Six Month Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine

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ABSTRACT

Background BNT162b2 is a lipid nanoparticle-formulated, nucleoside-modified RNA vaccine encoding a prefusion-stabilized, membrane-anchored SARS-CoV-2 full-length spike protein. BNT162b2 is highly efficacious against COVID-19 and is currently authorized for emergency use or conditional approval worldwide. At the time of authorization, data beyond 2 months post-vaccination were unavailable.

Methods In an ongoing, placebo-controlled, observer-blinded, multinational, pivotal efficacy study, 44,165 ≥16-year-old participants and 2,264 12-15-year-old participants were randomized to receive 2 doses, 21 days apart, of 30 μg BNT162b2 or placebo. Study endpoints reported here are vaccine efficacy (VE) against laboratory-confirmed COVID-19 and safety data, both up to 6 months post-vaccination.

Results BNT162b2 continued to be safe and well tolerated. Few participants had adverse events leading to study withdrawal. VE against COVID-19 was 91% (95% CI 89.0-93.2) through up to 6 months of follow-

up, among evaluable participants and irrespective of previous SARS-CoV-2 infection. VE of 86%-100% was seen across countries and in populations with diverse characteristics of age, sex, race/ethnicity, and COVID-19 risk factors in participants without evidence of previous SARS-CoV-2 infection. VE against severe disease was 97% (95% CI 80.3−99.9). In South Africa, where the SARS-CoV-2 variant of concern, B.1.351 (beta), was predominant, 100% (95% CI 53.5, 100.0) VE was observed.

Conclusion With up to 6 months of follow-up and despite a gradually declining trend in vaccine efficacy, BNT162b2 had a favorable safety profile and was highly efficacious in preventing COVID-19. (ClinicalTrials.gov number, NCT04368728)

Competing Interest Statement

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf

Clinical Trial

NCT04368728

Funding Statement

Supported by BioNTech and Pfizer.

Author Declarations

I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.

Yes

The details of the IRB/oversight body that provided approval or exemption for the research described are given below:

The trial was conducted in accordance with the protocol, the ethical principles derived from international guidelines including the International Council for Harmonisation Good Clinical Practice Guidelines, the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, and applicable laws and regulations (including applicable privacy laws). An independent data monitoring committee reviewed efficacy and unblinded safety data. Institutional Review Board or Ethics Committee approval was obtained for each site prior to enrollment of any study participant. The list of Institutional Review Board Committees is summarized at the end of the Supplementary Appendix.

All necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived.

Yes

I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance).

Yes

I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable.

Yes

Paper in collection COVID-19 SARS-CoV-2 preprints from medRxiv and bioRxiv

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Preprint discussion sites covering this article:

PUBPEER PubPeer, 25 Aug 2021

out work-up.

^ | v • Reply • Share ›

Red • 8 days ago

This paper is missing one very crucial piece of information: 6-month adverse event followup. Table S3 still reports only adverse event counts up to 1 month after the second dose, but nothing about longer followup periods. This is a violation of a commitment from the study's protocol where it was stated that 6-month safety data will be reported (section 9.5.1). And the only reason I can think of why such a data was not reported is because it suggests the treatment is not as safe as it is claimed.

13 ^ | v • Reply • Share ›

Medhat Khattar • 9 days ago

How is it correct to have used **only saline** as **placebo** injection, when the composition of the vaccine includes a range of compounds, most notably lipids?

1 ^ | v • Reply • Share ›

Madeline Harvey ↗ Medhat Khattar • 6 days ago

Saline is the correct placebo, a placebo should not have anything that would affect normal physiology. You are comparing something that shouldn't affect the body compared to something that will. In this case the vaccine (and all the components of the vaccine including the lipids).

3 ^ | v • Reply • Share ›

Anthony Loera • 10 days ago

Supplementary data shows deaths between Vaccine people and controls are close to even https://www.medrxiv.org/con...

2 ^ | v 1 • Reply • Share ›

ND ↗ Anthony Loera • 8 days ago

In table S4, the reported cause of deaths in vaccine arm like Arteriosclerosis, Cardiac arrest, Cardiac failure congestive and Hypertensive heart disease, which are not reported in the placebo arm could be a possible result of the microscopic blood clots described by Canadian physician Dr Charles Hoffe here https://www.globalresearch.... that he is finding via d-dimer test results in 62% of his vaccinated patients. It doesn't look like FDA asked Pfizer to provide d-dimer test data for clinical trial participants before approving the vaccine.

