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JAANA TAKALA

Planned Follow-up of Adult-onset Asthma in Primary Health Care

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ACADEMIC DISSERTATION
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the Faculty of Medicine and Health Technology
of Tampere University,
for public discussion in the Auditorium 2
of the Frami B building, Kampusranta 9B, Seinäjoki,
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ACADEMIC DISSERTATION
Tampere University, Faculty of Medicine and Health Technology
Seinäjoki Central Hospital, Department of Respiratory Medicine
Finland

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PunaMusta Oy – Yliopistopaino
Joensuu 2024

To my family

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The present dissertation was carried out at Tampere University and Wellbeing Services County of South Ostrobothnia. This thesis got its first spark when I was working at the Department of Respiratory Diseases in Seinäjoki Central Hospital in 2015-2016 during my specialization in general medicine.

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Jaana Takala

ABSTRACT

Adult-onset asthma is the predominant phenotype of asthma with a worse prognosis and lower remission rate than in childhood asthma. Primary health care has the main responsibility for managing adult-onset asthma; however, little is known about conducting a long-term follow-up of asthma in primary health care and how systematically asthma is assessed during the contacts.

The present thesis aims to evaluate how planned asthma follow-up contacts occur in primary health care during a long-term period and how factors affecting asthma are assessed during these contacts. Further aims were to investigate whether there was a difference in evaluating asthma depending on whether the general practitioner (GP), nurse, or both professionals participated in the follow-up and whether possible factors associated with non-participation in follow-up could be identified.

The present thesis investigated the data collected from adult-onset asthma patients in the Seinäjoki Adult Asthma Study (SAAS). The SAAS study is a real-life 12-year follow-up study of 203 patients who were diagnosed with asthma in adulthood in the respiratory department at Seinäjoki Central Hospital. The diagnosis of asthma was made by respiratory specialist based on typical symptoms and objective lung function measurements. Smokers and patients with concomitant chronic obstructive pulmonary disease (COPD) or other comorbidities were not excluded. Thus, this study population well represents the typical primary health care asthma population. In addition to the data gathered from all the asthma-related health care contacts of the 203 patients during the 12-year period, data from the medication purchased was obtained on patients entitled to asthma medication reimbursement from the Finnish Social Insurance Institution.

Most of the asthma patients in the Seinäjoki Adult Asthma Study population had asthma follow-up contacts mainly in primary health care. Based on the results, regular asthma follow-up contacts did not occur according to guidelines in primary health care in the Hospital District of South Ostrobothnia when only a third of patients attended a planned asthma contact per year, and most of the patients had <4 planned contacts during the 12-year period. Overall, 28% of patients in the SAAS -study population had only 0–1 planned asthma follow-up contacts during the study.

Heavy alcohol consumption was associated with poorer participation in follow-ups based on our results.

This thesis showed high adherence to performing lung function tests, especially to spirometry, in primary health care. Spirometry, peak flow monitoring, or both were conducted in almost 88% of contacts. Similarly, the documentation of possible respiratory symptoms was found in 79% of planned contacts. Lung function tests and symptoms were screened even more often if the GP and nurse both participated in the visit. Asthma medication names and recommendations for the next planned follow-up contact were found in over 60% of contacts. Instead, the documentation of smoking, pack-years, comorbidities, lifestyle factors, revision of inhalation technique, and asthma action plan (AAP) were poorly carried out during planned contacts, according to recorded patient data. Of all planned asthma contacts smoking status was only documented in 17% of contacts, while the pack-years, comorbidities, revision of inhalation technique, and AAP were assessed based on the recorded patient data under every tenth visit.

The usual division of labor between the nurse and physician can explain some of the differences observed between the GP and nurse in assessing asthma. Significant differences between professionals did not emerge in many respects, and the results emphasized that both professional groups should improve asthma assessment. The results indicated that the co-operation between a nurse and a GP could produce the best outcome in comprehensively evaluating asthma.

To conclude, based on a 12-year real-life follow-up study, this thesis showed that applicating evidence-based asthma guidelines in asthma follow-up has been only partially successful in primary health care. A need exists to improve regular asthma follow-up and systematic assessment and guidance of the patient during the planned contacts. The results may help identify potential health-care practice-related causes for uncontrolled and difficult-to-treat asthma not being controlled, and which areas of asthma assessment and follow-up require more attention in primary health care.

