

Shedding of Infectious SARS-CoV-2 Despite Vaccination

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Abstract

The SARS-CoV-2 Delta variant might cause high viral loads, is highly transmissible, and contains mutations that confer partial immune escape ^{1,2}. Outbreak investigations suggest that vaccinated persons can spread Delta ^{3,4}. We compared RT-PCR cycle threshold (Ct) data from 699 swab specimens collected in Wisconsin 29 June through 31 July 2021 and tested with a qualitative assay by a single contract laboratory. Specimens came from residents of 36 counties, most in southern and southeastern Wisconsin, and 81% of cases were not associated with an outbreak. During this time, estimated prevalence of Delta variants in Wisconsin increased from 69% to over 95%. Vaccination status was determined via self-reporting and state immunization records ([Supplemental Figure 1](#)).

Main text

We observed low Ct values (<25) in 212 of 310 fully vaccinated (68%; [Figure 1A](#)) and 246 of 389 (63%) unvaccinated individuals. Testing a subset of low-Ct samples revealed infectious SARS-CoV-2 in 15 of 17 specimens (88%) from unvaccinated individuals and 37 of 39 (95%) from vaccinated people ([Figure 1B](#)).

Low Ct values were detected in vaccinated people regardless of symptoms at the time of testing ([Figure 1C](#)). Ct values <25 were detected in 7 of 24 unvaccinated (29%; CI: 13-51%) and 9 of 11 fully vaccinated asymptomatic individuals (82%; CI: 48-97%), and 158 of 232 unvaccinated (68%, CI: 62-74%) and 156 of 225 fully vaccinated (69%; CI: 63-75%) symptomatic individuals. Time from symptom onset to testing did not vary by vaccination status ($p=0.40$; [Supplemental Figure 2](#)). Infectious virus was detected in the sole specimen tested from an asymptomatic fully vaccinated individual. Although few asymptomatic individuals were sampled, these results indicate that even asymptomatic, fully vaccinated people might shed infectious virus.

Combined with other studies ²⁻⁵, these data indicate that vaccinated and unvaccinated individuals infected with the Delta variant might transmit infection. Importantly, we show that infectious SARS-CoV-

2 is frequently found even in vaccinated persons when specimen Ct values are low. The inclusion of viruses from Pango lineages B.1.617.2, AY.2, and AY.3, and multiple counties without a linking outbreak, indicate that Delta-lineage SARS-CoV-2 can achieve low Ct values consistent with transmissibility in fully vaccinated individuals across a range of settings. Vaccinated and unvaccinated persons should get tested when symptomatic or after close contact with someone with suspected or confirmed COVID-19. Continued adherence to non-pharmaceutical interventions during periods of high community transmission to mitigate spread of COVID-19 remain important for both vaccinated and unvaccinated individuals.

