Journal of Asthma and Allergy

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

# Annual and Post-Exacerbation Follow-Up of Asthma Patients in Clinical Practice – A Large Population-Based Study in Sweden

Hanna Sandelowsky[1–3], Björn Ställberg[4], Fredrik Wiklund[5], Gunilla Telg[6], Sofie de Fine Licht[6], Christer Janson[7]

[1]Karolinska Institutet, Department of Medicine, Division of Clinical Epidemiology, Solna, Sweden; [2]Karolinska Institutet, Department of Neurobiology, Care Sciences and Society, Division of Family Medicine and Primary Care, Solna, Sweden; [3]Academic Primary Health Care Centre, Region Stockholm, Sweden; [4]Department of Public Health and Caring Sciences, Family Medicine and Preventive Medicine, Uppsala University, Uppsala, Sweden; [5]Statisticon AB, Uppsala, Sweden; [6]AstraZeneca Nordic, Södertälje, Sweden; [7]Department of Medical Sciences: Respiratory, Allergy and Sleep Research, Uppsala University, Uppsala, Sweden

Correspondence: Hanna Sandelowsky, Karolinska Institutet, Department of Medicine, Division of Clinical Epidemiology, Solna, Sweden, Tel +46738902565, Email hanna.sandelowsky@ki.se

**Background:** Symptom control has not improved in Swedish asthma patients during the last two decades. Guidelines recommend annual reviews for asthma patients treated with maintenance inhaled corticosteroids (ICS). We aimed to describe how visit patterns in an ICS-treated asthma population in Sweden were related to applicable asthma guidelines.

**Methods:** Swedish electronic health data for incident asthma patients, ≥18 years, with at least one ICS collection (index date) between 2006 and 2017 were included. Exacerbations were defined as hospitalizations, emergency visits, or collection of oral corticosteroids (OCS). Probability of an asthma-related regular follow-up visit and probability of a follow-up visit after an exacerbation, both within 15 months, were estimated using the cumulative incidence function, time-to-event analysis, and incident rate ratios.

**Results:** In 51,349 asthma patients (mean age 47.6 years, 63% females), 17,573 had a regular asthma visit in primary or secondary care within 15 months after the index, yielding an overall probability of a visit of 37.4%. Patients with a follow-up visit had higher ICS collection and lower OCS collection than patients without regular visits. Among 22,097 patients with acute exacerbations, the probability of a visit within 15 months after an exacerbation was 31.0%. The probability of having a visit increased during the study period.

**Conclusion:** Only one-third of ICS-treated asthma patients, regardless of asthma severity, had a regular or post-exacerbation follow-up visit within a 15-month period. The consequences of this lack of adherence to guidelines need further evaluation to secure optimal asthma management.

**Keywords:** asthma, disease management, follow-up visit, exacerbation

## Introduction

Asthma is a heterogeneous, chronic, inflammatory airway disease that is estimated to affect 339 million people worldwide.[1] Even though asthma is a rare cause of mortality in the Nordic countries,[1] it continues to cause considerable morbidity across the world.[2,3] Despite the availability of efficient anti-inflammatory treatments, many asthma patients lack full asthma control, as defined by international guidelines.[4]

In Sweden, the majority of patients with asthma are managed by primary care.[5] The publicly funded, primary care-based healthcare system aims to provide the same access and standard of care for all patients, independent of socio-economic status or geographical localization. There is a low patient fee for health-care visits and costs of medications. For chronic conditions, patients are typically prescribed medications for one year by their general practitioner, with collection at pharmacy every third month. In addition, it is possible to get a prescription renewed by telephone or email without visiting a doctor.

Received: 5 January 2022
Accepted: 1 April 2022
Published: 13 April 2022

According to the Swedish guidelines[5] and the current Global Initiative for Asthma (GINA) report,[4] well-controlled asthma patients on maintenance inhaled corticosteroids (ICS) treatment should have a review by their physician once annually, and patients with uncontrolled asthma should be reviewed at least twice per year.[4,5] Patients who have had an asthma exacerbation should have a follow-up within six weeks after the exacerbation, and after that at least twice annually. These consultations should address possible sources of poor asthma control, for instance by evaluating symptoms and physical activity, taking smoking and sick-leave history, controlling inhaler technique, and reviewing or developing a written individual action plan.[5] Planned asthma management with a systematic approach including regular follow-up visits in primary care has shown to improve asthma control.[6] However, previous studies and reports from Sweden have shown that 60% of asthma patients are uncontrolled – a proportion that has remained unchanged for the past two decades.[7,8]

The aim of this study was to describe asthma-related visit patterns in Swedish primary and secondary care, by the frequency of both regular follow-up visits and post-exacerbation visits, in an ICS-treated asthma population, and relate the findings to applicable asthma management guidelines. In addition, this study aimed to describe the baseline patient characteristics and respiratory medication collection during follow-up in those with and without a visit.

# Materials and Methods

## Study Design and Data Sources

In this observational cohort study, asthma patients were identified in primary care medical records. The primary health-care centers that were included in the study were either publicly funded (Stockholm county) or both publicly and privately funded (Uppsala county), and covered approximately 2.7 million inhabitants. Medical record data were extracted and linked by the Swedish National Board of Health and Welfare to data from Swedish national health registers (the National Patient Register, the Cause of Death Register, and the Swedish Prescribed Drug Register). Individual linkage between registers was possible due to the personal identification number assigned to all residents in Sweden. Once the patients were included in the study, the personal identification number was replaced with a study identification number. The linked database was managed by the Department of Medical Sciences, Respiratory Medicine at Uppsala University, Sweden. The study protocol was reviewed and approved by the regional ethics committee in Uppsala, Sweden (reference number 2016/486).

## Study Population

The study included an open cohort of patients with an asthma diagnosis between January 2006 and December 2017, with a rolling index date defined as the first collection of an ICS inhaler after the asthma diagnosis (Supplementary Figure 1). All patients aged ≥18 years with a main diagnosis of asthma (ICD-10 J45, J46) in primary care (as well as in secondary care in Uppsala county), who had had at least one collection of ICS (ATC code R03BA, R03AK) after the diagnosis of asthma were included. We excluded patients who had an asthma diagnosis registered prior to 2006; patients who were not residents in either of the two regions at the index date; and patients with comorbid diseases commonly treated with oral corticosteroids (OCS) (Crohn's disease, ulcerative colitis, rheumatoid arthritis or polymyalgia rheumatica before the index date) (Supplementary Table 1). These exclusions resulted in a cohort of 51,395 asthma patients in which we analyzed regular asthma follow-up visits after the index date. Analyses of follow-up visits after a moderate or severe exacerbation were performed in a cohort of 22,097 patients who had at least one exacerbation between 2006 and 2017.

