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The Association Between COVID-19 Vaccination and Health-related Quality of Life and Work Productivity: A Systematic Literature Review

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BACKGROUND

- Studies evaluating health-related quality of life (HRQoL) or work productivity via patient-reported outcomes (PROs) are warranted to assess the broader benefit of COVID-19 vaccination beyond clinical efficacy, effectiveness, and safety. Such studies are key to raising awareness of the full disease burden and informing evidence-based health policy decisions.
- The association between COVID-19 vaccination and PROs, such as HRQoL or work productivity, has not been fully characterized and remains an evidence gap.

OBJECTIVE

- **To identify and synthesize real-world observational studies that evaluate the association of COVID-19 vaccination with HRQoL and work productivity following SARS-CoV-2 infection or long-COVID.**

METHODS

- A systematic literature review (SLR) was conducted by searching in Embase and MEDLINE on October 8, 2024, to identify studies published since January 2021 reporting HRQoL or work productivity among individuals who received a primary, booster, or adapted vaccine of any BNT162b2, mRNA-1273, or NVX-CoV2373/NVX-CoV2601/NVX-CoV2705 formulation. The proceedings of two key international conferences on infectious diseases (Infectious Diseases Week and European Society of Clinical Microbiology and Infectious Diseases) were also hand searched.
  - Only studies comparing different vaccine brands, formulations, or doses or reporting data for vaccination vs. no vaccination were eligible for inclusion.
- Title/abstract screening was conducted by a single reviewer against the pre-defined eligibility criteria, with a second reviewer screening 10% of records. Double screening was employed at the full-text screening stage, with discrepancies resolved by a third reviewer. Data were extracted by one researcher and fully validated by a second, with conflicts resolved by a third. The quality of included studies was evaluated using the Newcastle-Ottawa Scale (NOS)[1] tool for non-randomized studies.
- Included studies were grouped by population to derive a narrative synthesis of results by vaccination status for each outcome.[2]

RESULTS

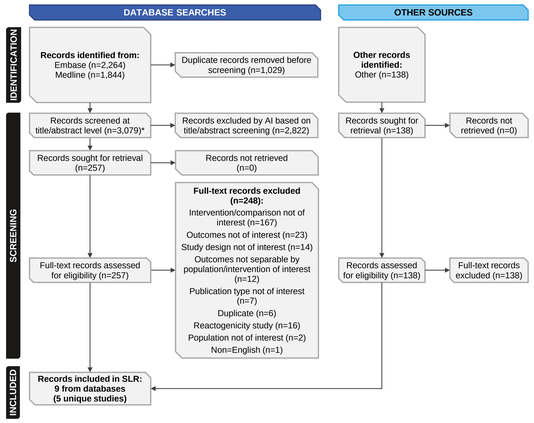
- Of 3,079 unique records screened, nine were included (representing five unique studies (**Figure 1; Table 1**).
- All included studies reported on the wildtype BNT162b2 vaccine (primary series or original booster) across various populations (**Figure 2**); two studies also reported on the adapted (bivalent BA.4/5) BNT162b2 vaccine.
- No studies reported outcomes of interest related to recently adapted vaccine formulations (XBB.1.5, JN.1, or KP.2).

Disclosures

CCC and **SP** are employees of PPD™ Evidera™ Health Economics & Market Access, Thermo Fisher Scientific, who received funding from Pfizer Inc. to conduct this study. **HB** was an employee of PPD™ Evidera™ Health Economics & Market Access at the time this study was conducted. **TH**, **CFM**, **HV**, **SMCL**, **JY** and **MD** are Pfizer employees and may receive Pfizer stock options.

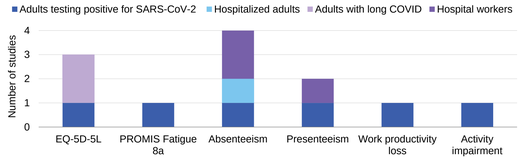
RESULTS (cont.)

