Side Effects After Vaccination Using the Pfizer-Biontech (Bnt162b2) Against Sars-Cov-2 in the Young Adults

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Research Article

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Abstract

Background:

In order to limit the spread of the SARS-CoV-2 virus, national immunization programs have started in many countries. Vaccinations are effective in preventing infection and severe clinical form of COVID-19, which affects 15% of patients. Despite the high efficacy of The Pfizer-BioNTech (BNT162b2) vaccine, the characterization of side effects in age-stratified populations is still not exhaustive in the literature.

Aim:

The aim of our study is to determine what side effects affect the population of young adults following vaccination with the Pfizer-BioNTech vaccine (BNT162b2).

Material and methods:

An anonymous survey was conducted. People vaccinated with two doses of the SARS-CoV-2 vaccine (BNT162b2) were qualified for the study. The Paired Wilcoxon and Fisher's exact tests were used for statistical analysis.

Results:

The main side effects after the first dose were increased pain, pain and swelling at the injection site. After the 2nd dose, the dominant side effects were weakness, fever and headache. In the case of the 2nd dose, no difference in side effects was observed between those who suffered of COVID-19 and those who had no symptoms of COVID-19 in their past medical history.

Key Messages

- Vaccination against SARS-CoV-2 is safe

- Local side effects dominate after the first dose

- Systematic side effects dominate after the second dose

Introduction

SARS-CoV-2 (primarily 2019-nCoV) infection causing the COVID-19 disease, only three months after the diagnosis of the first case, was declared as a pandemic by the World Health Organization on March 11, 2020[1].

Due to the lack of effective and cheap treatment of COVID-19, the main goal was prevention by using vaccines. Since December 2020 national vaccination programs have started in many countries in order to limit the transmission of the virus[2]. As of December 12, 2020, the European Commission has signed six advance purchase agreements with: Astra Zeneca, Sanofi-GSK, Janssen Pharmaceutica NV / Johnson & Johnson, Pfizer / BioNTech, CureVac and Moderna for a total of 62.06 million doses of vaccines. Vaccinations show clinically significant efficacy against contracting COVID-19 and a severe course of illness. At the moment, the literature does not exhaust the incidence and characteristics of adverse effects in stratified populations due to age. As of October 23, 2021, 38.6M doses have been administered to the Polish population and 19.8 M are fully vaccinated, which is 52.3% of the population.[3].

The aim of our study is to characterize side effects after the first and second dose. As well as their frequency and duration in the young adults. And also how the time interval beetwen doses, previous symptoms of COVID-19, positive antigen/RT-PCR results and the presence of Anti-SARS-CoV-2 antibodies affects duration and occurance of side effects.

Materials

Research procedure

An anonymous survey was conducted.

The questions concerned local side effects (NRS (numeric rating scale), shoulder pain, duration of arm pain, redness or swelling, lymphadenopathy) and systemic side effects (weakness, headache, fever, chills, weakness). In addition, a general medical history of the last 16 months was collected.

Before the survey had been made available on students forums, it was validated on 38 people. In numerical questions, Cronbach's Alpha was 0.891. The average time to complete the questionnaire was 4 min 39 seconds.

The time interval between vaccination and completion of the questionnaire did not show a normal distribution. It showed the features of a linear increasing function in proportion to the time interval of filling. The median was 76 days and the mod was 37.

Studied group

The survey was completed by 175 people. 123 people were included in the study. The study excluded people who did not meet the age criteria, who were vaccinated with only one dose, and who were vaccinated with a vaccine other than the Pfizer-BioNTech vaccine (BNT162b2).

The subjects included in the study were between 18-30 years old and were vaccinated with two doses of The Pfizer-BioNTech vaccine (BNT162b2) (Table 1).