## Outcomes and Variables

The main outcome was asthma-related follow-up visits defined as either a primary care nurse or physician visit with asthma as the main diagnosis, or a secondary outpatient visit with asthma as the main diagnosis. Two types of asthma-related visits were identified; I) regular follow-up visits after the index date, and II) follow-up visits after an exacerbation (post-exacerbation visit). Based on guideline recommendations, regular follow-up visits were identified within 15 months after the index date, and post-exacerbation follow-up visits were identified within 15 months after an exacerbation. The present study defined a moderate exacerbation as a deterioration of asthma which led to either a collection of OCS or an

emergency visit at hospital. A severe exacerbation was defined as a hospitalization with asthma as the main diagnosis. Recurrent exacerbations within 14 days were combined and considered as one exacerbation.

In this study, the ICS dose (budesonide equivalent) collected at the index date was used to indicate asthma severity at the time of inclusion in the study. Low/medium dose ICS (≤800 μg) with or without long-acting $\beta_2$-agonist (LABA) was considered as mild/moderate asthma and high dose ICS (>800 μg) was considered as severe asthma. Comorbidities were identified using primary and secondary diagnoses (ICD-10 codes) from all available data in primary care medical records and the national Patient Register at any time prior to the index. Asthma medications were identified in the national Prescribed Drug Register (ATC codes) (Supplementary Table 1).

## Statistical Analyses

Baseline characteristics were described as mean (standard deviation [SD]) for continuous variables and absolute and relative frequencies for categorical variables. For each individual, the follow-up period for regular asthma visits started on the index date (first ICS collection) and ended after 15 months. Similarly, the follow-up period for exacerbation-related visits started on the registered date of the exacerbation and ended 15 months later.

To evaluate the proportion of patients who had had regular follow-up visits within 15 months, the probability of regular and exacerbation-related visits was estimated using the cumulative incidence function with corresponding confidence intervals. In addition, the probabilities of having an asthma-related follow-up visit overall and by type of visit (primary care visit or outpatient secondary care visit) were analysed with a time-to-event analysis using Kaplan–Meier estimates. Follow-up visits after moderate and severe exacerbations were analysed separately, using the Kaplan–Meier function. Patients were censored in the event of an OCS-related diagnosis, exacerbation, emigration or death, whichever occurred first. These probabilities represent the chances of having an asthma-related follow-up visit in the absence of exacerbation, migration, and death and are thus useful for comparisons of visit probabilities across groups of patients and time.

The trends over time, regarding both regular follow-up visits and post-exacerbation visits, were explored by calculating the probability of a visit within 15 months for each year separately (2006–2017) using the cumulative incidence function with 95% confidence intervals (CIs).

To explore the effects of sex and age (18–34, 35–49, 50–64, 65+ years) on regular asthma-related follow-up visits, the calendar year was used as a continuous variable and the incidence rate ratios (IRR) of asthma-related follow-up visits with 95% CI were calculated using a negative binomial regression model.

To explore the changes in visit patterns over a longer follow-up period, the cumulative incidence of both a regular visit and a post-exacerbation visit with 30 months follow-up was calculated.

# Results

A total of 51,349 patients (mean age 47.6 years, 63% females) with a claim of an ICS inhaler after the first registered diagnosis of asthma in primary or secondary care between 2006 and 2017 were included in the study (Table 1). Of these, 48,458 patients had a mild/moderate asthma and 2891 patients had a severe asthma at the index. The most common chronic comorbidity was hypertension (19.5%), whereas 13.8% had allergies and 13.2% dermatitis/eczema (Table 1). Overall, 5.9% had a concomitant diagnosis of chronic obstructive pulmonary (COPD) disease.

## Regular Asthma Visits in Primary and Secondary Care

During the 15 months follow-up period after the index, 17,573 patients out of 51,349 had at least one regular asthma follow-up visit (33.9% of the patients with mild/moderate and 40.4% of patients with severe asthma), 10,276 had one visit and 7297 had two or more visits (Table 2). The overall probability of having a regular follow-up visit was 37.4% (95% CI: 37.0–37.8). The majority of follow-up visits occurred in primary care (Figure 1 and Table 2). Female sex and increasing age were associated with a higher rate (IRR) of a follow-up visit 15 months after the index (Supplementary Table 2). The overall probability of having a regular visit did not increase markedly over a follow-up period of 30 months (47.6%, 95% CI: 47.1–48.1).

