OCCUPATION AND INCIDENT BREAKTHROUGH INFECTIONS WITH SARS-COV-2 IN A COHORT OF FRONTLINE WORKERS DURING DELTA AND OMICRON PREDOMINANCE

by

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Final approval and acceptance of this thesis is contingent upon the candidate's submission of the final copies of the thesis to the Graduate College.

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LAND ACKNOWLEDGEMENT

We respectfully acknowledge the University of Arizona is on the land and territories of Indigenous peoples. Today, Arizona is home to 22 federally recognized tribes, with Tucson being home to the O'odham and the Yaqui. Committed to diversity and inclusion, the University strives to build sustainable relationships with sovereign Native Nations and Indigenous communities through education offerings, partnerships, and community service.

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LIST OF ACRONYMS

AZ HEROES	: Arizona Healthcare Emergency Response and Other Essential workers Surveillance study
CDC	: Centers for Disease Control and Prevention
COVID-19	: Coronavirus Disease 19
EMS	: Emergency Medical Services
OEW	: Other Essential Worker
FR	: First Responder
HCP	: Healthcare Personnel
HR	: Hazard Ratio
IQR	: Interquartile Range
PPE	: Personal Protective Equipment
RECOVER	: Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel
SD	: Standard Deviation
VE	: Vaccine Effectiveness
95% CI	: 95% Confidence Interval

ABSTRACT

Background

The SARS-CoV-2 virus has caused a pandemic with an unprecedented number of infections and deaths. Research conducted prior to vaccine availability has identified first responders at increased risk of experiencing infections, but occupational risk profiles accounting for vaccination status may have shifted. We examined data from the longitudinal cohort study The Arizona Healthcare Emergency Response and Other Essential workers Surveillance study (AZ HEROES) to determine if healthcare personnel, first responders, or other essential workers were at increased risk of experiencing a breakthrough COVID-19 infection between the periods of Delta and Omicron predominance.

Methods

Breakthrough infections within the AZ HEROES study were confirmed through laboratory specimens among participants. Within the Delta (06/14/2021-12/13/2021) and Omicron (12/14/2021-02/16/2022) periods, 697 were at risk for breakthrough infection during Delta and 1,260 were at risk during Omicron. Breakthrough infections were defined as infections occurring at least 14 days from the primary series of the vaccine, and assessed for each period, examining crude incidence among granular occupational categories and the association between breakthrough infection and occupation using cox proportional hazards models among healthcare personnel, first responders, and other essential workers. The models were adjusted for baseline demographics, underlying health status, days since vaccination, and mitigation behaviors.

Results

Fewer breakthrough infections were reported in the Delta period (n=46) compared to the Omicron period (n=241), despite fewer person-days at risk observed during Omicron (Median (IQR): 64 (0) vs 183 (0)) compared to Delta. Compared to healthcare personnel and other essential workers, first responders were more likely to experience a breakthrough infection. In the Delta period, first responders were 186% more likely to experience breakthrough infections (compared to the healthcare personnel: (HR: 2.86 (95% CI 1.21, 6.77) p=0.02) compared to other essential workers: (HR: 1.99 (95% CI: 0.92, 4.29) p=0.08)). In the Omicron period, first responders were 54% more likely to experience breakthrough infections (compared to healthcare personnel: (HR: 1.54 (95% CI 1.07, 2.21) p=0.02) compared to other essential workers: (HR: 1.92 (95% CI: 1.34, 2.75) p=0.0003)). Testing for interaction between occupation and predominant variant confirmed that the association between risk and breakthrough infection and occupation did not differ by variant (p=0.41).

Conclusion

The finding that first responders are at increased risk for breakthrough infection align with previous findings of elevated risk during the pre-vaccine era. This approach provides a unique perspective to better understand the role that occupation has as an exposure factor for COVID-19 infection. Future research should strive to examine the factors that put first responders at increased risk to develop targeted interventions.

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, is a respiratory disease noted for its impressive transmissibility that perpetuated a global pandemic.[1,2] As of March 31, 2022, the COVID-19 pandemic has been responsible for over 79 million infections in the United States since its discovery in 2019, resulting in over 978,000 deaths.[1,2] In Arizona 61.3% of the total population has received the primary series of the vaccine, defined as two doses of the mRNA vaccine or a single dose of the viral vector vaccine.[2–5] Despite over half of the population having the primary series of the vaccine, over 2,007,000 infections had been reported, with more than 29,000 deaths, with a strikingly high death rate of 407.1 deaths per 100,000 population.[1,2] Vaccination against COVID-19 protects against severe illness or death, but prevention of transmission of the SARS-CoV-2 virus proves to be more complex, with factors such as mutations in the virus, timing of vaccination, and individual level practices influencing rate of infections.[6,7] Infections that occur at least 14 days after the receipt of the primary series of the COVID-19 vaccine are termed breakthrough infections, which comprise an increasing proportion of all infections.[4] Data in Arizona from September 2021 reported breakthrough infections accounted for 21.1% of all infections.[2,8] By February 2022, 47.6% of all cases were attributed to breakthrough infections.[2,8]

State-level data is reported by the Arizona Department of Health Services, and despite detailed information on case counts, death, and demographic factors such as sex and age, there is no information reported on occupational category.[1,2] The labor force participation rate in Arizona ranges from 74.5-85.4% of the population aged 25-54 working at least part time.[9] Over half of the working population is employed in education and health services, government, trade, transportation and utilities, and professional and business services sectors.[9] Occupation is one of

the most powerful determinants of health, directly impacting income, wealth, education, and access to healthcare services as it is closely tied with socioeconomic status.[10,11] Type of occupation has been identified as a risk factor for outcomes such as premature mortality, stress, depression, risky lifestyle behaviors, and reduced access to screening programs that can prevent disease.[10,11] Varying mortality rates by occupation have been previously observed for respiratory diseases such as influenza, and chronic conditions such as cancer, which demonstrate that differences between occupations are apparent when it comes to reported health outcomes.[12–14] Understanding how COVID-19 infections occur by occupation is beneficial to understand occupation as a risk factor for negative health outcomes.

Essential workers – occupations that are necessary to be conducted in person despite stay at home recommendations across the United States – are at increased risk of infections from COVID-19.[15–17] These occupations can range from utility services to nurses, but are broadly grouped into healthcare personnel, first responders, and other essential workers.[16] Healthcare personnel provide medical care to patients and typically spend hours in close contact with others due to the nature of their occupation.[18,19] Vaccinations are often required by employers, and they tend to be compliant with general COVID-19 mitigation practices.[6,18–20] First responders encompass occupations that respond to emergency situations, such as fires, criminal activity, and medical emergencies.[9,15,20] Other essential workers encompass all other necessary in-person occupations.[15,17] These occupations are categorized differently by state, but in general they also work in close contact with others.[15] In Arizona, examples of these occupations include education, retail, financial institutions, media, and postal services.[15] Essential workers are distinct from other occupations as they are at increased risk of infection.[15] This can not only negatively impact their health, but the health of their family and communities that they serve.[15–17] Being in close

contact with others can have far-reaching consequences when infected, enabling the rapid spread of disease.[21,22]

An individual's occupation can directly impact their ability to undertake recommended mitigation practices, such as the ability to socially distance, wear personal protective equipment (PPE), access the healthcare system, and the ability to be informed with the most recent developments or safety measures.[14,21,22] Consequently, factors such as COVID-19 education, health literacy, vaccination status, PPE training and availability, and workplace environment have a high correlation with the likelihood of developing an infection with COVID-19.[6,14,20,23] PPE, in particular, plays a vital role in reducing the risk of disease transmission.[18] Throughout the course of the pandemic, the availability of PPE has varied significantly.[24–27] At the start of 2020, PPE was very limited and prioritized for healthcare personnel, which resulted in higher occupational risk for groups that did not have access to PPE.[24–27] Over time, appropriate PPE has become more readily available for all occupational groups.[24,26] Healthcare personnel, specifically individuals working in the inpatient setting, now report relatively low rates of COVID-19 infection compared to the general population, despite close contact with confirmed positive cases.[18,28,29] Numerous studies have shown that the proper use of PPE can prevent infection and is correlated with an understanding of and desire to adhere to mitigation protocols.[18,19,28–30]

Various longitudinal cohort studies have been initiated to understand the epidemiologic and immunologic aspects of infection and reinfection in frontline workers.[31] The Arizona Healthcare Emergency Response and Other Essential workers Surveillance study (AZ HEROES) is an example of a state-level study that began enrolling in July 2020.[31] Identifying the extent of COVID-19 transmission can prove difficult in studies that use passive testing data due to the proportion of SARS-CoV-2 infections that are mildly asymptomatic and not identified through

testing.[18] Active surveillance for both symptomatic and asymptomatic infections can allow for a more complete understanding of transmission characteristics and the characteristics that play a role in transmission among relatively healthy occupational cohorts, as done in AZ HEROES.[18] Before the availability of the COVID-19 vaccine, first responders in the AZ HEROES cohort were most at risk for incident COVID-19 infections.[32] An analysis of beliefs and practices regarding COVID-19 infection in this cohort found that endorsement of the COVID-19 vaccine strongly predicts vaccine uptake.[20] In this study, first responders were 42% less likely to believe in vaccine effectiveness compared to other occupational categories.[20] In parallel with these findings, research conducted in South Africa found that members of the police force reported a general knowledge of how to prevent the spread of COVID-19, but did not practice preventative measures due to not being required and a general indifference towards infection, thus aiding in the spread of the virus.[7] Trust in the federal government regarding COVID-19 is correlated with the belief in the effectiveness of the COVID-19 vaccine and the likelihood of undertaking vaccination and other preventative measures.[20] Collectively, the body of literature to date on occupation and COVID-19 has focused on risk factors for SARS-CoV-2 infection and vaccine effectiveness among essential workers.[20,23,31,33]