4 ^ | v • Reply • Share ›

vinu arumugham ↗ Anthony Loera • 8 days ago

https://www.medrxiv.org/con...

^ | v 1 • Reply • Share ›

circleofmamas ↗ Anthony Loera • 9 days ago

Did you see the 3 additional deaths after unblinding? They were all in people who had then received the vaccine. So not even.

2 ^ | v • Reply • Share ›

Dan Miller • 13 days ago

Where is table 4 ?

1 ^ | v • Reply • Share ›

vinu arumugham ➚ Dan Miller • 8 days ago

If you mean Table S4, it is in the supplementary material:
https://www.medrxiv.org/con...

^ | v 1 • Reply • Share ›

Steve Kirsch • 14 days ago

There were two people in the placebo group who got the drug after the unblinding. The paper never talks about the cause of death from those two people. This is EXTREMELY important. Does anyone know?

6 ^ | v • Reply • Share ›

carbsane • 17 days ago

Can someone PLEASE explain to me how there can be 850 cases of COVID among the placebo group through March 13th if most of that group was subsequently vaccinated?? According to Pfizer's website they began unblinding and vaccinating in December (pretty much after the EUA), as they reported that as of Jan 29th 3,624 placebos had been FULLY vaxxed. Their last reported numbers (before dropping the information from their weibsite) were on Feb 24th by which time 16,904 had received at least one dose of vaccine.

^ | v • Reply • Share ›

Dillon Burke ➚ carbsane • 14 days ago

The study started April 29, 2020 so what are you asking?
(ClinicalTrials.gov number, NCT04368728)

^ | v • Reply • Share ›

BiotechObserver ➚ carbsane • 15 days ago

There were over 20,000 in the placebo group to begin with, and most of the 850 cases occurred long before March. They state that the VE calculations in this paper only include still-blinded participants and events. Ie, if someone chose to unblind and/or switch from placebo to vax, cases that occur to them will not be included in the analysis. I believe that's what this sentence indicates:
"VE analyses during the blinded period are presented for all randomized ≥12-year-olds without known HIV infection who received ≥1 BNT162b2 or placebo dose"

^ | v • Reply • Share ›

questionable02848 • 21 days ago

I am interested in seeing a similar study done on Recovered versus Vaccinated cases over some years. It is **theoretically** possible that Recovery (despite original virus death rate) confers greater defense than Vaccinated (despite lower original virus death rate) because Recovery forms a superior, longer-lasting, or greater-breadth immune response. This is important to consider for coronavirus specifically due to its tendency to mutate. The studies I have seen indicate that the Recovered do have a greater immunity than the Vaccinated, as studied here: https://www.biorxiv.org/con...

And so, if Recovered do in fact fare better when exposed to mutations, we really want to know

this before we vaccinate the young, who do not face a statistically significant threat from coronavirus but have many years ahead of them facing its mutations.

4 ^ | v • Reply • Share ›

Jeff Brender ➚ questionable02848 • 15 days ago • edited

https://www.cdc.gov/mmwr/vo...
Kentucky residents who were not vaccinated had 2.34 times the odds of reinfection compared with those who were fully vaccinated (odds ratio [OR] = 2.34; 95% [CI] = 1.58–3.47) (likely the Alpha strain based on the date)

^ | v • Reply • Share ›

pasiii ➚ Jeff Brender • 8 days ago

More scientific theory being promoted as scientific fact. Did you read the assumptions? And what about this line: "Finally, this is a retrospective study design using data from a single state during
a 2-month period; therefore, these findings cannot be used
to infer causation. Additional prospective studies with larger
populations are warranted to support these findings.". I hate when people use this type of study to support their political agenda, and then claim that I don't believe in science. THIS IS NOT SCIENTIFIC FACT!

3 ^ | v • Reply • Share ›

Truenorth 1960 • 21 days ago

I'm not sure I understand this study. While I understand this is a report that is intended for professionals, the l language is not English, it is "technobable" for lack of a better expression. For covid , these studies should have a translation into something more akin to regular English. Narrative should help understand the results. In this case I find the narrative is not helpful, it is easier to look at the tables.