Figure 1. PRISMA Diagram



Other sources: conference hand searches.
Abbreviation: SLR = systematic literature review. AI=Artificial Intelligence

Figure 2. Number of Studies by Outcome and Population Type (Five Studies)



Note: Work Productivity and Activity Impairment was assessed by one study, which reported individual components for absenteeism, presenteeism, work productivity loss, and activity impairment among adults testing positive for SARS-CoV-2. Abbreviation: PROMIS = Patient Reported Outcome Measurement Information System

HRQoL (Two Studies) (Table 2)

EQ-5D-5L

- Patients with acute SARS-CoV-2 infection. Individuals in the US who were vaccinated with three doses of the original wild-type BNT162b2 vaccine in 2022 or the bivalent BA.4/5-adapted BNT162b2 vaccine in 2023 consistently had numerically higher utility indices (UIs) (better HRQoL) and lower symptom burden compared with unvaccinated participants at all follow-up timepoints.[3,4]

EQ-5D-5L (cont.)

- Patients with long COVID. Similar trends were observed for participants with long COVID in the US, with those vaccinated reporting higher UI values than those unvaccinated.[5] At 6 months, boosted patients had significantly lower symptom burden than their unvaccinated counterparts.[5]

PROMIS Fatigue 8

- Patients with acute SARS-CoV-2 infection. Fatigue had a substantial effect on both vaccinated and unvaccinated cohorts, with numerically higher PROMIS scores (worse fatigue) at week 1 and week 4 in the unvaccinated cohort.[4]

Table 2. Summary of HRQoL Results

Population	Country and Study Period	Vaccine	Outcome Description	Vaccinated Compared to Unvaccinated or Not Fully Vaccinated
EQ-5D-5L				
Symptomatic Adults	US 2022[3]	BNT162b2 primary series with or without booster (2 or 3 doses)	EQ-5D-5L UI mean CFB at 3 days post infection	**Significantly Lower** -0.105 vs -0.155 (p=0.007)
			EQ-5D-5L UI mean CFB at 4 weeks post infection	**Significantly Lower** -0.039 vs -0.074 (p=0.023)
	US 2023[4]	BNT162b2 bivalent BA.4/5-adapted vaccine	EQ-5D-5L UI mean CFB at 3 days post infection	No significant difference -0.108 vs -0.111 (p=0.859)
			EQ-5D-5L UI mean CFB at 4 weeks post infection	No significant difference -0.026 vs -0.035 (p=0.476)
Adults with long COVID at 6 months post infection	US 2023[5]	BNT162b2 primary series with booster; primary series	EQ-5D-5L UI mean change from pre-COVID at 4 weeks post infection	**Significantly Lower** -0.083 vs -0.164 (p=0.032)*
			EQ-5D-5L UI mean change from pre-COVID at 3 months post infection	**Significantly Lower** -0.029 vs -0.182 (p=0.002)*
			EQ-5D-5L UI mean change from pre-COVID at 6 months post infection	**Significantly Lower** 0.001 vs − 0.155 (p=0.014)*
PROMIS Fatigue 8a				
Symptomatic Adults	US 2023[4]	BNT162b2 bivalent BA.4/5-adapted vaccine	PROMIS Fatigue mean CFB at 1 week post infection	No significant difference 15.7 vs 15.3 (p=0.727)
			PROMIS Fatigue mean CFB at 4 weeks post infection	No significant difference 2.8 vs 3.1 (p=0.728)

Abbreviation: CFB = change from baseline; PROMIS = Patient Reported Outcome Measurement Information System; UI = utility index; *vs unvaccinated; p<0.05 = statistically significant; 0.05 > p <0.1 = marginally significant; p>0.1 = no significant difference

Work Productivity (Four Studies) (Table 3)