**Table 1** Baseline Characteristics of Study Population

| Patient Characteristics | All patients | Patients without visits | Patients with visits |
|---|---|---|---|
| Patients, n | 51,349 | 33,776 | 17,573 |
| Age, Mean (SD) | 47.6 (18.4) | 47.3 (18.4) | 48.3 (18.3) |
| Females, n (%) | 32,164 (62.6) | 21,017 (62.2) | 11,147 (63.4) |
| Index year | | | |
| 2006–2009 | 9048 (17.6) | 7040 (20.8) | 2008 (11.4) |
| 2010–2013 | 23,155 (45.1) | 15,066 (44.6) | 8089 (46.0) |
| 2014–2017 | 19,146 (37.3) | 11,670 (34.6) | 7476 (42.5) |
| ICS dose at index (budesonide equivalent) n, (%) | | | |
| Low/medium dose (≤800 µg) | 48,458 (94.3) | 32,052 (94.9) | 16,406 (93.4) |
| High dose (>800 µg) | 2891 (5.7) | 1724 (5.1) | 1167 (6.6) |
| Comorbidities, n (%) | | | |
| Respiratory related | | | |
| -Chronic rhinitis | 1221 (2.4) | 734 (2.2) | 487 (2.8) |
| -Nasal polyps | 1240 (2.4) | 787 (2.3) | 453 (2.6) |
| -Acute lower respiratory tract infections | 5861 (11.4) | 3677 (10.9) | 2184 (12.4) |
| -Chronic bronchitis | 905 (1.8) | 588 (1.7) | 317 (1.8) |
| -COPD | 3015 (5.9) | 2172 (6.4) | 843 (4.8) |
| -Pneumonia | 4772 (9.3) | 3182 (9.4) | 1590 (9.0) |
| -Acute upper respiratory tract infections | 15,526 (30.2) | 9825 (29.1) | 5701 (32.4) |
| Hypertension | 10,022 (19.5) | 6396 (18.9) | 3626 (20.6) |
| Allergies | 7065 (13.8) | 4613 (13.7) | 2452 (14.0) |
| Dermatitis and eczema | 6781 (13.2) | 4254 (12.6) | 2527 (14.4) |
| Depression | 4907 (9.6) | 3215 (9.5) | 1692 (9.6) |
| Malignant neoplasm | 3218 (6.3) | 2145 (6.4) | 1073 (6.1) |
| Diabetes, type 2 | 2772 (5.4) | 1809 (5.4) | 963 (5.5) |
| Ischaemic heart disease | 2627 (5.1) | 1776 (5.3) | 851 (4.8) |
| Heart Failure | 1426 (2.8) | 1013 (3.0) | 413 (2.4) |
| Osteoporosis | 770 (1.5) | 492 (1.5) | 278 (1.6) |

**Table 2** Asthma Follow-Up Visits During 15 Months After Index and 15 Months After an Exacerbation, by Type of Visit

| | Primary care visit | Outpatient secondary care visit | Any visit (primary or secondary care) |
|---|---|---|---|
| **Regular follow-up visits** | | | |
| Number of visits, n (%) | | | |
| 0 visits | 36,627 (71.3) | 46,951 (91.4) | 33,776 (65.8) |
| 1 visit | 9229 (18.0) | 3135 (6.1) | 10,276 (20.0) |
| 2 or more visits | 5493 (10.7) | 1263 (2.5) | 7297 (14.2) |
| Mean (SD) | 0.47 (1.10) | 0.14 (0.82) | 0.61 (1.38) |
| **Exacerbation-related visits** | | | |
| Number of visits, n (%) | | | |
| 0 visit | 17,891 (81.4) | 20,138 (91.7) | 16,699 (76.0) |
| 1 visit | 2578 (11.7) | 1270 (5.8) | 3015 (13.7) |
| 2 or more visits | 1503 (6.8) | 564 (2.6) | 2258 (10.3) |
| Mean (SD) | 0.31 (0.83) | 0.14 (0.76) | 0.45 (1.15) |

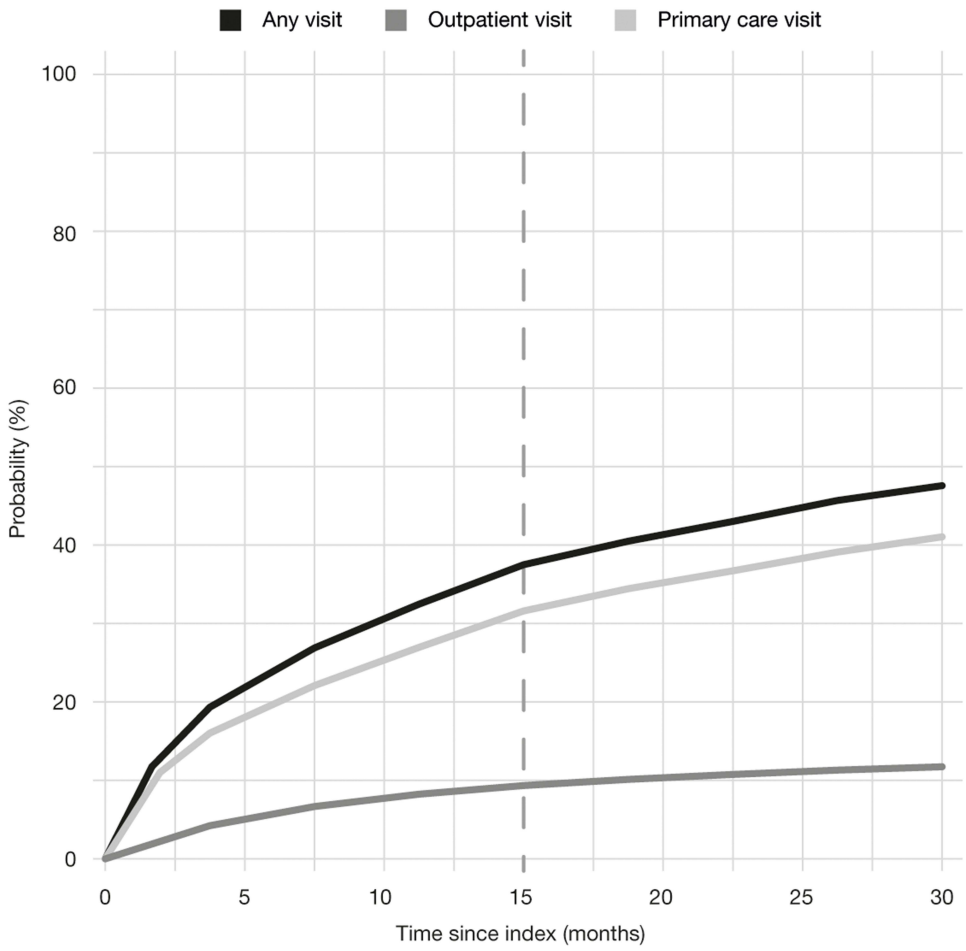


**Figure 1** Probability of having an asthma follow-up visit within 15 months after index date*.
**Note**: Patients are censored at time of first moderate or severe exacerbation.

## Characteristics of Patients with and without Follow-Up Visits

Respiratory-related comorbidities were slightly more common in patients who had had a follow-up visit and a slightly higher proportion of patients in this group collected a high dose ICS at index (Table 1). The follow-up visit patterns were similar in men and women, and the mean age was the same for those who had a follow-up visit and those who did not.

