COVID-19 vaccination acceptance, safety and side-effects in European patients with severe asthma

Apostolos Bossios [1,2,3], Alison M. Bacon [4], Katrien Eger [5], Dóra Paróczai[6], Florence Schleich [7], Shane Hanon [8], Svetlana Sergejeva[9], Eleftherios Zervas [10], Konstantinos Katsoulis[11], Christina Aggelopoulou[12], Konstantinos Kostikas [12], Eleni Gaki[12], Nikoletta Rovina[13], Zsuzsanna Csoma[14], Ineta Grisle[15], Kristina Bieksienė[16], Jolita Palacionyte[16], Anneke ten Brinke[17], Simone Hashimoto [5], Florin Mihălţan[18], Natalia Nenasheva[19], Biljana Zvezdin[20], Ivan Čekerevac[21,22], Sanja Hromiš [20,23], Vojislav Ćupurdija[21,22], Zorica Lazic[21,22], Rekha Chaudhuri[24], Steven James Smith[24], Hitasha Rupani [25], Hans Michael Haitchi [25], Ramesh Kurukulaaratchy[25], Olivia Fulton [26], Betty Frankemölle[27], Peter Howarth [28], Celeste Porsbjerg[29], Elisabeth H. Bel[5], Ratko Djukanovic[25] and Michael E. Hyland[30]

[1]Karolinska Severe Asthma Center, Department of Respiratory Medicine and Allergy, Karolinska University Hospital, Huddinge, Sweden. [2]Department of Medicine, Karolinska Institutet, Stockholm, Sweden. [3]Division of Lung and Airway Research, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden. [4]School of Psychology, University of Plymouth, Plymouth, UK. [5]Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands. [6]Csongrad County Hospital and Department of Pulmonology, University of Szeged, Szeged, Hungary. [7]CHU Liege, Liege, Belgium. [8]Respiratory Division, Universitair Ziekenhuis Brussel (UZ Brussel), Vrije Universiteit Brussel (VUB), Brussels, Belgium. [9]The North Estonian Medical Centre, Tallinn, Estonia. [10]7th Respiratory Department, Athens Chest Hospital, Athens, Greece. [11]Pulmonary Department, 424 Army General Hospital, Thessaloniki, Greece. [12]Respiratory Medicine Department, University Hospital of Ioannina, Ioannina, Greece. [13]1st Department of Pulmonary Medicine, "Sotiria" Hospital, Athens Medical School, National and Kapodistrian University of Athens, Athens, Greece. [14]National Koranyi Institute for Pulmonology, Budapest, Hungary. [15]Riga East University Hospital, Riga, Latvia. [16]Lithuanian University of Health Science, Kaunas, Lithuania. [17]Medical Centre Leeuwarden, Leeuwarden, The Netherlands. [18]National Institute of Pneumology, Bucharest, Romania. [19]Russian Medical Academy of Continuous Professional Education of the Ministry of Healthcare of the Russian Federation, Moscow, Russian Federation. [20]Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia. [21]Clinic for Pulmonology, University Clinical Center Kragujevac, Kragujevac, Serbia. [22]Department of Internal Medicine, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia. [23]Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia. [24]Gartnavel General Hospital, Glasgow, UK. [25]Southampton University Hospital, Southampton, UK. [26]European Lung Foundation, Patient Advisory Group, Edinburgh, UK. [27]European Lung Foundation, Patient Advisory Group, Heemskerk, The Netherlands. [28]GSK, Brentford, UK. [29]Bispebjerg University Hospital, Copenhagen, Denmark. [30]Plymouth Marjon University, Plymouth, UK.

Corresponding author: Apostolos Bossios (apostolos.bossios@ki.se)

Abstract

Background Vaccination is vital for achieving population immunity to severe acute respiratory syndrome coronavirus 2, but vaccination hesitancy presents a threat to achieving widespread immunity. Vaccine acceptance in chronic potentially immunosuppressed patients is largely unclear, especially in patients with asthma. The aim of this study was to investigate the vaccination experience in people with severe asthma.

Methods Questionnaires about vaccination beliefs (including the Vaccination Attitudes Examination (VAX) scale, a measure of vaccination hesitancy-related beliefs), vaccination side-effects, asthma control and overall safety perceptions following coronavirus disease 2019 (COVID-19) vaccination were sent to patients with severe asthma in 12 European countries between May and June 2021.

Results 660 participants returned completed questionnaires (87.4% response rate). Of these, 88% stated that they had been, or intended to be, vaccinated, 9.5% were undecided/hesitant and 3% had refused vaccination. Patients who hesitated or refused vaccination had more negative beliefs towards vaccination. Most patients reported mild (48.2%) or no side-effects (43.8%). Patients reporting severe side-effects (5.7%) had more negative beliefs. Most patients (88.8%) reported no change in asthma symptoms after vaccination, while 2.4% reported an improvement, 5.3% a slight deterioration and 1.2% a considerable

deterioration. Almost all vaccinated (98%) patients would recommend vaccination to other severe asthma patients.

Conclusions Uptake of vaccination in patients with severe asthma in Europe was high, with a small minority refusing vaccination. Beliefs predicted vaccination behaviour and side-effects. Vaccination had little impact on asthma control. Our findings in people with severe asthma support the broad message that COVID-19 vaccination is safe and well tolerated.

Introduction

Since the coronavirus disease 2019 (COVID-19) pandemic emerged in December 2019, around 769 million cases and more than 6.9 million deaths were reported by week 32 (August) of 2023 [1]. Although population immunity can be achieved through infection, vaccination is a safer means of achieving this objective while reducing the societal and financial burden of COVID-19. Vaccination hesitancy, defined as the "delay in acceptance or refusal of vaccination despite the availability of vaccination services" [2], is a major threat to achieving herd immunity without too many casualties. Hesitancy is not a modern phenomenon and was a feature of the first vaccine for smallpox in the 1790s [3]. Vaccination hesitancy is a top global health threat [4], an annual problem for preventing seasonal influenza and has presented challenges in previous pandemics, such as the 2009 H1N1 outbreak [5, 6]. Following the COVID-19 pandemic, vaccination hesitancy has become a global health problem [7, 8], with an increasing number of studies revealing decreased vaccine acceptance with a pattern of doubts about vaccine safety and effectiveness, exacerbated by ubiquitous unsubstantiated scientific misinformation [9] and distrust of politicians [10].

Vaccination hesitancy is often related to fears about personal safety. The main concern is the fear of a severe allergic reaction as a side-effect of vaccination contributes to COVID-19 hesitancy among people with allergic diseases [11], even though that risk is extremely low. Concerns may also focus on potential future effects; in COVID-19, these have been increased by a perception that the vaccine was developed more quickly than for previous vaccines and, therefore, may not have been rigorously tested [12]. Ideological concerns around profiteering by pharmaceutical companies and a general preference for natural immunity can also contribute to vaccine hesitancy, including in COVID-19 [6, 13]. A systematic review of 60 worldwide studies conducted from February to December 2020 reported that vaccination acceptance rates varied between 24% and 97% in different populations [8]. A further review and meta-analysis reported a similar range (28–93%) [14]. Overall, vaccination acceptance varies widely. A low vaccination intention was reported in healthcare personnel [15] as well as among vulnerable populations with a potentially decreased immune response, including HIV [16], cancer [17] and rheumatic diseases [18] in whom 38.4%, 28.3% and 35.5%, respectively, showed hesitancy to be vaccinated for one reason or another.

Around 3–10% of patients diagnosed with asthma experience severe disease [19] and these patients not only have many comorbidities [20] but often need treatment with high doses of inhaled steroids or oral corticosteroids [21] and/or biological therapies [22]. In patients with severe asthma, a dominating endotype of immune dysregulation is driven by type 2-high inflammation [23], with up to 80% having an allergic/atopic component. Underlying dysregulation of innate immunity can predispose individuals to viral infections [24]. Although asthma may be an independent risk factor for COVID-19 outcome, due to their comorbidities, severe asthma patients are likely to experience more severe disease and worse longer term outcomes [25–27]. Therefore, understanding or overcoming vaccine hesitancy in the population with severe asthma is particularly important. However, no studies to date have addressed this issue.

The aims of the study were to: 1) determine the proportion and characteristics of people with severe asthma in Europe who report that they have either been or will be vaccinated, are unsure whether to get vaccinated, or have decided not to be vaccinated against COVID-19; 2) examine the relationship between vaccination hesitancy beliefs and vaccination status, the relationship between vaccination hesitancy beliefs and perceived side-effects, and perceived asthma symptom change following vaccination; and 3) identify the extent to which patients who have received COVID-19 vaccination feel safe following vaccination and whether they would recommend vaccination to other patients with severe asthma.

Data were obtained using a survey involving patients with severe asthma from the "Severe Heterogeneous Asthma Research collaboration, Patient-centred" (SHARP) Clinical Research Collaboration. This collaboration is hosted by the European Respiratory Society and engages a network of severe asthma experts and patients from clinical centres across 28 countries to promote Europe-wide, patient-centred severe asthma research [28].

Methods

Design, survey development and patient population

This was a cross-sectional study in which the survey was sent to patients with severe asthma within Europe from 5 May to 30 June 2021. The survey was developed iteratively by severe asthma experts (physicians and scientists), health psychologists and patients. Members of the European Lung Foundation's asthma Patient Advisory Group had a central role, consistent with the international guidelines for patient reporting [29]. Professional translators translated the patient surveys into the native languages of the 12 participating European countries and the translations were checked for medical accuracy by asthma specialists. Physicians were asked to recruit severe asthma patients for the survey as they came into their outpatient clinic to prevent selection bias using online and paper versions of the survey according to individual preference. The online survey was hosted by SurveyMonkey (www.surveymonkey.com). Paper versions of the survey were used if online versions were unavailable to patients and results from these were transferred into the SurveyMonkey system by the local research team. All data collection was anonymous. Patients were eligible for inclusion if they had physician-diagnosed severe asthma and were under the care of a severe asthma clinic for at least 6 months prior to the onset of the COVID-19 pandemic.

Survey content

The survey consisted of 18 questions about demographics, asthma medication use, experience of COVID-19 infection, vaccination status and if the patient had been vaccinated, type of vaccine received. Those already vaccinated were asked about side-effects, whether they felt safer for being vaccinated and whether they would recommend vaccination to other patients with severe asthma. In addition, all patients were asked to complete the Vaccination Attitudes Examination (VAX) scale [30], a questionnaire which yields scores on four subscales representing beliefs that may underlie vaccination hesitancy: mistrust of vaccine benefit, worries about unforeseen future effects, concerns about commercial profiteering and preference for natural immunity. Participants responded to questions on a 5-point scale (1=agree strongly and 5=disagree strongly) and responses were averaged to obtain a score for each subscale. A higher score indicates a higher level of belief. The full survey is shown in the supplementary material.

Ethics

Approval for the study was obtained from the medical ethical board of Amsterdam University Medical Center (W20_463 # 20.512) and the ethical boards of every individual country where there was a requirement for approval for survey-based studies. All patients provided digital or written informed consent for participation in this study.

Statistical analysis

Descriptive statistics or proportions of positive ("Yes") responses were calculated for each question, as appropriate. Patients were grouped according to whether or not they had been, or intended to be, vaccinated and we also examined the extent to which they reported vaccination hesitancy according to scores on the VAX questionnaire. Groups were compared using independent samples t-tests, Pearson's Chi-squared or ANOVA with post-hoc tests with Bonferroni adjustment for multiple comparisons. p-values $\leqslant 0.05$ were regarded as statistically significant. Statistical analyses were performed using SPSS version 25 (IBM, Armonk, NY, USA).

Results

Patient demographics

In total, 798 surveys were sent through the SHARP network in 12 European countries and 697 patients were recruited, giving a response rate of 87.34%. 37 surveys were incomplete and were removed from the sample, leaving 660 for analysis (table 1). As the number of patients recruited from each country varied largely, no statistical comparisons between countries were possible. Vaccination rates for each country are presented in supplementary table S1. Thus we chose to address the whole population as one European population. The majority of patients were female (65%), over one-fifth (22%) were on daily oral corticosteroids and more than half (64%) were receiving biological therapy for their asthma. Most (70%) had not had a COVID-19 infection, 12% reported a positive COVID-19 test and only 22 (3%) reported hospitalisation due to COVID-19.

COVID-19 vaccination status

509 out of the 660 patients (77%) had already received at least one dose of vaccine at the time of the study, with a further 10.45% intending to be vaccinated, while 9.55% were still undecided and a smaller proportion (2.88%) had refused vaccination (figure 1).

TABLE 1 Participant details by country: numbers and characteristics of participating patients per country

	Participants	Age, years	Female	Daily prednisolone	Biologics
Belgium	166 (25)	59 (21–86)	95 (57)	33 (20)	98 (59)
Estonia	43 (7)	57 (22–86)	32 (74)	11 (26)	21 (49)
France	1 (0.15)	53 (53–53)	1 (100)	1 (100)	1 (100)
Greece	104 (16)	56 (18–80)	75 (72)	18 (17)	88 (85)
Hungary	73 (11)	57 (23–84)	49 (67)	12 (16)	47 (47)
Latvia	23 (3)	59 (42–81)	16 (70)	3 (3)	8 (35)
Lithuania	24 (4)	54 (31–78)	17 (71)	3 (3)	23 (96)
Netherlands	62 (9)	54 (25–75)	35 (82)	14 (14)	53 (85)
Romania	11 (2)	56 (38–77)	9 (82)	1 (9)	10 (91)
Russian Federation	19 (3)	49 (30–70)	11 (58)	3 (16)	5 (26)
Serbia	92 (14)	53 (26–76)	57 (62)	38 (41)	45 (49)
UK	42 (6)	51 (28–73)	30 (71)	7 (16.7)	21 (50)
All patients	660 (100)	55 (18–86)	427 (65)	144 (22)	420 (64)

Data are presented as n (%) or mean (range).

Of the 509 patients who had been vaccinated, 300 (59%) had received an mRNA-based vaccine, with the remainder receiving vector and protein subunit technology vaccines. We grouped patients into three categories according to their reported vaccination status: accepters (patients who are accepting vaccination; vaccinated/will be vaccinated), hesitant (undecided) and refusers (see table 2 for patient characteristics). Patients accepting vaccination were significantly older than those in the other groups (F(2,653)=5.08, p=0.006, η^2=0.02). Pearson's Chi-squared indicated that hesitators were most likely to have had a COVID-19 infection (χ^2(2)=39.45, p<0.001) and refusers were least likely to be on a biological treatment (χ^2(2)=6.19, p=0.05). Refusers were also least likely compared with other categories to use daily prednisolone, although this difference did not reach significance (p=0.23).

Vaccination hesitancy among patients with severe asthma

We then compared the three categories of patients in terms of their vaccination beliefs, as indicated by VAX scores (figure 2). ANOVA showed significant differences in all four beliefs as a function of vaccination status. Post-hoc tests with Bonferroni adjustment indicated that for mistrust of vaccine benefit, refusers and hesitators scored similarly (p=0.09) but more highly than accepters (patients who had been vaccinated or planned to be) (p<0.001). For worries about unforeseen future effects, refusers and hesitators scored very similarly (p=0.99) and more highly than accepters (p<0.04). In terms of concerns about
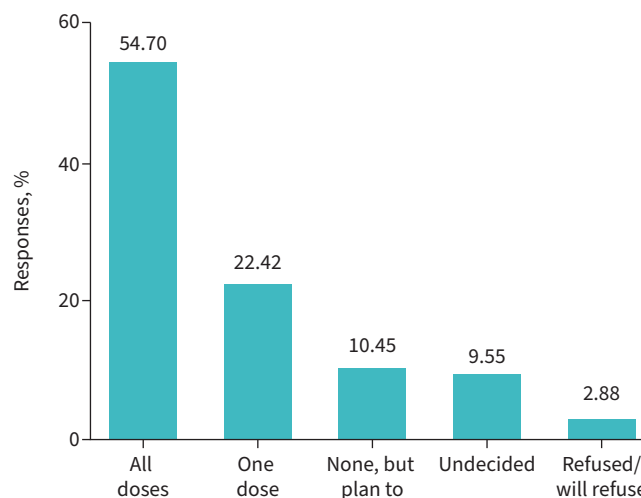

FIGURE 1 Coronavirus disease 2019 vaccination status in patients with severe asthma who completed the survey. Graph showing patients with severe asthma reporting their vaccination status. Data are presented as percentage of the total population who replied to the survey (n=660).

TABLE 2 Characteristics of patients according to their reported vaccination status: refusers, hesitant (undecided) and accepters (vaccinated/will be vaccinated)

	Refusers (n=18)	Hesitant (n=63)	Accepters (n=575)
Age, years	51.28±8.71	51.68±13.37	56.53±13.14
Female	61	76	64
Had COVID-19	17	41	12
Daily prednisolone	11	29	22
Biologics for asthma	44	54	65

Data are presented as mean±SD or %. COVID-19: coronavirus disease 2019.

commercial profiteering, refusers scored higher than hesitators (p=0.02) who, in turn, reported more concerns than accepters (p<0.001). Finally, the preference for natural immunity was similar in both hesitators and refusers (p=0.19) and higher than accepters (p=0.001).

Perceptions of vaccination safety, asthma symptoms and side-effects
The 509 patients who had received at least one dose of a COVID-19 vaccine were presented with a final set of questions about their perception of vaccination side-effects and effects on their asthma symptoms. These items required a "Yes" or "No" response. Most of the patients experienced mild or no side-effects; notably, only 7% reported a need for any treatment for side-effects (table 3). Markedly, the vast majority (89%) did not perceive a change in asthma symptoms following vaccination, with 12 patients (2%) reporting an improvement. 27 patients (5%) perceived that their asthma symptoms got slightly worse without needing any change in treatment, and only six (1%) patients reported that their asthma symptoms got worse and needed a treatment change. Little difference was observed as a function of the type of vaccine received.

We then considered whether general beliefs about vaccination (and, by implication, vaccination hesitancy) were related to the perception of side-effects (table 4). A comparison of the four VAX subscales regarding the level of reported side-effects (none, mild or severe) revealed significant differences in all but the natural immunity subscale. In each case, there was no significant difference in scores between patients with no or mild side-effects (p=0.25–0.99), but those who reported severe side-effects scored significantly higher on all three subscales (p=0.001 in every case). We observed no significant differences in preference for natural immunity (p>0.50).
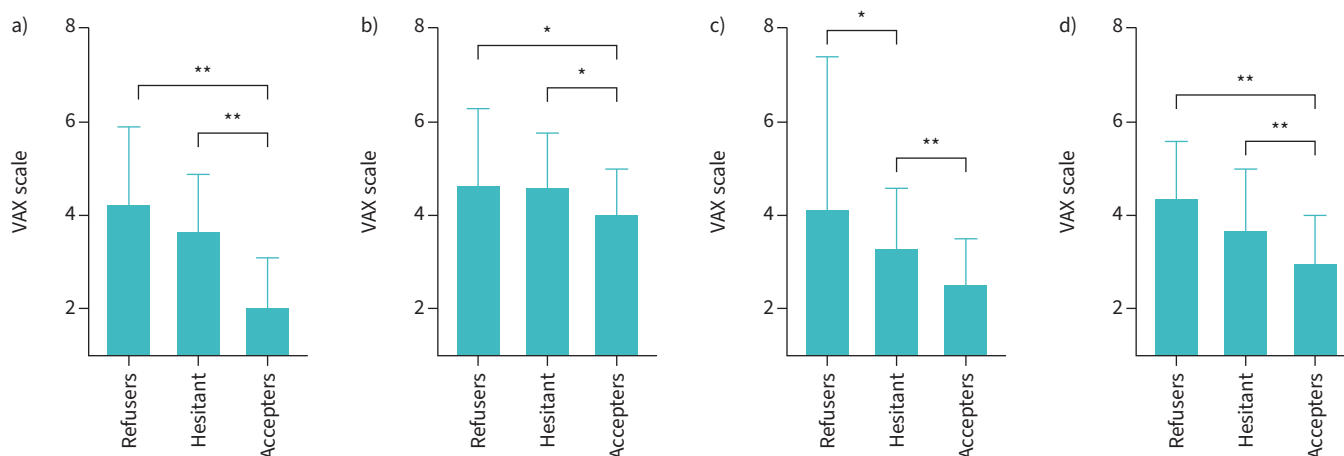

FIGURE 2 Vaccination hesitancy between patients with severe asthma (Vaccination Attitudes Examination (VAX) subscale scores) according to their vaccination status. Descriptive statistics for the VAX questionnaire by reported vaccination status for a) mistrust of vaccine benefit, b) worries about unforeseen future effects, c) concerns about commercial profiteering and d) preference for natural immunity. Patients grouped as "accepters" of vaccination (vaccinated/will be vaccinated), "hesitant" (undecided) and "refusers". Data show results of a 5-point scale (1=agree strongly and 5=disagree strongly) and responses were averaged to obtain a score for each subscale. Significance for paired comparisons with Bonferroni post-hoc tests: *: p<0.05; **: p<0.001.

TABLE 3 Perceptions of vaccination side-effects and effects on asthma symptoms following vaccination by patients who had received at least one dose of vaccine (n=509)

	"Yes" responses	Type of vaccine	
		mRNA	Other
Perceived side-effects of vaccination			
Severe side-effects	29 (5.70)	13 (2.55)	16 (4.00)
Mild side-effects	245 (48.16)	154 (30.26)	91 (17.88)
No side-effects	223 (43.81)	128 (25.15)	95 (18.66)
Treatment sought for side-effects	35 (6.88)	6 (1.18)	7 (1.38)
Perceived change in asthma symptoms following vaccination			
No change in symptoms	452 (88.80)	265 (52.06)	187 (36.74)
Symptoms got better	12 (2.36)	6 (1.18)	6 (1.18)
Symptoms slightly worse, no change in treatment needed	27 (5.30)	18 (3.54)	9 (1.77)
Symptoms worse, needed a change in treatment	6 (1.18)	6 (1.18)	0

Data are presented as n (%). Only 497 surveys had complete answers and were analysed. Percentages represent the proportion of "Yes" responses overall and in terms of the type of vaccine received.

Overall evaluation of vaccination experience

Finally, we were interested in how vaccinated patients felt concerning their safety. Importantly, the vast majority of patients (90%) felt safer following vaccination. Virtually all (98%) would recommend vaccination to other severe asthma patients, irrespective of the vaccine type they received.

Discussion

This survey was conducted in 12 European countries between May and June 2021, about 6 months after COVID-19 vaccines were authorised and at a time when COVID-19 was prevalent, causing significant societal disruption and burden on the healthcare systems. Most severe asthma patients had positive behaviour or intentions to COVID-19 vaccination, with 88% of the participant sample already vaccinated or intending to be. Less than 3% of the respondents said they did not intend to be vaccinated, with the remaining 9% being undecided. Vaccinated patients were slightly older than the other two groups and were less likely to be on a biological treatment. Patients who reported more negative beliefs about vaccination were more likely to be undecided about vaccination or to deny it. Among the vaccinated, those with more negative beliefs were more likely to report severe side-effects. Almost all patients who had received at least one vaccination dose (98%) stated that they would recommend vaccination to other patients with severe asthma.

Vaccination beliefs assessed through the VAX scale showed greater hesitancy for the refuser or undecided groups on all four VAX subscales: mistrust of vaccine benefit, worries about unforeseen future effects, concerns about commercial profiteering and preference for natural immunity. These results are broadly in line with those from general public samples. In terms of the subscales of the VAX, a recently published study reported worries about unforeseen future effects to be the most highly endorsed belief (mean 3.32), followed by a preference for natural immunity (mean 2.44), concerns about commercial profiteering (mean 2.17) and lastly mistrust of vaccine benefit (mean 1.97) [13]. Our survey showed a similar overall pattern.

TABLE 4 Vaccination hesitancy-related beliefs (Vaccination Attitudes Examination (VAX) subscale scores) for patients with severe asthma according to their perception of coronavirus disease 2019 (COVID-19) vaccination side-effects

	Participants	VAX subscale			
		Mistrust of vaccine benefit	Worries about unforeseen future effects	Concerns about commercial profiteering	Preference for natural immunity
Severe side-effects	29	2.34±0.82	4.42±1.18	3.14±1.19	3.08±1.08
Mild side-effects	245	1.99±0.83	3.99±0.98	2.42±0.97	2.80±1.02
No side-effects	221	1.85±0.80	3.82±1.04	2.41±1.01	2.87±1.11
Results of ANOVA		$F_{(2,492)}=5.04$, p=0.01, $\eta^2=0.02$	$F_{(2,492)}=5.01$, p=0.01, $\eta^2=0.02$	$F_{(2,492)}=7.08$, p=0.001, $\eta^2=0.03$	$F_{(2,492)}=0.99$, p=0.37, $\eta^2=0.004$

Data are presented as n or mean±SD (VAX questionnaire scores) and results of between-group ANOVA for patients who reported no, mild or severe side-effects following COVID-19 vaccination.

General public samples often report higher levels of hesitancy than observed in the present study. In a large-scale general population study from the UK, with 32 361 adults, 14% of the sample reported unwillingness to receive a vaccine, with a further 23% unsure/hesitant [31]. Some studies refer to patient groups that have reported high hesitancy rates. Notably, the severe asthmatic population sample in the current study showed more positive attitudes when compared with other chronic or malignant diseases and, generally, when comparing people from outside Europe. In HIV patients surveyed in India between January and February 2021, 38.4% reported being hesitant [16, 17]. Among cancer patients from Tunisia asked about COVID-19 vaccination acceptance between February and May 2021 (close chronologically to the present study), 28.3% were refusers and 21.2% were undecided [17]. Similarly, a survey of 521 adults with chronic disease in Saudi Arabia found COVID-19 vaccine acceptance as low as 52% [32]. Intentions to be vaccinated may change over time. UK hesitancy rates in the general public have been reported to fall from over 25% prior to vaccine development to just 13% once the UK vaccination programme was underway [12]. During the first wave of the pandemic (April 2020), COVID-19 vaccination acceptance was examined in two French high-risk groups: patients above 65 years old and patients with chronic airway disease, asthma or COPD (n=216; mean age 43.8 years). In the second group, most relevant to the present context, vaccination acceptance was 85% [33].

This survey showed that vaccines were well tolerated. Of the 509 participants who had received at least one vaccine dose, the majority reported mild or no side-effects. However, there was evidence of a nocebo effect: people with negative beliefs towards vaccination had more severe side-effects. A minority of patients reported an improvement in asthma symptoms or reported a worsening of symptoms following vaccination. Severe asthma exhibits idiopathic variation in symptoms, so these results may be due to natural variation in asthma control, and the slightly larger number of patients experiencing mild worsening can be explained by a nocebo effect.

Our results are in accordance with an Italian study that evaluated COVID-19 vaccination safety and its effect on asthma control in 253 patients with severe asthma [34]. Less than 20% of patients reported side-effects, and vaccination positively affected asthma symptoms and quality of life. Our present study corroborates these important findings with a larger and more diverse sample, including patients treated with biologics and oral corticosteroids (patients receiving >10 mg prednisolone were excluded from the Italian study). Furthermore, we examined the effects of mRNA and vector/protein subunit technology vaccines, with no differences reported in perceptions of either side-effects or changes in asthma symptoms. A recent meta-analysis of studies involving over 26 million vaccine recipients [34] reported a low prevalence of COVID-19 mRNA vaccine-associated anaphylaxis, with nonanaphylactic reactions occurring at a higher rate and being largely self-limited. This was the case in a study of patients with mastocytosis, a group with an increased risk of anaphylaxis where COVID-19 mRNA vaccination was well tolerated [35]. The low number of side-effects reported in our study supports this conclusion. An important finding in our study is that perception of side-effect severity is highest in patients with a general mistrust of vaccines, suggesting that perceptions may be influenced by psychological factors linked to negative expectations. The nocebo effect is recognised as a cause of side-effect reporting for COVID-19 vaccination [36], but we provide evidence for the first time that side-effect reporting is increased with negative beliefs about vaccination.

Finally, this study has shown that 90% of severe asthma patients feel safe following vaccination and 98% would recommend COVID-19 vaccination to other patients with severe asthma. The experience of vaccination in those patients who received the vaccine was positive.

The current recommendation on COVID-19 vaccination from the US Centers for Disease Control and Prevention is that everyone from the age of 5 years should get one dose of an updated vaccine to protect against serious illness from COVID-19 [37]. However, COVID-19 booster vaccination represents a challenge as it rises up to 30% globally [38]. Safety concerns and doubts about safety represent the main reasons [39, 40], which our report shows are unwarranted.

Our study has some limitations. We cannot exclude the possibility that patients with strong vaccination refusal beliefs chose not to respond, thereby introducing an element of bias. Different vaccine availability between countries may have affected the results. In addition, we conducted no clinical evaluations and our data, therefore, rely on self-reported perceptions, with their inherent limitations. However, patients with severe asthma tend to have accurate perceptions of their asthma and can be considered "experts by lived experience". In addition, people react to their perceptions of events, be they accurate or not, so understanding perceptions can be as important as measuring biomedical data. This survey also does not have the power to compare attitudes towards vaccination between individual countries.

Most of our population was on biologics (64%), which may increase the relationship between health practitioners and patients, as we presume frequent and more close contact, *i.e.* frequent visits for injections. This relationship could have made it easier for patients to accept vaccinations. However, patients with severe asthma, not on biologics, may have less frequent visits and thus might not have the same acceptance of the COVID-19 vaccination. We address this risk in table 2, where we found that the vaccine refusers were least likely to be on biological treatment. This finding points to the importance of developing regular contact and trust between health professionals and patients in agreement with earlier studies, where lack of trust has been identified among the reasons for vaccination hesitancy [41].

Conclusions and future implications

In our study, only 9% of patients with severe asthma remained undecided about the COVID-19 vaccine. This hesitant minority is important as they are still potentially persuadable. With this study, we provide evidence that might be able to persuade that hesitant minority. First, COVID-19 vaccines are medically safe for people with severe asthma, with no evidence of adverse asthma-related side-effects. Second, people with severe asthma feel safe after having vaccinations. Finally, 98% of patients who had received vaccination would recommend it to other asthma patients, sending a powerful message to patients with asthma and other chronic immune-related diseases who are hesitant about getting vaccinated. This message is valuable for convincing asthma patients and patients with other immune-related diseases, as well as other patients and healthy individuals, to receive a booster vaccine for COVID-19 [37] and overall our preparation for future pandemics [42].

Ethics statement: Approval for the study was obtained from the medical ethical board of the Amsterdam University Medical Center (W20_463 # 20.512) and the ethical boards of every individual country where there was a requirement for approval for survey-based studies. All patients provided digital or written informed consent for participation in this study.

Conflict of interest: A. Bossios reports support from Novartis for attending meetings, outside the submitted work; participation on a data safety monitoring or advisory board for AstraZeneca, GSK, Novartis, Teva and Sanofi, outside the submitted work; and is a member of the Steering Committee of SHARP, Secretary of Assembly 5 (Airway Diseases, Asthma, COPD and Chronic Cough) of the European Respiratory Society and Vice-chair of the Nordic Severe Asthma Network, outside the submitted work. K. Katsoulis reports payment or honoraria for lectures presentations, speakers bureaus, manuscript writing or educational events from GSK, Novartis and AstraZeneca; and support received from Menarini and Novartis for attending meetings and/or travel, outside the submitted work. K. Kostikas reports grants or contracts from AstraZeneca, Boehringer Ingelheim, Chiesi, Innovis, ELPEN, GSK, Menarini, Novartis and NuvoAir, outside the submitted work; consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, ELPEN, GSK, Menarini, Novartis and Sanofi-Genzyme, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, Boehringer Ingelheim, Chiesi, ELPEN, GSK, Menarini, Novartis, Sanofi-Genzyme and WebMD, outside the submitted work; and is a member of the GOLD Assembly, disclosures made outside the submitted work. N. Rovina reports receiving honoraria for lectures and presentations from Chiesi, AstraZeneca, Menarini, Gilead and Baxter, outside the submitted work. K. Bieksienė reports receiving lecture honoraria from Berlin-Chemie, AstraZeneca and Norameda, outside the submitted work. A. ten Brinke reports grants from Teva and GSK, outside the submitted work; consulting fees from AstraZeneca, GSK, Novartis, Sanofi-Genzyme and Teva, outside the submitted work; and payment or honoraria for lectures received from AstraZeneca, GSK, Sanofi-Genzyme and Teva, outside the submitted work; and is Chair of the Dutch severe asthma registry RAPSODI, outside the submitted work, and ERS SHARP CRC national lead for the Netherlands. R. Chaudhuri reports grants or contracts from AstraZeneca, outside the submitted work; payment of honoraria for lectures from GSK, AstraZeneca, Teva, Chiesi, Sanofi and Novartis, outside the submitted work; support for attending meetings and/or travel from Chiesi, Sanofi and GSK, outside the submitted work; and participation in advisory board meetings for GSK, AstraZeneca, Teva, Chiesi and Novartis, outside the submitted work.

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