Let's be cautious and first see the full data

Peter Doshi, PhD

Associate professor, University of Maryland School of Pharmacy

Associate editor, The BMJ

https://faculty.rx.umaryland.edu/pdoshi/

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FINANCIAL DISCLOSURES

I have received travel funds from the **European Respiratory Society (2012)** and **Uppsala Monitoring Center (2018)**; grants from the **Laura and John Arnold Foundation (2017-21), American Association of Colleges of Pharmacy (2015), Patient-Centered Outcomes Research Institute (2014-16), Cochrane Methods Innovations Fund (2016-18),** and **UK National Institute for Health Research (2011-14);** and am a paid editor at **The BMJ** and unpaid member of the **Reagan-Udall Foundation for the FDA**.

Summary

- Salary from University of Maryland & The BMJ
- Public, foundation, and non-profit funding of academic research
- Reimbursement (e.g. lodging, travel) from non-profits
- No industry funding

We need rigorous analyses of the raw data

1. **To be assured the study was not unblinded**
   - High rate of adverse events on vaccine may have informally unblinded trial through reasonable guessing
   - Without testing all symptomatics, a true Covid-19 case would go uncounted
   - Analysis needed of people with Covid-19 symptoms were referred for PCR testing

2. **To be assured that pain/fever relief drugs did not confound the analyses**
   - Greater use of medicines in vaccine arm → greater suppression of symptoms (including those from SARS-CoV-2 infection) → less testing → less likelihood of meeting primary endpoint
   - But apparent reduction in Covid-19 in this case was driven by medicines, not vaccine
   - What were patients told regarding use of pain/fever reducing medicines?
   - Analysis needed of pain/fever medicine use in vaccine vs. placebo group

3. **To be assured that all "severe Covid-19" cases in trial were actually severe disease**
   - A mild Covid-19 case with SpO2 ≤ 93% would meet the "severe Covid-19" case definition
   - Nov. 18 press release does not list any hospitalizations, ICU use, or deaths among 10 "severe cases"

Have these analyses been conducted?

Are data publicly available for independent verification?

Possible unblinding through reasonable guessing?

Overlap between Covid-19 symptoms & very common vaccine adverse events

Frequency of AEs in trials[1]

- fatigue (> 60%)
- headache (> 50%)
- myalgia (> 30%)
- chills (> 30%)
- arthralgia (> 20%)
- fever (> 10%)

Primary endpoint definition[2]

At least 1 of the following:

- Fever or chills
- Cough
- Shortness of breath or difficulty breathing
- Fatigue
- Muscle or body aches
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea

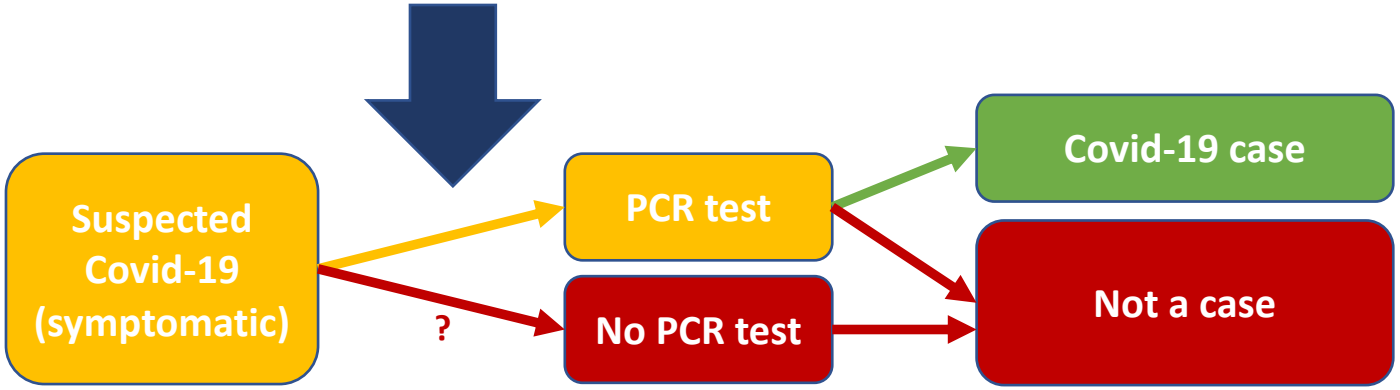
+ Lab-positive test

Sources

1 UK label. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/940565/Information_for_Healthcare_Professionals_on_Pfizer_BioNTech_COVID-19_vaccine.pdf