The proportion of patients who collected ICS, ICS/LABA, LABA, LTRA and SABA was higher among patients with a regular follow-up visit compared to those without a visit within 15 months after the index (Table 3). In contrast, the proportion of patients who collected OCS was higher in patients with no follow-up visit (Table 3).

## Follow-Up Visits After an Exacerbation (Post-Exacerbation Visits)

In total, 22,097 (43%) of the patients in this study had at least one acute exacerbation of asthma, of which 62.4% experienced a second exacerbation, within 15 months from the index date. The average time between the first and the second exacerbation was nine months (Interquartile range, IQR: 2.6–22.2).

Among patients who had had an exacerbation of asthma, 5273 patients had at least one follow-up visit within 15 months after the exacerbation; 3015 had one visit and 2258 had two or more visits (Table 2). The overall probability of having a visit due to asthma within 15 months after the exacerbation was 31.0% (95% CI: 30.3–31.8). The probability of

**Table 3** Respiratory Related Medications During 15 Months Following Index

| Respiratory Medications, n (%) | All patients (n=51,349) | Patients without visits (n=36,020) | Patients with visits (n=15,329) |
|---|---|---|---|
| ICS mono inhaler | 21,456 (41.8) | 12,428 (36.8) | 9028 (51.4) |
| ICS/LABA combinations | 18,241 (35.5) | 10,744 (31.8) | 7497 (42.7) |
| ICS/LABA/LAMA combinations | 3 (0.0) | 2 (0.0) | 1 (0.0) |
| Any ICS containing inhaler | 36,210 (70.5) | 21,607 (64.0) | 14,603 (83.1) |
| LABA | 5474 (10.7) | 3060 (9.1) | 2414 (13.7) |
| LAMA | 2499 (4.9) | 1649 (4.9) | 850 (4.8) |
| SABA | 23,790 (46.3) | 14,095 (41.7) | 9695 (55.2) |
| Leukotriene modifiers | 4710 (9.2) | 2301 (6.8) | 2409 (13.7) |
| Any oral corticosteroids | 9823 (19.1) | 7073 (20.9) | 2750 (15.6) |
| Regular oral corticosteroids* | 1275 (2.5) | 1019 (3.0) | 256 (1.5) |
| N-acetylcysteine | 6617 (12.9) | 4209 (12.5) | 2408 (13.7) |
| Nasal corticosteroids | 14,256 (27.8) | 8661 (25.6) | 5595 (31.8) |

**Note**: Medications claimed from pharmacy *Defined as at least 4 collections.

having a visit after a severe exacerbation was 47.2% (95% CI: 40.8–52.9) whereas after a moderate exacerbation the probability was 30.8% (95% CI; 30.0–31.5) (Figure 2). The probability of having an outpatient visit was higher if the exacerbation had been severe rather than moderate (Figure 2).

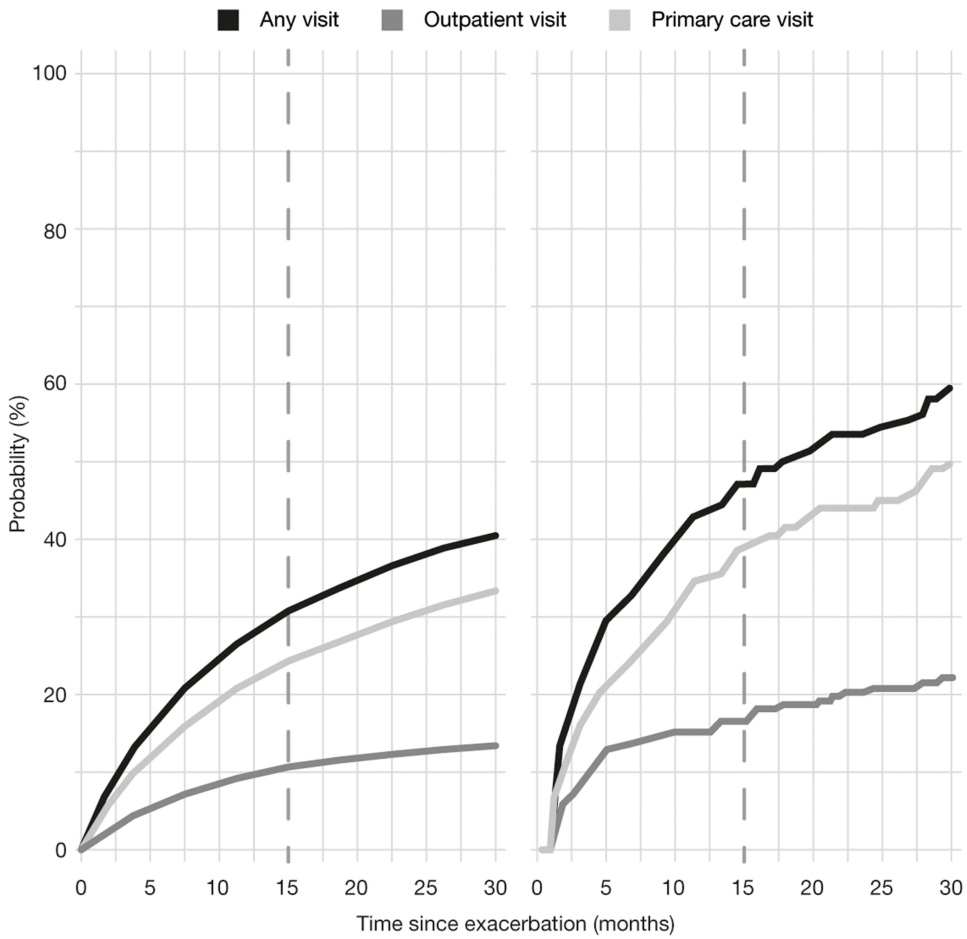


**Figure 2** Probability of having an asthma follow-up visit within 15 months after an exacerbation, by type of index exacerbation and type of follow-up visit.
**Note**: Patients are censored at time of second moderate or severe exacerbation.

The probability of having an asthma-related visit within 30 months after a moderate exacerbation was 40.8% (95% CI: 39.9–41.7) and 59.2% (95% CI: 52.2–65.2) after a severe exacerbation.