Table 1

Qualitative description of the medical history persons qualified to the research in the last 16 months

Variable and symptom		-
Age (years)	mean±SD	23,56±2,06
	median	24
	quartiles	23 - 24
Sex	Female	77 (62,60%)
	Male	46 (37,40%)
Feeling weak	No	42 (34,15%)
	Yes	81 (65,85%)
Raised temperature	No	67 (54,47%)
	Yes	56 (45,53%)
Sore throat	No	61 (49,59%)
	Yes	62 (50,41%)
Cough	No	71 (57,72%)
	Yes	52 (42,28%)
Taste or smell disturbances	No	103 (83,74%)
	Yes	20 (16,26%)
Diarrhea	No	81 (65,85%)
	Yes	42 (34,15%)
Rhinitis	No	54 (43,90%)
	Yes	69 (56,10%)
Enlarged lymph nodes	No	88 (71,54%)
	Yes	35 (28,46%)
Positive RT-PCR test	No	109 (88,62%)
	Yes	14 (11,38%)
Positive serological test	No	109 (88,62%)
	Yes	14 (11,38%)

The protocol of the study was approved by The Bioethics Committee of the Jagiellonian University (No. 1072.6120.92.2021). Every person was informed about methods and purpose of the research. Informed consent was obtained from each participant in the study. All methods were performed in accordance with the relevant guidelines and regulations.

Statistics

For group comparison we performed the Paired Wilcoxon test to compare two repeated measures of quantitative variables, Chi-squared test (with Yates' correction for 2x2 tables) was used to compare qualitative variables among groups. In case of low values in contingency tables, Fisher's exact test was used instead, Mann-Whitney test was used to compare quantitative variables between two groups.

Significance level for all statistical tests was set to 0.05 ($p < 0.05$, 95% CI)

R 4.1.1. was used for computations. The calculations were performed using the following programs: RStudio, R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/ for macOs Catalina v.10.15.4 (Apple, Inc., Cupertino, CA, USA)

Results

To comprare quantitive side-effect after 1st and 2nd dose, we used Wilcoxon paired test, that demonstrated that the Severity of Pain (NRS) and duration of pain or swelling at the injection site were significantly greater after the fisrt dose.

The duration of muscle or joint pain, weakness and headache was significantly longer after the second dose (Table 2), (Figure 1).

Table 2
Comparison of side-effect after 1st and 2nd dose, using p-wilcoxon paired test

Adverse effects		After dose 1	After dose 2	p
Pain [NRS]	mean±SD	3,89±1,88	3,07±2,31	p<0,001
	median	4	3	
	quartiles	3 - 5	1 - 5	
Pain or swelling of application place [days]	mean±SD	2,37±1,67	1,92±1,95	p=0,008
	median	2	2	
	quartiles	1 - 3	0 - 3	
Muscles and joints pain [days]	mean±SD	1,27±2,21	1,67±2,34	p=0,011
	median	0	1	
	quartiles	0 - 2	0 - 2	
Feeling weak [days]	mean±SD	1,82±2,63	2,42±2,59	p=0,001
	median	1	2	
	quartiles	0 - 2	0,5 - 3	
Shivers [days]	mean±SD	0,63±1,74	0,79±1,49	p=0,078
	median	0	0	
	quartiles	0 - 0	0 - 1	
Fever [days]	mean±SD	0,85±2,16	0,9±1,67	p=0,295
	median	0	0	
	quartiles	0 - 0	0 - 1	
Headache [days]	mean±SD	0,84±1,69	1,26±2,06	p=0,003
	median	0	0	
	quartiles	0 - 1	0 - 2	
Enlarged lymph nodes [days]	mean±SD	0,64±1,91	0,72±2,02	p=0,466
	median	0	0	
	quartiles	0 - 0	0 - 0	
Dyspnoea [days]	mean±SD	0,22±1,3	0,14±0,94	p=0,572
	median	0	0	
	quartiles	0 - 0	0 - 0	
Problems with memory [days]	mean±SD	0,34±1,71	0,37±1,75	p=0,832
	median	0	0	
	quartiles	0 - 0	0 - 0	

Qualitative Comparison of side-effect after 1st and 2nd dose with The Fisher's exact test showed that pain or swelling at the injection site was more common after dose 1. Feeling of weakness, chills, fever and headache were more common after dose 2. (Figure 2), (Table 3).