While risk factors for COVID-19 severe illness have been well established, risk factors for SARS-CoV-2 infection have become more complex in the context of vaccination, newly circulating variants, and shifts in mitigation adherence.[34–36] The SARS-CoV-2 virus continues to evolve at a rapid pace, which may result in the shifting of occupational risk profiles.[7,20,37] The Delta variant (lineage B.1.617.2) starting in summer 2021, and the Omicron variant (lineage B.1.1.529) starting in December 2021, have also demonstrated differences in transmissibility, vaccine escape and potential for reinfection.[33,37–39] In comparison to the Delta variant, the

Omicron variant has numerous mutations in the spike protein, a glycoprotein on the surface of the SARS-CoV-2 virus, which contributes to immune escape.[4,35] Vaccine effectiveness for the periods of Delta and Omicron predominance have been examined to better understand these differences.[4,5,40] Reported vaccine effectiveness during the period of Delta predominance was 65% after obtaining the primary series, and increased to 91% after receiving an additional dose of the vaccine, termed "booster".[34,35,40] During the period of Omicron predominance, obtaining the primary had a vaccine effectiveness of 46% and obtaining an additional dose increased vaccine effectiveness to only 60%.[4,34,35] Vaccine effectiveness varies substantially and is found to decrease with time, leading to "breakthrough" infections – infections that occur despite having the recommended doses of the vaccine.[3–5,40] Therefore, it is imperative to understand the differences in occupational risk of SARS-CoV-2 breakthrough infections between the time periods for each predominant variant among SARS-CoV-2 vaccinees.

There are many factors that influence the likelihood of becoming infected with SARS-CoV-2 and developing COVID-19.[3,4,36,41] Comparison of risk across occupational categories while monitoring for asymptomatic infections is vital to further understand the role that occupation plays in the risk of infection and subsequent risk of transmission to broader communities, something that is accomplished within AZ HEROES.[18,19,32] In addition, many studies have focused on pre-vaccine risk factors and vaccine effectiveness, with limited focus on the role that occupation plays in breakthrough infections during eras of differing variant predominance.[19,32,37,38] This analysis is intended to build on previous research and further examine how occupation functions as an exposure factor among vaccinees throughout periods of Delta and Omicron predominance.

The aims of this thesis are to:

1) Determine differences in the incidence of SARS-CoV-2 breakthrough infections by occupational category in Arizona frontline workers during Delta and Omicron predominant periods.
2) Examine occupation as a risk factor for breakthrough infection after adjusting for demographic, underlying health, and exposure factors.

2. METHODS

2.1 Study Design

The Arizona Healthcare Emergency Response and Other Essential workers Study (AZ HEROES) is a prospective cohort study throughout the state of Arizona which – at the start of recruitment in July 2020 -- enrolled essential workers to identify incident SARS-CoV-2 infections.[31] Recruitment is ongoing, with 4,140 individuals ever enrolled and 2,524 currently enrolled in the study as of March 31, 2022.[31] The study is funded by the Centers for Disease Control and Prevention (CDC), with a standardized protocol with 7 national sites in the larger Research on Epidemiology of SARS-CoV-2 in Essential Response Personnel (RECOVER) study.[42] AZ HEROES was reviewed and approved by the Arizona Institutional Review Boards (IRB) and all participants complete informed consent electronically.[31]

SARS-CoV-2 infections among participants were confirmed through home tests that are then sent through an expedited courier service for PCR laboratory testing conducted at Marshfield Laboratories, which serves as a research laboratory for CDC projects in Marshfield, Wisconsin.[31] Participants provide weekly self-collected mid turbinate samples, in addition to

blood samples upon enrollment, every three months, after a confirmed infection, and after vaccination.[31] The mid-turbinate swabs are collected weekly regardless of symptoms, with an additional sample submitted at the beginning of symptom onset.[31] Participants provide baseline demographic information upon enrollment, and complete weekly information on symptoms and overall health, with 4 different sets of weekly rotating questions (one set per month) focusing on exposure information, along with quarterly surveys collecting information about their health, occupational and personal exposures, and attitudes and beliefs surrounding COVID-19.[31]

2.2 Study Participants

Sampling targets for the AZ HEROES study were set at 40% healthcare personnel, 30% first responders, and 30% other essential workers.[31] Sampling targets were also used to oversample traditionally represented racial and ethnic groups, and were set at 50% Hispanic or American Indian.[31] Recruitment was accomplished through a multipronged strategy, through outreach from Arizona-based COVID-19 testing activities, partnering with community-based COVID-19 cohorts to recruit participants, and a marketing strategy to raise awareness and provide information on receipt of self-referrals.[31] Eligibility screening was accomplished through phone calls or email. Designated AZ HEROES staff members communicated regularly with participants to improve participant adherence to weekly specimen collection and assessment of symptoms, and to answer questions that participants may have through phone calls or email. Regular newsletters were sent to study participants to share findings and provide information regarding study updates. In addition, participants were offered monetary incentives through prize drawings for individuals who consistently completed study activities.[31]

2.3 Eligibility Criteria

Eligible participants included Arizona residents aged 18 to 85 years who worked at least 20 hours a week in a position that involves regular direct contact (three feet or less) with others. Participants also spoke and were able to write in English or Spanish, had a mailing address, and had access to a computer or smartphone with internet access. The participant occupations fell into three broad categories: healthcare personnel (HCP), first responders, and other essential workers (OEW). The HCP category included clinical providers and support staff in inpatient, outpatient, and institutional (i.e., long-term care or residential healthcare) settings. The first responder category included those working in fire service, non-fire emergency medical services, law enforcement (including border patrol), and corrections. The OEW category included education, agriculture and food processing, transportation services, waste collection, utilities, government and community-based services, childcare, and hospitality.[31]

Variant predominance in Arizona was determined through genomic surveillance conducted by The Translational Genomics Research Institute (Tgen).[43] When a given variant comprised 50% or greater of all specimens analyzed, it was considered the predominant variant.[43] Using T-gen reported percentages by variant, the Delta variant (B.1.617.2) became predominant in Arizona on June 21, 2021, and the Omicron variant (B.1.1.529) became predominant on December 21, 2021.[43] The dates used in the inclusion criteria were assessed one week prior to reported predominance to account for the seven-day delay in time to sequencing.[43] Participants were included for analyses if they were actively enrolled in the study and were compliant with study activities – meaning they had not missed more than 3 weeks between sample collections during the study period. The rationale for restricting to only those who were compliant with weekly samples was to reduce the number of potentially missed infections. The

sample was restricted to those at risk for breakthrough infections, so participants were also included if they received the primary series of the vaccine at least 14 days prior to the start of the respective periods. Additionally, those with previous infection at the beginning of each period were excluded. Individuals that had received the single dose of the Janssen vaccine were included in the analyses. The follow-up period for study participants used in the analysis is from June 13, 2022, to February 16, 2022.

2.4 Measures

2.4.1 Primary Outcome

Incident breakthrough infections – when an individual first tests positive for SARS-CoV-2 infection at least two weeks after receiving the primary series of the COVID-19 vaccine – were identified within Delta and Omicron predominant periods in Arizona.[3,4] The primary outcome of interest was laboratory confirmed breakthrough COVID-19 infections.

Time at risk for COVID-19 infection was assessed separately for each period of variant predominance. The person-time at risk for breakthrough infection began at the reported date of Delta predominance and continued until the date of the next predominant variant for participants with no breakthrough infection. For the Omicron period, person-time at risk for breakthrough infection continued until the dataset was withdrawn for analysis. Thus, the period for the Delta variant was June 14, 2021, to December 13, 2021, and the period for the Omicron variant was December 14, 2021, to February 16, 2022. For those with breakthrough SARS-CoV-2 infection, the time to event was calculated as the number of days from the start of the predominant period to infection or censoring (withdrawal or the end of the period).

2.4.2 Primary Exposure Variable of Interest

Exposure was defined as the occupational category determined at study enrollment. The broad categories were broken down into the list of occupations that were provided at the baseline enrollment survey. Occupational categories were defined as follows: HCP were categorized into inpatient, ambulatory, and institutional categories, 2) first responders were categorized into fire services, emergency medical services, corrections, and law enforcement, and 3) OEW were categorized into education/government/hospitality, and essential operations/infrastructure. The granular categories were used for crude incidence of breakthrough infections, and the broad categories were used for the adjusted analyses.

2.4.3 Covariates

Additional variables of interest included gender identity, race/ethnicity, age, level of education, number of comorbidities, and hours worked weekly, measured at enrollment. Weekly responses to rotating questions regarding mitigation practices included number of hours spent in close contact (three feet or less) with others at work, percent of time PPE used at work according to employer specifications, number of hours in close contact within the community, and percent of time masks were used outside of work. These variables were assessed monthly because they rotated once every four weeks on the weekly symptom assessment text-based questionnaire. The rotating questions resulted in sparse data, and to account for sparseness the averages for the four questions were taken for each period. To examine a meaningful difference in these four weekly surveillance variables, the upper 25^{th} percentile was compared to the lower 75^{th} percentile for the adjusted analysis. Participant vaccination status was uploaded at the time of vaccination and verified through quarterly surveys and participant follow-up. For this analysis, vaccination status

determined at the start of each Delta and Omicron study periods. The number of days since the receipt of the primary series was also assessed, in addition to the receipt of the booster dose of the vaccine in the Omicron period.