## Pharmacological Treatment

Overall, 70.5% of the asthma patients collected at least one ICS inhaler, either in mono or fixed combinations, during the 15 months of follow-up after the index (Figure 3). Among these, 26.2% collected ICS inhalers at least four times

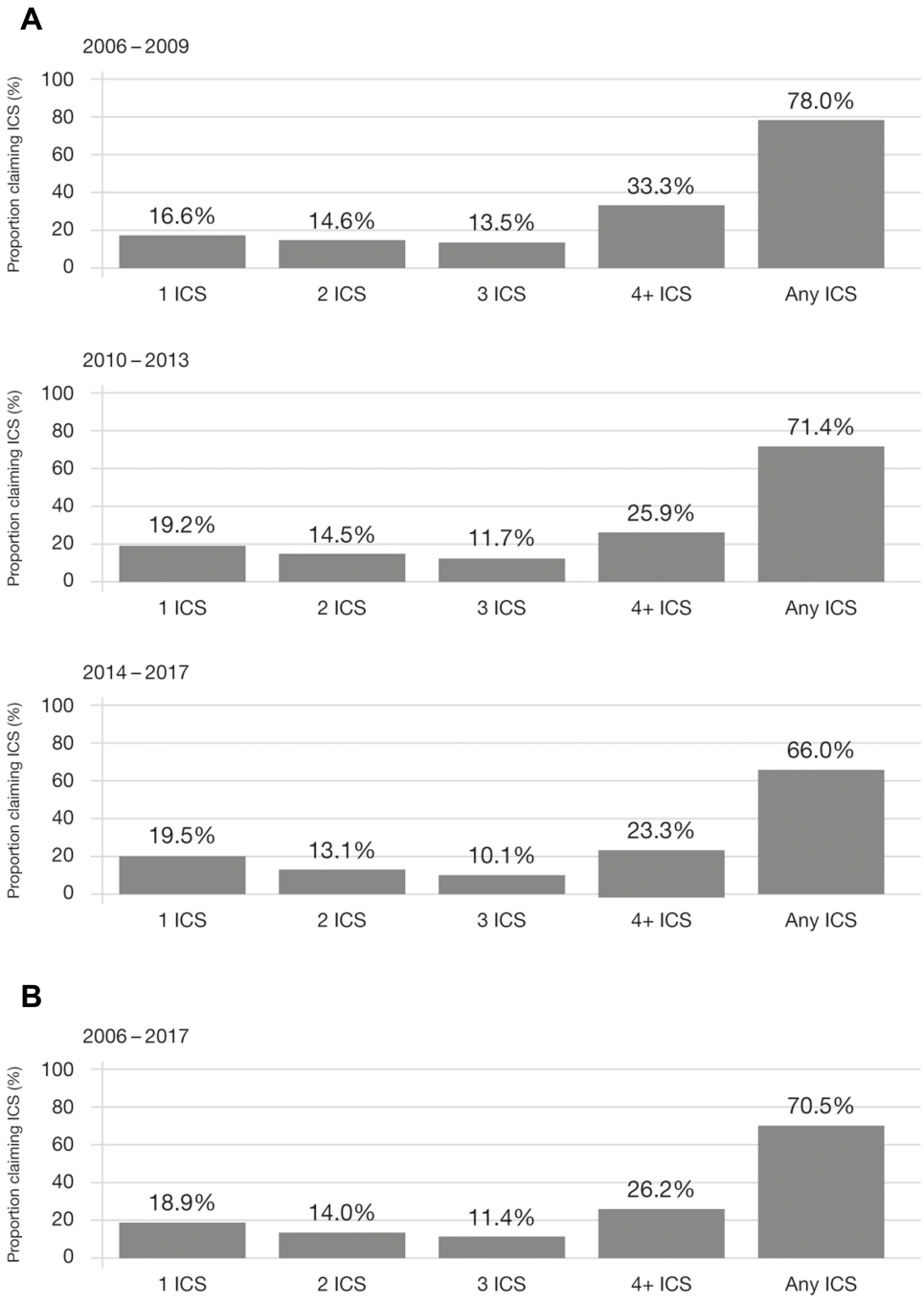


**Figure 3** Proportion of patients with 1, 2, 3, ≥4 claims of ICS* at pharmacy during 15 months follow-up after index, stratified by (**A**) calendar period of inclusion; 2006–2009, 2010–2013, 2014–2017 as well as (**B**) the full follow-up period 2006–2017.
**Notes**: ICS collection at pharmacy includes both mono- and combination treatment.
**Abbreviation**: ICS, inhaled corticosteroid.

(Figure 3), most commonly as mono inhalers (42% of all dispensed ICS inhalers) (Table 3). Short-acting $\beta_2$-agonist (SABA) was collected by 46.3% and OCS by 19.1% whereof 2.5% were collecting OCS regularly.

Among patients who had acute asthma exacerbations, 74.8% collected at least one ICS inhaler and 43.9% collected OCS during the 15 months follow-up period after the exacerbation.

## Changes in Visit Patterns and ICS Collection Over Time

The probability of having at least one follow-up visit within 15 months after the index increased over the study period, from 20.1% in 2006 to 48.0% in 2017. Also, the probability of a visit after the first exacerbation increased slightly over time, from 27.6% in 2006 to 32.8% in 2017 (Figure 4). In contrast, the proportion of patients who collected at least one ICS inhaler within 15 months after the index decreased over time, from 78% for patients who were included during 2006–2009 to 66% for patients included in 2014–2017 (Figure 3).

