Open Forum Infectious Diseases

LETTER TO THE EDITOR

RE: Incidence of SARS-CoV-2 Breakthrough Infections After Vaccination in Adults: A Population-Based Survey Through 1 March 2023

Dear Editor,

As the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic unfolds and new variants emerge, updating estimates of breakthrough infection after primary series vaccination is essential. This letter updates the previous report on the incidence of breakthrough infections through July 1, 2022, across 5 pandemic waves in Texas.

We used the data from the Texas Coronavirus Antibody REsponse Survey (Texas CARES). Briefly, Texas CARES is an ongoing prospective population-based seroprevalence program designed to assess infection- and vaccine-induced antibody status over a long period among a volunteer population throughout Texas. The design of Texas CARES has been described previously in detail [1–3].

As of March 9, 2023, the Centers for Disease Control and Prevention (CDC) defines a breakthrough as follows: "When someone who is vaccinated with either a primary series or a primary series plus a booster dose gets infected with the virus that causes COVID-19, it is referred to as a vaccine breakthrough infection" [4]. Accordingly, we have defined a breakthrough participant as one who self-reports a coronavirus disease 2019 (COVID-19) infection diagnosis via polymerase chain reaction test after vaccination completion +14 days, up to their last survey completion date. A nonbreakthrough participant is defined as one who did not report any COVID-19 infection 14 days after vaccination completion, up to their last survey completion date. For breakthroughs, self-reported infections were confirmed with a positive nucleocapsid protein test (Roche) from serial blood draws, as described in DeSantis et al. [5]. Further, if a participant seroconverted in the time frame from N negative to N positive, they were included as a breakthrough (even if unreported). For nonbreakthrough cases, survey reports were used. Verification was not possible for every single report because a participant could have had an infection before primary series vaccination and thus would have a positive N test.

We calculated variant wave dates using the CDC's Laboratory Surveillance reports [6] per the detailed calculations described in DeSantis et al. [5]. We used the data reported for Health and Human Services Region 6 (consisting of Arkansas, Louisiana, New Mexico, Oklahoma, and Texas) to calculate the beginning of each wave in Texas. The date chosen for each variant wave was the week before that in which the proportion share for a given variant of all variants measured reached 50%. The week prior was chosen to account for the incubation period.

The breakthrough incidence per 10 000 person-days was 1.51 (95% CI, 1.17–1.85) during pre-Delta, 3.53 (95% CI, 3.17–3.90) during Delta, 15.75 (95% CI, 13.34–18.15) during Omicron, 4.13 (95% CI, 3.94–4.31) during Omicron BA.2, and 8.38 (95% CI, 7.46–9.30) during BQ and XBB. Figure 1*A* shows a clear peak in breakthroughs per 10 000 person-days in BQ and XBB in red, with the blue dotted curve showing the person-days contribution. We note that the BQ and XBB total person-time contribution and total number of breakthrough infections observed (n = 29) were small; however, their ratio still indicates that the incidence is high, as seen in Figure 1*B*.

Notably, the breakthrough frequency for Omicron BA.2 was less than that for BQ and XBB, potentially due to greater population-level immunity after the very large Omicron wave of December 2021. The Omicron BA.2 wave was dominant for ~7 months; at this point, natural immunity may have begun to decay [6], leading to a higher observed incidence of breakthrough infections in the subsequent BQ and XBB wave. Another possibility is that new infections were underreported vs during the Omicron wave, but that would not account for the increase during the BQ and XBB wave. Further evaluation will be needed as variants emerge and become dominant.

Although this survey is subject to potential selection and misclassification biases, as described in detail in DeSantis et al., a thoughtful design limited these; for example, having similar follow-up time between breakthroughs and nonbreakthroughs and similarly scheduled serial blood draws to test for the nucleocapsid protein (every 3–4 months) to confirm the existence of an infection/breakthrough, when possible. Further, early analyses of the survey showed >80% agreement between self-reported infection and a positive N test. Other studies ensuring that biases are minimized by enforcing similar follow-up times have yet to be conducted. The current study controlled for biases that arise when follow-up time for breakthroughs and nonbreakthroughs is not necessarily commensurate (eg, Malato et al.) [7].

