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RESEARCH ARTICLE

Efficacy and safety parameters of a novel COVID-19 vaccine

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Abstract: Considering the fact that vaccine efficacy may be a difficult concept for physicians and health officials alike, we decided to explain it using data from the first publication on the efficacy and safety of a COVID-19 vaccine produced by Pfizer/BioNTech. We examined the published data and calculated common epidemiological parameters such as RRR (relative risk reduction), RR (relative risk), ARR (absolute risk reduction) and NNT (number needed to treat) for 3 groups of patients as described in the original paper. Further, we calculated safety parameters for the vaccine as NNH (number needed to harm) for any, related and severe side effects as mentioned by the investigators. We argue that both NNT and NNH are necessary estimates of how a vaccine might perform in real life and that a robust understanding of efficacy is vital for patients and health care providers as well as health officials in order to make responsible and balanced policy decisions regarding vaccination.

Keywords: COVID-19, vaccine, efficacy and safety, RRR, RR, ARR, NNT, NNH

1 Introduction

We are presenting here our viewpoint on the data shown in the paper by Polack *et al*. published Dec 31 2020 in N Engl J Med [1]. This article, the first that was peer-reviewed and published on the subject of efficacy and safety of a COVID-19 vaccination produced by Pfizer/BioNTech, will soon be a reference for further studies. It already constitutes a basis for decision making on public health policies around the world (*e.g.* massive vaccinations). However, according to us, the paper does not sufficiently explain how the efficacy is to be understood against the background of common epidemiological knowledge and a few important parameters are missing.

2 Methods

To follow the logic of the authors and examine their calculations we divided their results into 3 groups, Group I: Cases with no evidence of existing or prior infection and with onset at least 7 days after the second dose; Group II: Cases with and without evidence of prior infection and with onset at least 7 days after the second dose and Group III: cases between the first and second dose. Then we calculated the estimates of efficacy, that we consider necessary, for each of the group I, II, III (Table 1 ,Table 2 ,Table 3 , respectively). The summary of safety parameters as calculated by us are presented separately, in Table 4.

3 Results

In the section Statistical Analysis, the authors write as follows: "Vaccine efficacy was estimated by 100×(1-IRR), where IRR is the calculated ratio of confirmed cases of COVID-19 illnesses per 1000 person-years of follow-up". According to us, the above formula is an equivalent of RRR (relative risk reduction), shown as a percentage, *i.e.* 100×(1-RR), a parameter commonly used in epidemiological studies (2). The fact that we calculated **RRR** in the three groups as 95%, 94.6%, 53%, respectively, and the values are almost identical with what was presented as corresponding efficacies in the paper confirms the logic behind it. Calculating backwards we estimated **RR** (relative risk) as ratios: 0.05, 0.0536 and 0.474, respectively and **ARR** (absolute risk reduction) as percentages: 0.836%, 0.795%, 0.2%, respectively. However, both RR and ARR are missing from the original paper, which makes it difficult for less

Table 1 Group I: Cases with no evidence of existing or prior infection and with onset at least 7 days after the second dose

	BNT162b2	Placebo
Cases	8	162
Participants (available for efficacy evaluation: total 36523)	18198	18325
AR	0.00044 = 0.044%	0.0088 = 0.88%
ARR	0.88%-0.044% = 0.836%	N.A.
NNT	100: 0.836 = 120	120 (people must be vaccinated in order to protect 1 person from developing symptoms of COVID-19)
RR	0.00044: 0.0088 = 0.05	N.A.
RRR = efficacy	1-0.05 = 0.95 = 95%	N.A.

Table 2 Group II: Cases with and without evidence of prior infection and with onset at least 7 days after the second dose

	BNT162b2	Placebo
Cases	9	169
Participants (available for efficacy evaluation: total 40137)	19965	20172
AR	0.00045= 0.045%	0.0084 = 0.84%
ARR	0.84% - 0.045% = 0.795%	N.A.
NNT	100: 0.795 = 125.7	126 (people must be vaccinated in order to protect 1 person from developing symptoms of COVID-19)
RR	0.00045:0.0084 = 0.0536	N.A.
RRR = efficacy	1-0.0536 = 0.946 = 94.6%	N.A.