TIIVISTELMÄ

Aikuisiällä alkava astma on yleisin astman ilmenimismuoto. Se eroaa lapsuusiällä alkaneesta astmasta muun muassa huonomman ennusteensa ja matalamman remissioasteensa osalta. Päävastuu aikuisiän astman diagnostiikasta, hoidosta ja seurannasta on perusterveydenhuollossa. Astman pitkäaikaisesta seurannasta ja siitä, miten astmaa perusterveydenhuollon seurantakäynneillä arvioidaan, tiedetään kuitenkin hyvin vähän.

Tämän väitöskirjatutkimuksen tavoitteena oli selvittää, miten astman suunnitellut seurantakäynnit perusterveydenhuollossa toteutuvat pitkän seurantajakson aikana, ja kuinka systemaattisesti astmaan vaikuttavia tekijöitä käynneillä arvioidaan. Tavoitteena oli myös tutkia, onko astman arvioinnissa eroa sen mukaan, osallistuuko käyntiin lääkäri, hoitaja vai molemmat, sekä onko mahdollista tunnistaa riskitekijöitä sille, ettei potilas osallistu seurantakäynneille.

Tutkimus toteutettiin Seinäjoki Adult Asthma Study (SAAS) -kohortin potilaista kerättyä aineistoa hyödyntäen. Seinäjoki Adult Asthma Study on 12-vuotinen seurantatutkimus, johon osallistui 203 aikuisiällä Seinäjoen keskussairaalan keuhkopoliklinikalla astmadiagnoosin saanutta potilasta. Astmadiagnoosi asetettiin tyypillisten oireiden ja objektiivisten keuhkofunktiomittausten perusteella keuhkosairauksien erikoislääkärin toimesta. Tupakoitsijat ja potilaat, jotka olivat aiemmin tupakoineet, tai joilla oli todettu samanaikainen keuhkoahtaumatauti tai muita liitännäissairauksia, otettiin tutkimusjoukkoon mukaan. Näin ollen tutkimuspopulaatio kuvaa hyvin tavanomaista perusterveydenhuollon potilasaineistoa. Potilaista 12 vuoden seurantajakson aikana kerättyjen terveydenhuollon käyntitietojen ja potilasasiakirjamerkintöjen lisäksi käytettävissä oli Kansaneläkelaitokselta saatuja tietoja astmalääkitysostoja tehneistä potilaista, joilla oli astmalääkityksen erityiskorvausoikeus.

Suurimmalla osalla SAAS-tutkimuskohortin potilaista astman seurantakäynnit toteutuivat pääosin perusterveydenhuollossa. Säännöllinen astman seuranta ei kuitenkaan toteutunut hoitosuositusten mukaisesti perusterveydenhuollossa Etelä-Pohjanmaan sairaanhoitopiiri alueella: yksi kolmesta potilaasta kävi seurantakäynnillä vuosittain, ja valtaosalla oli 12 vuoden seurantajakson aikana alle neljä suunniteltua kontaktia perusterveydenhuoltoon. Kaiken kaikkiaan koko SAAS-aineiston potilaista

28 %:lla oli vain 0–1 suunniteltua astman seurantakäyntiä seurantajakson aikana. Runsas alkoholin käyttö oli tulostemme perusteella yhteydessä huonompaan seurantakäynnille osallistumiseen.

Perusterveydenhuollon sitoutuminen keuhkojen toimintakokeiden, erityisesti spirometrian, suorittamiseen osana astman seurantaa oli korkea: joko spirometria, pef-seuranta tai molemmat tutkimukset tehtiin lähes 88 %:ssa kaikista perusterveydenhuollon seurantakäynneistä. Samoin mahdollisten astmaoireiden kirjaaminen oli suoritettu noin 79 %:ssa seurantakäynneistä. Keuhkojen toimintakokeiden ja hengitystieoireiden seulonta tehtiin vielä useammin, mikäli sekä lääkäri että sairaanhoitaja osallistuivat käyntiin. Astmalääkkeiden nimet ja suositus seuraavan seurantakäynnin ajankohdasta löytyivät kirjattuna yli 60 %:ssa käynneistä. Sen sijaan tupakointitietoja, askivuosihistoriaa, mahdollisia liitännäissairauksia, elintapoja sekä lääkkeen inhalaatiotekniikan ja omahoito-ohjeiden tarkastamista suoritettiin seurantakäynneillä huonosti tehtyjen potilasasiakirjamerkintöjen perusteella. Potilaan tupakkatausta mainittiin vain 17 %:ssa käynneistä. Tupakoitu askivuosihistoria, liitännäissairaudet, inhalaatiotekniikan tarkistaminen ja astman omahoitosuunnitelma arvioitiin alle joka kymmenellä käynnillä 12 vuoden seurannan aikana.