Figure

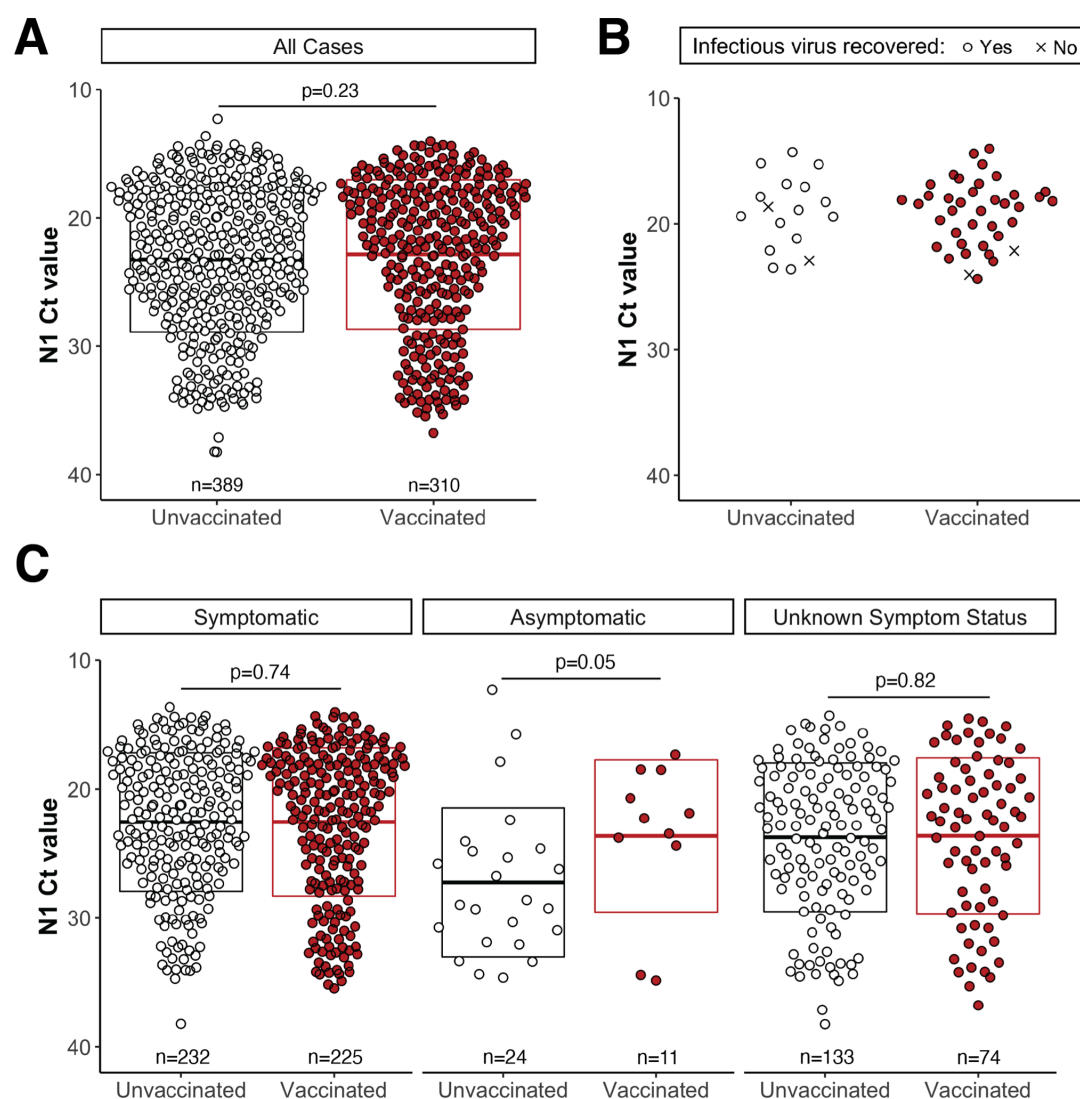
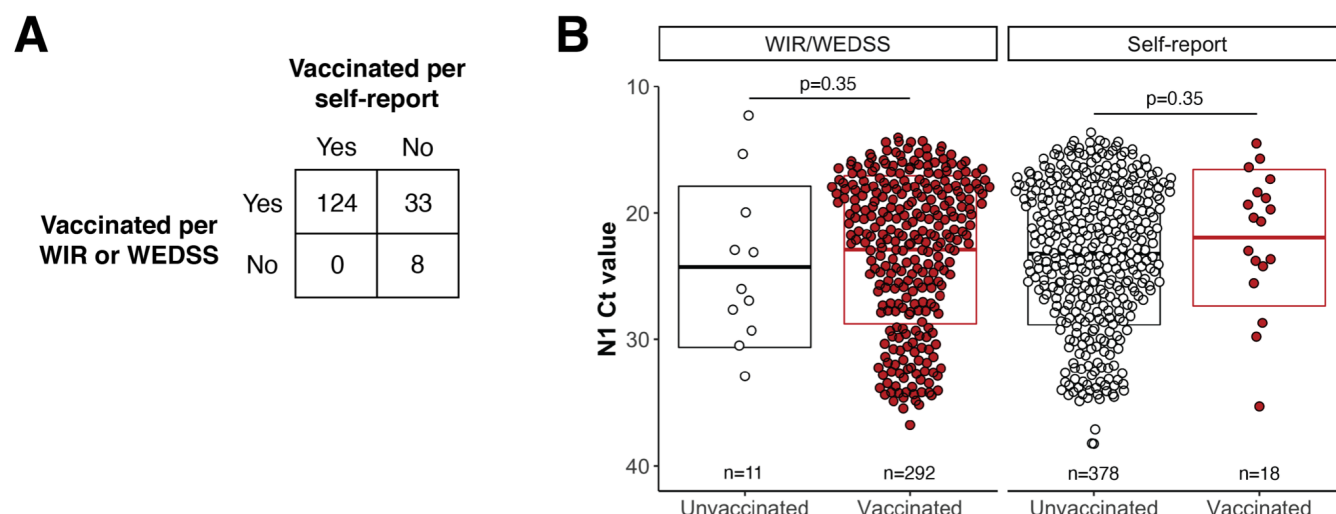