Table 3
Comparison of side-effect after 1st and 2nd dose, fisher's exact test

Adverse effects	Dose		p
	After dose 1 (N=123)	After dose 2 (N=123)	
Pain or swelling of application place	112 (91,06%)	90 (73,17%)	p<0,001
Muscles and joints pain	56 (45,53%)	69 (56,10%)	p=0,126
Feeling weak	71 (57,72%)	92 (74,80%)	p=0,007
Shivers	24 (19,51%)	46 (37,40%)	p=0,003
Fever	23 (18,70%)	50 (40,65%)	p<0,001
Headache	39 (31,71%)	57 (46,34%)	p=0,026
Enlarged lymph nodes	17 (13,82%)	20 (16,26%)	p=0,721
Dyspnoea	6 (4,88%)	6 (4,88%)	p=1
Problems with memory	6 (4,88%)	6 (4,88%)	p=1

Comparison side effects after 1st dose with and without positive RT-PCR. Based on the qualitative comparisons made using Fisher's exact test after the first dose among people who were positive for RT-PCR compared to those who were negative "fever" occurred more often in the group with a positive RT-PCR test", Fever: Fisher's exact test (Positive RT-PCR 14 (12.84%), No-RT-PCR 9 (64.29%), p <0.001).

The quantitive comparison In people with positive RT-PCR or serological tests "chills, fever, headache and memory problems appeared more often in the group with positive RT-PCR or serological tests", Shivers 15 (14.71%): 9 (42.86%) p = 0.006, Fever 13 (12.75%): 10 (47.62%) p = 0.001, Headache 28 (27.45%): 11 (52.38%) p = 0.048, Problems with memory 1 (0.98%): 5 (23.81%) p = 0.001 .

Analogical calculations performed using Fisher's exact test showed no statistically significant differences after the second dose.

A qualitative comparison of the occurrence of side effects depending on the difference in the time interval between doses intake (below and above 25 days) was also performed, showed no statistically significant difference.

To compare quantitative side-effect after 1st dose with and without positive RT-PCR, P - Mann-Whitney test showed that the duration of pain or swelling at the injection site, feelings of weakness, fever and headache was significantly greater in the group with positive RT-PCR results, after the first dose (Table 4), (Figure. 3).

Table 4
Comparison of side-effet after 1st dose with and without positive RT-PCR and Positive RT-PCR or serological test.