Tässä väitöskirjatutkimuksessa havaitut erot astman arviointikäytännöissä lääkärin ja hoitajan välillä voidaan osin selittää näiden ammattiryhmien välisellä tavanomaisella työnjaolla. Monilta osin merkittäviä eroja ammattilaisten välillä ei kuitenkaan ilmennyt, vaan ennemminkin sekä lääkärien että hoitajien tulisi parantaa astman arviointia. Sairaanhoitajan ja lääkärin yhteistyö voisi kuitenkin tuottaa parhaan tuloksen astman kokonaisvaltaisen arvioinnin onnistumisessa tässä väitöskirjassa esitettyjen tulosten perusteella.

Yhteenvetona voidaan todeta, että tämä 12-vuotiseen seurantaan perustuva väitöstutkimus osoitti, että näyttöön perustuvien astmaohjeiden toteuttaminen on onnistunut vain osittain perusterveydenhuollossa. Astman säännöllistä seurantaa, mutta myös potilaan systemaattista arviointia ja ohjausta suunniteltujen seurantakontaktien aikana on parannettava. Tämä tutkimus voi auttaa tunnistamaan mahdollisia terveydenhuollon käytäntöihin liittyviä syitä huonoon astman hallintaan. Lisäksi tulokset osoittavat, mitkä osa-alueet astman seurannassa ja arvioinnissa vaativat tarkempaa huomiota perusterveydenhuollossa.

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ABBREVIATIONS

AAP	Asthma Action Plan
ACT	Asthma Control Test
AQ20	Airways Questionnaire 20
BD	Bronchodilatation
BMI	Body mass index
CAT	COPD Assessment Test
CDT	Carbohydrate-deficient transferrin
COPD	Chronic obstructive pulmonary disease
FEV1	Forced expiratory volume in one second
FeNO	Fraction of exhaled nitric oxide
GINA	Global Initiative for Asthma
GP	General practitioner
GT	γ-glutamyltransferase
ICS	Inhaled corticosteroid
IgE	Immunoglobulin E
IQR	Interquartile range
LABA	Long-acting beta$_2$-agonist
NSAID	Non-steroidal anti-inflammatory drug
OCS	Oral corticosteroid
PEF	Peak expiratory flow
SAAS	Seinäjoki Adult Asthma Study
SABA	Short-acting beta$_2$-agonist

ORIGINAL PUBLICATIONS

This thesis is based on the following original communications, referred to in the text by their Roman numerals (I–IV).

I Takala J, Ilmarinen P, Tuomisto LE, Vähätalo I, Niemelä O, Kankaanranta H. 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: 8. doi: 10.1038/s41533-020-0166-2.

II Takala J, Vähätalo I, Tuomisto LE, Niemelä O, Ilmarinen P, Kankaanranta H. Participation in scheduled asthma follow-up contacts and adherence to treatment during 12-year follow-up in patients with adult-onset asthma. BMC Pulm Med. 2022; 22: 63. doi: 10.1186/s12890-022-01850-1.

III Takala J, Vähätalo I, Tuomisto LE, Niemelä O, Ilmarinen P, Kankaanranta H. Documentation of smoking in scheduled asthma contacts in primary health care: a 12-year follow-up study. npj Prim Care Respir Med. 2022; 32: 44. doi: 10.1038/s41533-022-00309-4

IV Takala J, Vähätalo I, Tuomisto LE, Niemelä O, Ilmarinen P, Kankaanranta H. Documentation of comorbidities, lifestyle factors, and asthma management during primary care scheduled asthma contacts. npj Prim Care Respir Med. In press.

AUTHOR'S CONTRIBUTION

The author of this thesis was the main author in Publications I, II, III and IV. The author's contributions to each publication, are described below.

Publication I The author contributed to the study design, interpreted the data, wrote the manuscript, and submitted the work for publication as the corresponding author.

Publication II The author participated to the study designing, analyzed and interpreted the data, draw the pictures to the publication, wrote the manuscript, and submitted the work for publication as the corresponding author.

Publication III The author participated to the study designing, conducted to the additional data collection, analyzed and interpreted the data, draw the pictures to the publication, wrote the manuscript, and submitted the work for publication as the corresponding author.

Publication IV The author contributed to the study designing, and participated in defining, coding, and interpreting the additional data to be collected. The author analyzed and interpretated all data, draw the pictures to the publication, wrote the manuscript, and submitted the work for publication as the corresponding author.