- Individuals vaccinated with BNT162b2 presented lower work and activity impairment due to COVID-19 compared to those unvaccinated.[3,4,8,9,11]
- Trends towards improvement were consistent between vaccine doses (primary series and primary series + original booster) in the early waves of the pandemic (2020–2021),[3,7,8,11] with no significant difference between vaccination with the bivalent BA.4/5-adapted vaccine and unvaccinated/partially vaccinated in the later wave of the pandemic (2022–2023), especially after 4 weeks post-infection.[4,9]

Table 3. Summary of Work Productivity Results

Population	Country and Study Period	Vaccine	Outcome Description	Vaccinated Compared to Unvaccinated or Not Fully Vaccinated
Absenteeism				
Symptomatic Adults	US 2022[3]	BNT162b2 primary series with or without booster (2 or 3 doses)	WPAI mean score CFB at 1 week post infection	**Significantly Lower** 42.5 vs 55.5 (p=0.006)
			WPAI mean score CFB at 4 weeks post infection	**Significantly Lower** 1.4 vs -7.7 (p=0.006)
	US 2023[4]	BNT162b2 bivalent BA.4/5-adapted vaccine	WPAI mean score CFB at 1 week post infection	No significant difference 43.1 vs 49.7 (p=0.112)
			WPAI mean score CFB at 4 weeks post infection	No significant difference -1.8 vs -5.2 (p=0.13)
Hospitalized Adults	Greece 2021–2022[11]	BNT162b2 primary series and at least one booster	Mean days absence from work	**Significantly lower** 17.3 vs 20.1 (p=0.03)
Hospital Workers	Greece 2020–2021[7]	BNT162b2 primary series	Mean days absence from work	**Significantly lower** 6.9 vs 11.9 (p<0.001)
	Greece 2021–2022[8]	BNT162b2 primary series and at least one booster	Mean days absence from work	**Significantly lower** 8.1 vs 9.7 (p<0.001)
	Greece 2022–2023[9]	BNT162b2 primary series and BA.4/5 bivalent vaccine	Mean days absence from work	No significant difference 5.1 vs 5.2 (p=0.771)
Presenteeism (working while being ill)				
Symptomatic Adults	US 2022[3]	BNT162b2 primary series with or without booster (2 or 3 doses)	WPAI mean score CFB at 1 week post infection	No significant difference 33.0 vs 38.2 (p=0.268)
			WPAI mean score CFB at 4 weeks post infection	**Significantly Lower** 1.4 vs 10.7 (p=0.006)
	US 2023[4]	BNT162b2 bivalent BA.4/5-adapted vaccine	WPAI mean score CFB at 1 week post infection	**Lower (marginally significant)** 37.7 vs 43.4 (p=0.095)
			WPAI mean score CFB at 4 weeks post infection	No significant difference 1.2 vs 1.0 (p=0.917)
Hospital Workers	Greece 2020–2021[7]	BNT162b2 Primary series	Number of presenteeism episodes	No significant difference 24% vs 26% (p value NR)
	Greece 2021–2022[8]	BNT162b2 primary series and at least one booster	Number of presenteeism episodes	No significant difference 19.1% vs 15.4% (p=0.315)
	Greece 2022–2023[9]	BNT162b2 primary series and BA.4/5 bivalent vaccine	Number of presenteeism episodes	No significant difference 21.2% vs 19.8% (p=0.279)
Work Productivity				
Symptomatic Adults	US 2022[3]	BNT162b2 primary series with or without booster (2 or 3 doses)	WPAI mean score CFB at 1 week post infection	No significant difference 46.7 vs 53.2 (p=0.203)
			WPAI mean score CFB at 4 weeks post infection	No significant difference 1.4 vs 7.7 (p=0.113)
	US 2023[4]	BNT162b2 bivalent BA.4/5-adapted vaccine	WPAI mean score CFB at 1 week post infection	**Lower (marginally significant)** 45.3 vs 51.2 (p=0.069)
			WPAI mean score CFB at 4 weeks post infection	No significant difference -3.1 vs -2.3 (p=0.749)
Activity Impairment				
Symptomatic Adults	US 2022[3]	BNT162b2 primary series with or without booster (2 or 3 doses)	WPAI mean score CFB at 1 week post infection	No significant difference 36.1 vs 37.0 (p=0.801)
			WPAI mean score CFB at 4 weeks post infection	**Lower (marginally significant)** 2.3 vs 8.8 (p=0.053)
	US 2023[4]	BNT162b2 bivalent BA.4/5-adapted vaccine	WPAI mean score CFB at 1 week post infection	No significant difference 42.8 vs 45.4 (p=0.285)
			WPAI mean score CFB at 4 weeks post infection	No significant difference 3.6 vs 3.7 (p=0.959)