Adverse effects		Positive RT-PCR test 1st dose (p-Mann-Whitney test)		p	Positive RT-PCR or serological test 1st dose (P - MANN-WHITNEY TEST)		p
		No (N=109)	**Yes (N=14)**		**No (N=102)**	**Yes (N=21)**	
Pain [NRS]	mean±SD	3,8±1,88	4,57±1,79	p=0,166	3,75±1,86	4,57±1,89	p=0,094
	median	4	4,5		3,5	4	
	quartiles	3 - 5	3 - 5		3 - 5	3 - 6	
Pain or swelling of application place [days]	mean±SD	2,26±1,55	3,29±2,27	p=0,04	2,2±1,5	3,24±2,17	p=0,012
	median	2	3		2	3	
	quartiles	1 - 3	2 - 4		1 - 3	2 - 4	
Muscles and joints pain [days]	mean±SD	1,12±1,97	2,43±3,44	p=0,087	1±1,76	2,57±3,46	p=0,032
	median	0	1		0	1	
	quartiles	0 - 1	0 - 2,75		0 - 1	0 - 4	
Feeling weak [days]	mean±SD	1,61±2,47	3,43±3,32	p=0,034	1,48±2,39	3,48±3,14	p=0,005
	median	1	2,5		1	3	
	quartiles	0 - 2	0,25 - 5,75		0 - 2	0 - 6	
Shivers [days]	mean±SD	0,46±1,36	2±3,28	p=0,058	0,38±1,24	1,86±2,99	p=0,002
	median	0	0		0	0	
	quartiles	0 - 0	0 - 3,25		0 - 0	0 - 2	
Fever [days]	mean±SD	0,45±1,46	4±3,74	p<0,001	0,41±1,36	3±3,65	p<0,001
	median	0	4		0	0	
	quartiles	0 - 0	0 - 7,5		0 - 0	0 - 6	
Headache [days]	mean±SD	0,72±1,63	1,79±1,89	p=0,011	0,67±1,56	1,67±2,08	p=0,01
	median	0	1,5		0	1	
	quartiles	0 - 1	0 - 3,75		0 - 1	0 - 3	
Enlarged lymph nodes [days]	mean±SD	0,6±1,77	1±2,8	p=0,894	0,54±1,72	1,14±2,63	p=0,391
	median	0	0		0	0	
	quartiles	0 - 0	0 - 0		0 - 0	0 - 0	
Dyspnoea [days]	mean±SD	0,16±1,01	0,71±2,67	p=0,654	0,15±1,03	0,57±2,2	p=0,272
	median	0	0		0	0	
	quartiles	0 - 0	0 - 0		0 - 0	0 - 0	
Problems with memory [days]	mean±SD	0,28±1,55	0,86±2,68	p=0,088	0,1±0,99	1,52±3,34	p<0,001
	median	0	0		0	0	
	quartiles	0 - 0	0 - 0		0 - 0	0 - 0	

First dose comparison comparison Positive RT-PCR or serological test P - Mann-Whitney test showed that the duration of pain or swelling at the injection site, muscle or joint pain, feelings of weaknes, chills, fever, headache, and memory problems was significantly longer in the RT-PCR or serology-positive group after the first dose (Table 4), (Figure. 4).

To compare person after second dose with Positive RT-PCR or serological test to person without, we performed P - Mann-Whitney test that showed no statistically significant difference. (Table 5)

Table 5
Comparison of side-effet after 2nd dose with and without positive RT-PCR and Positive RT-PCR or serological test. The comparison of side effects depending on time beetwen doses also was made.