2 ^ | v • Reply • Share ›

Josie Richardson ➚ Truenorth 1960 • 6 days ago

That is the role of scientific reporters/journalists to translate this kind of information. Scientific papers are written for their peers in the scientific community and regulatory bodies. For this reason it needs to be in technobabble and follow certain standards. It is not designed to be a widely read article with a narrative. While the research in this Covid arena has been made available for lay people, there is no expectation that we would all understand it.

^ | v • Reply • Share ›

Jeff Brender ➚ Truenorth 1960 • 15 days ago • edited

Vaccine effectiveness went down roughly 3% a month after the second shot (Table 2)
No side effects showed up beyond what you get in the first few days

^ | v 1 • Reply • Share ›

Maria Ranetti ➚ Jeff Brender • 5 days ago

No side effects showed up, if you don't count the deaths, neurological problems, etc.

1 ^ | v • Reply • Share ›

Magnus Thorssten ➚ Jeff Brender • 13 days ago

Please inform the CDC! They were just on television today telling us effectiveness drops so low boosters are recommended 8 months after second dose. They will be glad to here it's not so bad per what you have astutely pointed out in this study.

2 ^ | v • Reply • Share ›

vinu arumugham • 25 days ago • edited

Table S4 shows 4 deaths in the vaccine arm and 1 death in the placebo arm due to cardiac arrest.
The probability that this outcome is a chance occurrence is 1.5%.

(((21999÷22000)^21996)×((1÷22000)^4)×(22000!))÷(21996!×4!) =0.0153 or 1.5%.
So 98.5% chance that the vaccine CAUSED the excess cardiac arrest deaths.

Table S4 also shows 1 excess COVID-19 related death in the placebo arm.
So to prevent 1 COVID-19 related death, the vaccine causes at least 3 deaths due to cardiac arrest.

8 ^ | v 1 • Reply • Share ›

paul S ➚ vinu arumugham • 3 days ago • edited

That chance of rolling snake eyes with two die is 2.7%. If you roll snakes eyes twice in a row (.08%), that is not a sign you have loaded dice. The correct approach is below, Fisher Exact Test which demonstrates your, "4 deaths in the vaccine arm and 1 death in the placebo arm" is not statistically significant.

^ | v • Reply • Share ›

circleofmamas ➚ vinu arumugham • 17 days ago

Good finding Vinu. Also really appreciate your paper on food proteins in vaccines, I reference it often :)

Another troubling finding from this paper, is the 5 additional deaths after unblinding, 3 from the vaccine group, and 2 originally from the placebo group who then got the vaccine, and died. So this brings another numerical imbalance: 20 deaths in the vaccine group / 14 deaths in the placebo group.

No additional deaths in the placebo group after unblinding who did not get the vaccine.

7 ^ | v 2 • Reply • Share ›

Tim Freeman ➚ vinu arumugham • 23 days ago

You picked that row out of 26 other rows, so you have to correct for multiple analyses. To a first approximation that multiplies the odds of seeing something like that by accident by 26, so not significant.

4 ^ | v 2 • Reply • Share ›

Joe ➚ Tim Freeman • 7 days ago • edited

Exactly!, same table S4, myocardial infarction in control group =2, and in vaccinated = 0. Do that means that vaccine protects for myocardial infarction?, NO!. Stop fear mongering VINU ARUMUGHAM. Learn to read phase 2/3 trial data. Look at the comorbities across patients and statistical significance as

data. Look at the comorbities across patients and statistical significance as mentioned below.

Reply • Share ›

vinu arumugham ➚ Tim Freeman • 22 days ago

Why would the other 26 rows affect this outcome?

2 | 1 • Reply • Share ›

Isaac Demme ➚ vinu arumugham • 14 days ago

For a humorous explanation of why, see https://xkcd.com/882/

Reply • Share ›

Ken ➚ vinu arumugham • 14 days ago

Everything is wrong with your calculations. The correct test is Fishers exact which gives a p-value of 0.375. This is the sum of the probability of the observed or more extreme data under the null. So no difference. The 26 rows are important, as under the null hypothesis the distribution of the p-value is uniform on 0,1. If I randomly take a sample of 26 uniform(0,1) there is a high probability that one of them will be less than 0.05, so we use a correction for multiple comparisons. No need as the p-value is 0.375.