2.5 Statistical Methods

Summary statistics were generated for the two distinct study populations: participants at risk for incident SARS-CoV-2 breakthrough infections within the period of Delta predominance (06/14/2021-12/13/2021) and those at risk during the period of Omicron predominance (12/14/2021-02/16/2022). Participant characteristics included: demographic information, average percentage of submitted weekly samples, average days at risk for breakthrough infection, total number of breakthrough infections, average days at risk, days since receipt of final vaccine the primary series of the COVID-19 vaccine, vaccination status at the beginning of the period, receipt of booster vaccine (during omicron period only), average hours in close contact with others at work and in the community, and the average percent of time wearing PPE required by employer at work or a mask in the community.

2.5.1 Primary Analysis

Crude incidence was assessed for the granular occupational categories, comparing the number of events over the total person-days-at-risk for breakthrough infection, reported per 1,000 person-days-at-risk.

The association of time to incident COVID-19 breakthrough infection and occupation was tested using Cox Proportional Hazards regression models to estimate the hazard ratio and 95% confidence intervals. Hazard ratios were assessed, comparing the incident infection for the

broad occupational categories to HCP as the reference category.[28,29] The effect of experiencing a breakthrough infection by occupation dependent on predominant variant was examined by modelling an interaction term.

Hazard ratios were adjusted for risk factors for COVID-19 fixed at baseline, including gender, age in ten-year increments, reported comorbid conditions, days since receipt of the primary series of the vaccine, and booster status at the start of the Omicron predominant period only. Hazard ratios were then adjusted for covariates that mitigate risk of infection only, including hours each week in close contact with others at work, percent of time spent wearing PPE recommended by employer, hours each week in close contact with members of the community, and the percent of time wearing masks in public while not at work. Hazard ratios were then fully adjusted for baseline risk factors and mitigation practices. The models were pre-specified, and the choice of covariates was based on background knowledge. The proportional hazards assumption was visually assessed from the survival curves.

2.5.2 Sensitivity Analysis

To assess the robustness of the results, study participants that were previously excluded due to non-compliance with study activities – meaning they had missed 3 or more weeks between sample collections during the study period - were reincorporated into the fully adjusted models for both the Delta and Omicron predominant periods.

All statistical analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC), Microsoft Excel v.2203 (Microsoft Corporation, Redmond, WA) and RStudio v.2021.9.0.351 (RStudio, PBC, Boston, MA).

3. RESULTS

3.1 Participant Characteristics

Among the 2,970 participants in the Delta period, a total of 165 individuals experienced prior infections, and 827 had a least 3 missed weekly samples. Excluding those without the primary series resulted in 697 at risk for breakthrough infections in the Delta period (Figure 1). Among the 1,838 participants in the Omicron period, 94 experienced prior infections, and 93 had a least 3 missed weekly samples. 391 participants did not receive the primary series, leaving 1,260 participants at risk for breakthrough infections during the Omicron period.

During the Delta period, a total of 115,298 person-days were contributed over the 183-day study period (Table 1). During the Omicron period, a total 72,498 person-days were over the 64-day study period. Due to person-days at risk not being normally distributed, and median and interquartile range (IQR) were assessed for person-days at risk for breakthrough infection. Despite the difference in person-days at risk between the predominant variants, a total of 46 breakthrough infections were examined in the Delta period, contrasted by 241 infections in the Omicron period.

Participants in both the Delta and Omicron periods were predominantly female (63.1%, 65.8%), white (71.4%, 72.9%) had a college education or above (96.9%, 97.8%), had a mean age of 46.8 (SD 11.2) and 47.7 (SD 13.9), did not have any reported comorbidities (64.1%, 63.7%), and reported working at least full time at baseline (Mean (SD): 42.3 (13.9), 42.3 (13.9)), respectively. After removing individuals who were not compliant with weekly sample collection, average weekly compliance was very similar for both periods (Mean (SD): 74.5 (29.9), 75.1 (14.0)).

Figure 1: Participant Flow Diagram

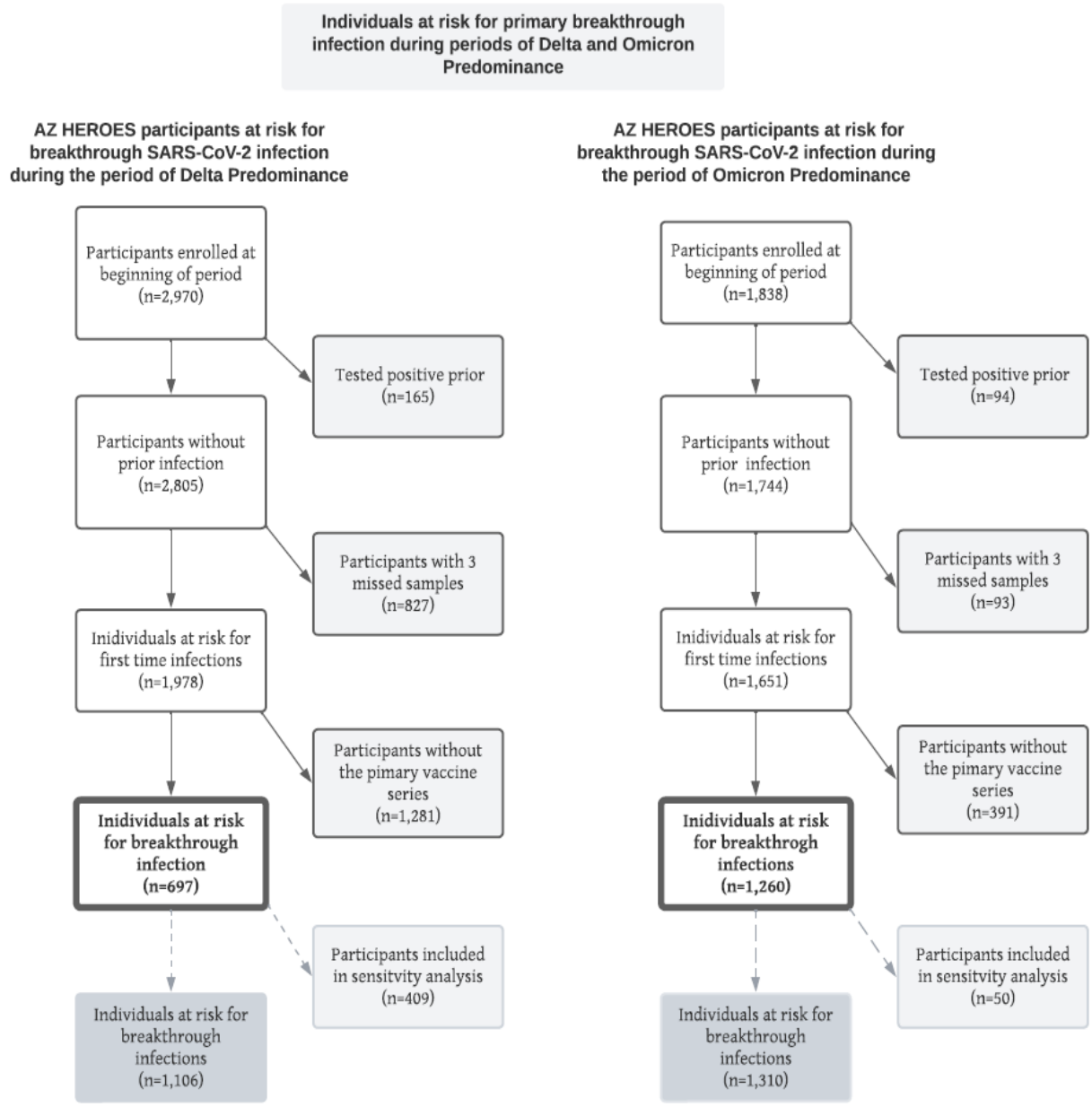


Table 1. Participant characteristics of individuals at risk for first-time breakthrough infections during Delta Predominance (06/14/2021-12/13/2021, n=697) and Omicron Predominance (12/14/2021-02/16/2022, n=1260)