# Discussion

In this study of more than 51,000 asthma patients treated with ICS at some point between 2006 and 2017, we found that the probability of an asthma-related follow-up visit either in primary or secondary care was only 37% within 15 months after the index date of first collection of ICS, regardless of disease severity at the index. Almost half of the patients experienced an exacerbation and among those, the overall probability of a follow-up visit within 15 months after the

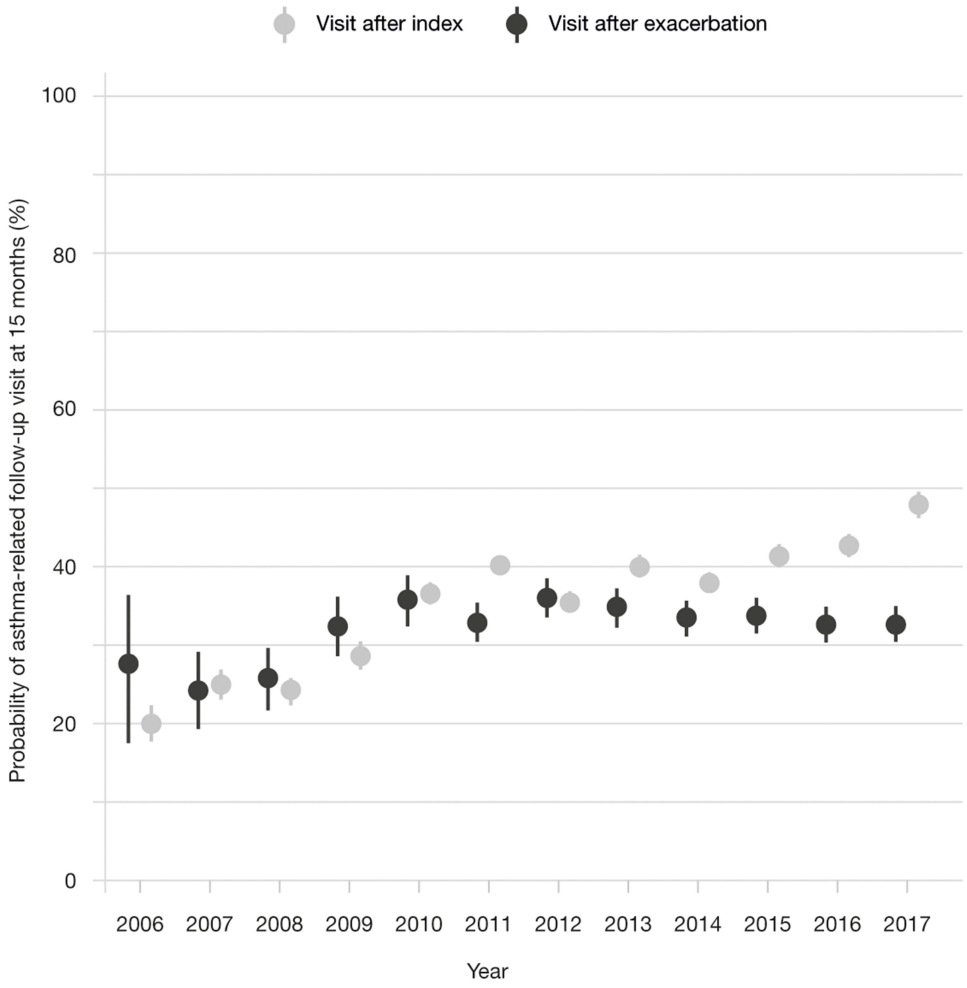


**Figure 4** Probability of having an asthma follow-up visit at 15 months after index date and after first exacerbation, by calendar year of inclusion.

exacerbation was only 31%. A positive finding was that the probability of follow-up visits increased over time during the study period. However, over the same period the proportion of patients collecting ICS inhalers decreased.

The clinical guidelines recommend that exacerbating patients should be evaluated within 6 weeks after an exacerbation.[5] Thus, one of the most alarming findings in our study was that less than half of the patients with severe exacerbations had a follow-up visit to evaluate treatment and symptoms and even fewer had a follow-up visit after a moderate exacerbation. Overall, the findings of this study highlight that adherence to asthma management guidelines in general was low. This is in line with previous research that indicates that only one-third of patients with severe asthma and only one in five of patients with mild to moderate asthma had a contact with primary care in Sweden.[9] Also, a recent Finnish study showed that asthma patients had in average only four regular asthma reviews during a 12-year period.[10]

Regular asthma reviews improve asthma outcomes,[6,11] and the current Swedish guidelines recommend regular follow-up of patients with uncontrolled asthma and define in detail the contents of the clinical asthma reviews.[5] These guidelines were published in 2007, and as expected we found an overall increase in the proportion of patients with an asthma follow-up visit during the study's 11-year observation period (2006–2017), even though the follow-up rate still remained clearly insufficient.

Suboptimal adherence to guidelines is a common worldwide problem seen not only in asthma,[12–15] and in particular in severe asthma,[16] but also in chronic obstructive pulmonary disease and other common chronic conditions, such as cardiovascular diseases and diabetes.[17–21] Asthma reviews are known to be significantly associated with a reduced risk of severe asthma exacerbations.[22] Additionally, the risk of a subsequent, acute exacerbation is increased in patients who previously have had a severe asthma exacerbation, indicating that these patients need high-intensity post-exacerbation treatment. Therefore, the findings in our study on the low frequency of asthma reviews after acute exacerbations were particularly worrying, although poor follow-up routines in asthma care have been reported also from other countries,[23,24] regardless of the healthcare system or demographics.

In Sweden, the organizational challenges of the health-care system, mainly due to the lack of general practitioners and increased workloads in primary care, may have contributed to the low frequency of follow-up visits and increased discontinuity in asthma care over the past decades.[25] Alternatives to traditional face-to-face consultations with a physician, such as telephone and video consultations and consultations with an asthma/COPD nurse, have become more common.[26,27] As our results were based on registered, face-to-face visits with a physician, the alternative consultation ways may have affected the results of our study. Particularly, telephone consultations have been a part of routine primary care in Sweden for a long time. Although nurse-led clinics in primary care have shown to improve the quality of asthma care,[26] only a minority of patients have a care contact with such a clinic.[8] A well-structured video or telephone consultation can be a complement to a traditional follow-up visit.[28,29] However, as there has been an increasing shortage of resources and staff in the Swedish primary care in recent decades, prescription renewals without paying attention to evaluating asthma control, inhaler technique, and prescribed medications are likely to be common. Patients with chronic conditions are typically prescribed medications to last for one year, and it is possible for the patient to contact their general practitioner by telephone or email to get a prescription renewal without talking to or visiting a health-care professional. This saves time, both for patients and physicians, but it may also be a missed opportunity to provide patient education and adjust treatments. In our study, we found that patients without an asthma follow-up visit collected less inhaled asthma treatments including ICS than those who had a visit, but they also collected more OCS. This is a sign of an insufficient asthma treatment, suboptimal asthma control, and an increased risk of disease deterioration[30] in patients who had not had a follow-up visit, which highlights the importance of a face-to-face visit with a health-care provider.

