



Rapid Rollout and Initial Uptake of a Booster COVID-19 Vaccine Among Israel Defense Forces Soldiers

Tomer Talmy^{1,2} · Itay Nitzan^{1,2}

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Abstract

The surge of breakthrough COVID-19 among fully vaccinated individuals has raised the prospects of booster dose administration. In Israel, concerns of waning immunity and dominance of the B.1.617.2 (delta) variant resulted in approval of a third-dose (booster) vaccination for the entire eligible population starting on August 29, 2021. This study aims to evaluate vaccine uptake for booster doses among a population of previously vaccinated individuals during a rapid rollout and to analyze socio-demographic characteristics associated with vaccine uptake. A cross-sectional study among Israel Defense Forces soldiers with high access to booster doses of BNT162b2. Subjects eligible for booster doses were voluntarily vaccinated at three vaccine sites constructed within soldiers' bases. We analyzed associations between subjects' socio-demographic characteristics and booster vaccine uptake at the culmination of vaccine rollout using logistic regression models. 1157 soldiers from an IDF brigade were eligible for third dose vaccination (received second dose > 5-months before rollout), with 978 (84.5%) receiving a third, booster dose during the study's timeframe. Subjects' median age was 20.5 (IQR 19.7–21.5) and 791 (68.4%) were male. Notable socio-demographic characteristics associated with increased vaccine uptake in a multivariable model included increased age (OR 1.16, 95% CI 1.02–1.31), high socio-economic status (OR 2.12, 95% CI 1.25–3.59) and female sex (OR 1.87, 95% CI 1.26–2.74). Below-average cognitive function score was associated with decreased vaccine uptake (OR 0.61, 95% CI 0.39–0.95). This study demonstrates that real-world vaccine hesitancy remains a major obstacle, even among a population previously acceptant to COVID-19 vaccines. Decreased uptake for vaccines may be associated with socio-demographic variables in spite of high-access vaccine rollouts. Reasons for vaccine hesitancy among previously vaccinated individuals, along with the benefits of population-wide booster administration should be further investigated.

Keywords COVID-19 · SARS-CoV-2 · Vaccine · Military · Hesitancy · Acceptance · Booster

Introduction

The surge in breakthrough COVID-19 cases among vaccinated individuals has raised concerns of waning immunity (Bergwerk et al., 2021; Keehner et al., 2021; Levine-Tiefenbrun et al., 2021; Lopez Bernal et al., 2021), potentially necessitating the administration of a third, booster dose, of the COVID-19 mRNA vaccines (Bar-On et al., 2021; Keehner et al., 2021). In Israel, a rapid nationwide mass vaccination program (Dagan et al., 2021; Gurwitz, 2021) exclusively utilizing the BNT162b2 (Pfizer–BioNTech) mRNA vaccine, nearly eradicated the disease, resulting in a miniscule daily case rate between April–June, 2021 (Levine-Tiefenbrun et al., 2021; Ritchie et al., 2020). However, since early June, 2021, a steep rise in cases was recorded, ascribed to a decline in vaccine-induced immunity, the dominance of the B.1.617.2 (delta) variant (Levine-Tiefenbrun et al., 2021; Lopez Bernal et al., 2021), and the relaxation of gathering restrictions and masking mandates (Israel Ministry of Health, 2021).

Due to the resurgence of cases, on July 30, 2021, the Israeli Ministry of Health approved inoculation of a third, booster dose for those aged 60 years or older (Levine-Tiefenbrun et al., 2021), with additional age groups included incrementally. On August 29, 2021, the third dose was approved for the entire population aged 12 years or older, five months from the date of the second dose (Israel Ministry of Health, 2021). Consequently, the Israel Defense Forces (IDF) commissioned a rapid, high access rollout of the third dose to all eligible military personnel starting on September 1, 2021, with vaccine sites being constructed within military bases at over 70 locations.