Figure 1. Individuals infected with SARS-CoV-2 despite full vaccination have low Ct values and shed infectious virus. A. Ct values for SARS-CoV-2-positive specimens grouped by vaccination status. RT-PCR was performed by Exact Sciences Corporation, responsible for over 10% of all PCR tests in Wisconsin during this period, using a qualitative diagnostic assay targeting the SARS-CoV-2 N gene (oligonucleotides identical to CDC's N1 primer and probe set) that has been authorized for emergency use by FDA (<https://www.fda.gov/media/138328/download>). **B.** Infectiousness was determined for a subset of N1 Ct-matched specimens with Ct <25 by inoculation onto Vero E6 TMPRSS2 cells and determining presence of cytopathic effects (CPE) after 5 days in culture. Specimens were selected by N1 Ct-matching between fully vaccinated and not fully vaccinated persons, then specimens from persons with unknown vaccination status were excluded from the analysis. Circles indicate presence of CPE; 'X' indicates no CPE detected. **C.** N1 Ct values for SARS-CoV-2-positive specimens grouped by vaccination status for individuals who were symptomatic or asymptomatic, or those whose symptom status was not determined, at the time of testing. In **A** and **C**,

boxplots represent mean N1 Ct values +/- one standard deviation. P-values were calculated by comparing mean Ct values by independent two-group Mann-Whitney U tests.

Supplemental materials

Supplemental figure 1



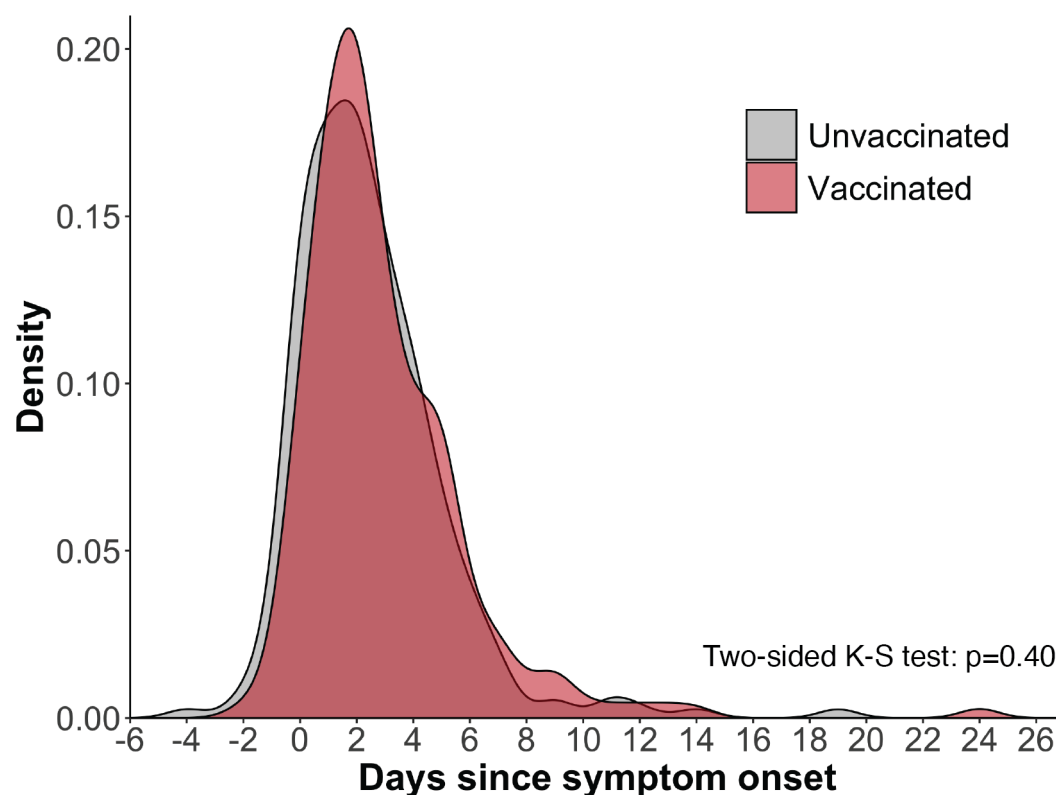
Supplemental figure 1. Concordance between self-reported vaccination status and the Wisconsin Immunization Registry (WIR) or Wisconsin Electronic Disease Surveillance System (WEDSS). For all individuals, vaccination status was determined using WIR/WEDSS electronic registries when data were available. Individuals were identified as unvaccinated at the time of testing if WIR/WEDSS data indicated receipt of a first SARS-CoV-2 vaccine dose after the test date.