Adverse effects		Positive RT-PCR test 2nd dose (p - Mann-Whitney test)		p	Positive RT-PCR or serological test 2nd dose (p - Mann-Whitney test)		p	Time between doses (p - Mann-Whitney test)		p
		No (N=109)	**Yes (N=14)**		**No (N=102)**	**Yes (N=21)**		**Up to 25 days (N=90)**	**Over 25 days (N=33)**	
Pain [NRS]	mean±SD	3,09±2,31	2,86±2,38	p=0,681	3,04±2,31	3,19±2,34	p=0,752	3,16±2,41	2,82±2,02	p=0,547
	median	3	2,5		3	3		3	3	
	quartiles	1 - 5	1 - 3,75		1 - 5	1 - 4		44317	44288	
Pain or swelling of application place [days]	mean±SD	1,95±1,96	1,64±1,86	p=0,608	1,88±1,93	2,1±2,07	p=0,618	1,83±1,93	2,15±2	p=0,315
	median	1	2		1	2		1	2	
	quartiles	0 - 3	0 - 2		0 - 3	0 - 3		0 - 3	44228	
Muscles and joints pain [days]	mean±SD	1,62±2,23	2±3,11	p=0,98	1,54±2,18	2,29±2,97	p=0,388	1,77±2,44	1,39±2,03	p=0,532
	median	1	1		1	1		1	1	
	quartiles	0 - 2	0 - 1,75		0 - 2	0 - 3		0 - 2	0 - 2	
Feeling weak [days]	mean±SD	2,42±2,62	2,43±2,44	p=0,755	2,28±2,51	3,1±2,88	p=0,165	2,71±2,76	1,64±1,87	p=0,041
	median	2	2		2	2		2	1	
	quartiles	44256	0,25 - 3,75		0 - 3	44287		1 - 3,75	0 - 2	
Shivers [days]	mean±SD	0,81±1,47	0,64±1,65	p=0,263	0,8±1,51	0,71±1,42	p=0,723	0,9±1,64	0,48±0,91	p=0,25
	median	0	0		0	0		0	0	
	quartiles	0 - 1	0 - 0		0 - 1	0 - 1		0 - 1	0 - 1	
Fever [days]	mean±SD	0,92±1,73	0,79±1,19	p=0,885	0,9±1,67	0,9±1,73	p=0,846	1±1,79	0,64±1,29	p=0,483
	median	0	0		0	0		0	0	
	quartiles	0 - 1	0 - 1		0 - 1	0 - 1		0 - 1	0 - 1	
Headache [days]	mean±SD	1,32±2,16	0,79±1,05	p=0,654	1,28±2,12	1,14±1,8	p=0,854	1,3±2,2	1,15±1,66	p=0,864
	median	0	0		0	0		0	0	
	quartiles	0 - 2	0 - 1,75		0 - 2	0 - 2		0 - 2	0 - 2	
Enlarged lymph nodes [days]	mean±SD	0,68±1,92	1,07±2,73	p=0,569	0,67±1,91	1±2,53	p=0,664	0,86±2,18	0,36±1,45	p=0,184
	median	0	0		0	0		0	0	
	quartiles	0 - 0	0 - 0		0 - 0	0 - 0		0 - 0	0 - 0	
Dyspnoea [days]	mean±SD	0,16±1	0±0	p=0,376	0,16±1,03	0,05±0,22	p=0,964	0,16±1,08	0,09±0,38	p=0,725
	median	0	0		0	0		0	0	
	quartiles	0 - 0	0 - 0		0 - 0	0 - 0		0 - 0	0 - 0	
Problems with memory [days]	mean±SD	0,32±1,6	0,71±2,67	p=0,662	0,22±1,4	1,1±2,83	p=0,03	0,36±1,81	0,39±1,58	p=0,742
	median	0	0		0	0		0	0	
	quartiles	0 - 0	0 - 0		0 - 0	0 - 0		0 - 0	0 - 0	

The duration of the feeling of weakness after 2nd dose was significantly greater in the group that took the second dose up to 25 days after the first dose (Table 5).

Disscusion

Results presented by Fernando P. Polack et al. also showed a trend towards more systemic symptoms after the 2nd dose. The prevalence of local side effects in our work defined the occurrence of pain after the 1st dose at 91% and 73% after the 2nd dose (in the study mentioned above 87% and 66%, respectively.

Tendencies to increase in systemic symptoms in articles "Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine", "A randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers", "Side effects after COVID-19 vaccinations among residents of Poland" are similar as in our results.

Results presented by Fernando P. Polack et al. in “Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine” a randomized trial was made included results related to local side effects (pain, redness, swelling) and systematic side effects (fever, fatigue, headache, chills, vomiting, diarrhea, muscle pain and joint pain). In the age group of 16-55 after the first dose 83% reported pain, 5% redness, and 7% swelling. Systemic symptoms: fever 4%, fatigue 47%, headache 42%, chills 14%, vomiting 1%, diarrhea 11%, muscle pain 21% and joint pain 11%. In the age group of 16-55 after second dose reported local side effects were as follows: pain 66%, 7% redness, 7% swelling

Systemic side effects: fever 16%, fatigue 59%, headache 52%, chills 35%, vomiting 2%, diarrhea 10%, muscle pain 37% and joint pain 22%

The data in the study was classified qualitatively and categorically (scales of severity of various symptoms) [4].