1 INTRODUCTION

Asthma is a heterogenous respiratory disease affecting all age groups and 1%–29% of the population worldwide (GINA 2023). Most asthma cases are diagnosed in adulthood (Honkamäki et al. 2019; Kankaanranta et al. 2017; Sood et al. 2013). Despite improvements in understanding, evidence-based guidelines, and asthma medications, poor disease control is common, and remission of adult-onset asthma is rare (Almqvist et al. 2020; Honkamäki et al. 2021; Ilmarinen et al. 2019; Larsson et al. 2020; Tuomisto et al. 2016). Reasons for poor control can be complex and may include patient-, therapy-, and healthcare-related factors, such as smoking, poor adherence to asthma medication, inhaler technique errors, lack of self-care instructions, and inadequate follow-up (Larsson 2020). Lung function, comorbidities, and lifestyle factors also affect disease control (GINA 2023; Porsbjerg & Mendiez-Gow 2017). The aspects above underscore why regular holistic assessment and guidance of asthma patients is essential.

Evidence-based asthma guidelines recommend that patients have regular follow-up contacts with a comprehensive assessment of asthma (Asthma: Current Care Guidelines 2022; GINA 2023). However, suboptimal adherence to asthma guidelines is considered a worldwide problem, and the gaps between evidence-based recommendations and practice are considered to cause poor health outcomes concerning asthma (Baldacci et al. 2019; Chapman et al. 2017; Cloutier 2018; Flecher et al. 2020; Price et al. 2019). During the Finnish National Asthma Programme, the main responsibility for asthma management shifted to primary health care (Erhola et al. 2003; Haahtela et al. 2006). No long-term real-life studies exist on how implementation of asthma guidelines has succeeded in primary health care asthma follow-up. Based on the above, follow-up and assessing of asthma in primary health care must be more accurately evaluated.

This thesis investigates how planned asthma follow-up contacts occurs in primary health care during long-term follow-up and how asthma is assessed in planned contacts. The aim was also to explore if the asthma assessment differs depending on whether a GP, nurse or both professionals participate in the visit and whether factors associated with non-participation in a planned follow-up can be identified.

2 REVIEW OF LITERATURE

2.1 Asthma

2.1.1 Description of asthma

Asthma is a respiratory disease that can strike at any age (GINA 2023; Papi et al. 2018). It is characterized by chronic airway inflammation leading to variable expiratory airflow limitation and causing typical asthma symptoms, including wheezing, coughing, chest tightness, dyspnoea, and increased bronchial mucus production (Porsbjerg et al. 2023). Due to the fluctuating inflammatory activity in the bronchus, asthma symptoms vary in intensity and over time (Hammad & Lambrecht et al. 2021; Papi et al. 2018). If untreated, ongoing bronchial inflammation can cause structural changes in the bronchial mucosa and submucosal tissue (Papi et al. 2018). Over time, these changes can lead to irreversible airway remodelling that progressively worsens pulmonary function (Hammad & Lambrecht 2021; Papi et al. 2018).

In Finland, asthma is the third most common disease, entitling one to special medication reimbursement rights after hypertension and diabetes (Asthma: Current Care Guidelines 2022). Asthma is one of the most common diseases in the world affecting 1%–29% of the population in different countries, placing an enormous burden on individuals and society (GINA 2023; Papi et al. 2018; Reddel et al. 2015). The incidence of asthma has been increasing globally during previous decades, partly due to improved recognition. Signs show the prevalence is levelling off but not yet universally (Papi et al. 2018; Porsbjerg et al. 2023). In Finland, the prevalence of physician-diagnosed asthma is reportedly around 10%–12% (Honkamäki et al. 2019). A recent study has indicated the prevalence of asthma is plateauing also in Finland (Hisinger-Mölkänen et al. 2019). Preventing asthma has proven to be challenging, although several potential risk factors are known (Beasley et al. 2015; Tanno et al. 2017). Public health efforts should focus on measures that can improve lung and general health, such as reducing tobacco smoking and exposure to environmental tobacco smoke, lowering obesity, encouraging a healthy diet, and

decreasing social inequalities to help prevent asthma epidemics, as previously suggested (Beasley et al. 2015).