Vaccine hesitancy for COVID-19 vaccines among young adults remains a major obstacle worldwide towards achieving extensive inoculation with the aim of reaching herd immunity (Adams et al., 2021; Troiano & Nardi, 2021). The rapid surge in breakthrough COVID-19 cases has prompted administration of a booster dose in several countries. However, the lack of extensive evidence on the efficacy of such booster doses, along with calls for reallocation of vaccine doses (Chagla & Pai, 2021; Krause et al., 2021) make vaccine hesitancy a heightened concern at this juncture. Socio-demographic variables have been demonstrated to potentially influence initial COVID-19 vaccine uptake among young adults (Shapiro et al., 2022). The aim of this study was to describe a high access vaccine rollout conducted in an IDF brigade and analyze associations between socio-demographic characteristics and booster vaccine uptake among individuals who had previously received the first two doses of the BNT162b2 vaccine.

Materials and Methods

Study Design, Setting and Population

In Israel, most Jewish citizens and some minorities are obligated to serve in the Israeli Defense Forces starting at the age of 18 years. As part of the pre-recruitment evaluation, mostly at age 17 years, subjects undergo a comprehensive socio-demographic and medical evaluation (Geva et al., 2019; Nitzan et al., 2021). We conducted a cross-sectional study to assess initial real-world acceptance of a COVID-19 booster dose among soldiers serving in a frontline IDF brigade. The study population consisted of all soldiers in the brigade deemed eligible to receive a third dose of the Pfizer-BioNTech BNT162b2 COVID-19 vaccine. Data was collected at three vaccine sites stationed within the brigade's bases with the aim of vaccinating the entire eligible population. In accordance with the vaccination policy set forth by the Israel Ministry of Health, we excluded subjects who had tested positive for SARS-CoV-2 via PCR testing at any timepoint, received the second dose of the vaccine during the previous five months or had yet to receive two doses of the vaccine (Fig. 1). During the study's timeframe,

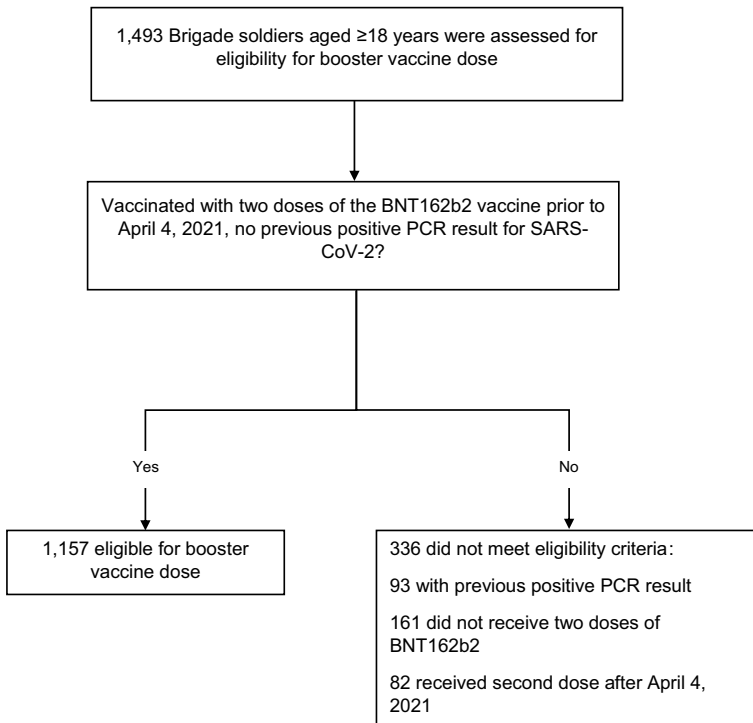


Fig. 1 Study population eligible for booster vaccine dose

all eligible soldiers were allowed to freely vaccinate with no prioritization made according to demographics, including age, rank and military occupation.