Results presented by Kadali et.al in “A randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers”. In a randomized cross sectional study in which HCWs (medical workers) were included in the study, the side effects were obtained after the 1st or 2nd dose. Local symptoms: 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), lymphadenopathy (axillary or regional) (3.36%, 27/803). Systemic symptoms: Myalgia (muscle pain) (45.7%, 367/803), arthritis or joint pain (16.56%, 133), weakness or fatigue (58.9%, 473/803), headache (44.83%, 360/803), chills (35.99%, 289/803), fever (22.04%, 177/ 803) decrease in memory (0.75%, 6/803), decreased sleep quality (5.35%, 43/803)[5]

In the publication “Side effects after COVID-19 vaccinations among residents of Poland” Among 196 people vaccinated with the first dose of Pfizer, 124 (63.3%) reported pain at the injection site, 143 (73%) reported shoulder pain, 21 (10.7%) reported muscle aches, 31 (15.8%) reported headaches, 13 (6.6%) reported fever, 13 (6.6%) reported chills, and 47 (24%) reported weakness.

After the second dose of the Pfizer vaccine among 177 individuals who had received the second dose, 101 (57.1%) reported injection site pain, 30 (16.9%) reported shoulder pain, 62 (35%) reported muscle aches, 60 (33.9%) reported headaches, 50 (28%) reported fever, 57 (32.2%) reported chills, and 89 (50.3%) reported weakness[6].

Limitatations

The limitations of the study resulted mainly from the anonymous, not guarded questionnaires. The research group was only 123 but there were enough number of people to show statistically significant data. Another limitation was the time between vaccination and the completed questionnaire. However, it was assumed that due to the young age and the relatively low incidence of memory disorders, these data would not be able to distort the results and conclusions.

Conclusion

1. The Pfizer-BioNTech vaccine (BNT162b2) is safe and the local and systemic side effects are relatively limited in relation to potential severe course of COVID-19 or complications from the disease.
2. The most common side effects after the first dose were the increase in pain, pain duration and swelling at the injection site, local side effects are more common, in case of the second dose, the most common side effects were weakness, fever and headache (generalized side effects).
3. In people who suffered from COVID-19, systemic symptoms dominated after the 1st dose; they resembled side effects after the 2nd dose in people who were not ill.
4. The duration of the feeling of weakness was significantly longer in the group of people vaccined with the second dose up to 25 days after the first.

Declarations

Author Disclosures Conflicts of interest:

None.

