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Table 3: Adherence to SARS-CoV-2 vaccination, related factors and vaccine side effects assessed 6 months after the full course.

Total individuals (n)	**Healthcare workers n1 (%)**	**Nursing Students n2 (%)**
	146	81
Fully vaccinated	143 (97.9)	81 (100)
Reasons for vaccination:	**Multi-response n1 (%)**	**Multi-response n2 (%)**
Social responsibility	54 (43.9)	27 (33.8)
Benefits of immunity	45 (36.9)	21 (26.3)
Confidence in vaccine effectiveness	30 (24.8)	14 (17.5)
Working in health care	101 (84.4)	71 (89.9)
Other reasons	1	-
Previous vaccinations (flu):	**n1 (%)**	**n2 (%)**
Flu campaign 2021-22 (Yes)	89 (62.5)	44 (55)
Previous flu campaigns (Yes)	74 (52.1)	22 (27.5)
Type of vaccine:	**n1 (%)**	**n2 (%)**
BioNTech/Pfizer	143 (100)	42 (51.9)
Astra Zeneca	-	37 (45.7)
Moderna	-	2 (2.5)
Exposure to factors related to immunity:	**n1 (%)**	**n2 (%)**
Active smokers	25 (17.6)	7 (8.6)
Weekly alcohol consumption	18(13.2)	6 (7.4)
Adverse reactions 1ª dose	**Vacuna BioNTech/Pfizer n (%)**	**Vacuna Oxf/Astra-Zeneca n (%)**
Insomnia (*)	-	7 (18.9)
Dizziness (*)	4 (2.2)	14 (37.8)
Swelling at injection site	20 (10.9)	7 (19.4)
Shivers (*)	11 (6.0)	32 (86.5)
Fatigue (*)	8 (4.4)	22 (62.9)
Nausea/vomiting (*)	2 (1.1)	13 (35.1)
Diarrhoea (*)	2(1.1)	5 (13.5)
Decreased appetite (*)	2 (1.1)	9 (24.3)
Pain at injection site (*)	92 (50.3)	31 (83.8)
Fiver (*)	10 (5.5)	31 (83.8)
General discomfort (*)	25 (13.7)	31 (83.8)
Myalgia (*)	10 (5.5)	19 (51.4)
Arthralgia (*)	10 (5.5)	19 (51.4)
Pain in the extremities (*)	64 (35.0)	26 (70.3)
Drowsiness (*)	14 (7.7)	29 (78.4)
Adverse reactions 2nd dose	**Vacuna BioNTech/Pfizer n (%)**	**Vacuna Oxf/Astra-Zeneca n (%)**
Dizziness	12 (6.6)	4 (10.8)

Citation: Delicado-Useros Victoria, Navarro-Rodenas Esther, Ortega-Martínez Carmen, Pérez-Domenech Teresa, García-Alcaraz Francisco, Pérez-Serra Juan Daniel and Sánchez-Onrubia Indalecio Miguel. Impact of SARS-CoV-2 Infection in Healthcare Workers and Nursing Students: Incidence, Adherence to Vaccination and Effects of Vaccines . Archives of Microbiology and Immunology. 7 (2023): 405-419.

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Nausea/vomiting	5 (2.7)	4 (10.8)
Swelling at injection site	24 (13.1)	2 (5.4)
Shivers	38 (20.8)	6(16.7)
Fatigue	24 (13.1)	6 (16.7)
Pain at injection site	88 (48.1)	19 (51.4)
Fever	41 (22.4)	11 (29.7)
General discomfort	72 (39.3)	16 (43.2)
Myalgia	33 (18.0)	7 (18.9)
Arthralgia	22 (12.0)	7 (18.9)
Pain in the extremities	65 (35.5)	19 (51.4)
Drowsiness	35 (19.1)	11 (29.7)

Adverse effects: *Those reported in at least 10% of cases in either group are cited. Significant differences were found in the adverse effects of the first dose of BioNTech/Pfizer and Oxf/Astra-Zeneca vaccines. Comparison of proportions was conducted using the Chi-square test (*) p-value <0.001. Differences between side effects in the second dose of BioNTech/Pfizer and Oxf/Astra-Zeneca vaccines were not statistically significant.*

Source: own preparation. Population from the ICM of Almansa (Albacete) and the Albacete Faculty of Nursing (2021). Non-responses have not been reflected but the percentages were calculated for valid data.

Immune response of the groups according to dose and related factors.