In the present study, all patients had an asthma diagnosis prior to the collection of the index ICS. However, 75% of the patients did not collect enough of ICS inhalers to cover their daily treatment during the 15-months follow-up, and 30% did not collect any ICS inhalers after the index collection. Low adherence to treatments with ICS has been described in other recent reports from Sweden: one study[31] showed that 60% of patients with asthma did not collect ICS after an asthma-related hospitalization, and another study reported an overuse of SABA parallel to a nearly doubled number of patients not claiming ICS during the observation period.[30] As such undertreatment leads to poor asthma control, it is not

surprising that previous research consistently shows insufficient asthma control in patients in Sweden over the last two decades.[7,8]

### Strengths and Limitations

A major strength of this study is that it includes an unselected, population-based cohort of Swedish asthma patients, which limits the risk of selection bias. Furthermore, it includes real-world data from both primary and secondary care settings. The data extraction from primary care electronic medical records linked with mandatory, and thus comprehensive national health-care registers provides solid and unique data. However, there are also some methodological limitations that should be considered when interpreting the results. Data about collections of prescription medications are used as a proxy for medication use, but leave the level of actual use unknown. ICS dose collected at the index date was used as a proxy for disease severity. The large sample size in our study is likely to counteract possible bias due to missing data and misclassifications of asthma visits. Such bias could, for instance, occur if general practitioners have discussed the patient's asthma management passingly at a visit scheduled for another reason than asthma, thus possibly not having registered the asthma diagnosis. Additionally, some patients may have had a remote review with no registered visit as a consequence, or they have seen a physician outside the counties of Stockholm and Uppsala. Further, we do not have access to all comorbidities in our dataset, why there may be some patients treated with OCS for other diseases than asthma, also after excluding patients with Crohn's disease, ulcerative colitis, rheumatoid arthritis and polymyalgia rheumatica.

## Conclusion

In this study about the management of asthma in Sweden, we found that the adherence to national guidelines is insufficient as only approximately a third of asthma patients, regardless of asthma severity, have a regular asthma follow-up visit within a 15-month period. In addition, only one of three patients with an acute asthma exacerbation had a follow-up visit with a health-care provider and only two out of five patients with severe exacerbations had a follow-up visit. Patients without an asthma follow-up visit collected less inhaled maintenance treatments and more OCS than those who had a visit. This indicates a poor quality of maintenance asthma treatment and poor asthma control in patients without asthma reviews. This study highlights the need for intensification of asthma follow-up, especially in patients who exacerbate, in order to treat uncontrolled asthma and prevent future exacerbations.

## Abbreviations

ATC, Anatomical Therapeutic Chemical; CI, confidence intervals; COPD, cChronic obstructive pulmonary disease; GINA, Global Initiative for Asthma; ICD, International Classification of Diseases; ICS, inhaled corticosteroids; IQR, interquartile range; IRR, incident rate ratios; LABA, long-acting $\beta_2$-agonists; LTRA, leukotriene antagonists; OCS, oral corticosteroids; SABA, short-acting $\beta_2$-agonist: SD, standard deviation.

## Data Sharing Statement

The dataset supporting the conclusions of this article can be available upon request.

## Ethics Approval and Informed Consent

This study was performed in accordance with applicable legislation on non-interventional studies and/or observational studies. The study was approved by the Uppsala regional ethics committee (reference number 2016/486). The linkage of registers data was approved and performed by the Swedish National Board of Health and Welfare. Individual patient consents to participate were not collected as they are not required in Sweden when public register data is used for research.

## Consent for Publication

All authors read and approved the final manuscript. All authors gave consent to publish these data.

## Author Contributions

All authors contributed to the study design, data analysis, drafting or revising the article and have agreed to submit the current version to Journal of Asthma and Allergy.

## Funding

The study was sponsored by AstraZeneca.

## Disclosure

GT and SdFL are employed by AstraZeneca. FW is employed at Statisticon for which AstraZeneca is a client.

CJ has received payments for educational activities from AstraZeneca, Boehringer Ingelheim, Chiesi, Novartis, and Teva, and has served on advisory boards arranged by AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, and Teva. BS has received honoraria for educational activities and lectures from AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Novartis and Teva, and has served on advisory boards arranged by AstraZeneca, Novartis, Meda, GlaxoSmithKline, Teva and Boehringer Ingelheim. HS has received honoraria for educational activities from Boehringer Ingelheim, Novartis, AstraZeneca, Chiesi, and TEVA, an unrestricted research grant from AstraZeneca, and has served on advisory boards arranged by AstraZeneca, Novartis, Chiesi, and GlaxoSmithKline. The authors report no other conflicts of interest in this work.

