# Side effects of BNT162b2 mRNA COVID-19 vaccine: A randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers.

Concerns are prevailing about the safety and side effects of the BNT162b2 mRNA vaccine for coronavirus disease 2019 (COVID-19).

A randomized, cross-sectional study was performed to investigate the side effects of the BNT162b2 vaccine using an independent online questionnaire gathering responses from healthcare workers (HCWs) with detailed review of organ systems.

Of all HCWs, 87.98% (1245/1415) completed the survey. Of them, 64.5% (803/1245) received the BNT162b2 mRNA vaccine and reported at least one or more symptoms (classified based on organ systems and occurrence rate) post vaccination. Of these, 640/803 (79.7%) were able to continue activities of daily living (ADL), 103/803 (12.83%) had trouble temporarily to perform ADL, 99/803 (12.33%) took time off work temporarily, 20/803 (2.49%) required help from an outpatient provider, 5/803 (0.62%) required help from an emergency department and 2/803 (0.25%) required hospitalization. Despite this, 97.61% intended to have the second dose and 92.9% had already received it.

Commonly reported symptoms (occurrence in descending order) were soreness, fatigue, myalgia, headache, chills, fever, joint pain, nausea, muscle spasm, sweating, dizziness, flushing, feelings of relief, brain fogging, anorexia, localized swelling, decreased sleep quality, itching, tingling, diarrhoea, nasal stuffiness and palpitations. Despite this, remarkable acceptance for the second dose of the BNT162b2 vaccine was found among HCWs.



Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has caused a global pandemic in a short period of time, imposing challenges on medical services, researchers, epidemiologists and policy makers about the nature of the virus; and posing challenges for a successful vaccine outcome (

Umakanthan et al., 2020

Middeldorp et al., 2020

Rodriguez-Morales et al., 2020

The US Food and Drug Administration has authorized two mRNA vaccines to prevent COVID-19: the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech) on 11 December 2020, and the mRNA-1273 COVID-19 vaccine (Moderna) on 18 December 2020. On 12 December 2020, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for the use of a two-dose regimen of the BNT162b2 mRNA vaccine (which was shown to have 95% efficacy in protection against COVID-19) in persons aged ≥16 years (

CDC COVID-19 Response Team, 2021b

Overall, the COVID-19 mRNA-based vaccination programme has generated many concerns, questions and continuing arguments concerning the safety issues of both the new mRNA vaccines among HCWs and the general population in the USA. A recent study on self-reported side effects with the mRNA-1273 vaccine among HCWs showed a broad spectrum of symptomatology, with most symptoms being non■life threatening, and high acceptance of the vaccine among HCWs (

Design and sample selection

After obtaining institutional review board approval, a cross-sectional study was conducted by circulating an independent online survey questionnaire through an internet-based survey platform (Survey Monkey), which gathered anonymous responses from HCWs from verified healthcare communities representing various parts of the country during the early phase of COVID-19 vaccination. No personal identifications were obtained. The Survey Monkey web link was distributed to coordinators of healthcare institutions and verified communities of HCWs via social media (e.g. Facebook). Informed consent was obtained at the beginning of the survey. Participants who voluntarily agreed and consented to proceed and who chose to receive one of the two mRNA-based COVID-19 vaccines were automatically allowed to move forward to answer subsequent questions about the side effects and other variables. Those who chose ‘None of them’ were diverted to a disqualified page. The study obtained feedback in anonymous mode regarding the side-effect and benefit profile during the post-vaccination period.

The Survey Monkey web link was left open and kept active to collect responses for approximately 6 weeks. The responses were collected between 24 January 2021 and 10 March 2021.

Responses were obtained from 1415 HCWs (

Classification of survey responses from healthcare workers (HCWs).

This study primarily focused on the BNT162b2 mRNA vaccine. Of the 1245 vaccine recipients who completed the survey, 803 (64.5%) received the BNT162b2 mRNA vaccine and 35.5% (442) received

the mRNA-1273 vaccine (

Demographic data of study participants reporting receipt of BNT162b2 mRNA vaccine.

Percentage responded (%)

Doctorate or professional medical degree

High school graduate (working in healthcare setting)

HCWs, healthcare workers.