Table 4 shows the descriptive values of the IgG levels in each group at 6 months after full vaccination. It should be noted that, in all cases, the immune response was positive (100% seropositivity) and mean IgG values of 3017.4 AU/ml were recorded in (n1) and 2484.6 in (n2). Comparison of the log of these mean IgG values with the t-Student test indicates shows the differences are not statistically significant.

We examined possible variations in IgG levels associated with personal characteristics, such as age and gender, without finding differences that could be considered random, as shown in Table 4, in both the healthcare worker and student populations. The participants were asked about habits related to immunity, such as smoking and alcohol consumption. We found differences between the two populations, which were statistically significant in the case of smoking, with a lower proportion of smokers among the nursing students (n2), where 8.6% were active smokers, than among the healthcare professionals (n1), where 16,7 % smoked. As can be seen in Table 4, IgG levels in the n1 population differ according to smoker status, with significantly lower levels in active smokers than in non-smokers or ex-smokers. This smoking-related variation in IgG is not confirmed in the sample of nursing students. There are also differences in the responses between the two groups in the case of alcohol consumption: weekly alcohol consumption was reported by 13.1% of the healthcare workers (n1) and 7.4% of the students (n2). However, these differences are not statistically significant and are not associated with the mean IgG levels. Another of the study variables found to be associated with significant variations in IgG is the history of COVID-19 infection prior to vaccination, the so-called hybrid immunity. The data in Table 4 show significantly higher mean IgG levels in infected healthcare workers (7520.05 AU/ml) than in their uninfected counterparts (1567.62 AU/ml) (p= 0.000). These significant differences (p= 0.01), albeit not so notable, are also found in the mean IgG values of the students (infected 3802.72 AU/ml; non-infected 2326.04 AU/ml).

Discussion

Populations in studies on healthcare workers consist largely of females, with a high proportion of young adults, which is consistent with our results. For example, a hospital study in Spain [20] found 85.3% women and a mean age of 41 years. Meanwhile, a European study with HCWs from more than 40 countries [21] reported a population with 66% women and a mean age of 42 (±11) years. The COVID-19 pandemic has had a higher incidence in healthcare workers than in the general population. This was revealed in the three-wave ENE-COVID study conducted in Spain in 2020, which estimated an overall prevalence in infected persons of 9.9% and of 16.8% in healthcare workers, a figure close to that found in our work in both groups [22]. Data from a systematic meta-analysis of seroepidemiological studies from 2020 show that seroprevalence was low in the general population (mean 4.5% and IQR 2.4-8.4%), although it varied widely across specific populations and different regions of the world [23]. The work performance and overall health of healthcare workers have been greatly impacted by the pandemic. Working in pandemic conditions exposes health workers to the risk of infection and psychological stress. A European study on HCWs from more than 40 countries revealed a fear of infection at the onset of

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Table 4: Immunity, associated factors and IgG levels in vaccinated population at 6 months. Descriptive statistics and variations.

	Healthcare workers (n1) Ig G 6 months	**Nursing students (n2) Ig G 6 months**
Total individuals (n)	141	79
Mean IgG (95% CI)	3017.4 (2124.48-3910.31)	2484.62 (1590.13-3379.10)
SD	5362.91	3993.45
Minimum	62.6	87.7
Maximum	36644.7	24912.4
Median	1132.6	1266
Interquartile range (IQR)	2020.7	1900
Comparison of IgG log means at 6 months between the two groups: t- Student=0,537 p =0,592		
Sex (mean)	**Healthcare workers (n1) Ig G 6 months**	**Nursing students (n2) Ig G 6 months**
Women	(106) 2782.91	(71) 2546.62
Men	(35) 3727.57	(8) 1934.38
Statistic and p-value	t-Student *=1.117; p=0.266	U-Mann Whitney=272; p=0.845
Age groups	**Healthcare workers (n1) Ig G 6 months**	**Nursing students (n2) Ig G 6 months**
< 35 years	3131.5	Not applicable
35-49 years	2642.8	
≥ 50 years	3663.1	
Statistic and p-value	K-Wallis= 3,847; p = 0.08 (NS)	
Smoking	**Healthcare workers (n1) N (%) and Ig G 6 meses**	**Nursing students (n2) N (%) and Ig G 6 months**
Non-smokers	75(50%) 3912.23	69(85%) 2632.54
Smokers	25(16.7%) 1267.7	7(8.6%) 1113.42
Ex-smokers	42(28.0%) 2701.7	5(6.2%) 2422.10
Statistic and p-value	K-Wallis= 9,916; p= 0.01	K-Wallis=2,256; p=0.324 NS
Occupation exposure to COVID-19	**Healthcare workers (n1) Ig G 6 meses**	**Nursing students (n2) Ig G 6 months**
Yes	(107) 2112.61	(30) 2086.91
No	(22) 7232.53	(41) 2467.81
Statistic and p-value	U de Mann Whitney = 937; P=0.133	U de Mann Whitney = 599,0 p=0.898
COVID-19 history (prior to vaccination)	**Healthcare workers (n1) Ig G 6 meses**	**Nursing students (n2) Ig G 6 months**
Yes	(33) 7520.05	(9) 3802.72
No	(101)1567.62	(65) 2326.04
Statistic and p-value	U de Mann Whitney = 676.0 p = 0.000	U de Mann Whitney= 139 p=0.011