Table 3 Group III: cases between the first and second dose

	BNT162b2	Placebo
Cases	39	82
Participants	21669	21686
AR	0.0018=0.18%	0.0038 = 0.38%
ARR	0.38% - 0.18% = 0.2%	N.A.
NNT	100: 0.2 = 500	500 (people must be vaccinated in order to protect 1 person from developing symptoms of COVID-19)
RR	0.0018: 0.0038 = 0.474	N.A.
RRR = efficacy	1 - 0.474 = 0.526 = 52.6% = 53%	N.A.

Table 4 Safety (provided for 43252 participants with variable follow-up time after the 1^{st} dose)

	BNT162b2	Placebo
Any adverse events	27% = 0.27	12% = 0.12
Attributable risk	27% - 12% = 15% = 0.15	N.A.
NNH	1: 0.15 = 6.6	1 in ca. 7 vaccinated persons developed any adverse events
Related adverse events	21% = 0.21	5% = 0,05
Attributable risk	21% - 5% = 16% = 0.16	N.A.
NNH	1: 0.16 = 6.25	1 in ca. 6 vaccinated persons developed related adverse events
Serious adverse events	0.6%	0.5%
Attributable risk	0.6% - 0.5% = 0.1% = 0.001	N.A.
NNH	1: 0.001 = 1000	1 in 1000 vaccinated persons experienced serious adverse events

epidemiologically versed physicians, as well as the lay public to translate the vaccine efficacy into real life situations.

It is important to stress that the relative risk (RR) is a ratio of infection risks of vaccinated to non-vaccinated persons in a trial and cannot make any predictions about whether and how many vaccinated people will get ill when exposed to the virus.

NNT (number needed to treat) is missing from the report. We find it disturbing because it is the single most important parameter for a clinician as well as a health policy official to estimate the effectiveness of the intervention. According to us, the NNT of the BNT162b2 is high: 120, 126, 500, respectively, which shows that either the condition was rare or the intervention was relatively not effective.

Our calculations on safety of BNT162b2 are based on the data presented in the paper and are summarised for 3 different groups of adverse effects: any adverse effects, related adverse effects and serious side effects (see Table 4). However, from the paper's section Safety, the **NNH** (number needed to harm) is missing. It is unfortunate as both NNT and NNH are necessary to make a sound benefit-side effects analysis as well as a cost-effectiveness evaluation. We estimated NNH for BNT162b2 in the corresponding groups (any, related and severe side effects) as ca. 7, 6 and 1000, respectively.

4 Conclusions

The incorrect understanding of efficacy is currently influencing public health policies in many countries, *e.g.* in Germany on the "vaccination consent form" for patients we can find the following explanation: "According to the current level of knowledge, approx. 95 out of 100 vaccinated persons are protected from becoming ill" [3] (status from the 16.01.2021), which was never examined in the first place. The paper's authors themselves, however unintentionally, may suggest this interpretation by writing "A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age and older" in the Conclusions section.

Further, as the paper is translated into other languages the word "efficacy" may be mistaken for "effectiveness" and presented as such by the media ("efficacy" being translated into German as "Wirksamkeit" and Polish as "skutecznosc", both meaning more or less the same as "effectiveness" in the two languages). However, efficacy trials like described by Polack *et al.* [1] are not the same as effectiveness trials. The difference between efficacy and effectiveness known as "implementation gap" [2] should be kept in mind when establishing health policy measures.

In respect to safety, the frequency of severe adverse reactions (NNH = 1000) seems to be problematic in a situation of (semi-mandatory) vaccinating of at least 50% of the population (as planned by some governments, *e.g.* in Poland) [4]. It is also important not to neglect to mention that the increase in harmful effects in the vaccine arm as compared with the placebo was twofold (27% versus 12%) regarding any adverse events, and fourfold regarding related adverse events (21% *vs.* 5%).

We have decided to present our viewpoint on the recently published data in order to start a well-meaning and inclusive discussion among healthcare workers and health authorities towards more transparency around the important issue of vaccination as well as to provide a balanced view of a novel Covid-19 vaccine.

References

[1] Polack FP, Thomas SJ, Kitchin N, *et al*. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. The New England Journal of Medicine, 2020, **383**(27): 2603-2615. http://doi.org/10.1056/NEJMoa2034577

[2] Fletcher R. Clinical epidemiology: The Essentials. Lippincott Williams & Wilki; 5. Edition, 2012.

[3] Aufklärungsmerkblatt zur COVID-19-Impfung mit mRNA-Impfstoff (rki.de).

[4] Rzad chce zaszczepić na COVID-19 połowe Polaków. Start już w lutym (wyborcza.pl).