In total, 92.9% of the HCWs who received the BNT162b2 mRNA vaccine had received both doses and 7.1% had only received the first dose at the time of this study. Those who had received the BNT162b2 vaccine reported various symptoms based on their complete review of organ systems: localized symptom/s, 719/803 (89.54%); generalized symptom/s, 610/803 (75.97%); musculoskeletal symptom/s, 428/803 (53.3%); gastrointestinal symptom/s, 172/803 (21.42%); psychological/psychiatric symptom/s, 133/803 (16.56%); neurological symptom/s, 102/803 (12.7%); head/ear/eyes/nose/throat symptom/s, 97/803 (12.08%); endocrine symptom/s, 83/803 (10.34%); cardiovascular symptom/s, 48/803 (5.98%); respiratory symptom/s, 21/803 (2.61%); urinary symptom/s, 10/803 (1.24%); and allergic symptom/s (other than localized/generalized rash), 10/803 (1.24%) (

Event rate classified based on review of organ systems and descending order of occurrence.

Symptoms after the first and/or second dose of the BNT162b2 mRNA vaccine

Number of HCWs reporting symptom (

Generalized symptom/s

Generalized weakness/fatigue

Localized swelling at the injection site

Lymphadenopathy (axillary or regional)

Residual skin discoloration

Musculoskeletal symptom/s

Arthritis/joint pains

Muscle stiffness/spasm

Gastrointestinal symptom/s

Psychological and/or psychiatric symptom/s

Feelings of joy/relief/gratitude

Decreased sleep quality

Manic/hypermanic mood changes

Neurological symptom/s

Brain fogging or reduced mental clarity/attention/concentration

Vertigo like symptoms

Paralysis/extremity weakness

Reactivation of shingles

Loss of consciousness/fainting

Head/ear/eyes/nose/throat symptom/s

Ringing sensation in ears

Heat/cold intolerance

Increased urine production

Cardiovascular symptom/s

Blood pressure changes

Respiratory symptom/s

Urgent need to urinate

Frequent urination at night

Difficulty in urination

Pain or burning on urination

Swelling in mouth/ throat

Swelling of lips or tongue

Effect on activity or need for medical attention

Trouble to perform regular daily living activities temporarily

Required transient time off from work

Required to seek help from outpatient provider

Required to seek help from emergency department provider

Required to hospitalize and subsequent inpatient care

HCWs, healthcare workers.

Included in localized and allergic symptom classification.

Included in gastrointestinal and endocrine symptom classification.

The main generalized symptoms that were reported were generalized weakness or fatigue (58.9%, 473/803), headache (44.83%, 360/803), chills (35.99%, 289/803), fever (22.04%, 177/803), sweating (9.22%, 74/803), dizziness (8.34%, 67/803) and flushing (7.1%, 57/803).

Approximately 88.04% (707/803) of HCWs reported a sore arm or pain at the injection site as their primary localized side effect, followed by localized swelling at the injection site (5.48%, 44/803), itching (5.35%, 43/803), lymphadenopathy (axillary or regional) (3.36%, 27/803), rash (2.49%, 20/803), residual skin discoloration (1.25%, 10/803) and bleeding (0.37%, 3/803).

Musculoskeletal symptoms

Myalgia (muscle pain) (45.7%, 367/803), arthritis or joint pain (16.56%, 133), and muscle stiffness/spasm (9.59%, 77/803) were reported by the recipients. Of note, paradoxically, two HCWs (Participants #38 and 915) with a prior history of chronic psoriasis reported improvement in their psoriatic symptoms.

Gastrointestinal symptoms

Nausea (15.94%, 128/803), diarrhoea (4.61%, 37/803), decreased appetite (5.73%, 46/803), abdominal pain (3.11%, 25/803), vomiting (1.49%, 12/803), heartburn (1.12%, 9/803) and constipation

(0.37%, 3/803) were reported by the recipients.

Psychological or psychiatric symptoms

Decreased sleep quality (5.35%, 43/803), feelings of joy/relief/gratitude (6.35%, 51/803), anxiety (2.49%, 20/803), increased sleep (2.12%, 17/803), psychological stress (0.75%, 6/803), decrease in memory (0.75%, 6/803), manic/hypermanic mood changes (0.37%, 3/803), depression (0.37%, 3/803) and behavioural changes (0.12%, 1/803) were reported by the recipients.