IgG values expressed in AU/ml. All comparisons of IgG means have been performed with non-parametric tests.

The comparison statistic and p-value are shown.

(*) This comparison was conducted using the IgG log mean.

Source: own preparation. Population from the ICM of Almansa and the Albacete Faculty of Nursing (2021). Non-responses have not been reflected although the percentages were calculated for valid data.

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the pandemic: HCWs reported a high level of concern about the risk of COVID-19 infection for themselves (71%) and their family (82%) as a result of their work. A total of 40% of HCWs felt that becoming infected with COVID-19 was beyond their control (21).

In the Spanish salaried population, the impact of temporary incapacity (TI) due to COVID after the early months of the pandemic was evident, and the incidence was multiplied in healthcare and social-health workers compared to the general population (3.6% in the total population, compared to 17.0% in senior carers, 10.5% in nurses and 6.6% in medical staff). The Work and Health Conditions Study, which surveyed more than 20,000 workers in Spain and was published in June 2020 (24), collected data on individuals that had gone to work during the state of emergency with symptoms compatible with COVID-19, finding 13.1% in the study as a whole and much higher proportions in healthcare and social-healthcare occupations (25% in practical nurses, 23% in nurses and senior carers [24]. Our study collected data on the changes in healthcare workers' positions in the early months of the pandemic, which affected one in five professionals. Seroprevalence studies have shown higher values in specific populations and, in particular, the risk for healthcare workers in contact with infected persons is estimated to have been 2.1 times higher compared to their counterparts with no known contact [23]. Studies in specific populations, such as German critical care and emergency doctors, evidence that contact with infected patients increased the risk of infection (overall positive rate of 3.5%), and a large proportion of these (39%) were unaware of their infection [25]. However, the overall rate in German doctors was low compared to other countries, arguably because the German health system was not overwhelmed by the first wave of the pandemic, as occurred in other countries, including Spain. Seroprevalence in healthcare workers was high during the first wave of the pandemic, with two studies conducted in the UK reporting rates of 20% [26] and 27% [27], which are close to our findings, while another work reports a figure as high as 29% [28]. The international study on healthcare workers from 37 countries found that one fifth had previously been infected with COVID-19 [29]. In a study conducted in paediatric and maternity hospital services in Spain, the proportion of healthcare professionals infected with SARS-CoV-2 during the first wave of the pandemic was 20.9% [20], confirming healthcare workers' increased risk of SARS-CoV-2 infection, even in services where the risk of exposure to COVID-19 patients is considered medium. Nonetheless, the data are highly disparate. A systematic review and meta-analysis estimated a weighted mean seroprevalence among healthcare workers before vaccination of 8% (95% CI 6-10%), with variations in this prevalence associated with several circumstances, often external to their professional performance [30]. The study reported that working on the front line was not consistent with higher seroprevalence. Most infected healthcare workers did not present complications, with mild cases predominant in various studies. Less severe symptoms, such as headaches, loss of smell, fever and cough were cited as affecting 40-60% of infected individuals. In one study, the proportion of severe cases requiring hospitalisation was 8% (20) a result that is similar to our findings, albeit slightly higher. Following full vaccination, the incidence of COVID-19 decreased notably [31]. So-called breakthrough infections were rare, mostly mild and asymptomatic cases, with a rate of 2.6% reported among workers at an Israeli hospital (32), which is consistent with our findings. Additionally, the same study reports cases of persistent symptoms (more than 6 weeks) in 19% of those infected post-vaccination [32], a somewhat higher percentage compared to our study.