Vaccine Sites and Administration

On August 30, 2021, the IDF ordered the construction of on-base vaccine sites at 70 different locations, with the aim of vaccinating its primarily young adult population with a third, booster COVID-19 vaccine. Data was collected at three vaccination sites, located within participating units' bases, between September 1 and 2, 2021. One of the sites also operated on September 5, 2021, serving soldiers unable to attend the first two administration days. Sites operated starting at 9:00 AM each day until 11:00 PM to ensure ample time for soldiers to receive vaccinations, taking into consideration prior time commitments and tasks. Each site was directed by a single, primary care physician who supervised all on-site procedures including vaccine handling, storage, preparation, dilution and administration. The latter tasks were all performed by IDF medics who underwent a two-hour instruction prior to vaccine arrival. Vials of the Pfizer-BioNTech BNT162b2 vaccine arrived thawed and were stored in Helmer SLR104™ refrigerators at all sites. Notably, vaccination was entirely voluntary, and soldiers did not receive any reward or time off from duties following vaccination. Figure 2 describes the suggested construction of vaccination sites.

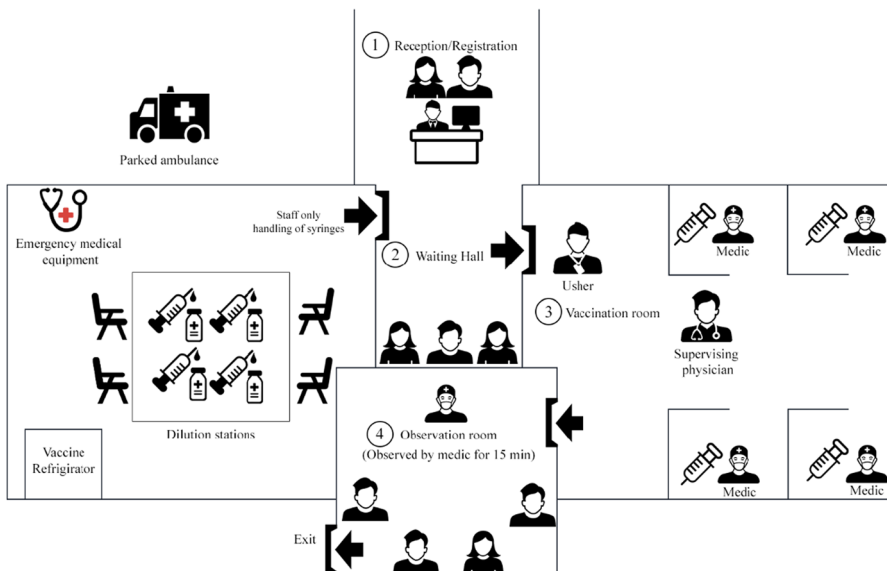


Fig. 2 Suggested mock of vaccination site with limited specialized healthcare staff

Study Variables

Documented variables of subjects included age, sex, cognitive function score (CFS), socio-economic cluster, country of birth and type of military service. Date of birth and sex were obtained from soldiers' personal records. Age at booster administration (years) and time from second dose (days) were treated as continuous variables. Prior to their recruitment, all candidates for military service undergo cognitive assessment that yields the CFS, which is normally distributed and correlated with the Wechsler Adult Intelligence Scale (Megreli et al., 2020). The CFS assesses subjects' verbal and non-verbal intelligence via four different subsets which then construct a validated cumulative score (1–9) reflecting general intelligence (Rabinowitz et al., 2000). CFS was classified into three groups: below average (1–3), average (4–6) and above average (7–9). Socio-economic cluster was determined according to the classification methodology of the Israel Central Bureau of Statistics (ICBS), based on current city of residence as assessed by subjects' registered address (Tzibel, 2009). The Bureau categorizes each municipality to one of ten socio-economic clusters ranked from low to high, considering age distribution, available labor force, level of unemployment, level of education, average per capita income and proportion of income support recipients. Socio-economic clusters were categorized into three groups: low (1st-4th clusters), medium (5th-7th clusters) and high (8th-10th clusters). Country of birth was classified into two groups: Israel and immigrants (born outside of Israel). Baseline health was assessed according to the IDF medical profiling system. Prior to enlisting, all IDF recruits are assigned a medical profile score according to their current health status and medical histories. Soldiers included in the study were classified as having unimpaired health in the absence of any chronic comorbidity requiring medical therapy, including history of malignancy or a major operation, as previously described (Geva et al., 2019). Soldiers' military occupation was classified to combat and non-combat occupation, based on current service role.