Neurological symptoms

Brain fogging or reduced mental clarity/attention/concentration (5.85%, 47/803), tingling of the extremity at the injection site (4.86%, 39/803), numbness (2.86%, 23/803), vertigo-like symptoms (2.49%, 20/803), paralysis/extremity weakness (0.62%, 5/803), lack of coordination (0.5%, 4/803), loss of consciousness/fainting (0.25%, 2/803), facial weakness (0.12%, 1/803) and seizures (0.12%, 1/803) were reported by the recipients. Of note, two participants reported reactivation of herpes or shingle-like lesions after receiving the vaccine.

Head/eyes/ears/nose/mouth/throat symptoms

Nasal stuffiness (4.61%, 37/803), sore throat (2.99%, 24/803), runny nose (2.24%, 18/803), ringing sensation in the ears (1.99%, 16/803), ear pain (0.87%, 7/803), blurred vision (0.5%, 4/803), eye pain (0.87%, 7/803), changes in hearing (0.37%, 3/803), flashing lights (0.25%, 2/803), hoarseness (0.37%, 3/803), ear discharge (0.12%, 1/803) and bleeding gums (0.12%, 1/803) were reported by the recipients.

Decreased appetite (5.73%, 46/803), heat or cold intolerance (3.24%, 26/803), increased thirst (1.2%, 9/803), increased appetite (0.87%, 7/803) and increased urine production (0.25%, 2/803) were reported by the recipients.

Cardiovascular symptoms

Palpitations/racing heart (4.36%, 35/803), chest pain (1.12%, 9/803), and blood pressure changes and syncope (0.87%, 7/803) were reported by the recipients.

Shortness of breath (1.99%, 16/803), coughing (0.87%, 7/803) and wheezing (0.25%, 2/803) were reported by the recipients.

Allergic/skin symptoms (except for rash)

Hives (0.62%, 5/803), swelling of the lips (0.12%, 1/803), swelling in the mouth/throat (0.37%, 3/803) and atopic eczema (0.25%, 2/803) were reported by the recipients.

Urgent urination (0.75%, 6/803), increased frequency of urination (0.37%, 3/803), difficulty in urination (0.12%, 1/803) and dysuria (0.12%, 1/803) were reported by the recipients.

The extent of the impact of these symptoms on the vaccine recipients was evaluated. Overall, 640/803 (79.7%) had no issues and were able to continue their daily routine activities, 103/803 (12.83%) had trouble to perform regular daily activities temporarily, and 99/803 (12.33%) required time off work temporarily. Only 20/803 (2.49%) needed help from an outpatient provider, 5/803 (0.62%) needed help from an emergency department provider, and 2/803 (0.25%) needed hospitalization and subsequent inpatient care (

Infection rate among vaccinated group

In total, 10/803 HCWs (1.25%) reported that they had tested positive for COVID-19 during the period between the first and second doses of the BNT162b2 vaccine, and no HCWs reported that they had tested positive for COVID-19 after the second dose of the BNT162b2 vaccine.

Benefits of vaccines other than for COVID-19

In total 2.14% (12/803) HCWs reported improvement or resolution of chronic symptoms after receiving the BNT162b2 vaccine. Specifically, two HCWs with a prior history of chronic psoriatic arthritis reported improvement in their psoriatic joint pain.

This study aimed to analyse the safety and detailed side-effect profile of the BNT162b2 vaccine among HCWs in the USA. Based on the above results, vaccine recipients can primarily expect the following symptoms during the early phase of the post-vaccination period: localized soreness; generalized weakness; myalgia; headache; chills; fever; joint pain; and nausea. Muscle stiffness or spasm, sweating, dizziness, flushing, feelings of joy/relief/gratitude, brain fogging or reduced mental clarity/attention/concentration, decreased appetite, localized swelling at the injection site, decreased sleep quality, itching, tingling, diarrhoea, nasal stuffiness, palpitations and/or high heart rate were reported as other predominant symptoms. Of note, 97.61% of the BNT162b2 vaccine recipients intended to receive a second dose of the vaccine irrespective of side effects after the first dose, conflicting schedules and personal apprehension. Moreover, 92.62% of the BNT162b2 vaccine recipients had already received their second dose by the time they responded to the survey.