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Figures

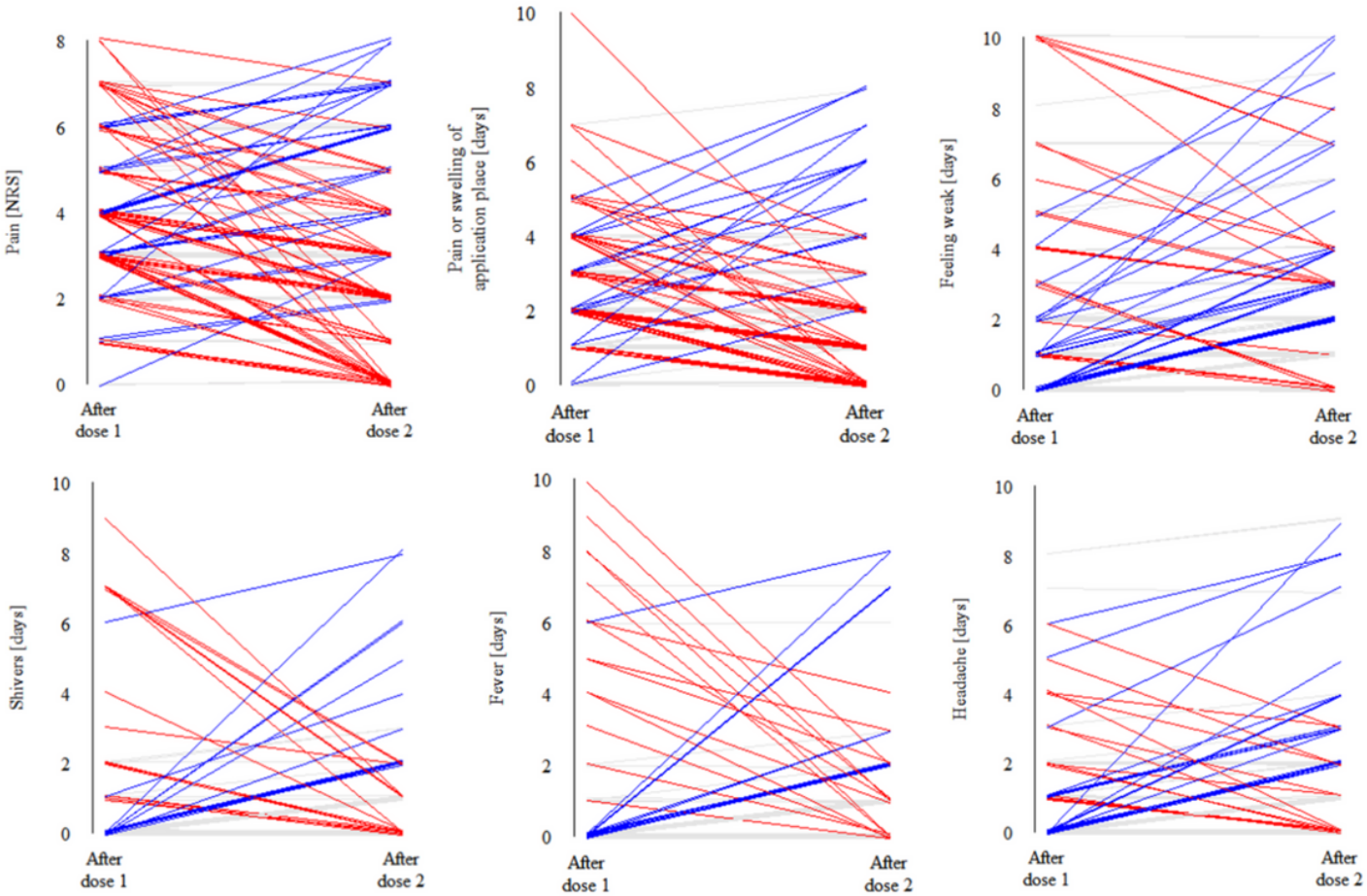

Figure 1

Paralel coordinates plot compares the side effects. Increase side effects blue lines. Deacreasing red lines. Constant Gray lines.

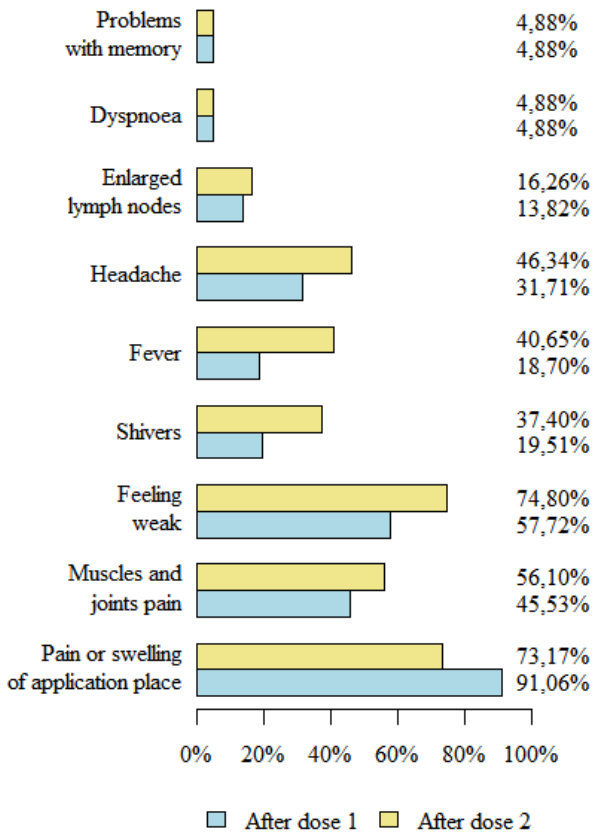

Figure 2

Comparison of side-effect after 1st and 2nd dose, p-chi-squared or fisher's exact test (Tabel. 3)

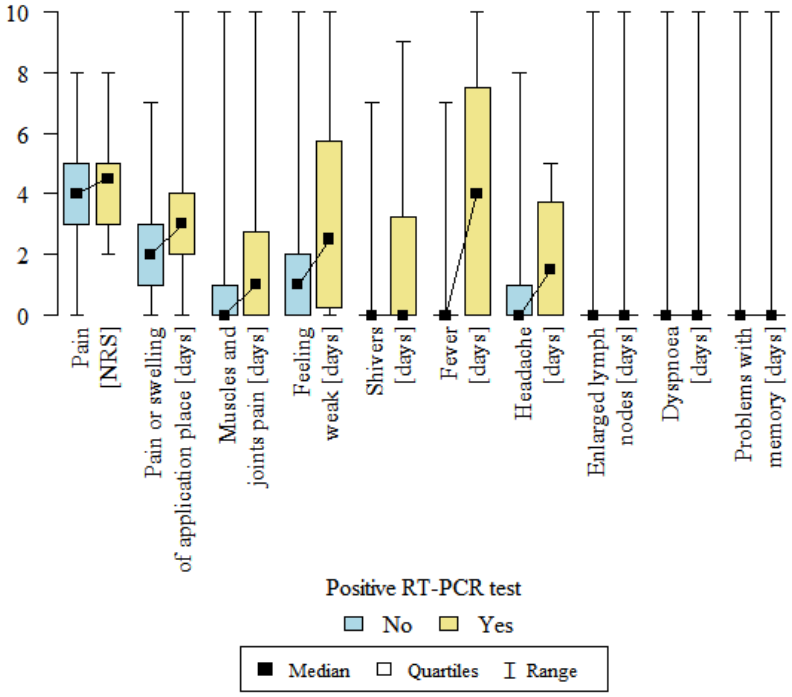

Figure 3

Comparison of side-effect after 1st dose with and without positive RT-PCR, p-Mann-Whitney test (Tabel. 4)

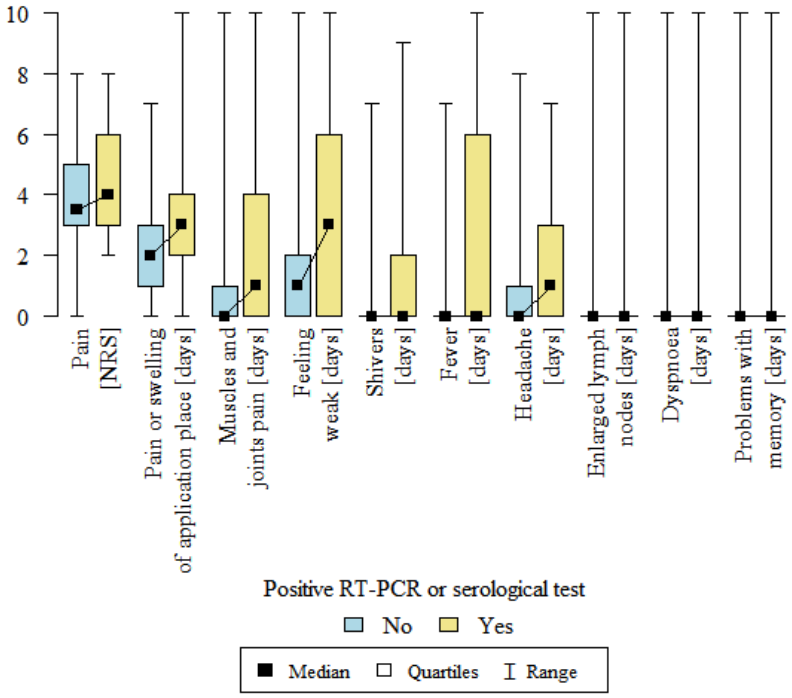

Figure 4

Comparison of side effects after the 1st dose between people with positive RT-PCR or serology versus people who did not have positive tests, p - mann-whitney test (**Tabel. 4)**