Participant Characteristics[a]	**Delta Predominance n (%) or mean (sd)**	**Omicron Predominance n (%) or mean (sd)**
Person-days at risk for COVID-19[b]	183 (0)	64 (0)
Breakthrough Infections	46 (6.6)	241 (19.1)
Participant compliance[c,d]	74.5 (29.9)	75.1 (14.0)
Gender		
Male	225 (36.6)	426 (33.8)
Female	440 (63.1)	829 (65.8)
Transgender	1 (0.1)	1 (0.1)
Refused	1 (0.1)	4 (0.3)
Age[c]	46.8 (11.2)	47.7 (13.9)
Education		
Highschool or less	21 (3.1)	28 (2.3)
College or above	658 (96.9)	1216 (97.8)
Race		
Non-Hispanic White	494 (71.4)	913 (72.9)
Black	23 (3.3)	49 (3.9)
Hispanic	142 (20.5)	241 (19.3)
Asian	19 (2.8)	29 (2.3)
Refused	14 (2.0)	20 (1.6)
Vaccination Status[e]		
Primary Series	697 (100.0)	586 (46.5)
Primary Series + Booster	0 (0.0)	674 (53.5)
Days since second dose[c,f]	112.9 (34.6)	283.9 (58.2)
Number of Comorbid conditions		
0	428 (64.1)	778 (63.7)
1+	240 (35.9)	443 (36.3)
Hours worked each week[c]	42.3 (13.9)	42.3 (13.9)
Occupation		
Healthcare Personnel	253 (36.3)	447 (35.5)
Inpatient Healthcare Personnel	123 (17.7)	257 (20.5)
Ambulatory Healthcare Personnel	103 (14.8)	225 (17.9)
Institutional Healthcare Personnel	39 (5.6)	63 (5.0)
First Responder	131 (18.8)	144 (11.4)
Non-Fire Emergency Medical Service	15 (2.2)	22 (1.8)
Fire Services	72 (10.4)	89 (7.1)
Law Enforcement	48 (6.9)	71 (5.7)
Corrections	12 (1.7)	15 (1.2)
Other Essential Worker	267 (38.3)	428 (34.0)
Hospitality/Retail/Food Service	24 (3.5)	42 (3.4)
Educator/Government/Grocery	190 (27.4)	353 (28.1)
Essential Operations	24 (3.5)	43 (3.4)
Essential Infrastructure	44 (6.3)	75 (6.0)
Work and Community Exposure		
Hours of close contact with others at work[c,g]	28.9 (18.0)	27.8 (18.9)
Percent of time wearing appropriate PPE at work[c,g,h]	57.9 (37.4)	71.5 (37.6)
Hours of close contact with others in the community[c,g]	28.4 (19.5)	26.6 (20.2)
Percent of time wearing masks in the community[c,g]	52.1 (31.7)	69.0 (30.6)

a: Frequencies are reported as n, (%)
b: Median (Interquartile Range)

c: mean (SD)
d: Average percentage of weekly samples submitted during the respective period of variant predominance
e: Status at the start of the period predominance
f: Vaccinations for COVID-19 include mRNA vaccines manufactured by Pfizer and Moderna, and viral vector vaccine manufactured by Janssen.
g: Average reported from weekly rotating surveys during the respective period of variant predominance
h: Minimum PPE recommended by employer

Due to the timing of the availability of the COVID-19 booster dose, the participants in the Delta period had only received the primary series. 46.5% of the participants in the Omicron period had the primary series only, and 53.5% had received the booster dose. The largest occupational category for the Delta period was other essential worker (38.3%) and HCP in the Omicron period (35.5%). Within the weekly rotating surveys, the average hours spent in close contact with others at work in the community were relatively similar (mean (SD): 28.9 (18.0) vs 28.4 (19.5) for Delta period; 27.8 (18.9) vs 26.6 (20.2) for Omicron period) and the percent of time wearing recommended PPE was higher at work compared to close contact within the community (mean (SD): 57.9 (37.4) vs 52.1 (31.7) for Delta period; 71.5 (37.6) vs 69.0 (30.6) for Omicron period). The percent of time wearing appropriate PPE was higher in the Omicron period for both hours in close contact at work and in the community compared to the Delta period.

3.2 Crude Incidence

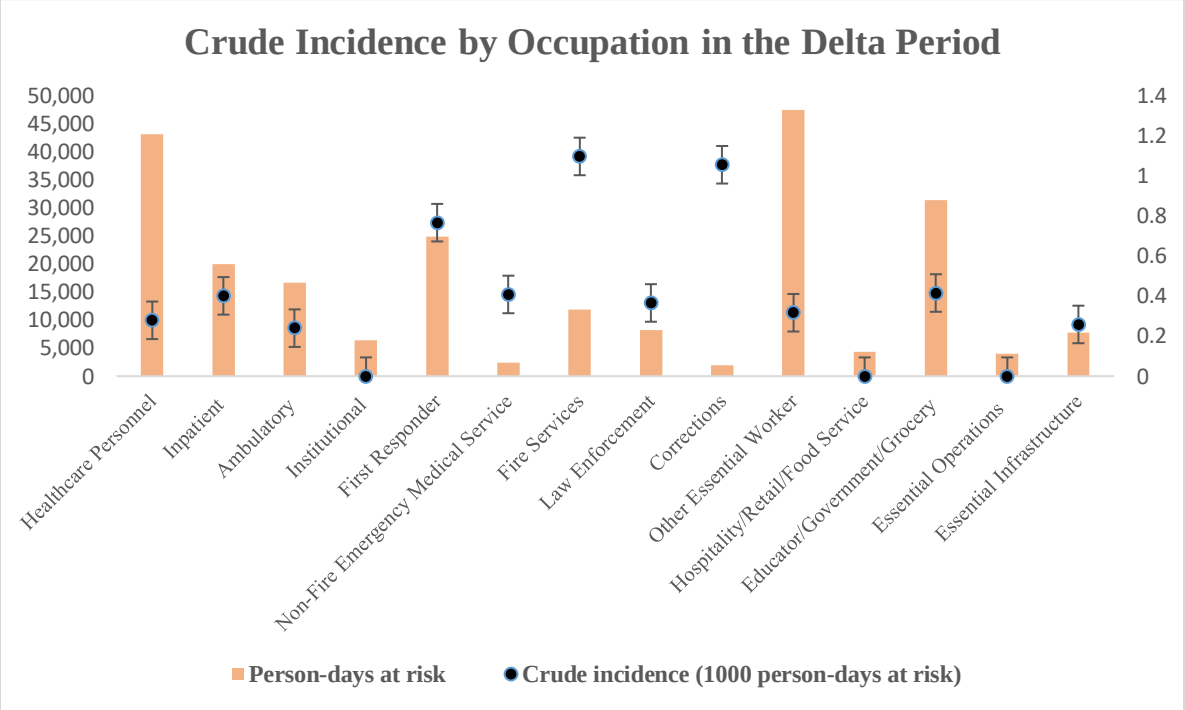
Crude incidence (Table 2) of breakthrough infection was consistently highest in the broad first responder category for both the Delta and Omicron periods (0.77 & 5.28 per 1,000 person-days at risk). Within the granular categories, fire services in the Delta period experienced the highest crude incidence (1.10 per 1,000 person-days at risk). Within the Omicron period, corrections experienced the highest crude incidence for breakthrough infections (13.10 per 1,000 person-days at risk).

Table 2. Crude incidence by broad occupation categories per 1,000 person-days at risk for breakthrough infection

	Delta Period (n=697)				Omicron Period (n=1,260)			
Occupational Category	**n**	**Infections**	**Person-days at risk**	**Crude incidence (1000 person-days at risk)**	**n**	**Infections**	**Person-days at risk**	**Crude incidence (1000 person-days at risk)**
Healthcare Personnel	**253**	**12**	**43,073**	**0.28**	**447**	**98**	**31,541**	**3.11**
Inpatient	123	8	19,970	0.40	257	50	14,808	3.38
Ambulatory	103	4	16,695	0.24	225	42	12,935	3.25
Institutional	39	0	6,408	0.00	63	6	3,798	1.58
First Responder	**131**	**19**	**24,817**	**0.77**	**144**	**58**	**10,987**	**5.28**
Non-Fire Emergency Medical Service	15	1	2,453	0.41	22	4	1,270	3.15
Fire Services	72	13	11,863	1.10	89	22	4,976	4.42
Law Enforcement	48	3	8,215	0.37	71	21	3,812	5.51
Corrections	12	2	1,897	1.01	15	9	687	13.10
Other Essential Worker	**267**	**15**	**47,408**	**0.32**	**428**	**85**	**29,970**	**2.84**
Hospitality/Retail/ Food Service	24	0	4,347	0.00	42	4	2,560	1.56
Educator/Government/Grocery	190	13	31,338	0.41	353	64	20,380	3.14
Essential Operations	24	0	3,971	0.00	43	3	2,643	1.14
Essential Infrastructure	44	2	7,752	0.26	75	14	4,387	3.20

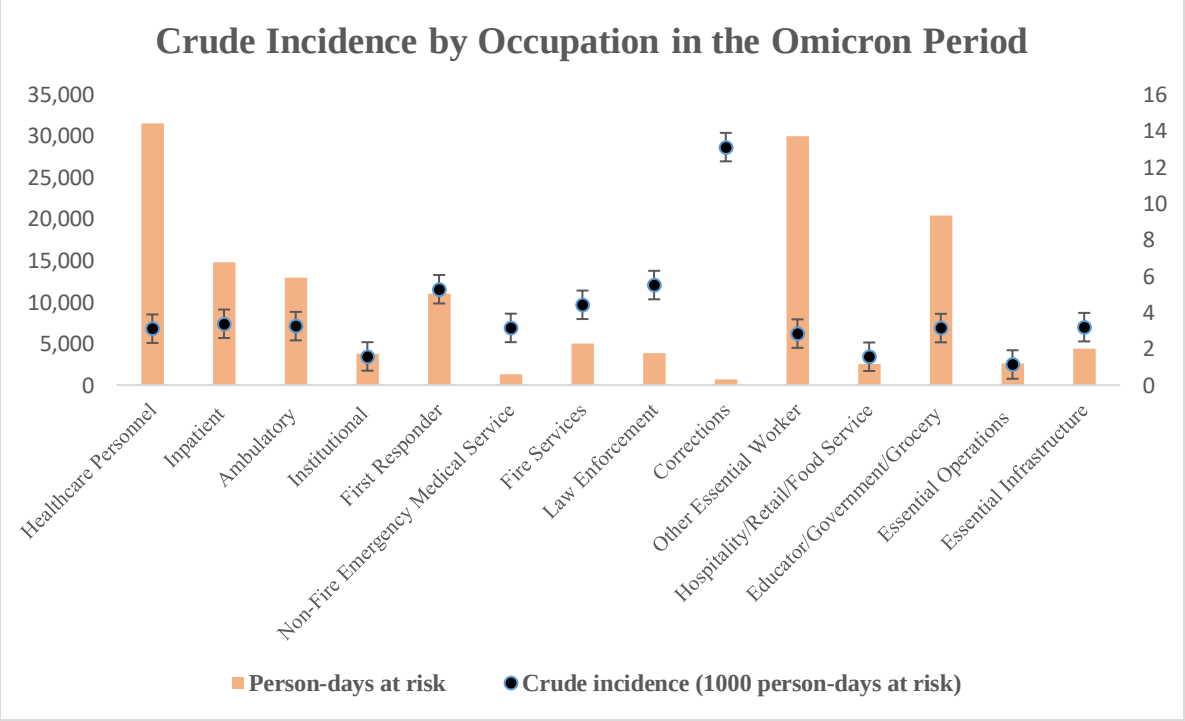
Figure 2. Person-days at risk (Orange bars) and crude incidence with standard error[a] (black circles) by occupational category within the Delta (a) and Omicron (b) Predominant Periods