Statistical Analysis

The socio-demographic characteristics of the study population are presented as medians and interquartile range for continuous variables and proportions for categorical variables. Student's *t*-test and the Chi-square test were used to compare differences in continuous and categorical variables, respectively. Among included subjects, the association between booster vaccination uptake, as an outcome variable, and each of the independent socio-demographic variables, was evaluated using univariable logistic regression models. Variables with *p* value < 0.1 upon univariable analysis were considered to be potential determinants of vaccine uptake and were selected for multivariable logistic regression analysis. The results of the regression models are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Multicollinearity of independent variables was assessed

computing the variance inflation factor (VIF). A two-sided p value <0.05 was considered statistically significant. Statistical analyses were performed with syntax-based SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Subgroup Analysis

All soldiers enlisting in the IDF commit to a minimal mandatory service of two years for females and approximately three years for males (typically ages 18–21). A small portion of soldiers commit to additional, “permanent” service and therefore serve to older ages. To attenuate for potential confounding by type of service, we limited the subgroup analysis to soldiers in mandatory service, excluding soldiers who opted for permanent service. To minimize confounding by coexisting morbidities that might affect vaccination acceptance (Soares et al., 2021), we restricted the main analysis to subjects with unimpaired health status at time of vaccination.

Study Ethics

The IDF’s institutional review board approved the use of deidentified vaccination and socio-demographic data. Subjects’ anonymity was strictly kept during data handling and processing.

Results

Demographics

A total of 1157 soldiers from a single IDF brigade met the eligibility criteria for receiving a booster dose of the BNT162b2 vaccine (Fig. 1). Eligible subjects had a median age of 20.5 (IQR 19.7–21.5), 791 (68.4%) were male and 74 (6.4%) were immigrants. Most belonged to the medium socio-economic cluster ($n = 588$; 50.9%) and 484 (44.7%) had an average cognitive function score (CFS). The socio-demographic characteristics of the study population are displayed in Table 1.

Vaccine Uptake

During the study timeframe, 978 (84.5%) received a third, booster dose of the BNT162b2 COVID-19 vaccine (Table 1). Among vaccinated soldiers, the proportion of those with higher socio-economic status (p value = 0.001) and above average CFS (p value = 0.002) were significantly higher as compared with those unvaccinated with the third dose. The vaccinated group had a significantly higher proportion of soldiers with unimpaired health (p value = 0.008) and serving in combat roles (p value <0.001) as opposed to unvaccinated soldiers. There was a higher proportion of females among vaccinated soldiers, but this difference was not statistically significant (p value = 0.092).

Table 1 Socio-demographic characteristics of the study population stratified according to booster vaccination status