## References

1. Global Asthma Network. The global asthma report 2018. Available from: http://www.globalasthmareport.org. Assessed July 2021.
2. Soriano JB, Abajobir AA, Abate KH. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the global burden of disease study 2015. *Lancet Respir Med*. 2017;5(9):691–706. doi:10.1016/S2213-2600(17)30293-X
3. Ebmeier S, Thayabaran D, Braithwaite I, et al. Trends in international asthma mortality: analysis of data from the WHO mortality database from 46 countries (1993–2012). *Lancet*. 2017;390(10098):935–945. doi:10.1016/S0140-6736(17)31448-4
4. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. Available from: http://ginasthma.org/gina-reports/. Updated 2021. Accessed July 2021.
5. National Board of Health and Welfare. Nationella riktlinjer för astma och KOL; 2020. [National guidelines for asthma and COPD, 2020]. Available from: www.socialstyrelsen.se. Accessed January, 2022.
6. Backer V, Bornemann M, Knudsen D, et al. Scheduled asthma management in general practice generally improve asthma control in those who attend. *Respir Med*. 2012;106(5):635–641. doi:10.1016/j.rmed.2012.01.005
7. Stallberg B, Lisspers K, Hasselgren M, et al. Asthma control in primary care in Sweden: a comparison between 2001 and 2005. *Prim Care Respir J*. 2009;18(4):279–286. doi:10.4104/pcrj.2009.00024
8. Lisspers K, The PRAXIS-study, asthma report; 2017. Available from: www.praxisstudien.se. Acessed april 04, 2022.
9. Larsson K, Ställberg B, Lisspers K, Telg G, Johansson G, Thuresson M, Janson C. Prevalence and management of severe asthma in primary care: an observational cohort study in Sweden (PACEHR). *Respir Res*. 2018;19(1):12. doi:10.1186/s12931-018-0719-x
10. Takala J, Ilmarinen P, Tuomisto LE, et al. Planned primary health care asthma contacts during 12-year follow-up after Finnish national asthma programme: focus on spirometry. *NPJ Prim Care Respir Med*. 2020;30(1):8. doi:10.1038/s41533-020-0166-2
11. Pinnock H, Fletcher M, Holmes S, et al. Setting the standard for routine asthma consultations: a discussion of the aims, process and outcomes of reviewing people with asthma in primary care. *Prim Care Respir J*. 2010;19(1):75–83. doi:10.4104/pcrj.2010.00006
12. Yawn BP, Rank MA, Cabana MD, et al. Adherence to Asthma guidelines in children, tweens, and adults in primary care settings: a practice-based network assessment. *Mayo Clin Proc*. 2016;91(4):411–421. doi:10.1016/j.mayocp.2016.01.010
13. Weidinger P, Nilsson JL, Lindblad U. Adherence to diagnostic guidelines and quality indicators in asthma and COPD in Swedish primary care. *Pharmacoepidemiol Drug Saf*. 2009;18(5):393–400. doi:10.1002/pds.1734
14. Chapman KR, Hinds D, Piazza P, et al. Physician perspectives on the burden and management of asthma in six countries: the Global Asthma Physician Survey (GAPS). *BMC Pulm Med*. 2017;17(1):153. doi:10.1186/s12890-017-0492-5
15. Cloutier MM, Salo PM, Akinbami LJ, et al. Clinician agreement, self-efficacy, and adherence with the guidelines for the diagnosis and management of asthma. *J Allergy Clin Immunol Pract*. 2018;6(3):886–894.e4. doi:10.1016/j.jaip.2018.01.018
16. Most JF, Ambrose CS, Chung Y, et al. Real-world assessment of asthma specialist visits among U.S. patients with severe asthma. *J Allergy Clin Immunol Pract*. 2021;9:3662–3671.e1. doi:10.1016/j.jaip.2021.05.003
17. Hill MN, Miller NH, DeGeest S, et al. Adherence and persistence with taking medication to control high blood pressure. *J Am Soc Hypertens*. 2011;5(1):56–63. doi:10.1016/j.jash.2011.01.001
18. Gyberg V, De Bacquer D, De Backer G, et al. Patients with coronary artery disease and diabetes need improved management: a report from the EUROASPIRE IV survey: a registry from the EuroObservational research programme of the European Society of Cardiology. *Cardiovasc Diabetol*. 2015;14:133. doi:10.1186/s12933-015-0296-y
19. Eder S, Leierer J, Kerschbaum J, et al. Guidelines and clinical practice at the primary level of healthcare in patients with type 2 diabetes mellitus with and without kidney disease in five European countries. *Diab Vasc Dis Res*. 2019;16(1):47–56. doi:10.1177/1479164118795559

20. Giezeman M, Arne M, Theander K. Adherence to guidelines in patients with chronic heart failure in primary health care. *Scand J Prim Health Care*. 2017;35(4):336–343. doi:10.1080/02813432.2017.1397253
21. Geary L, Hasselström J, Carlsson AC, et al. Secondary prevention after stroke/transient ischemic attack: a randomized audit and feedback trial. *Acta Neurol Scand*. 2019;140(2):107–115. doi:10.1111/ane.13109
22. Park HJ, Byun MK, Kim HJ, et al. Regular follow-up visits reduce the risk for asthma exacerbation requiring admission in Korean adults with asthma. *Allergy Asthma Clin Immunol*. 2018;14(1):29. doi:10.1186/s13223-018-0250-0
23. Suruki RY, Daugherty JB, Boudiaf N, et al. The frequency of asthma exacerbations and healthcare utilization in patients with asthma from the UK and USA. *BMC Pulm Med*. 2017;17(1):74. doi:10.1186/s12890-017-0409-3
24. Sarinho E, Queiroz GRESD, Dias MLCDM, et al. Asthma-related hospitalizations and lack of outpatient follow-up treatment. *J Bras Pneumol*. 2007;33(4):365–371. doi:10.1590/S1806-37132007000400004
25. Johannessen A, Lehmann S, Omenaas ER, et al. Post-bronchodilator spirometry reference values in adults and implications for disease management. *Am J Respir Crit Care Med*. 2006;173(12):1316–1325. doi:10.1164/rccm.200601-023OC
26. Lisspers K, Ställberg B, Hasselgren M, et al. Primary health care centres with asthma clinics: effects on patients knowledge and asthma control. *Prim Care Respir J*. 2009;19(1):37–44. doi:10.4104/pcrj.2009.00043
27. Ljungberg H, Carleborg A, Gerber H, et al. Clinical effect on uncontrolled asthma using a novel digital automated self-management solution: a physician-blinded randomised controlled crossover trial. *Eur Respir J*. 2019;54(5):1900983. doi:10.1183/13993003.00983-2019
28. Wherton J, Shaw S, Papoutsi C, et al. Guidance on the introduction and use of video consultations during COVID-19: important lessons from qualitative research. *BMJ Lead*. 2020;4(3):120–123. doi:10.1136/leader-2020-000262
29. IPCRG. Remote respiratory consultations. desktop helper. No 11; January, 2021. First Edition. Available from: https://www.ipcrg.org/dth11. Accessed January 2021.
30. Nwaru BI, Ekström M, Hasvold P, Wiklund F, Telg G, Janson C. Overuse of short-acting β 2 -agonists in asthma is associated with increased risk of exacerbation and mortality: a nationwide cohort study of the global SABINA programme. *Eur Respir J*. 2020;55(4):1901872. doi:10.1183/13993003.01872-2019
31. Ekström M, Nwaru BI, Wiklund F, Telg G, Janson C. Risk of rehospitalization and death in patients hospitalized due to asthma. *J Allergy Clin Immunol Pract*. 2021;9(5):1960–1968.e4. doi:10.1016/j.jaip.2020.12.030