a) Delta Predominant Period



a: Standard error: SD/$\sqrt{n}$

b) Omicron Predominant Period



a: Standard error: SD/$\sqrt{n}$

3.3 Delta Predominant Period

Among 697 participants at risk for breakthrough infections in the Delta predominant period, breakthrough infections were higher in the first responder category compared to HCP and OEW (Tables 3 & 4). Prior to adjustment, first responders were 177% more likely to experience breakthrough infections compared to HCP (HR: 2.77 (95% CI: 1.34, 5.70) p=0.01) and OEW (HR: 2.77 (95% CI: 1.34, 5.70) p=0.01). After adjusting for participant characteristics, the likelihood of breakthrough infection increased in the first responder category to 192% compared to HCP (HR: 2.92 (95% CI: 1.27, 6.73) p=0.01) and 104% compared to OEW (HR: 2.02 (95% CI: 0.94, 4.42) p=0.07). Decreased likelihood of experiencing a breakthrough infection was observed if one or more comorbid conditions were reported (HR: 0.86 (95% CI: 0.45, 1.65) p=0.65). After adjustment for mitigation practices only, first responders were 176% more likely to experience a breakthrough infection compared to HCP (HR: 2.76 (95% CI: 1.30, 5.87) p=0.01), and 130% more likely compared to OEW (HR: 2.30 (95% CI: 1.17, 5.56) p=0.02). Adjusting for all mitigation practices resulted in increased likelihood of experiencing a breakthrough infection in the upper 25^{th} percentile of hours in close contact with others at work (HR: 2.11 (95% CI: 1.04, 4.26) p=0.04).

After adjusting for both participant characteristics and mitigation practices, first responders were 186% more likely to experience breakthrough infections compared to the HCP (HR: 2.86 (95% CI 1.21, 6.77) p=0.02) and 99% more likely compared to OEW (HR: 1.99 (95% CI: 0.92, 4.29) p=0.08). The results were further supported by the sensitivity analysis that included individuals who had been excluded due to lack of compliance comparing first responders to HCP (HR:2.51 (95% CI 1.22, 5.17) p=0.01) and OEW (HR: 1.50 (95% CI: 0.78, 2.88) p=0.29). OEW were more likely to experience breakthrough infections compared to HCP

(HR: 1.44 (95% CI: 0.62, 3.44) p=0.41). Across the various models, the overall effect of occupation remained statistically significant.

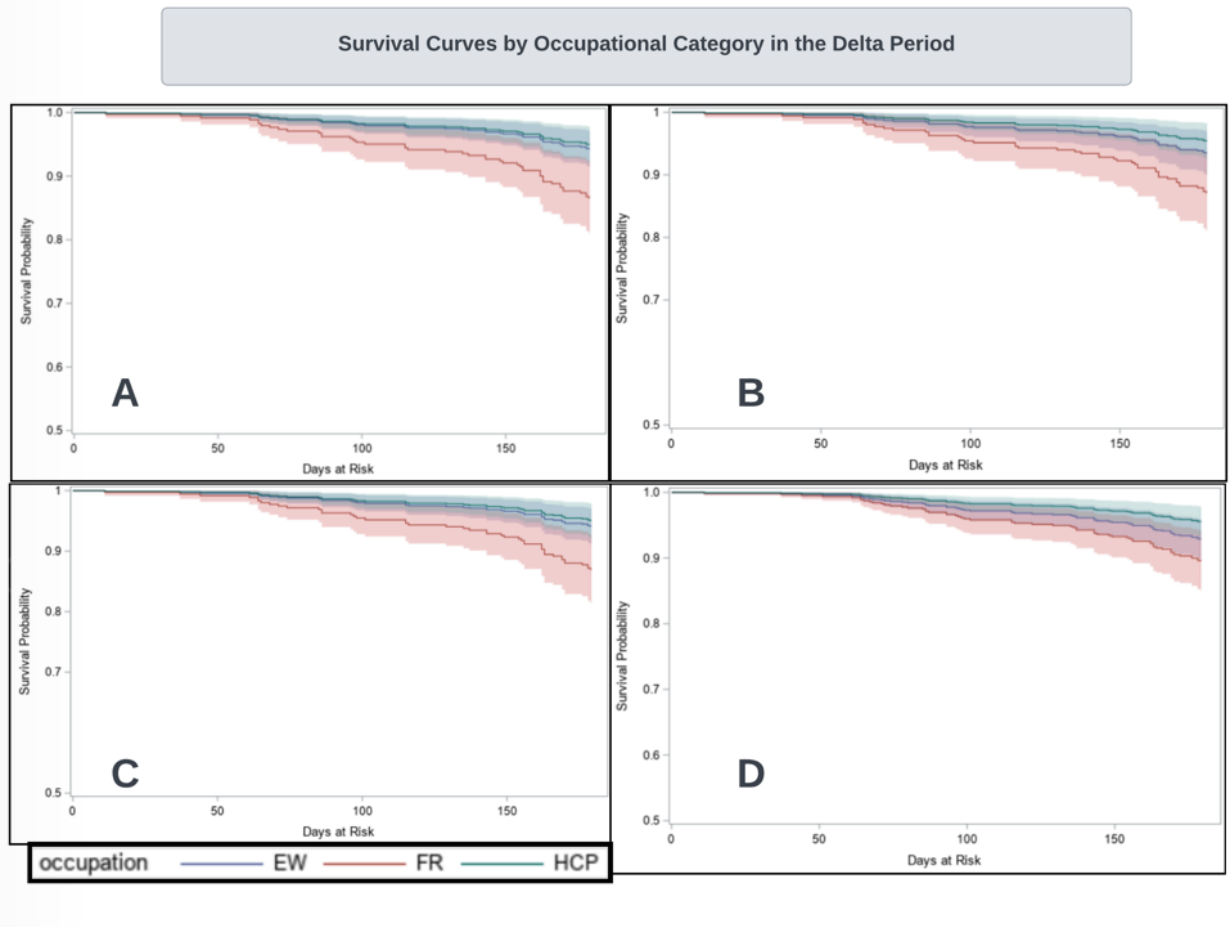
Survival curses in the Delta predominant period (Figure 4) supported the observed hazards ratios. First responders had a higher probability of experiencing a breakthrough infection, followed by OEW and HCP among the various models.

Table 3. Unadjusted and adjusted Cox Proportional Hazards Models among breakthrough infections for the period of Delta Predominance, healthcare personnel as reference category (n=697)

	Unadjusted Model	**Model 2[a]**	**Model 3[b]**	**Model 4[c]**	**Sensitivity[c,d] (n=1,106)**
Occupational Category	**HR[e] (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Healthcare Personnel	Ref	Ref	Ref	Ref	Ref
First Responder	**2.77* (1.34, 5.70)**	**2.92* (1.27, 6.73)**	**2.76* (1.30, 5.87)**	**2.86* (1.21, 6.77)**	**2.51* (1.22, 5.17)**
Other Essential Worker	1.34 (0.53, 2.43)	1.43 (0.60, 3.40)	1.20 (0.55, 2.61)	1.44 (0.60, 3.44)	1.65 (0.81, 3.35)
Female		0.97 (0.50, 1.89)		0.97 (0.50, 1.89)	0.87 (0.50, 1.53)
Age		1.09 (0.82, 1.45)		1.10 (0.83, 1.46)	1.01 (0.79, 1.28)
Comorbidities: 1+		0.86 (0.45, 1.65)		0.87 (0.45, 1.68)	0.94 (0.54, 1.62)
Days since primary series		1.01 (0.99, 1.02)		1.00 (0.99, 1.01)	1.01 (1.00, 1.01)
Hours in close contact at work[f]			**2.11* (1.04, 4.26)**	1.82 (0.88, 3.76)	1.78 (0.96, 3.30)
Percent of time wearing appropriate PPE at work[f]			1.03 (0.45, 2.38)	1.07 (0.46, 2.49)	1.00 (0.50, 1.99)
Hours in close contact in the community[f]			0.65 (0.29, 1.45)	0.73 (0.33, 1.65)	0.68 (0.34, 1.35)
Percent of time wearing a mask in the community[f]			0.73 (0.31, 1.71)	0.71 (0.30, 1.69)	0.70 (0.34, 1.44)

a: Adjusted for gender, age in increments of 10 years, comorbid conditions, and days since second dose of the vaccine
b: Adjusted for average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
c: Adjusted for gender, age in increments of 10 years, comorbid conditions, days since second dose of the vaccine, average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
d: Including previously excluded individuals who missed 3 consecutive weekly nasal swabs
e: Hazard ratio and 95% confidence interval
f: Upper 25th percentile compared to the lower 75th percentile
*: P value < 0.05