Study population characteristics	COVID-19 booster vaccination status			<i>p</i> value ^a
	Vaccinated with booster (N = 978)	Unvaccinated with booster (N = 179)	Total (N = 1157)	
Age—Median (IQR), years	20.5 (19.7–21.6)	20.2 (19.6–21.2)	20.5 (19.7–21.5)	0.001*
Sex—N (%)				
Male	659 (83.3%)	132 (16.7%)	791 (68.4%)	0.092
Female	319 (87.2%)	47 (12.8%)	366 (31.6%)	
Country of birth—N (%)				
Israel	919 (84.9%)	164 (15.1%)	1083 (93.6%)	0.238
Immigrants	59 (79.7%)	15 (20.3%)	74 (6.4%)	
Socio-economic cluster—N (%) ^y				
Low	114 (77.6%)	33 (22.4%)	147 (12.7%)	0.001*
Medium	488 (83.0%)	100 (17.0%)	588 (50.9%)	
High	375 (89.1%)	46 (10.9%)	421 (36.4%)	
Cognitive function score (CFS)—N (%) ^{yy}				
Below average	172 (76.4%)	53 (23.6%)	225 (20.8%)	0.002*
Average	417 (86.2%)	67 (13.8%)	484 (44.7%)	
Above average	323 (86.4%)	51 (13.6%)	374 (34.5%)	
Medical profile—N (%)				
Unimpaired health	836 (85.7%)	139 (14.3%)	975 (84.3%)	0.008*
Impaired health/ comorbidity	142 (78.0%)	40 (22.0%)	182 (15.7%)	
Military occupation—N (%)				
Combat	703 (87.7%)	99 (12.3%)	802 (69.3%)	< 0.001*
Non-combat	275 (77.5%)	80 (22.5%)	355 (30.7%)	
Time from second dose vaccination—Median (IQR), days	210 (199–219)	205 (196–219)	210 (199–219)	0.003*

**p* value < 0.05^a*p* values acquired from Chi-square test or Student's *t*-test^yMissing data for 1 soldier. ^{yy}Missing data for 74 (6.4%) soldiers

Associations in Regression Models

Age, sex, socio-economic cluster, CFS, medical profile, service type and time from second dose vaccination were found to be associated (*p* value < 0.1) with receiving a booster vaccine in univariable models (Table 2). Multicollinearity of socio-demographic variables was not observed (highest VIF value was 1.29). Overall, in the multivariable model, females had higher odds of receiving a booster vaccine compared to males (OR 1.87, 95% CI 1.26–2.74). Subjects with a below average

Table 2 Associations of socio-demographic characteristics with booster vaccine uptake in univariable and multivariable models

Socio-demographic characteristics	Univariable logistic regression			Multivariable logistic regression		
	OR	95% CI	p value for category	OR	95% CI	p value for category
Age	1.07	1.02, 1.13	–	1.16	1.02, 1.31	0.024
Sex						
Male	Reference			Reference		
Female	1.36	0.95, 1.95	0.093	1.87	1.26, 2.74	0.002
Country of birth						
Israel	Reference			–		
Immigrants	0.7	0.39, 1.27	0.24			
Socio-economic cluster						
Low	Reference			Reference		
Medium	1.41	0.91, 2.20	0.127	1.38	0.86, 2.21	0.178
High	2.36	1.44, 3.87	0.001	2.12	1.25, 3.59	0.005
Cognitive function score (CFS)						
Below average	0.52	0.35, 0.78	0.001	0.61	0.39, 0.95	0.027
Average	Reference			Reference		
Above average	1.02	0.69, 1.51	0.931	0.91	0.61, 1.37	0.660
Medical profile						
Unimpaired health	Reference			Reference		
Impaired health/comorbidity	0.59	0.40, 0.86	0.009	0.77	0.48, 1.24	0.284
Military occupation						
Combat	Reference			Reference		
Non-Combat	0.48	0.35, 0.67	<0.001	0.62	0.41, 0.94	0.024
Time from second dose vaccination in days	1.02	1.01, 1.03	–	1.01	1.00, 1.02	0.078

OR, odds ratio; CI, confidence interval

*p value < 0.1 therefore variable included in multivariable logistic regression model

cognitive function and those in non-combat positions had lower odds for vaccination (OR 0.61, 95% CI 0.39–0.95 and OR 0.62, 95% CI 0.41–0.94, respectively). High socio-economic clusters were associated with raised odds for vaccination (OR 2.12, 95% CI 1.25–3.59), whereas the association with the medium clusters was not statistically significant ($p=0.178$). Each incremental increase in subjects' age increased the odds of vaccination by 16% (95% CI 1.02–1.31), while the time (days) from inoculation with the second dose vaccination was not statistically significant (p value =0.078).

