.80(0.65-0.98)	
White	1.00		1.00	
Other	1.33(1.07-1.64)		1.17(0.94-1.46)	
IMD quintile				
1-most deprived	1.19(1.08-1.32)	0.005	1.13(1.02-1.26)	0.148
2	1.11(1-1.24)		1.09(0.98-1.22)	
3	1(0-0)		1(0-0)	
4	1.02(0.91-1.14)		1.01(0.9-1.13)	
5-least deprived	1.06(0.94-1.2)		1.05(0.92-1.18)	

(continued)

Table 2 (Continued)

	Household Transmission			
	OR (95% CI)	P value	Adjusted OR (95% CI)	P value
No. of household contacts				
1	1(0-0)	<0.001	0(0-0)	<0.001
2	1.28(1.17-1.4)		1.33(1.21-1.46)	
3	1.66(1.52-1.82)		1.75(1.59-1.92)	
≥4	1.88(1.71-2.07)		1.97(1.77-2.18)	
Vaccination status of index case				
Unvaccinated	1.00	0.002	1.00	0.03
<21 days post dose 1	1.1(0.97-1.24)		0.91(0.79-1.03)	
≥21 days post dose 1	1.19(1.08-1.3)		0.94(0.84-1.05)	
≥14 days post dose 2	0.93(0.77-1.13)		0.73(0.58-0.9)	
Unknown	0.97(0.87-1.1)		0.9(0.8-1.02)	

Table 2: Univariable and multivariable conditional logistic regression of odds of household transmission in genomically sequenced confirmed SARS-CoV-2 cases, in England 18 March – 7 June, 2021.

Discussion

Our study found a 70% increase in the odds of household transmission associated with infection with SARS-CoV-2 Delta variant compared to Alpha, following adjustment for the index cases' vaccination status, as well as sex, ethnicity, IMD, age group and number of household contacts. This study provides early, real-world evidence of the effect of Delta variant on household transmission. The findings support existing evidence that the Delta variant has a substantially increased transmissibility advantage over the Alpha variant. This advantage has contributed to the rapid increase in the number of Delta variant cases in the UK over the study period and may explain the rapid surge in cases seen in other countries where this variant has been observed.^{2,8,15}

This study also found evidence of increased household transmission in households with an index case of Asian ethnicity, a finding consistent with studies of the previously dominant Alpha variant.^{14,16} These results add important new evidence to help understand the underlying reasons for increased susceptibility to COVID-19 infection, and possibly reflect differences in household composition and inter-household mixing between ethnic groups, with specific groups more likely to live in large or multi-generational households.

The analysis of household clustering has previously been used to characterise the transmissibility of different variants such as Alpha variant when this initially emerged,¹⁶ and similar observations followed in other countries.^{17,18} The key strength of this method is the comprehensive genomic sequencing programme in England co-ordinated by COG-UK which delivers large-scale whole genome sequencing of SARS-CoV-2 cases

allowing for surveillance, early detection of variants and the increased understanding of viral transmission, both nationally and internationally.

The sampling strategy for sequencing in England is not random, however, some effects of this non-random sampling were addressed by removing households that received targeted testing. Despite the sampling strategy for sequencing not being random, with over 50% of positive COVID-19 cases sequenced during the study period, the sequenced cases included in this study are likely representative of the population testing positive for COVID-19.

This analysis covers a time period when both Delta and Alpha variants were circulating in the population, allowing comparison of risk with sufficient power to detect a difference in transmission. By the end of May 2021, Delta had become the dominant SARS-CoV-2 virus in England, accounting for over 90% of all new cases and has been a key driver for the rapid rise in cases seen in England in Spring 2021.¹

The inclusion of vaccination data further strengthens this study. By linking COVID-19 case data to vaccination status we were able to partially adjust for the effect of vaccination on onward transmission to secondary cases. This adjustment is an important factor in assessing transmissibility, as other studies have shown vaccination is effective in reducing secondary cases in households with a symptomatic index case.¹¹ However, our assessment of this effect was limited as most cases included in the analysis were unvaccinated.

This study also benefits from the enrichment of COVID-19 case data with residential address data and travel information to create a large sample of cases and controls for inclusion in the analysis.

There are several limitations to this study. Firstly, as we did not have information on household makeup, which is likely to have an effect on the estimates of transmissibility, an amount of unmeasured confounding was introduced to the analysis. For example, characteristics of household contacts, such as age, is likely to influence vaccination status and overall risk of transmission. The trends observed in transmissibility by age group are in line with the findings of passive and active surveillance studies.^{19,20} Moreover, without data on the vaccination status of household contacts, the extent to which this would impact onward transmission in this setting was unknown. Despite this, variation in household makeup was somewhat mitigated by matching on local geography and property type.

Further studies that include all individuals' vaccination status are needed to provide improved estimates of household transmission and allow for the calculation of household secondary attack rates.

Although we excluded co-primary case households (defined as a household with more than one case having the same earliest positive specimen date), as index cases were defined by their specimen date, we were unable to exclude individuals who were in fact co-primary cases but were tested sequentially in the household. Furthermore, the advantage for the Delta variant observed may also be associated with escape from immunity induced by prior infection.