Figure 3. Cox proportional Hazards Regression Survival Curves for the Delta Period (n=697)



a: Unadjusted survival curve
b: Adjusted for gender, age in increments of 10 years, comorbid conditions, and days since second dose of the vaccine
c: Adjusted for average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
d: Adjusted for gender, age in increments of 10 years, comorbid conditions, days since second dose of the vaccine, average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community

3.4 Omicron Predominant Period

Among 1,260 participants at risk for breakthrough infections in the Omicron period, breakthrough infections were higher in the first responder category compared to the HCP and OEW (Tables 5 & 6). Prior to adjustment, first responders were 71% more likely to experience breakthrough infections compared to HCP (HR: 1.71 (95% CI: 1.24, 2.37) p=0.0002) and 87% more likely compared to OEW (HR: 1.87 (95% CI: 1.34, 2.62) p=0.0002). After adjusting for

participant characteristics, the likelihood of breakthrough infections in the first responder category were 65% compared to HCP (HR: 1.65 (95% CI: 1.15, 2.35) p=0.01) and 101% compared to OEW (HR: 2.01 (95% CI: 1.41, 2.86) p=0.0001). Receiving a booster dose of the vaccine increased the likelihood of experiencing a breakthrough infection (HR: 1.58 (95% CI: 1.19, 2.07) p=0.001). After adjustment for mitigation practices only, first responders were 63% more likely to experience a breakthrough infection compared to HCP (HR: 1.63 (95% CI: 1.17, 2.28) p=0.004), and 81% more likely compared to OEW (HR: 1.81 (95% CI: 1.29, 2.54) p=0.001). The upper 25th percentile of hours in close contact with others at work experienced increased likelihood of experiencing a breakthrough infection (HR: 1.11 (95% CI: 0.82, 1.52) p=0.49), and hours of close contact in the community (HR: 1.13 (95% CI: 0.82, 1.56) p=0.45).

After adjusting for both participant characteristics and mitigation practices, first responders were 54% more likely to experience breakthrough infections compared to the HCP (HR: 1.54 (95% CI 1.07, 2.21) p=0.02) and 92% more likely compared to OEW (HR: 1.92 (95% CI: 1.34, 2.75) p=0.0003). The results were further supported by the sensitivity analysis comparing first responders to HCP (HR: 1.60 (95% CI 1.11, 2.29) p=0.01) and OEW (HR: 1.92 (95% CI: 1.35, 2.74) p=0.003). HCP were more likely to experience breakthrough infections compared to OEW (HR: 1.25 (95% CI: 0.92, 1.71) p=0.16). Across the various models, the overall effect of occupation remained statistically significant.

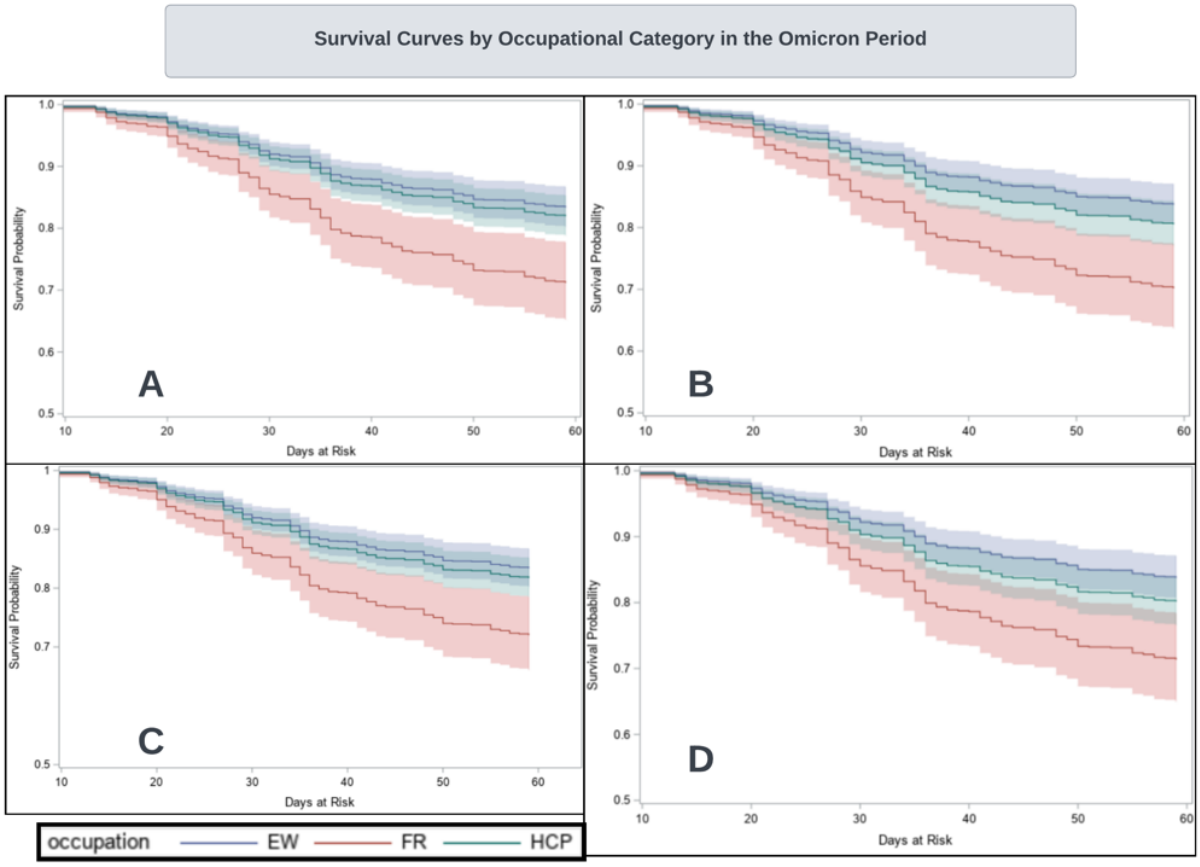
Survival curses in the Omicron predominant period (Figure 5) supported the observed hazards ratios. First responders had a higher probability of experiencing a breakthrough infection, followed by HCP and OEW among the various models.

Table 4. Unadjusted and adjusted Cox Proportional Hazards Models among breakthrough infections for the period of Omicron predominance, healthcare personnel as reference category (n=1,260)

	Unadjusted Model	**Model 2[a]**	**Model 3[b]**	**Model 4[c]**	**Sensitivity[c,d] (n=1,310)**
Occupational Category	**HR[e] (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Healthcare Personnel	Ref	Ref	Ref	Ref	Ref
First Responder	**1.71* (1.24, 2.37)**	**1.65* (1.15, 2.35)**	**1.63* (1.17, 2.28)**	**1.54* (1.07, 2.21)**	**1.60* (1.11, 2.29)**
Other Essential Worker	0.91 (0.68, 1.22)	0.82 (0.60, 1.12)	0.90 (0.67, 1.21)	0.80 (0.59, 1.09)	0.83 (0.61, 1.13)
Female		0.92 (0.70, 1.22)		0.91 (0.69, 1.20)	0.92 (0.70, 1.22)
Age		0.93 (0.82, 1.04)		0.93 (0.82, 1.05)	0.94 (0.83, 1.06)
Comorbidities: 1+		0.94 (0.72, 1.24)		0.93 (0.71, 1.23)	0.94 (0.71, 1.23)
Days since primary series		**1.00* (0.99, 1.00)**		**1.00* (0.99, 1.00)**	**1.00* (0.99, 1.00)**
Received booster dose		**1.58* (1.19, 2.07)**		**1.62* (1.23, 2.15)**	**1.58* (1.20, 2.07)**
Hours in close contact at work[f]			1.11 (0.82, 1.52)	1.06 (0.78, 1.45)	1.15 (0.85, 1.56)
Percent of time wearing appropriate PPE at work[f]			1.01 (0.77, 1.33)	0.94 (0.71, 1.23)	0.94 (0.72, 1.23)
Hours in close contact in the community[f]			1.13 (0.82, 1.56)	1.19 (0.86, 1.63)	1.09 (0.80, 1.49)
Percent of time wearing a mask in the community[f]			0.73 (0.52, 1.02)	0.73 (0.52, 1.03)	0.74 (0.53, 1.04)

a: Adjusted for gender, age in increments of 10 years, comorbid conditions, and days since second dose of the vaccine
b: Adjusted for average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
c: Adjusted for gender, age in increments of 10 years, comorbid conditions, days since second dose of the vaccine, average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
d: Including previously excluded individuals who missed 3 consecutive weekly nasal swabs
e: Hazard ratio and 95% confidence interval
f: Upper 25th percentile compared to the lower 75th percentile
*: P value < 0.05

Figure 4. Cox proportional Hazards Regression Survival Curves for the Omicron Period (n=1,260)



a: Unadjusted survival curve
b: Adjusted for gender, age in increments of 10 years, comorbid conditions, and days since second dose of the vaccine
c: Adjusted for average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
d: Adjusted for gender, age in increments of 10 years, comorbid conditions, days since second dose of the vaccine, average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community

The test for interaction did not find a statistically significant association between occupation and experiencing a breakthrough infection dependent on predominant variant on ($p=0.41$).