2 Phase 3 trial protocol. https://pfe-pfizercom-d8-prod.s3.amazonaws.com/2020-09/C4591001_Clinical_Protocol.pdf

Were all symptomatic cases tested?



Study protocol:

"During the 7 days following each vaccination, potential COVID-19 symptoms that overlap with solicited systemic events (ie, fever, chills, new or increased muscle pain, diarrhea, vomiting) should not trigger a potential COVID-19 illness visit unless, in the investigator's opinion, the clinical picture is more indicative of a possible COVID-19 illness than vaccine reactogenicity."[1]

Source: Protocol page 88. https://pfe-pfizercom-d8-prod.s3.amazonaws.com/2020-09/C4591001_Clinical_Protocol.pdf

Were all "severe Covid-19" cases actually severe?

Trial definition allows mild Covid-19 cases with SpO2 ≤ 93% to qualify

SpO2 ≤92% in 1 in 20 normal, asymptomatic, community dwelling ≥65+ population

Table 2. Peripheral Blood Oxygen Saturation According to Age and Sex

Method	%, Median (Interquartile Range)	Percentile 5,%	Percentile 1,%	N
≥65				
Total				
Method 1	96.0 (94.0–97.0)	91.0	85.0	636
Method 2	96.0 (94.0–97.0)	**91.8**	80.0	182
Female				
Method 1	96.0 (95.0 -97.0)	91.0	86.4	418
Method 2	96.0 (94.0–97.0)	**91.0**	87.6	106
Male				
Method 1	95.0 (94.0–97.0)	88.0	84.4	218
Method 2	95.0 (94.0–97.0)	**92.0**	80.0	76
≥80				
Total				
Method 1	96.0 (94.0–97.0)	89.0	83.9	399
Method 2	95.0 (94.0–97.0)	**90.7**	84.4	77
Female				
Method 1	96.0 (94.0–97.0)	89.0	81.6	264
Method 2	96.0 (94.0–97.0)	**90.2**	87.0	52
Male				
Method 1	95.0 (94.0–97.0)	89.0	85.2	135
Method 2	95.0 (94.0–97.0)	**89.1**	84.0	25

Method 1: excluding cases with factors influencing the results, according to the multivariate analysis (dyspnea at the moment of examination and history of chronic obstructive pulmonary disease).

Method 2: (author's recommended limit in bold face): more-restrictive analysis excluding cases with factors influencing the results, according to the bivariate analysis. Dyspnea and history of asthma, chronic obstructive pulmonary disease, use of specific respiratory medications, cardiac disease, anemia, or smoking were excluded.

Source: Rodríguez-Molinero et al. 2013 J Am Geriatr Soc, 61: 2238-2240. https://doi.org/10.1111/jgs.12580

Conclusions

- **The most crucial questions about BNT162b2 remain unanswered**
  - Does it reduce **severe Covid-19, hospitalization, ICU use, or death?**
  - Does it reduce **spread of SARS-CoV-2?**
  - Is it equally effective in **subgroups at highest risk** (e.g. elderly, frail)?
  - What is its **duration of protection** and **safety** e.g. at 3/6/12 months?

- **An EUA will undermine placebo-controlled follow-up**
  - **Expanded access** can provide vaccine to those who cannot wait for evidence that benefits outweigh risks

- **Only full transparency and rigorous scrutiny of the data will allow for informed decision making**

Contact: Peter Doshi, PhD, https://faculty.rx.umaryland.edu/pdoshi/