The report published by the Spanish Association of Public Health and Healthcare Administration describes the impact of the pandemic on primary care (PC), reporting a highly disturbing situation of saturated and exhausted staff, as the large number of patients to be attended was exacerbated by the lack of resources that had accumulated in previous years. A new approach to care orientation was generated, neglecting the capacity of PC to resolve chronic and acute health problems, interrupting health programmes and prioritising tele-care as the predominant model. Continued pressure on care laid bare the crisis in PC, highlighting a high level of dissatisfaction among professionals and users. No solutions have been found, in terms of either investment (human and financial resources) or organisational changes [33]. The various groups of healthcare personnel have shown a high adherence to the pandemic prevention measures, constituting a positive reference for the general population. The capacity to vaccinate large numbers of the population in a short time, with safe and effective vaccines, has proven to be the most powerful tool, bolstering the role of nurses in prevention. Healthcare workers have emerged as the most trusted and influential advisors on vaccination decisions, and, hence, the success of the COVID-19 vaccination programme is primarily influenced by these professionals. As the provision of COVID-19 vaccines generated some controversial reluctance, albeit among a minority, we considered it important to assess adherence to COVID-19 vaccination in healthcare workers, understood as consent or refusal to receive the vaccine. Additionally, we thought it important to examine the reasons that led them to decide to be vaccinated (or to have doubts and avoid vaccination, if applicable). In our study, we found high adherence to the vaccination programme, although 2% of our participants delayed the first dose. A large survey of HCWs in more than 37 countries, conducted at the beginning of the SARS-CoV-2 vaccination process, found that the majority (93%) had been vaccinated

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against COVID-19 or were willing to do so, especially those working on the frontline. In contrast, 6.6% were hesitant and the respondents' main concern was safety or possible side-effects (29). Being a healthcare worker (or similar) is reported as the main motivation in our population groups (more than 85%) and, to a lesser extent (< 50%), participants indicate reasons such as social responsibility, expected benefits and confidence in the vaccines.

In recent years, vaccination for flu has been linked to that for COVID-19, with the aim being to protect the most vulnerable population and alleviate the strain on the health system. We consider that adherence to these vaccines might be related, although the perceived risk is different for each disease. Our data reveal low adherence to flu vaccination in pre-pandemic years, being higher in healthcare workers than in nursing students, and an increase in 2021-2022 compared to previous campaigns. Other studies report similar results, with variations depending on whether the study concerns the general population (lower adherence) or healthcare workers. For example, in 2020, in the autonomous region of Castilla and León, 33.40% of the population was vaccinated against flu, while only 22.3% had been vaccinated in the year before [34].

Our findings are important for the implementation of vaccination strategies for COVID-19 booster doses. The debate on how to enhance vaccine adherence includes determining the reasons for mistrust and whether the information available to the target population is sufficient or could be expanded and doubts resolved. The international study on HCWs launched from the UK [29] clearly shows that unfounded beliefs, distrust and denialism are also present in the small proportion of health workers that were vaccine-hesitant or preferred to wait to see the effect of vaccines in the population. In contrast, the majority of those adherent to vaccines were concerned that vaccines should be available to the world's entire population, being convinced they were the best measure against the pandemic. Among the main reasons for not being vaccinated, 5% cited concerns about safety or potential side effects of vaccines. Although few studies have reported adverse effects of the vaccines, the main findings are substantially consistent: non-serious adverse events, such as pain at the injection site, fever and fatigue, were reported with certain frequency, and no serious adverse events have been evidenced [35], not even those cited as most frequent, such as traumatic venous and arterial traumatic events, facial paralysis, myocarditis and pericarditis, as indicated in the 2023 review by Sadehalvad [36]. The prevalence of complications was higher after the first dose than after the second one [37], coinciding with our findings .