4. DISCUSSION

4.1 Summary

Crude incidence for breakthrough infections was highest for the first responder category in the Delta and Omicron periods (0.77 & 5.28 per 1,000 person-days at risk). Within this category, fire services had the highest crude incidence in the Delta period (1.10 per 1,000 person-days at risk). In the Omicron period, corrections had the highest crude incidence of breakthrough infections (13.10 per 1,000 person-days at risk).

Models adjusted for participant only characteristics or mitigation behaviors did not show consistent changes in the likelihood of experiencing a breakthrough infection, but first responders were consistently at increased risk of breakthrough infection. In the Delta period, decreased likelihood of experiencing a breakthrough infection was observed if one or more comorbid conditions were reported (HR: 0.86 (95% CI: 0.45, 1.65) p=0.65). Adjusting for mitigation practices resulted in increased likelihood of experiencing a breakthrough infection in the upper 25th percentile of hours in close contact with others at work (HR: 2.11 (95% CI: 1.04, 4.26) p=0.04). In the Omicron period, receiving a booster dose of the vaccine increased the likelihood of experiencing a breakthrough infection (HR: 1.58 (95% CI: 1.19, 2.07) p=0.001). The upper 25th percentile of hours in close contact with others at work experienced increased likelihood of experiencing a breakthrough infection (HR: 1.11 (95% CI: 0.82, 1.52) p=0.49), and hours of close contact in the community (HR: 1.13 (95% CI: 0.82, 1.56) p=0.45).

After adjustment for participant characteristics and mitigation practices, first responders were 186% more likely to experience breakthrough infections compared to HCP (HR: 2.86 (95% CI 1.21, 6.77) p=0.02) and 99% more likely compared to OEW (HR: 1.99 (95% CI: 0.92, 4.29) p=0.08) in the Delta period. First responders were 54% more likely to experience breakthrough

infections compared to HCP (HR: 1.54 (95% CI 1.07, 2.21) p=0.02) and 92% more likely compared to OEW (HR: 1.92 (95% CI: 1.34, 2.75) p=0.0003) in the Omicron period. OEW were more likely to experience breakthrough infections compared to HCP in the Delta period (HR: 1.44 (95% CI: 0.62, 3.44) p=0.41). However, compared to OEW, HCP were more likely to experience breakthrough infections (HR: 1.25 (95% CI: 0.92, 1.71) p=0.16) in the Omicron period.

Testing for interaction did not find that breakthrough infections by occupation was dependent on predominant variant (p=0.41).

4.2 Interpretation

Previous research has identified first responders at higher risk of experiencing infections compared to HCP and OEW prior to availability of the vaccine, which was consistently observed across the Delta and Omicron periods.[32] Individuals with preexisting chronic conditions may be more likely to adhere to mitigation behaviors compared to those without preexisting conditions.[44–46] This serves as a potential explanation for the decreased hazards in the Delta period among those with reported comorbidities.[44–46] Receiving a booster dose of the COVID-19 vaccine can give a false sense of security, which may explain why increased hazards were observed in the Omicron period among those who had received the booster.[45–49] Spending prolonged periods of time in close contact with others increases the likelihood of experiencing a COVID-19 infection, which potentially explains the increased risk observed among those in the 25th percentile.[21,50,51] Despite higher percentage of average reported PPE use in the Omicron period, the enhanced transmissibility of the variant resulted in almost five times the number of breakthrough infections compared to the Delta period.[4,5] The higher average PPE use could be explained by timing of the

surveys, which may have occurred later in the omicron period when participants became aware of the increased number of infections.

Prevention of COVID-19 infection is a complex, multilayered process that cannot be mitigated by a singular action.[21,22,36,52] Other factors may have driven the increased incidence of breakthrough infections that were not measured in this study. These factors include attitudes or beliefs towards prevention, a false sense of security, especially if the booster dose was recently obtained, and differences in work practices by occupation.[3,4,34,52] First responder occupations such as fire services may work prolonged shifts and spend many hours around other employees.[16,21,32] Law enforcement may share confined spaces with colleagues and the communities that they serve, all of which may contribute to the risk of infection.[7,32]

Individuals in the Delta period did not have access to the booster dose of the vaccine, coupled with participants having a relatively long duration of time since the receipt of the primary series. It has been demonstrated that vaccine effectiveness decreases over time, which may have contributed to the higher likelihood of experiencing a breakthrough infection.[3–5,34,35]

Even after accounting for receipt of a booster dose of the COVID-19 vaccine, first responders were most likely to experience a breakthrough infection compared to OEW and HCP. While the receipt of the vaccine may play an important role in prevention of severe infection from COVID-19, occupation still has a significant relationship with experiencing a breakthrough infection.

4.3 Limitations

This study had several limitations. First, a lack of breakthrough infections was observed in the Delta period. This prevented assessing the granular occupational categories in the cox

proportional hazards models and a lack of statistical power. The limited number of breakthrough infections impacted the precision of the measures of effect, and the inability to establish definitive associations. The structure of the rotating weekly COVID-19 exposure questions resulted in sparse data, which prevented the covariates to be assessed as time-varying. More robust approaches such as multiple imputation could have been utilized to account for missing data, but arbitrary decisions would have been required to determine which survey response to use for those without breakthrough infections, which arguably could have introduced more bias into the analyses than taking the average.

The study sample was over 60% female in both periods, impacting generalizability due to over representativeness. The racial/ethnic groups in the study sample deviated from the sampling targets in the AZ HEROES protocol, which severely limits generalizability to racial groups outside of White or Hispanic individuals. Most of the sample had a college education, which has shown to be correlated with uptake of the vaccine and mitigation practices.[45,47,53] In addition to education, those who are already vaccinated tend to have more positive attitudes towards mitigation practices.[45–47,53] The results may be biased towards those who inherently are more cautious. Other factors influencing breakthrough infections may have not been measured in the study, including hours spent at work each day, the ability to socially distance, individual attitudes and beliefs, and exposures that occurred at home.[46,47,49–51] Not accounting for these factors leaves the study susceptible to residual confounding.

Monitoring for weekly infections among study participants enabled surveillance of both symptomatic and asymptomatic infections. Even after excluding individuals who were noncompliant with weekly samples, the sensitivity analysis confirmed the findings in the primary analysis. The AZ HEROES study benefits from a large sample size, which without it may not

have been possible to examine the breakthrough infections by occupational category. The longitudinal nature of the study provides accurate timing of COVID-19 infection, and the ability to establish temporal relationships.

5. CONCLUSION

This study provided a unique perspective on the role that occupation plays in experiencing a breakthrough infection, by assessing only individuals who had received the primary series of the vaccine. Breakthrough infection by occupation was contrasted for the Delta and Omicron predominant periods. These results intend to serve as a supplement to previous vaccine effectiveness studies, coupled with reported state data, demonstrating that despite receiving the vaccine, infections are still occurring at a higher rate in the first responder category. Despite the inability to examine specific occupations, the results confirmed previous findings in other studies. Identifying the occupation most at risk for breakthrough infections can enable focused interventions to prevent the spread of the virus more effectively.

5.1 Future Recommendations

Recommendations for future research include a mixed methods approach to understand why first responders experience COVID-19 infections at a higher rate compared to other occupational categories. A risk factor analysis among the first responder occupations could help identify factors that drive incidence rates among fire services and corrections. In addition, examining differences by sex and educational levels may prove beneficial to understanding differences among this occupational category.

APPENDIX A

Supplementary Tables

Unadjusted and adjusted Cox Proportional Hazards Models among breakthrough infections for the period of Delta Predominance, other essential worker as reference category (n=697)

	Unadjusted Model		**Model 2[a]**		**Model 3[b]**		**Model 4[c]**		**Sensitivity[c,d] (n=1,106)**	
Occupational Category	**HR[e] (95% CI)**	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Occupation[f]		0.01		0.03		0.01		0.04		0.06
Healthcare Personnel	0.88 (0.41, 1.88)	0.74	0.70 (0.29, 1.66)	0.42	0.84 (0.38, 1.82)	0.65	0.69 (0.29, 1.66)	0.41	0.62 (0.31, 1.26)	0.18
First Responder	**2.77* (1.34, 5.70)**	0.01	2.04 (0.94, 4.42)	0.07	**2.30* (1.17, 4.56)**	0.02	1.99 (0.92, 4.29)	0.08	1.50 (0.78, 2.88)	0.29

a: Adjusted for gender, age in increments of 10 years, comorbid conditions, and days since second dose of the vaccine
b: Adjusted for average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
c: Adjusted for gender, age in increments of 10 years, comorbid conditions, days since second dose of the vaccine, average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
d: Including previously excluded individuals who missed 3 consecutive weekly nasal swabs
e: Hazard ratio and 95% confidence interval
f: P values comes from Type 3 test of model effects
*: P value < 0.05

Unadjusted and adjusted Cox Proportional Hazards Models among breakthrough infections for the period of Omicron predominance, other essential worker as reference category (n=1,260)