At this point, the aetiology of side effects or reactions to the BNT162b2 vaccine remains unclear. The CDC estimates suggest that anaphylaxis (trouble with breathing, swelling of the face and throat, rash, low blood pressure) occurs soon after vaccination in 11 cases per million doses among recipients of the BNT162b2 vaccine (

CDC COVID-19 Response Team, 2021b

As such, in accordance with the CDC guidelines, it is recommended that all vaccine recipients should be observed for at least 15 min after receiving the vaccine, with adrenaline available at the vaccination site in case it is needed. It is the inactive ingredients or excipients (including egg protein, gelatin, formaldehyde, thimerosal and neomycin), rather than the active ingredients, that cause the allergic reactions. CDC recommends that individuals with a history of anaphylaxis to polyethylene glycol (PEG), PEG derivatives or polysorbate should avoid both mRNA COVID-19 vaccines (

In this study, 10 HCWs (1.25%) reported that they had tested positive for COVID-19 during the period between the first and second doses of the BNT162b2 vaccine. There are concerns about whether COVID-19 can be caused by the vaccine; however, this is unlikely because these mRNA vaccines did not use live SARS-CoV-2 virus in their development. If COVID-19 is observed soon after vaccination, it is improbable that it is caused by the vaccine; instead, the infection may have been caused by failure of the vaccine (studies on this are in progress), pre-existing infection before vaccine administration or infection at the time of vaccination.

There is a need to monitor further reports on the side effects of the vaccines as the vaccination programme continues. Approximately 6.35% of vaccine recipients reported feelings of joy/relief/gratitude post vaccination, and less than 2.5% of participants stated that they have decided not to have the second dose. These can be taken as positive signs. At best, most of the vaccine recipients (HCWs) took the challenge to end the deadly pandemic, irrespective of side effects experienced by them. Nevertheless, before receiving an mRNA vaccine that acts against this deadly virus, which has caused millions of deaths worldwide within 1 year, vaccine recipients need to balance the risks of possible non-life threatening adverse events with the potential benefit.

This study has several limitations. As this was an independent study investigating detailed self-reported symptoms through anonymous responses, the receipt of vaccine doses by study participants and their reported symptoms were not verified or confirmed, or recorded or documented officially by the study investigators. Most of the symptoms reported above occurred in the early post-vaccination phase of the vaccine. The latent effects of this vaccine were not studied or included in this study. No specific data on the initial timing of the onset of symptoms after vaccine administration or the duration of symptoms were obtained in this study. Some respondents may have incorrectly blamed the vaccine for several systemic side effects that they developed soon after vaccination, although symptoms of their pre-existing chronic medical problems may have contributed to these side effects, or they could be an unfortunate coincidence from new underlying medical problems that were not related to the vaccine. Chronic medical problems, such as heart attacks, blood disorders, cancer, stroke and other rare illnesses, occurred before the pandemic and will continue to occur. Acute and chronic health issues may be triggered after vaccine administration, as shown in this study, where two HCWs reported reactivation of herpes or shingle-like infections. The vaccine could be found to be responsible if a thorough investigation is performed and if certain health problems occur at a higher-than-normal rate. If not, it is more likely to be an unfortunate coincidence that these effects occurred after administration of the vaccine. Other examples, including rare cases of Bell’s palsy and other neurological diseases, have been reported since administration of the COVID-19 vaccine; however, to date there is no clear suggestion that the vaccine played any role. Similarly, it was reported that a physician in Florida developed a fatal blood disorder after receiving a COVID-19 vaccine, which raised concerns that it was triggered by the vaccine, although this condition did not occur among the tens of thousands of subjects in the clinical trials (

This detailed review of organ systems found that localized soreness, generalized weakness, myalgia, headache, chills, fever, joint pain and nausea were the most commonly reported symptoms, followed by muscle stiffness or spasm, sweating, dizziness, flushing, feelings of joy/relief/gratitude, brain fogging or reduced mental clarity/attention/concentration, decreased appetite, localized swelling at the injection site, decreased sleep quality, itching, tingling, diarrhoea, nasal stuffiness, palpitations and/or high heart rate. The majority (97.61%) of the vaccine recipients intended to receive a second dose of the vaccine, irrespective of side effects after the first dose, conflicting schedules and personal apprehension. This

indicates a remarkable acceptance rate for this vaccine, which can be considered as a positive sign. At best, most of the vaccine recipients (HCWs) took the challenge to end the deadly pandemic, irrespective of side effects experienced by them. If COVID-19 occurs after vaccination (1.25% of vaccine recipients in this study reported that they had tested positive for COVID-19 in the period between the first and second doses), this is unlikely to be caused by the vaccine; instead, the infection may



## Citation

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