Acknowledgments

Potential conflicts of interest. All authors: no reported conflicts.

Patient consent. This study's protocol was reviewed and approved by the University of Texas Health Science Center in Houston Institutional Review Board. A consent form and survey questionnaires are administered online over all time points, and participants proceed to a convenient lab location for the antibody test at each time point.

Stacia M. DeSantis,[1] Ashraf Yaseen,[1] Tianyao Hao,[1] Luis León-Novelo,[1] Yashar Talebi,[1] Melissa A. Valerio-Shewmaker,[2] Cesar L. Pinzon Gomez,[1]

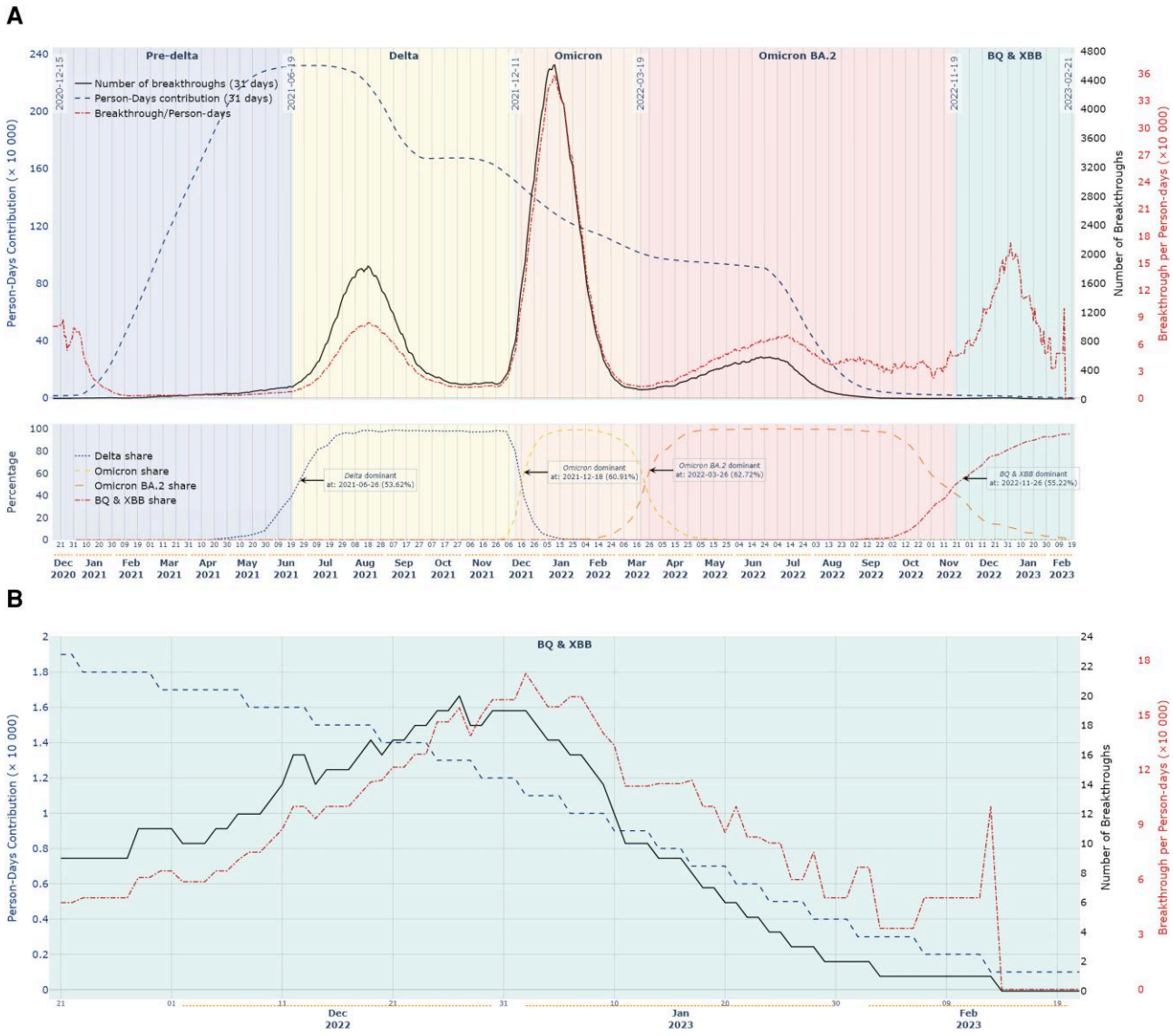

Figure 1. A, Breakthrough infections and person follow-up time by SARS-CoV-2 wave (colored areas) for each wave of infection (top). Dates of waves and variant shares (bottom). Top: Dates are on the horizontal axis. The black curve shows the number of breakthroughs (within a 31-day period centered at day 15), the dotted curve shows the person-days contribution × 10 000 d (within a 31-day period centered at day 15), and the red curve shows the number of breakthroughs per 10 000 person-days (also within a 31-day period centered at day 15). B, The same as (A) but only for the BQ and XBB timeframe, which is enlarged for readability. Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Sarah E. Messiah,[3,4] Harold W. Kohl III,[5,6] Steven H. Kelder,[5] Jessica A. Ross,[1] Lindsay N. Padilla,[1] Mark Silberman,[7] Samantha Wylie,[7] David Lakey,[8,9] Jennifer A. Shuford,[10] Stephen J. Pont,[10] Eric Boerwinkle,[1] and Michael D. Swartz[1]

[1]School of Public Health in Houston, The University of Texas Health Science Center at Houston, Houston, Texas, USA; [2]School of Public Health in Brownsville, The University of Texas Health Science Center at Houston, Brownsville, Texas, USA; [3]School of Public Health in Dallas, The University of Texas Health Science Center at Houston, Dallas, Texas, USA; [4]Center for Pediatric Population Health, UTHealth School of Public Health, Dallas, Texas, USA; [5]School of Public Health in Austin, The University of Texas Health Science Center at Houston, Austin, Texas, USA; [6]The University of Texas at Austin, Austin, Texas, USA; [7]Clinical Pathology Laboratories, Austin, Texas, USA; [8]The University of Texas System, Austin, Texas, USA; [9]The University of Texas at Tyler Health Science Center, Tyler, Texas, USA; and [10]Texas Department of State Health Services, Austin, Texas, USA