2 | 1 • Reply • Share ›

paul S ➚ Ken • 4 days ago • edited

I got 0.39. If you find the time, can you show a bit more work for me. It has been a long time. Thanks

Reply • Share ›

vinu arumugham ➚ Ken • 8 days ago

What is the probability that 4 deaths in the vaccine arm and 1 death in the placebo arm due to cardiac arrest, are due to chance?

Reply • Share ›

Jeff Brender ➚ vinu arumugham • 15 days ago • edited

The odds of finding some apparently unusual result in a large amount of random data is high.\
https://en.wikipedia.org/wi...
https://en.wikipedia.org/wi...

1 • Reply • Share ›

circleofmamas ➚ Jeff Brender • 14 days ago

I don't know why you three are dismissing this, because there is already a signal for increased risk of myocarditis and pericarditis after mRNA vaccination. The elevated risk was observed for both females and males, male ages spanning 12-49 were at an increased risk of heart inflammation. We should be paying attention, not dismissing potential signals.

6 | Reply • Share ›

Tim Freeman ➚ circleofmamas • 5 days ago

I already says why I am dismissing this. "correct for multiple analyses" works as search keywords with high ranking results that explain the statistics. If you already have a signal for increased risk of myocarditis, then use that, but the claim I replied to is junk.

^ | v 1 • Reply • Share ›

zega ➚ circleofmamas • 12 days ago

Muddying the waters for some reason, if it is known that spike-protein is causing endothelial damage, hence makes sense that vaccine causes myocarditis and pericarditis and other CVD events, hence you should keep close eye on that group, but no, we should care about car crash deaths and cancer deaths in this short period of time...just muddy the water

2 ^ | v • Reply • Share ›

Giannis Liasis • 25 days ago

- In the treatment group (N=21,926), 1 covid death
- In the placebo group (N=21,921), 2 covid deaths

So, one reading is that the treatment reduces 50% the deaths.
Another reading is that the covid death rate in the placebo group is 0.00009 (2 / 21,921 = 0.00009), which is double than the treatment group, but Influenza and pneumonia deaths (15.2 / 100.000 = 0.000152 (1)) are 68,8% higher (0.000152 / 0.00009 = 1.688) than the covid deaths.

So, should we have this treatment in our arsenal ?
Yes.

Should it be mandatory for everyone ?
Considering the fact that the treatment for influenza is not mandatory, then this treatment should also not be mandatory.

However, this is just my opinion which may be wrong, and if it is wrong I would like to hear why it is wrong

1. https://www.cdc.gov/nchs/fa...

6 ^ | v 2 • Reply • Share ›

BiotechObserver ➚ Giannis Liasis • 15 days ago

These participants were followed for covid deaths only for about a 6 month period. The "rate" you calculated is not static and only reflects the 6 month timeframe. Most of us plan to live longer than 6 months. Deaths go up over time as the virus spreads and more get infected. We've seen multiple waves of this virus now. So the relative risk reduction is what matters.

1 ^ | v • Reply • Share ›

Holger L. ➚ BiotechObserver • 6 days ago

The relative risk reduction is never what matters, because a relative reduction from 0,0001% to 0,00005% may be 50%, but as anybody can see will be practically meaningless overall. In fact, such a treatment will be detrimental if

there is *any* chance of side effects which is higher than that and a monetary cost associated with the treatment.

According to the original Pfizer study, the relative risk reduction is 94,6%, whereas the total risk reduction is only 0,73% (within that study, from 0,77% to 0,04%). It is still a significant reduction, however that will also diminish with certain age groups, especially children.

https://www.nejm.org/doi/fu...

And now you shouldn't even begin arguing with the "risk over a certain time span", such as multiple years, because then you'd also have to take into account that a virus may develop immune evasion and/or booster shots will be necessary.