Abbreviations: CFB = change from baseline; WPAI = Work Productivity and Activity Impairment
p<0.05 = statistically significant; 0.05 > p <0.1 = marginally significant; p>0.1 = no significant difference

Table 1. Overview of All Studies Included in the SLR

Study, Year, Country	Population	Time since Vaccination	Sample Size	Dominant Circulating Variant	Outcomes Reported
Symptomatic outpatients					
NCT05160636 (Di Fusco 2022,[3] 2023[4,5]) US	Symptomatic adults testing positive for SARS-CoV-2 (January – April 2022 cohort)[3]	Mean 186 (SD: 105) days	BNT162b2 Primary series with or without booster: 233 (54.2%) [of which 2 doses: 140 (32.6%) and 3 doses: 93 (21.6%)] Unvaccinated: 197 (45.8%)	Omicron	HRQoL Work productivity
	Symptomatic adults testing positive for SARS-CoV-2 (January – April 2022 cohort)[5] with and without long-COVID (follow-up to October 2022)	Boosted cohort: mean 2.3 months (SD: 1.9) Vaccinated cohort: mean 6.9 months (SD: 3.0)	BNT162b2 Primary series and a booster: 87 (26.5%) BNT162b2 Primary series: 86 (26.2%) Unvaccinated: 155 (47.3%)	Omicron	HRQoL Work productivity
	Symptomatic adults testing positive for SARS-CoV-2[4] (March – May 2023 cohort)	Mean: 165 (SD: 45) days	BNT162b2 Primary series and bivalent BA.4/5-adapted BNT162b2 booster: 316 (49.1%) Unvaccinated: 327 (50.9%)	Omicron (XBB)	HRQoL Work productivity
Kuodi 2023[6] Israel	Adults with a positive SARS-CoV-2 test between March 15, 2020 and June 15, 2022, with and without long-COVID (follow up to June 2022)	NR	One BNT162b2 dose: 231 (24.3%) BNT162b2 Primary series: 227 (23.9%) BNT162b2 Primary series and a BNT162b2 booster: 250 (26.3%) Unvaccinated: 243 (25.6%)	Pre-omicron/omicron (assumed based on study period)	HRQoL[f]
Hospital workers with absenteeism from infection (SARS-CoV-2, RSV, or influenza)					
Maltezou 2021,[7] 2022,[8] 2024[9] Greece	Hospital workers with absenteeism November 2020 – April 2021 cohort [7]	NR	BNT162b2 Primary series (1 or 2 doses): 4,823 (64.8%) Unvaccinated: 2,622 (35.2%)	Pre-omicron (assumed based on study period)	Work productivity
	Hospital workers November 2021 – April 2022 cohort[8]	Individuals with absenteeism: mean 17.0 weeks (SD: 10.3)	BNT162b2 Primary series and a BNT162b2 booster[a]: 6,496 (85.6%) Partially vaccinated: 953 (12.5%)[b] Unvaccinated: 143 (1.9%)	Delta (B.1.617.2), Omicron (B.1.1.529)	Work productivity
	Hospital workers with absenteeism November 2022 – May 2023 cohort[9]	NR	BNT162b2 Primary series and a bivalent BA.1 or BA.4/5-adapted BNT162b2 booster[c]: 530 (9.2%) Partially vaccinated: 5,222 (90.8%)[b]	Omicron BA.2, BA.2.75, XBB1.5	Work productivity
Lee 2021[10] US	Hospital workers with absenteeism May 2020 – May 2021	NR	NR – can assume predominately BNT162b2 vaccinated cohort as hospital workers[d]	Pre-omicron (assumed based on study period)	Work productivity
Patients hospitalized with COVID-19					
Maltezou 2023[11] Greece	Adult patients hospitalized with COVID-19 November 2021 – April 2022	128.9 (81.1) days (from vaccine to diagnosis)	BNT162b2 Primary series and a BNT162b2 booster[e]: 386 (33.9%) Partially vaccinated: 172 (15.1%)[b] Unvaccinated: 580 (51.0%)	Delta, Omicron	Work productivity