Among the sub-group of mandatory service soldiers ($n=904$), the association between high socio-economic clusters, combat service and booster uptake persisted, while the association with female sex accentuated (Supplementary table 1). Associations also persisted among sub-group of soldiers with unimpaired health, besides the association with service type that was insignificant (Supplementary table 2).

Discussion

This study describes the initial real-world uptake of a booster dose of COVID-19 vaccines during a rapid and highly accessible rollout in an IDF brigade. In this current study, 84.5% of eligible individuals (previously receiving two-doses) received a booster dose within an initial, highly accessible rollout. This study also demonstrates the feasibility of establishing rapid vaccination sites within a community setting, utilizing limited resources and short onboarding of non-specialized medical staff (Fig. 2).

The vast surge in cases worldwide, spearheaded by emerging variants and potentially waning immunity among vaccinated individuals, may necessitate widespread booster administration (Bar-On et al., 2021; Bergwerk et al., 2021; Keehner et al., 2021; Levine-Tiefenbrun et al., 2021). Booster COVID-19 mRNA vaccines have been administered in Israel since July 30, 2021, when the Israel Ministry of Health approved a booster dose for those over the age of 60. Initial efficacy data has demonstrated an > 11-fold decrease in relative risk for infection among those receiving a booster dose (Bar-On et al., 2021). On November 19, 2021, the U.S. Food and Drug Administration (FDA) approved booster administration for individuals 18 years of age or older who had previously completed a two-dose regimen of the Moderna or Pfizer-BioNTech COVID-19 vaccines (FDA, 2021). Therefore, booster doses are expected to be utilized worldwide with vaccine hesitancy posing a major obstacle for containment of the pandemic, even among previously vaccinated individuals.

Population-wide vaccination has been demonstrated as a highly effective measure in controlling the pandemic (Dagan et al., 2021; Lopez Bernal et al., 2021). However, vaccine hesitancy has hindered such efforts in many regions worldwide, with vaccine hesitant individuals often questioning vaccine safety and efficacy (Adams et al., 2021; Aw et al., 2021). The abundance of breakthrough cases among vaccinated individuals (Bar-On et al., 2021; Levine-Tiefenbrun et al., 2021) may deepen concerns of safety among this population and jeopardize acceptance of a third dose. Furthermore, concerns regarding allocation of vaccine doses to lower-income countries (Chagla & Pai, 2021) and older individuals (Adams et al., 2021) may arise

among younger, previously vaccinated individuals. In this study, we did not aim to identify causes of vaccine hesitancy, however, 15.5% of our target population remained unvaccinated with the booster dose. Considering the high availability of vaccines within the premises of soldiers' bases, we assume that portion of unvaccinated subjects may represent the portion of hesitant individuals. It should be noted that during our vaccine rollout, evidence supporting administration of a booster dose was scarce, raising controversy within the scientific community (Krause et al., 2021), potentially influencing vaccine hesitancy in our study population.

Previous studies have demonstrated inequities in vaccine acceptance by certain socio-demographic characteristics (Adams et al., 2021; Kadoya et al., 2021; Robertson et al., 2021; Soares et al., 2021; Troiano & Nardi, 2021). Our results highlight several socio-demographic factors associated with booster vaccine uptake, including older age, higher CFS and higher socio-economic status. These findings are consistent with a recent review of COVID-19 vaccine hesitancy, which points to lower education, lower income, and younger age being linked to increased hesitancy (Aw et al., 2021). Our results suggest that these factors may also play a role in booster vaccine uptake, even in the settings of high access for vaccination. Though previous works suggest that females are less acceptant of COVID-19 vaccines (Aw et al., 2021; Robertson et al., 2021), the odds of booster acceptance were higher among females in our study population (OR 1.87, 95% CI 1.26–2.74). Suggested reasons for this trend include concerns of vaccine effect on pregnancy and breastfeeding (Aw et al., 2021; Mohan et al., 2021). Our study sample included women in fertile ages, however pregnant women do not serve in frontline IDF units and therefore were not represented within our study population, potentially explaining this finding.