Individuals were considered fully vaccinated based on WIR/WEDSS data if the registries indicated receipt of a final vaccine dose at least 14 days prior to testing. For individuals whose vaccination status could not be verified in WIR/WEDSS, self-reported data collected at the time of testing were used. Individuals were considered unvaccinated based on self-report only if there was an explicit declaration of unvaccinated status in the self-reported data. Individuals were considered fully vaccinated based on self-report if they fulfilled all of the following criteria: (1) indicated that they had received a COVID vaccine prior to testing; (2) indicated that they did not require another vaccine dose; and (3) reported a date of last vaccine dose that was at least 14 days prior to testing.

Specimens lacking data on vaccination status were excluded from the study. Specimens from partially vaccinated individuals (incomplete vaccine series, or <14 days post-final dose) were also excluded. Fully vaccinated status was determined by WIR/WEDSS for 292 specimens and by self-reported data for 18. Unvaccinated status was determined by WIR/WEDSS for 11 and by self-reported data by 378. **A.** Of the 699 specimens with vaccination status available from at least one source, 165 specimens had data available from both sources. For self-reporting, under-reporting of full vaccination status (33/157) was more common than over-reporting (0/124). **B.** N1 Ct values for SARS-CoV-2-positive specimens grouped by vaccination status for individuals whose vaccination status was determined by WIR/WEDSS or by self-reported data. Boxplots represent mean N1 Ct values +/- one standard

deviation. P-values were calculated by comparing mean Ct values by independent two-group Mann-Whitney U tests.

Supplemental figure 2



Supplemental figure 2. Density distributions of unvaccinated and vaccinated specimen collection dates by day since symptom onset. Day 0 on the x-axis denotes self-reported day of symptom onset. Negative values for days indicate specimen collection prior to symptom onset. Symptom onset data were available for n=263 unvaccinated cases and n=232 vaccinated cases.

Conflict of interest

The authors declare no conflicting interests.

Ethics statement

Per the University of Wisconsin-Madison IRB, this project qualifies as public health surveillance activities as defined in the Common Rule, 45 CFR 46.102(l)(2). As such, the project is not deemed to be research regulated under the Common Rule and therefore, does not require University of Wisconsin-Madison IRB review and oversight.

The opinions expressed by authors contributing to this journal do not necessarily reflect the opinions of the Centers for Disease Control and Prevention or the institutions with which the authors are affiliated.

Data availability

Data and processing workflows are available at <https://go.wisc.edu/p22116>. To protect potentially personally identifiable information, the publicly available dataset contains only PCR Ct values, vaccine status, symptom status, culture status, and days from symptom onset to testing for each specimen.

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