Abbreviations: HRQoL = health-related quality of life; NR = not reported; RSV = respiratory syncytial virus. [a] Outcomes were not reported by vaccine brand. Vaccination rates were as follows: BNT162b2: 94.7%; Ad26.COV2.S: 3.1%; mRNA-1273: 2.0%; and ChAdOx1-S: 0.2%. Therefore, it was assumed that the results reflected the effect of BNT162b2 vaccine.[b] Partial COVID-19 vaccination was defined as a history of COVID-19 vaccination not fulfilling the criteria for full COVID-19 vaccination (e.g., incomplete primary series, complete primary series not followed by a booster dose six months later).[c] >94% of the vaccinations were the BNT162b2 vaccine; based on the study period, booster vaccines were assumed to be bivalent BA.1 or BA.4/5-adapted vaccines.[d] Conference abstract (sample size not reported). [e] Outcomes were not reported by vaccine brand, but BNT162b2 was received by 80.6% of the sample. Therefore, it was assumed that the results reflected the effect of the BNT162b2 vaccine. [f] Outcome was not reported as change from baseline and therefore is omitted from **Table 3**.

DISCUSSION

- The identified body of evidence exclusively reported on BNT162b2. No studies were found that reported on other approved vaccine brands (mRNA-1273 or NVX-CoV2373/NVX-CoV2601/NVX-CoV2705).
- Findings from this SLR showed an association between receipt of original BNT162b2 vaccines and improved HRQoL and reduced work productivity loss compared to partially vaccinated individuals or those unvaccinated.
  - Although the evidence on HRQoL is limited to two studies, significant improvements in HRQoL compared with unvaccinated individuals were found. This improvement was driven by a reduction in the number of SARS-COV-2 symptoms experienced, in the short-term setting (symptomatic outpatients) and in the long-term setting (long-COVID).
  - Vaccination with BNT162b2 (primary series, original booster) was consistently associated with improved absenteeism, presenteeism, work productivity loss, and activity impairment compared with unvaccinated individuals.

Limitations

- A limited number of studies were identified, which were conducted in only three countries (US, Greece, and Israel) across various time periods. Consequently, findings may not be generalizable to all individuals eligible for vaccination, including populations considered to be at increased risk for severe COVID-19 outcomes (e.g., those at high-risk such as the elderly or immunocompromised).
- All studies identified reported outcomes following BNT162b2 vaccination. More research is needed to assess whether other COVID-19 vaccines and more recent formulations (XBB.1.5, JN.1 or KP.2) offer the same benefits for HRQoL and work productivity following SARS-CoV2 infection.
- Further, despite the value of EQ-5D and WPAI data, no studies used COVID-specific instruments, which could provide disease-specific HRQoL information.

CONCLUSION

- **Studies consistently showed that vaccination with BNT162b2 (primary series and booster) is associated with smaller reductions in HRQoL and work productivity following SARS-CoV-2 infection compared with being partially vaccinated or unvaccinated, primarily due to reduction in symptom burden.**
- **These data support the broader benefits of COVID-19 vaccination beyond traditional measures of vaccine effectiveness to enhance overall HRQoL.**
- **Future studies are needed to better understand the impact of updated vaccines on HRQoL and work productivity within the context of the evolving COVID-19 landscape.**

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