• Reply • Share ›

BiotechObserver ➚ Holger L. • 3 days ago

"because a relative reduction from 0,0001% to 0,00005% may be 50%"
This would only be true if we were dealing with a problem we knew nothing about, pretended to know nothing about, or if we operated under the mistaken idea that Covid is not an issue. But we know that it is. Telling me in vague terms the absolute rate of covid hospitalization is "low" or the absolute covid mortality risk is "low" - Well, congrats, but that does not accurately portray the gravity of this disaster.
There are hundreds of thousands who died in the US.

"virus may develop immune evasion" is always another last resort fantasy like "what about long term effects" --- All imagination. If that would happen, bets would be off, but that hasn't happened. In the meantime, the vaccine is beneficial. It's been 8 months now. There is no evading variant. And you could make the exact same argument about immunity via infection recovery. What if one day the virus evades that immunity? So what? At this point, it hasn't.

• Reply • Share ›

Michael Kowalik ➚ Giannis Liasis • 21 days ago • edited

In a randomised controlled study the only controlled properties are those of Intervention vs No-Intervention; everything else is speculation, not a controlled part of the study. All we get from these figures is that the relative risk of death is 12.5% higher for the vaccinated vs the unvaccinated: (18-16)/16. Because all the pre existing conditions and health factors are distributed randomly between Intervention and non-Intervention arms, the necessary causal conclusion in RCT is that the 12.5% extra deaths are in fact CAUSED by the intervention. This clarity of conclusion is literally the only reason to undertake RCTs.

1 3 • Reply • Share ›

circleofmamas ➚ Michael Kowalik • 21 days ago

Where did you get this? "All we get from these figures is that the relative risk of death is 12.5% higher for the vaccinated vs the unvaccinated: (18-16)/16."

Are you looking at overall deaths?

1 • Reply • Share ›

Michael Kowalik ➚ circleofmamas • 19 days ago

Yes, cumulative deaths in both arms of the study, including 5 additional deaths recorded after unblinding. I just had another read and it turns out that all these 5 additional deaths were among the vaccinated; 3 previously vaccinated and 2 from the placebo arm but then died only after being vaccinated. So we now have 20 dead after the vaccine and 14 among the unvaccinated. The Relative Risk of Death for the Vaccinated post unblinding is (20-14)/14 = 43% more than for the unvaccinated. If we count just the deaths during the blinded period, we get 7%; (15-14)/14.

4 ^ | v 1 • Reply • Share ›

paul S ➚ Michael Kowalik • 4 days ago • edited

Inclusion of deaths during the open-label period raises the number to 18 BNT162b2 and 16 placebo. Where do you get 20 .... never mind. Got it.

^ | v • Reply • Share ›

questionable02848 ➚ Michael Kowalik • 21 days ago

Michael, how would we determine whether this 12.5% difference in death is not “noise” given the small number of deaths? Is it not the case that were you to randomly split 40,000 people into two groupings without any intervention, that you would see one group have a higher death rate than the other, simply due to chance?

1 ^ | v • Reply • Share ›

Michael Kowalik ➚ questionable02848 • 8 days ago

The authors indeed do not give us the p-value for the relative risk of death, so it is possible that statistical significance was not established, but this is a moot point anyway. If this result is not statistically significant then Pfizer has failed to show that their product does not kill more people than it saves, and the product should be withdrawn as safety is in doubt. If the result is statistically significant then the product kills more people than it saves and should be withdrawn, because it is proven to cause net harm.

In either case, even a statistically insignificant result that suggests the product kills more people than it saves should raise alarm bells, pending statistically significant evidence to the contrary.

1 ^ | v • Reply • Share ›

Ewin Barnett • a month ago

Am I the only person wondering where the discussion of the autopsy results was published? In fact VAERS is now easily over 5,000 vaccine-related deaths yet zero autopsies.

4 ^ | v 2 • Reply • Share ›

Giannis Liasis ➚ Ewin Barnett • 22 days ago

Please, be evidence based and share the source that supports your claim (5,000 deaths)

4 ^ | v 2 • Reply • Share ›

pedro paulo castro ➚ Giannis Liasis • 20 days ago

It's VAERS

2 ^ | v 1 • Reply • Share ›

Giannis Liasis ➚ pedro paulo castro • 18 days ago

Where is the exact link that supports the claim ?

^ | v • Reply • Share ›

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