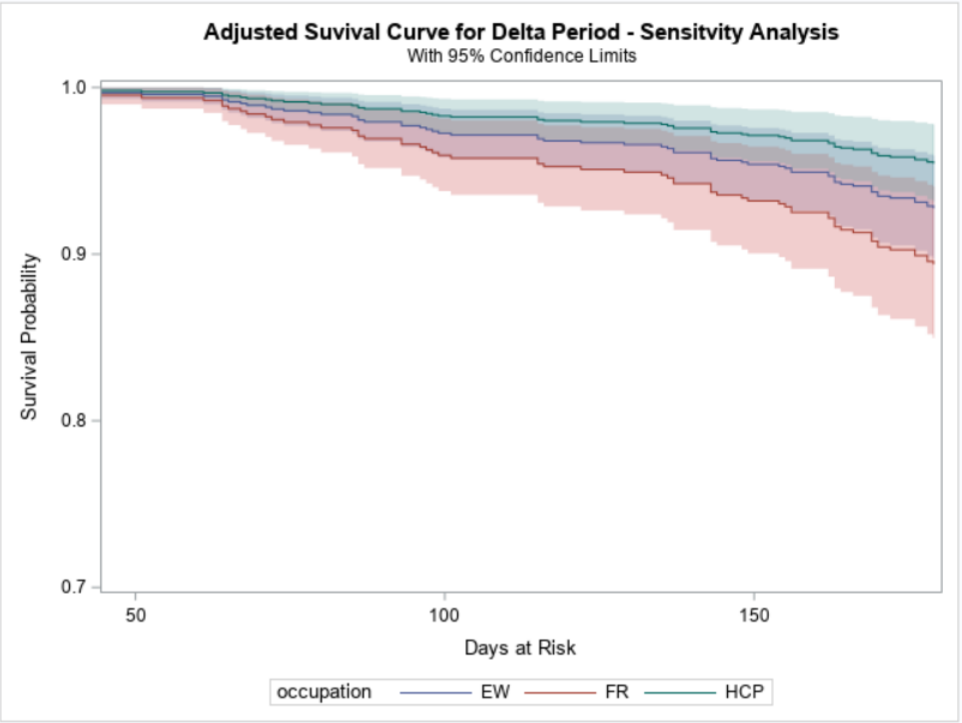
	Unadjusted Model		**Model 2[a]**		**Model 3[b]**		**Model 4[c]**		**Sensitivity[c,d] (n=1,310)**	
Occupational Category	**HR[e] (95% CI)**	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Occupation[f]		0.001		0.001		0.002		0.002		0.001
Healthcare Personnel	1.10 (0.82, 1.47)	0.54	1.22 (0.90, 1.66)	0.21	1.11 (0.83, 1.49)	0.48	1.25 (0.92, 1.71)	0.16	1.21 (0.89, 1.64)	0.23
First Responder	**1.87* (1.34, 2.62)**	0.0002	**2.01* (1.41, 2.86)**	0.0001	**1.81* (1.29, 2.54)**	0.0001	**1.92* (1.34, 2.75)**	0.0003	**1.92* (1.35, 2.74)**	0.0003
Other Essential Worker	Ref		Ref		Ref		Ref		Ref	

a: Adjusted for gender, age in increments of 10 years, comorbid conditions, and days since second dose of the vaccine
b: Adjusted for average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
c: Adjusted for gender, age in increments of 10 years, comorbid conditions, days since second dose of the vaccine, average hours in close contact with individuals at work and in the community, and average percent of time wearing PPE at work and in the community
d: Including previously excluded individuals who missed 3 consecutive weekly nasal swabs
e: Hazard ratio and 95% confidence interval
f: P values comes from Type 3 test of model effects
*: P value < 0.05

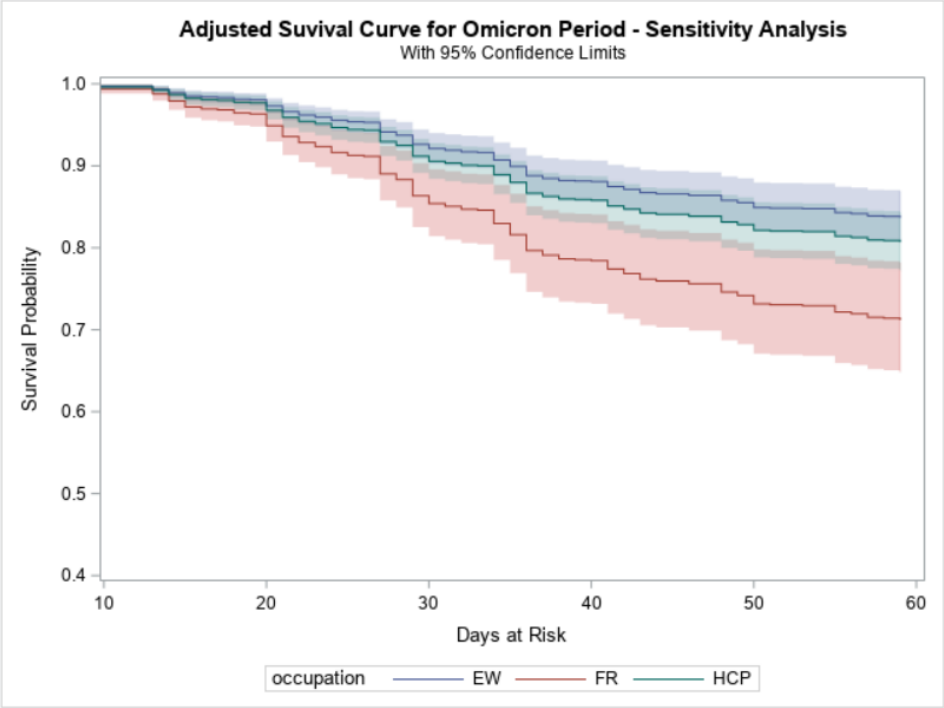
APPENDIX B

Supplementary Figures

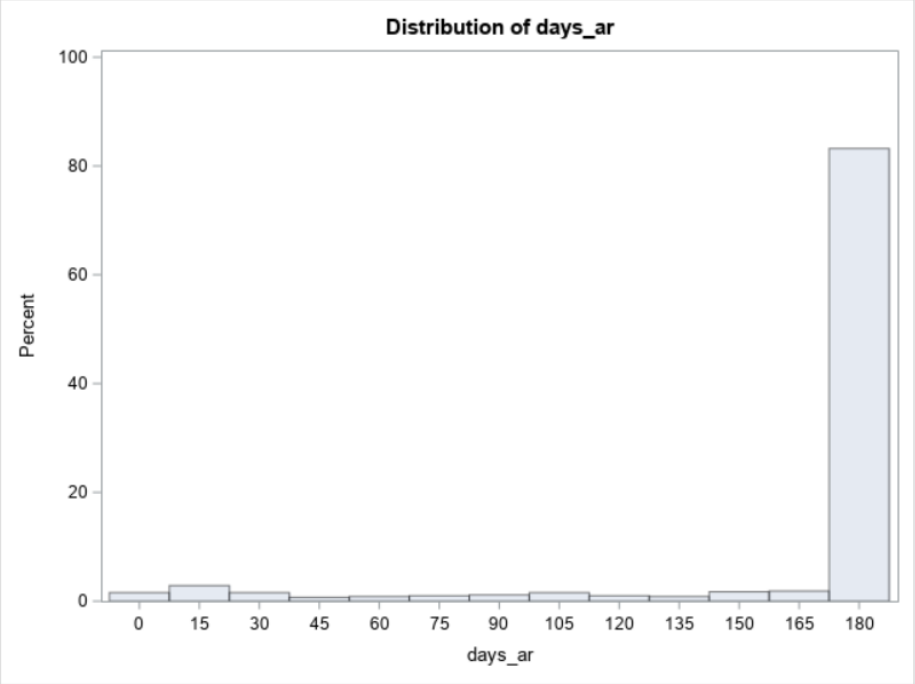
Adjusted Survival Curves for Sensitivity Analysis during Delta Period (n=1,106)



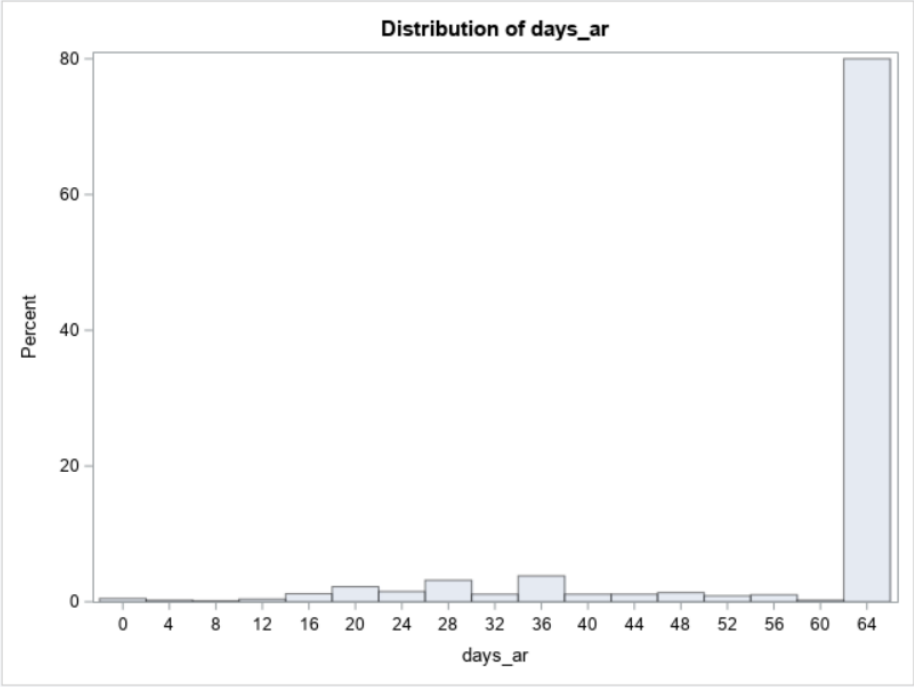
Adjusted Survival Curves for Sensitivity Analysis during Omicron period (n=1,310)



Distribution of person-days at risk for the Delta Period.



Distribution of person-days at risk for the Omicron period.



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