The immune response after the second dose of the vaccine (full course) has been studied, with multiple publications detailing the results according to the type of vaccine and at different times after follow-up. Our findings refer to the IgG level 6 months after full vaccination and are broadly consistent with the findings of works using similar approaches (by vaccine type, population and time of measurement). In studies with a follow-up of several months, a drop in IgG levels was observed between the first month and subsequent measurements (at 4 and 6 months after full vaccination, although almost 100% of the participants showed a reactive antibody response [38] (2) [39]. With regard to variations in IgG levels, there is substantial agreement on a history of previous SARS-CoV-2 infection being a factor that increases immune response, what is known as hybrid immunity [39, 2, 40], as evidenced by our results. This increased robustness of the hybrid immune response led to the proposal of delaying the second vaccination dose in infected individuals in order to make more efficient use of vaccines [39]. Across all the studies evaluating factors associated with variations in IgG levels, some agree with our findings, such as non-smokers having higher antibody titres than smokers [41]. In contrast, some works have reported differences related to age and sex - lower antibody levels in those over 65 years of age and higher levels in women - which were not corroborated in our data, as well as lower IgG values in participants with immunosuppression [42, 38, 41]. It has been suggested that daily alcohol consumption may hinder or limit the level of antibodies post-vaccination. Tamura reports a 15% lower IgG level in daily drinkers compared to non-drinkers [43]. Our study found no association between alcohol consumption and antibody levels, although the most frequent consumption reported in our study population was weekly or occasional. Our study is a further contribution to the body of literature assessing the efficacy of vaccines, where similar conclusions are drawn, demonstrating the high efficacy of the COVID-19 vaccine in Spanish healthcare workers [31]. This work is part of a prospective observational study on the evolution of acquired immunity after vaccination against SARS-CoV-2 in healthcare workers, the partial findings of which have already been published, evidencing antibody levels that remain positive 6 and 9 months after vaccination [44].

Limitations

The sample of students could not be completed by means of simple random sampling, and we were hence obliged to resort to a convenience sample from the study population that had shown interest in participating. Consequently, the sampling was not equiprobabilistic. Additionally, we did not achieve the sample size calculated for this group, and the inference of the results is thus limited. We must also note the limitations of this type of observational study, in which part of the data is self-reported, involving the possibility of information or memory biases in the reporting of symptoms, adverse effects or dates of positive tests. In this sense, a possible information bias could have occurred in the assessment of the incidence

of COVID-19 as no screening tests were carried out in the health care workers or students as a whole, and therefore, asymptomatic or mildly clinical cases that were not detected by PCR or Ag-test could have been missed.

Conclusion

The occupational exposure of our participants to persons with active SARS-CoV-2 infection was high, being 83% in the healthcare workers and 42% in the nursing students. Both groups presented a higher incidence of COVID-19 in the year prior to vaccination than that estimated for the general Spanish population (19.3% in HCWs and 13.6% in NS). The source of infection was not always known but was attributed to a different origin in the two groups studied: occupational origin was attributed in a high proportion of cases among the healthcare workers (41%), while among the nursing students, non-occupational origin was predominant (46%). In both groups, the clinical cases were primarily mild (77% in NS and 85% in HCWs). However, no moderate or severe clinical cases were found among the nursing students, nor cases of long COVID, which was reported by 11% of the healthcare workers affected. Post-vaccination, the incidence of COVID-19 decreased notably in both groups in the first 6 months. Adherence to the vaccine was high in both groups, with 100% of the nursing students and 97.5% of healthcare workers being vaccinated. Working in health care (or similar) is cited as the main reason for vaccination in both population groups, with social responsibility, expected benefits and confidence in vaccines being less frequently identified. The immune response 6 months after the full course of vaccination shows a reactive antibody response in 100% of the cases, with mean IgG values of 3017 AU/ml in the HCWs and 2484 AU/ml in the NS, indicating protection levels against SARS-CoV-2. The efficacy of the vaccines is also demonstrated by the decrease in post-vaccination infections and the clinical mildness of the cases. Factors impacting the immune response that have been reported in this and other studies are previous SARS-CoV-2 infection, which enhances the immune response (hybrid immunity), and smoking, which lowers the immune response in active smokers compared to the non-smoking population. The adverse reactions to the vaccines were frequent but transient (disappearing within 24h), mild and mostly local, with some differences found depending on the vaccine administered (more with AstraZeneca than with BioNTech/Pfizer) and the vaccine dose (more in the first dose than in the second). No severe adverse reaction was reported.