In a previous paper, we suggested several strategies to increase vaccine acceptance among hesitant individuals at the primary-care level (Talmy et al., 2021). Although much research has been conducted around COVID-19 vaccine hesitancy, vaccinated individuals (two-doses) reluctant of receiving a third dose represent a unique population which has yet to be characterized. As the duration of the COVID-19 pandemic prolongs, widespread periodic administration of vaccinations has become a plausible scenario. Under such conditions, decision-makers should be wary of incrementally decreased uptake among the population acceptant to previous doses. The prospects of a novel, broad-spectrum COVID-19 vaccine (Tan et al., 2021), targeting viral variants is therefore of a high-priority and may aid in swaying individuals wary of the added benefit of additional vaccinations. Further investigation as to specific concerns for booster vaccines among previously vaccinated individuals is warranted, with the objective of steering advocacy measures.

There are several limitations to this study. We included soldiers from a single IDF brigade, potentially reducing the generalizability toward other young adult and civilian populations. However, our results, as further exemplified by the subgroup analysis, may be representative of mandatory service IDF soldiers (18–21 years of age). Self-reported reasons for vaccine hesitancy were not investigated and the cross-sectional design is insufficient to inferring causality of associations. We did not have access to additional factors potentially influencing acceptance, such as vaccination status within individuals' families or side effects encountered with previous doses. Finally, a small proportion of unvaccinated

soldiers may have been willing to vaccinate but had not been able to attend the vaccination sites due to remote missions and personal or medical leave, despite the vaccine rollout being tabbed as the top priority for all soldiers during the study timeframe. The strengths of this study include the systematic data collection, the high access setting of vaccine sites, and the expedited rollout, allowing recognition of hesitant individuals for COVID-19 third dose.

Conclusion

This study demonstrates COVID-19 booster vaccine uptake during a rapid rollout among a military population. The results demonstrate that real-world hesitancy for a booster dose may be substantial among the population previously acceptant to initial doses of COVID-19 vaccines. Such vaccine hesitancy may be associated with socio-demographic variables such as lower cognitive assessment and lower socio-economic status. These findings call for further investigation and informative efforts regarding the efficacy of a booster COVID-19 vaccine, and its role in addressing breakthrough cases globally.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s10935-022-00702-2>.

Author Contributions TT: Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing—original draft. IN: Methodology, Software, Formal analysis, Investigation, Data curation, Writing—review & editing.

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Availability of Data and Materials Materials used to conduct the study are not publicly available.

Data Availability Full demographic data pertaining to individuals cannot be disclosed in order to ensure subjects' anonymity and data security policies in the IDF. Additional data is available in the supplementary appendix.

Code Availability The statistical software syntax used in this study may be available by emailing the corresponding author.

Declarations

Conflict of Interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: TT is a former employee of Emedgene Technologies, unrelated to the work reported in this paper.

Ethical Approval All data analyses were approved by the Israel Defense Forces Institutional review board.

Consent to Participate The Israel Defense Forces institutional review board approved the use of deidentified vaccination and socio-demographic data. Subjects' anonymity was strictly kept during data handling and processing.

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Authors and Affiliations

Tomer Talmy^{1,2}  · Itay Nitzan^{1,2} 

✉ Tomer Talmy
ttalmy@gmail.com

Itay Nitzan
itayn30@gmail.com

- ¹ Israel Defense Forces, Medical Corps, Tel Hashomer, Ramat Gan, Israel
- ² Department of Military Medicine and “Tzameret”, Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel