ORIGINAL RESEARCH

Disease Impact and Perception of Biologics in Adults with Type 2 Inflammation Respiratory Disease: International Survey Results

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Purpose: There is a growing interest in developing approaches that reduce the impact of Type 2 inflammatory conditions, such as asthma and chronic rhinosinusitis with nasal polyps (CRSwNP), on well-being. The aim of this international survey was to understand the impact of asthma and CRSwNP on people living with these conditions and to seek insight into the perception of biologics, which are often used to treat them.

Patients and Methods: A cross-sectional survey was conducted anonymously online from February to May 2024. International participants were recruited through social media and by Survey Monkey. Individuals aged \geq 18 years diagnosed by a medical professional with asthma and/or CRSwNP who lived in the US, Canada, UK, Germany, Italy, France, or Spain were eligible to participate.

Results: Of the 1566 survey participants (56.7% asthma, 24.8% CRSwNP, 18.5% both), 52.5% were female, and 65.3% were ages 25–54 years. Approximately two-thirds (64%) reported thinking once/day or at least once/week about managing their condition. Nearly half (44%) find it difficult to manage their disease. Of those currently using a biologic (14%), only 37% inject it themselves and feel confident doing so, and 42% felt it was a repeating reminder of their chronic condition. The top reason for stopping biologic treatment was that the injection/ device was too difficult. The possibility of a lower frequency injection increased the likelihood participants would consider a biologic.

Conclusion: The study further raises awareness of the personal burden from asthma and CRSwNP and their associated treatments in different countries. Beyond the goal of achieving clinical disease control for these diseases, a holistic approach to care delivery should include culturally appropriate emotional health support to improve overall well-being. Access to biologics administered with less frequency may alleviate some of the burden of self-injection.

Plain Language Summary: Asthma and chronic rhinosinusitis with nasal polyps (CRSwNP) are chronic (ongoing) diseases that can affect many aspects of life, and people often have both diseases. Biologic drugs can be used to treat asthma and CRSwNP not responding well to other treatments. These drugs need to be injected at home or in a doctor's office every 2–8 weeks. An online survey of patients around the world was done to understand the effects of these diseases on daily life and how people with these conditions feel about biologics. Of the 1566 participants, almost 57% had asthma, 25% had CRSwNP, and 19% had both. Participants said they worry about their disease, with 64% thinking every day or at least once/week about managing their condition and 44% finding it hard to take care of their disease. Of the people using a biologic drug, only 37% felt confident injecting it themselves, and 42% felt it was a reminder of their disease. The main reason for stopping a biologic was that the injection/device was too difficult. Patients said they would be more likely to take a biologic if the injection was needed less often. These results tell us asthma and/or CRSwNP negatively impacts well-being. For patients on biologics, worrying about injections and the constant reminder of their condition adds to their perception of burden. Emotional health supports and shared decision making with providers may help give patients confidence and lower anxiety. Having to get injections less often may lower the burden and anxiety people feel about self-injection.

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Keywords: asthma, chronic rhinosinusitis with nasal polyps, injection, burden

Introduction

Asthma and chronic rhinosinusitis with nasal polyps (CRSwNP) are chronic conditions of the lower and upper airway, respectively. Worldwide, approximately 300 million people have asthma,¹ and population studies have demonstrated a prevalence of approximately 2.6–2.7% for CRSwNP.^{2,3} Asthma and CRSwNP share some common pathophysiology related to Type 2 inflammation, which is characterized by the recruitment of eosinophils to the site of inflammation, airway remodeling, activation and degranulation of mast cells, and epithelial barrier dysfunction.⁴ Because of these shared disease mechanisms, it is not uncommon for patients to have both conditions. In a real-world study of patients with moderate-to-severe Type 2 disease in the US and Europe, 17% of those with asthma also had CRSwNP, and 46% of the patients with CRSwNP also had asthma.⁵

Treatment for asthma includes several types of drugs with different mechanisms of action, whereas treatment for CRSwNP can encompass pharmacotherapy as well as surgery. Biologic therapies for both conditions are available for patients who are unable to achieve disease control with standard of care treatment. Because of the shared underlying Type 2 inflammation, some of the same biologics that target these pathways are used to treat both asthma and CRSwNP.⁶ These biologics are administered subcutaneously, typically, every 2 to 8 weeks, but sometimes more or less frequently depending on the specific biologic and prescribed dose. The injections can be self-administered at home, by a friend or family member, or by a medical professional in a clinical setting.

As chronic diseases, the burdens of asthma and CRSwNP on the patient are multifaceted – the physical burden of discomfort and pain, the time burden to attend healthcare visits and fill prescriptions, and the financial burden from disease management and missed work days. These diseases can also take a toll on emotional health. There is a growing interest in developing approaches that reduce the impact of asthma and CRSwNP on well-being. Furthermore, while there is some information on the patient perception of biologics for asthma, no information is available from a large scale international perspective or for patients with CRSwNP.^{7–12} Thus, the aim of this international survey was to understand the impact of asthma and CRSwNP on people living with these conditions and to seek insight into the perception of biologics, which are often used to treat them.

Methods

Survey Methodology and Characteristics

The cross-sectional survey was conducted anonymously online via the Survey Monkey platform from February to May 2024. International participants for the survey were recruited through social media accounts (ie, Instagram, Facebook, X, and LinkedIn) of patient advocacy organizations and by Survey Monkey. The survey and social media recruitment posts were originally written in English and then translated into Spanish, French, German, and Italian by certified translators (Alboum Translation Services, Arlington, VA). The survey contained questions designed to assess participant demographics, disease history, disease management, impact of disease on daily activities and emotional health, and attitude toward biologics (Supplemental Table S1). Survey questions were pretested by 4 of the authors, and the translated versions were tested by native speakers. Once the survey was launched, the link could only be used once per IP address to prevent individuals from completing the survey multiple times.

This survey complied with the Declaration of Helsinki. As the research study team with access to data is based in the US, and the survey included US participants, the recruitment text and images, consent form, and survey were submitted to a central institutional review board in the US (BRANY, Lake Success, NY). Exemption from review was granted because the information obtained was recorded by the investigators in such a manner that the identity of the human subjects could not be readily ascertained, directly or indirectly through identifiers linked to the subjects (no names or personal identifying information were collected). Notably, by seeking exemption from an independent US ethics committee, we emulated the approach reported by similar large international surveys, for example, a recent survey conducted by the European Lung Foundation determined using a UK National Health Institute online tool that ethical

approval was not necessary.¹³ Online consent to participate in the survey was obtained from all individuals. Participants were informed that their survey answers and text responses/quotes were fully anonymized and would help in the creation of educational materials for patients and providers. No incentives were given for participation in the survey. Reporting of the survey is in accordance with the Consensus-Based Checklist for Reporting of Survey Studies.¹⁴

Individuals aged 18 years and over who self-reported being diagnosed by a medical professional with asthma and/or CRSwNP and who lived in the US, Canada, UK, Germany, Italy, France, or Spain were eligible to participate.

Analysis

A goal of 1800 participants was set for the survey, with a geographic distribution goal of 600 participants from the US and 200 participants each from Canada, UK, Spain, France, Germany, and Italy.

Analyses were descriptive only, with the percentage of participants calculated for each categorical response. There was no adjustment of results based on a non-response to a question. Denominators used to calculate responses to each question are the number of participants who responded to the question.

Results

Participant Characteristics and Disease History

A total of 2775 individuals entered the survey; 1566 individuals fulfilled eligibility criteria and provided survey responses. The majority (52.5%) of eligible participants were female, most (65.3%) were between the ages of 25–54 years, and the majority had an undergraduate or graduate degree (Table 1). Just over half (56.7%) of the participants self-

Characteristic	Survey Population N=1566
Female, n (%)	822 (52.5)
Age, y, n (%)	
18–24	217 (13.9)
25–34	386 (24.7)
35-44	341 (21.8)
45–54	295 (18.8)
55–64	182 (11.6)
65+	145 (9.3)
Country of primary residence, n (%)	
Canada	165 (10.5)
France	209 (13.4)
Germany	174 (11.1)
Italy	176 (11.2)
Spain	47 (9.4)
UK	156 (10.0)
United States	539 (34.4)

Table I Demographics and Disease Characteristics

(Continued)

Characteristic	Survey Population N=1566
Level of education completed, n (%)	
Less than high school	42 (3.1)
High school	272 (19.8)
Associate degree, professional, technical, vocational, or trade school	262 (19.1)
College/undergraduate degree	515 (37.5)
Graduate degree	262 (19.1)
Prefer not to answer	19 (1.4)
No response	194 (12.4)
Diagnosis, n (%)	
Asthma only	889 (56.7)
CRSwNP only	388 (24.8)
Asthma and CRSwNP	289 (18.5)

Table I (Continued).

Abbreviation: CRSwNP, chronic rhinosinusitis with nasal polyps.

reported being diagnosed with asthma only, approximately one-quarter (24.8%) had CRSwNP only, and approximately 1 in 5 participants (18.5%) had both diseases (Table 1).

Participants were commonly using intranasal corticosteroids, oral medications (eg corticosteroids, leukotriene receptor antagonists), nebulized corticosteroids, and inhaled medications (eg short-acting β -agonists, corticosteroids); 14% were using a biologic for asthma or CRSwNP. Only 6% (83/1410 responses) indicated they were not taking any medication regularly. Of the participants with asthma, 55% (639/1170 responses) had ever visited the emergency department, 39% (457/1170 responses) had ever taken oral steroids because of their asthma. Of those with CRSwNP, 59% (401/674 responses) had ever had surgery to remove nasal polyps.

Impact of Asthma and/or Nasal Polyps on Daily Activities and Well-Being

Approximately two-thirds (64%) of participants reported thinking about managing their condition once a day or at least once per week (ie, collecting prescriptions, scheduling doctor visits; Figure 1). Nearly half (44%; 458/1042 responses) of participants find it difficult or very difficult to manage their disease, with a notable difference for younger (25–34 years) and older (65+ years) participants (55% vs 34%, respectively; <u>Supplemental Figure S1</u>).

The most common negative impacts of their disease reported by participants were experiencing anxiety (feeling nervous) (46%), their ability to exercise (44%), and getting enough sleep (37%; Figure 2). When analyzed by age, the percentages of participants reporting anxiety and an impact on the ability to attend work/school was approximately 10% higher in younger individuals (<55 years; 47–48% and 33–36%, respectively) vs older (\geq 55 years; 36–38% and 12–21%, respectively, data not shown) individuals. Free text comments from participants indicate that their asthma or CRSwNP impacts their feelings, school and social activities, and sexual relations, although individuals over age 55 years tend to be more adjusted to life with their disease (Table 2).

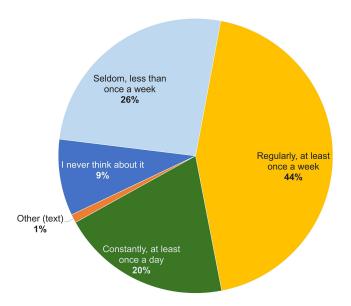


Figure I Frequency of thinking about the overall management of asthma and/or CRSwNP (n=1413 responses). "Other" comments were generally in regard to seasons (eg, "start of spring", "birch season").

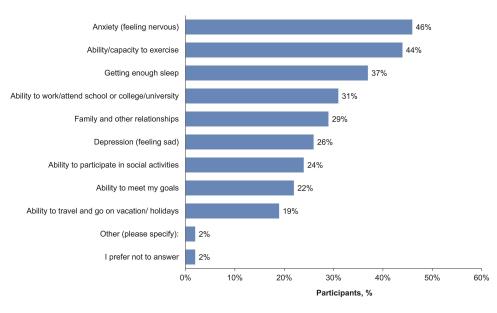


Figure 2 Impact of asthma and/or CRSwNP on daily lives (n=1413 responses); free text responses to "other" are included in Table 2.

Participant Attitude Toward Biologics

Self-injectable medicine for any health condition was currently being used or had been used in the past by 55% of participants (778/1411 responses). When asked if they were afraid of injecting themselves, 55% (781/1411 responses) were at least moderately afraid; participants over 55 years were less fearful of self-injection (Figure 3).

Of all the participants, 14% (195/1410 responses) were currently using a biologic for asthma and/or CRSwNP; 69% (135/195 responses) had been on the biologic for less than 2 years. Of those receiving a biologic, 37% (73/195 responses) inject it themselves and feel confident doing so (Figure 4). The remaining 63% either worry they are not doing it correctly or have someone else do the injection. On average, participants over age 45 years tend to be more likely than participants less than age 45 years to self-inject and feel confident doing so, but 25% of those over the age of 65 receive the injection from a family member or friend (Figure 4). Nearly half (42%; 82/195 responses) felt that taking the biologic was a repeating reminder of the chronic nature of their condition; 33% worry about missing a dose or forgetting to take

Participant Age Group, y	Quotes
18–24	"I like running a lot. I got worse at sports after getting asthma"
25–34	"I can't do what I want for fear of an asthma attack" (Spanish)
	"in recent years, due to lung conditioning through exercise, my quality of life has drastically improved"
	"extremely overwhelming" (Spanish)
35-44	"Ability to sing (do my job as a professional singer) at 100% at times. Especially when extremely cold out or super humid out"
	"Sex"
	"Eating, personal hygiene, dressing" (Spanish)
	"Mentally, feeling the symptoms of the disease causes me anxiety and physically, depending on the severity of the symptoms, they limit me from all day-to-day activities" (Spanish)
	"Work" (Spanish)
45–54	"Self confidence"
	"I cannot run or get to [sic] physically exhausted"
	"I need to live in brand new homes and clean every night to control my allergies"
55–64	"It doesn't. I treat it and live with it. I don't let it affect my day-to-day life more than absolutely necessary"
	"Actually, not at all anymore" (German)
65+	"I also have sleep apnea and hearing loss, partially due to congestion. I have been using CPAP successfully for about 15 years. Congestion is limiting the duration of my sleep and causing the events per hour to increase near the end of my sleep."
	"No impact"
	"Does not impact my life"
	"Since surgical removal, no problems"

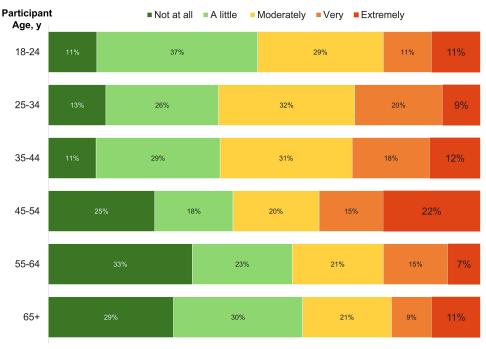
Table 2 Participant Free Text Quotes in Response to the Question "How Does Your Asthma and/or Nasal Polyps Impact Your DailyActivities and How You Worry About Your Disease?" by Age

Abbreviation: CPAP, continuous positive airway pressure.

their injection (Figure 5). A relatively small percentage reported having fatigue with having to regularly take an injection or worrying about receiving and storing their injection (Figure 5).

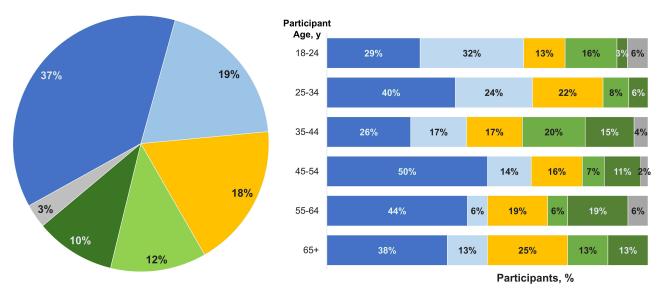
When given a list of reasons why people may not take their medications exactly as prescribed by their doctor, participants selected frequency of the medication (eg too often) as the top reason, followed by how the medication needs to be taken (eg by injection) (<u>Supplemental Figure S2</u>). Thirty-three percent of the participants (464/1401) reported that dosing once a month would make it easier for patients to take their injectable treatment exactly as the doctor instructed, and 22% (n=313) indicated that being able to have an injection at home rather than going to a healthcare provider would make it easier (<u>Supplemental Figure S3</u>).

Of those participants not currently on a biologic, a third (34%; 390/1156 responses) reported they had taken an injectable biologic in the past, which they had stopped taking. The top reasons for stopping treatment were that the injection/device was too difficult, getting to the clinic was too difficult, and the biologic injection was too expensive (Figure 6). Participants reported that having a reduced injection frequency would have made it easier to have stayed on treatment; frequency was more important than factors such as a different device, fewer side effects, or financial help (Supplemental Figure S4).



Participants, %

Figure 3 Participant rated fear of self-injecting by age group (n=1411 responses).



I inject it myself (self-administered) and I feel confident doing so

- I inject it myself but I worry that I am not doing it correctly
- The injection is given by my family member or friend
- The injection is given by a nurse at my home
- I get the injection at the clinician office, hospital, or infusion center
- I prefer not to answer/not sure

Figure 4 Administrator of the injection in those receiving a biologic overall and by age group (n=195 responses).

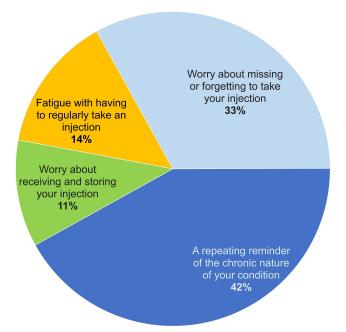


Figure 5 Participant perceptions when taking their biologic (n=195 responses).

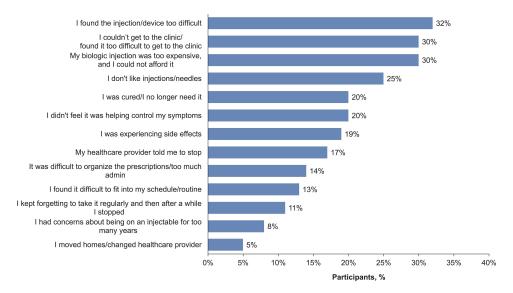


Figure 6 Reasons participants stopped using a biologic (n=389 responses). Participants could select all that apply.

More than two-thirds of participants (68%; 934/1378 responses) would consider a biologic injection if it was once every 6 months as part of their regular checkup; approximately half would consider a biologic treatment if the injection was twice a month (48%), once a month (53%), or every other month (56%; Figure 7). Participants agreed that there could be many advantages to getting a biologic injection every 6 months as part of their regular checkup (Supplemental Figure S5).

Association Between Emotional Health and Disease Impact

Participants reporting feelings of anxiety associated with their asthma and/or CRSwNP (n=644) had an overall greater negative impact on daily activities compared with the full survey population (Figure 8). When assessing the impact of disease on those with anxiety, 49% reported an impact on the ability to exercise, 44% reported an impact on sleep, 36% reported an impact on work/school, and 37% reported depression (Figure 8). Among those with anxiety who were taking

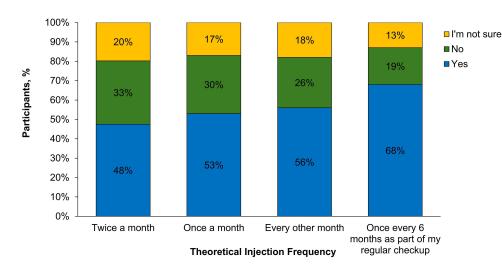


Figure 7 Participant perspective on considering a biologic treatment based on injection frequency (n=1378 responses).

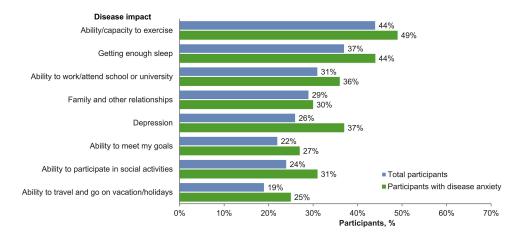


Figure 8 Percentage of total participants (n=1413 responses) and participants with disease-related anxiety (n=644 responses) reporting an impact of asthma and/or CRSwNP on daily activities. Participants could select all that apply.

an injectable treatment, 43% (48/112 responses) reported that the injection was a repeated reminder of the chronic nature of their condition and 29% (32/112 responses) worried about missing or forgetting to take it.

Discussion

Results from this international patient survey demonstrate that people with asthma and CRSwNP selected response options that demonstrated a negative impact on well-being, physical activity, sleep, sexual relations, work or school, and social activities. Use of a biologic seems to affect emotional health as participants indicated that it serves as a repeated reminder of the chronic nature of their disease, and they worry about injecting it incorrectly. Participants also find the injections difficult and inconvenient. Participants indicated that a biologic with a lower frequency could make it easier to stay on treatment and reduce the emotional burden and inconvenience of higher frequency treatments.

The presence of a physical and emotional burden related to asthma and CRSwNP indicated by participants has been well documented and was therefore not surprising.^{15–18} The survey results go beyond a quantitative assessment of the emotional burden and assess how the participants think and feel about their disease, revealing how it specifically affects their day-to-day life. Physically, participants indicated that asthma and CRSwNP inhibit exercise, sexual activity, sleep, and work performance. A notable finding was that the burden of disease on well-being appeared somewhat less with older participants (\geq 55 years), who were less likely to report an impact and were less afraid of doing self-injections than

younger participants. This may reflect lifestyle adjustment and disease acceptance by the older participants, which was further supported by the free text comments.

The survey found that the majority of participants on biologics are self-injecting, but younger patients (<55 years) tend to be less confident they are doing it correctly. Older patients who self-inject their biologic tend to be more confident in doing so, perhaps because they are less afraid of self-injecting. These findings differ from studies of subcutaneous selfinjection of rheumatoid arthritis (RA) treatments, which found that self-confidence in injecting correctly was significantly higher in younger patients than in older patients.^{19,20} Another survey of patients who self-inject a biologic for severe asthma reported that 44% worried about "making a mistake while injecting" and 44% expressed a desire for more injection training.¹² Clearly, many patients lack confidence in their ability to correctly self-inject biologics. Despite labeling requirements of healthcare-provided training for self-injection of several biologics, studies have found that patients generally learn how to self-inject through trial and error because they receive little to no education on how to do the injection.^{21,22} Patients often seek instruction from online resources such as YouTube videos.^{22,23} which are not regulated and may provide inaccurate information.²⁴ This in turn can lead to habitual incorrect injection technique and anxiety each time an injection is due.²¹ Eventually, the patient may become frustrated with the process and stop treatment. Indeed, the top reason survey participants indicated that they stopped a biologic was because they found the injection or device too difficult. These data indicate that education and training are a necessity when initiating selfinjected treatment, but such training during office visits is hampered by time constraints of healthcare providers.²¹ At a minimum, patients could be provided with instructional information, including digital resources such as videos for selfinjecting, although these methods may not be as satisfactory to patients as in-person training.²⁵

Both the current survey and a study of RA found that older patients tend to prefer someone else do the injection.²⁰ In the RA study, those who chose intravenous administration in a medical setting over subcutaneous administration were more likely to identify "contact with other patients/meeting others" and "staff availability if problems arise" as factors that influenced their choice.²⁰ Again, this indicates a lack of confidence that may be improved with adequate training.

Participants are somewhat fearful of injections but indicated they would be more willing to take them and stay on them if they were less frequent. The high frequency of the biologic injections has important implications; it serves as a reminder of their chronic condition and intensifies the inconvenience. Participants agreed that a biologic with a lower frequency, such as an injection every 6 months as part of their regular checkup, would have many advantages over a higher-frequency biologic. A previous survey of patients on biologics for asthma found that those with experience with multiple biologics preferred the one with the lowest frequency.⁸ In reality, the choice of a lower frequency biologic is not always possible because of restrictions by a country's healthcare system.²¹ Payers typically have a structured "step up" approach that starts with more affordable products and requires proof of treatment failure before covering more expensive options. Often these pathways to a biologic is not only an issue for payers. Even with financial assistance, the cost of biologics to the patient can be considerable. Survey participants indicated that the inability to afford the treatment was a top reason they stopped a biologic. Another survey of patients on biologics for asthma also noted that cost was a major barrier for treatment.⁷

A limitation of this survey is a potential selection bias since participants needed to have access to the internet and social media and also be willing to take an online survey. The survey included questions that evaluated the impact of Type 2 inflammatory disease on well-being, however, validated self-administered anxiety and depression screening tools were not used, thereby limiting the ability to determine the disease impact on mental health. Also, the survey did not assess the level of disease control, which is associated with the physical and emotional burden of disease.^{26–28}

Conclusions

This study further raises awareness of the personal burden from asthma and CRSwNP and their associated treatments. Beyond the goal of achieving clinical disease control for these diseases, a holistic approach to care delivery should include culturally appropriate emotional health support to improve overall well-being. Access to affordable biologics that can be administered at a lower frequency and in an easier manner may alleviate some of the burden of self-injection.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

This survey complied with the Declaration of Helsinki. The consent form and survey were submitted to an institutional review board (BRANY, Lake Success, NY) and granted an exemption from review.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

RTS is a retiree and shareholder of GSK and reports personal fees from AstraZeneca, Boehringer Ingelheim, ENA Respiratory, Roche, Vocalis Health, Teva, ImmunoMet, Renovion, Samay Health, GSK, ItayAndBeyond, COPD Foundation, Global Skin and the Global Allergy and Airways Patient Platform. AV is an employee and shareholder of GSK. JR is employed by Asthma Canada, which has received funding from AstraZeneca, GSK, Novartis, and Sanofi. HJ is employed by the Asthma and Allergy Foundation of America, which has received grants for research and unbranded initiatives from Amgen, AstraZeneca, Genentech, GSK, Johnson & Johnson, Novartis, Pfizer, Regeneron, Sanofi, and Viatris. RW has received consulting fees from AbbVie, AstraZeneca, Galderma, GSK, Sanofi-Regeneron, and Bristol Myers Squibb and has received grant support from AstraZeneca, Sanofi-Regeneron, Chiesi, and Verona. KW, ML, IM, MS, SN, CJ and VGM have nothing to disclose.

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