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SUPPLEMENTARY FILES

Table S1: Professional Characteristics and Occupational Exposure to Sars-Cov-2 tn Health Professionals

Professional experience (year): Mean (SD)= 17.87 (8.99); 95% CI %= 16.30-19.43 Minimum value= 1; Maximum value=47 years; Median: 17; Range=46; Mode (MD)= 15			
Departments /Workplaces	**n1 (%)**	**Departments/Workplaces in the last year**	
Special services*	52 (37.4)	**n1 (%)**	
Wards**	13 (9.5)	One	106 (70.2)
Central services	10 (7.3)	Two	23 (15.2)
Outpatients	30 (22.1)	Three	9 (6)
Management and administration	13 (9.6)	four	1 (0.7)
Primary care centers	13 (8.9)		
Care homes	5 (3.7)		
Length of service in position: Mean (SD) = 5.53 (5.21); Minimum value= 1 month; Maximum value= 18 years; Range=18 years; Median (Mn)= 3.12; Mode (MD)= 1 year			
Occupational exposure to COVID-19	**n (%)**	**Year qualified:** Ranges between 1978 & 2019 Range =41 years Mean= 2000 Median= 2001 Mode= 2001	
Yes	113 (74.8)		
No	23 (15.2)		

Legend: * Includes: Emergency, Critical Care and Surgery ** Includes Internal Medicine, Surgery and Obstetrics – Pediatrics
Lost values not included. Percentages are calculated over valid data. Data on the study population (n1) from ICS Almansa (Albacete) 2022.

Tabla S2: Adverse Reactions to Sars-Cov-2 Vaccines in Two Populations: Health Workers (n1) and Nursing Students (n2)

Organ and system involvement:	**1st dose**		**2nd dose**	
- Adverse reaction	**n1 (%)**	**n2 (%)**	**n1 (%)**	**n2 (%)**
Disorders of the blood and lymphatic system: - - Lymphadenopathy	5 (3,5)	-	6 (4,3)	-
Immune system disorders:				
- Anaphylaxis	-	1 (1,2)	-	-
- Hypersensitivity	-	2 (3,5)	-	-
Psychiatric disorders:				
- Insomnia	-	7 (8,6)	2 (1,4)	-
Nervous system disorders:				
- Dizziness	2 (1,4)	16 (18,9)	7 (5)	9 (11,1)
- Facial paralysis	- 9 (6,4)	-	-	-
- Drowsiness/ Tiredness	1 (0,7)	34 (42,5)	25 (17,7)	21 (25,9)
- Paresthesias		1 (1,2)	1 (0,7)	-
Gastrointestinal disorders:				
- Nausea	1 (0,7)	14 (17,3)	4 (2,8)	5 (6,2)
- Diarrhoea / Vomiting	1 (0,7)	6 (7,4)	4 (2,8)	5 (2,9)
Musculoskeletal and connective tissue disorders:				
- Limb pain	43 (30,5)	47 (58)	42 (29,8)	42 (51,9) (*)
- Arthralgia	9 (6,4)	20 (24,7)	18 (12,8)	12 (13,6)
- Myalgia	8 (5,7)	21 (25,9)	22 (15,6)	18 (22,2)
General disorders and local disturbances at the injection site:				
- General malaise	18 (12,8)	38 (46,9)	48 (34,0)	40 (49,4) (**)
- Fever / Febrile Fever	8 (5,7)	33 (40,7)	22 (15,6)	30 (37,0) (*)
- Local pain (injection site)	62 (44)	61 (75,3)	58 (41,1)	49 (60,5) (**)
- Fatigue	6 (4,3)	23 (30,4)	13 (9,2)	17 (21,0) (**)

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- Chills	10 (7,1)	33 (40,7)	25 (17,7)	19 (23,8)
- Local swelling	16 (11,3)	11 (13,8)	20 (14,2)	6 (7,4)
- Local redness	6 (5,3)	5 (6,2)	10 (7,1)	3 (3,7)
- Itching at injection site	1 (0,7)	1 (1,2)	2 (1,4)	-
Skin and subcutaneous tissue disorders:				
- Hyperhidrosis	-	1, (1,2)	-	-
- Generalised exanthema	-	-	-	-
- Generalised itching	-	-	-	-
Metabolic and nutritional disorders:				
- Decreased appetite	-	11 (13,6)	3 (2,1)	5 (6,3)
Other (specify):				
- Menstrual disorders	1 (0,7)	1 (1,2)	- 1 (0,7)	1 (1,2)
- Elevation of blood pressure	1 (0,7)	-	2 (1,4)	- 1(1,2)
- Headache				

Source: Self-administered questionnaire. Population n1 (141) and n2 (81). Calculated as % of valid data.

Classification of adverse effects according to the Ministry of Health Strategy 2021.

Legends: Significant differences in Chi-square test (*) $p<0.001$; (**) $p<0.05$.