References

1. Valerio-Shewmaker MA, DeSantis S, Swartz M, et al. Strategies to estimate prevalence of SARS-CoV-2 antibodies in a Texas vulnerable population: results from phase I of the Texas Coronavirus Antibody Response Survey. Front Public Health **2021;** 9: 753487.
2. Messiah SE, DeSantis SM, Leon-Novelo LG, et al. Durability of SARS-COV-2 antibodies from natural infection in children and adolescents. Pediatrics **2022;** 149:e2021055505.
3. Swartz MD, DeSantis SM, Yaseen A, et al. Antibody duration after infection from SARS-CoV-2 in the Texas Coronavirus Antibody Response Survey. J Infect Dis **2022;** 227:193–201.
4. Centers for Disease Control and Prevention. COVID-19 after vaccination: possible breakthrough infection. Available at: https://web.archive.org/web/20230309153306/https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/why-measure-effectiveness/breakthrough-cases.html. Accessed March 9, 2023.
5. DeSantis SM, Yaseen A, Hao T, et al. Incidence and predictors of breakthrough and severe breakthrough infections of SARS-CoV-2 after primary series vaccination in adults: a population-based survey of 22,575 participants. J Infect Dis **2023;** 227:1164–72.

6. Lambrou AS, Shirk P, Steele MK, et al. Genomic surveillance for SARS-CoV-2 variants: predominance of the Delta (B.1.617.2) and Omicron (B.1.1.529) variants—United States, June 2021—January 2022. MMWR Morb Mortal Wkly Rep **2022;** 71:206–11.
7. Malato J, Ribeiro RM, Fernandes E, et al. Stability of hybrid versus vaccine immunity against BA.5 infection over 8 months. Lancet Infect Dis **2023;** 23: 148–50.

Correspondence: Stacia M. DeSantis, PhD, Department of Biostatistics and Data Science, School of Public Health, The University of Texas Health Science Center at Houston, 1200 Pressler Street, Houston, TX 77030 (Stacia.M.Desantis@uth.tmc.edu).

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