This analysis is specific to residential households and excluded cases occurring in other residential settings that are susceptible to SARS-CoV-2 outbreaks, such as prisons or care homes, or in other vulnerable populations such as homeless people. As data is based on residential address, we were also not able to include outbreaks in education or occupational settings. Care must therefore be taken when applying conclusions from this study to such settings.

It is important to note that although COVID-19 vaccines administered in England are still highly effective against the Delta variant, the high transmissibility of this variant has still resulted in a substantial rise in the number of COVID-19 cases reported following its emergence. As this variant has now been detected globally, this evidence of increased transmissibility will be relevant to other industrialised countries and will be important in considering mitigation in public health responses, particularly in countries with low vaccination coverage.

Overall, we found increased household transmission of COVID-19 associated with the Delta compared to the Alpha variant. Our study shows that households are important settings for the transmission of the Delta variant and with household settings being an important factor in wider community spread, it is vital to maintain policies to prevent transmission of COVID-19 in these settings.

With the results of this analysis suggesting increased transmissibility of this variant and the Delta variant now

having been detected in many countries worldwide, the understanding of the transmissibility of this variant is important for informing public health policies internationally to control the COVID-19 pandemic.

Declarations

Data Availability Statement

Data are incorporated into the article and material contained within. Individual level data cannot be shared due to ethical/privacy reasons.

Code availability

Custom code using Stata15.

Authors' contributions

AV and HA were the principal investigators and led the writing of this report. HA, AV, MK, JF, KT and GD made significant contributions to conception of the study design. All authors contributed to the interpretation of results and critical review.

Ethics approval

All data were collected within statutory approvals granted to Public Health England for infectious disease surveillance and control. Information was held securely and in accordance with the Data Protection Act 2018 and Caldicott guidelines.

Consent to participate

All data were collected within statutory approvals granted to Public Health England for infectious disease surveillance and control. Information was held securely and in accordance with the Data Protection Act 2018 and Caldicott guidelines.

Consent for publication

All data were collected within statutory approvals granted to Public Health England for infectious disease surveillance and control. Information was held securely and in accordance with the Data Protection Act 2018 and Caldicott guidelines.

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Declaration of interests

GD's employer, Public Health England, has received funding from GlaxoSmithKline for a research project related to seasonal influenza and antiviral treatment; this project preceded and had no relation to COVID-19, and GD had no role in and received no funding from the project. All other authors declare no competing interests.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.lanepe.2021.100252](https://doi.org/10.1016/j.lanepe.2021.100252).

References

- Public Health England. National flu and COVID-19 surveillance reports.
- Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 11 2021.
- World Health Organisation. World Health Organisation 2021. <https://www.who.int/>.
- ECDC. Emergence of SARS-CoV-2 B.1.617 variants in India and situation in the EU/EEA, 11 May 2021, 2021.
- Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 14, 2021.
- Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 10 2021.
- Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 20 2021.
- Robert C, Louise D, Chris O, Laura G-R, Leon D, Julia G. Briefing note: Potential community transmission of B.1.617.2 inferred by S-gene positivity. 2021.
- Sheikh A, McMenamin J, Taylor B, Robertson C. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. *Lancet North Am Ed*.
- Bernal JL, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, Stowe J, Tessier E, Groves N, Dabrera G, Myers R. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. *N Engl J Med* 2021 Jul 2021.
- 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.
- Haroon S, Chandan JS, Middleton J, Cheng KK. Covid-19: breaking the chain of household transmission. *BMJ* 2020;370:m3181.
- Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 12, 2021.
- Genomics P. Standardised Variant Definitions. 2021. https://github.com/phe-genomics/variant_definitions (accessed 09/06/2021).
- Kucharski A, Davies N, Eggo R, Funk S. Modelling importations and local transmission of B.1.617.2 in the UK, 2021.
- Chudasama DY, Flannagan J, Collin SM, et al. Household clustering of SARS-CoV-2 variant of concern B.1.1.7 (VOC-202012-01) in England. *J Infect* 2021.
- Tanaka H, Hirayama A, Nagai H, Shirai C, Takahashi Y, Shinomiya H, Taniguchi C, Ogata T. Increased transmissibility of the SARS-CoV-2 Alpha variant in a Japanese population. *Int J Environ Res Public Health* 2021;18(15):7752. Jan.
- Althaus CL, Baggio S, Reichmuth ML, Hodcroft EB, Riou J, Neher RA, Jacquerioz F, Spechbach H, Salamun J, Vetter P, Williamson C. A tale of two variants: spread of SARS-CoV-2 variants Alpha in Geneva, Switzerland, and Beta in South Africa. *medRxiv* 2021.
- Miller E, Waight PA, Andrews NJ, McOwat K, Brown KE, Katja H, Ijaz S, Letley L, Haskins D, Sinnathamby M, Cuthbertson H. Transmission of SARS-CoV-2 in the household setting: a prospective cohort study in children and adults in England. *J Infect* 2021.
- 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.