2.1.2 Asthma phenotypes and endotypes

Asthma is a heterogenous disease with different clinical phenotypes having different features and prognoses with different underlying endotypes (Hammad & Lambrecht et al. 2021; Ilmarinen et al. 2015; Ilmarinen et al. 2023; Khusial et al. 2017; Papi et al. 2018; Wenzel 2012). The phenotype can be defined as a cluster or group with similar visible and measurable properties whereas the endotype defines the disease based on underlying pathogenic mechanisms (Hammad & Lambrecht et al. 2021; Kuruvilla et al. 2019; Wenzel 2012). Classification of asthma phenotypes can be done, for example, by clinical characteristics of the disease, pathophysiology, risk factors, time of asthma onset, cell type prevailing in the inflammatory reaction, and drug response or degree of asthma severity (Ilmarinen et al. 2023, Khusial et al. 2017; Kuruvilla et al. 2019; Wenzel 2012). Asthma phenotypes frequently overlap and may change over time (Ilmarinen et al. 2023). The main inflammatory endotypes of asthma are allergic eosinophilic, non-allergic eosinophilic, neutrophilic, and paucigranulocytic asthma (Kuruvilla et al. 2019). Asthma endotypes have also been divided based on the status of type 2 helper (Th2) cell inflammation to Th2-high and non-Th2 asthma (Hammad & Lambrecht et al. 2021; Kuruvilla et al. 2019; Wenzel 2012). Since group 2 innate lymphoid cells (ILC2) are also crucial in regulating type 2 (T2) inflammation with cytokines, the terminology has changed to T2-high and T2-low asthma (Hammad & Lambrecht et al. 2021; Kuruvilla et al. 2019). T2-high asthma can be identified for example by elevated blood eosinophil counts or with elevated fraction of exhaled nitric oxide (FeNO) (Hammad & Lambrecht et al. 2021). In T2-low-asthma the inflammation is suggested to be more neutrophilic or paucigranulosytic (Kuruvilla et al. 2019). T2-high asthma has been shown to associate, for example, with earlier onset of the disease, allergy, and nasal polyposis, whereas T2-low is associated with a later age at onset, smoking, obesity, and corticosteroid resistance (Hammad & Lambrecht et al. 2021). Within one phenotype, several distinct types of inflammation exist and, thus different endotypes. Therefore, a single treatment probably does not work equally well for all patients, even if the manifestation of asthma is otherwise the same (Kuruvilla et al. 2019). Assessing asthma endotype and phenotype is useful for choosing the correct treatment and evaluating asthma prognosis (Ilmarinen et al. 2023; Khusial et al. 2017; Lommatzsch et al. 2023). The figure 1 presents different

asthma phenotypes according to disease onset and the theoretically predominant inflammation type.

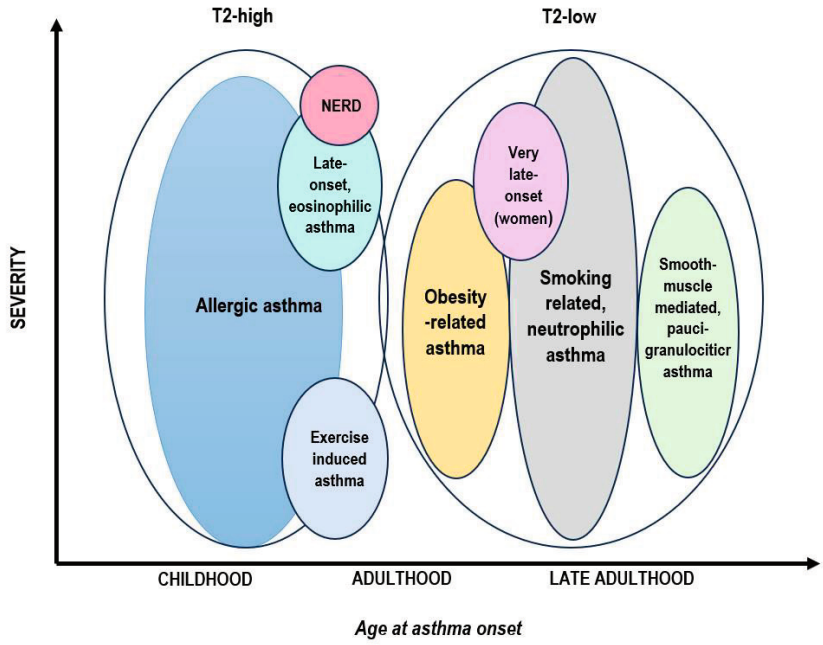

Figure 1. Different asthma phenotypes according to disease onset and the theoretically predominant inflammation type (Modified from Wenzel 2012). T2=type 2 inflammation; NERD=non-steroidal anti-inflammatory drug (NSAID) exacerbated respiratory disease.

2.1.3 Adult-onset asthma

Age at asthma onset is one of the most used differentiating factors when dividing asthma into different phenotypes in childhood- and adult-onset asthma. Most asthma cases are diagnosed during adulthood (Honkamäki et al. 2019; Kankaanranta et al. 2017; Sood et al. 2013). The prevalence of asthma in childhood is higher in boys than girls, but in adulthood, it is higher in women than men (Honkamäki et al. 2019; Kankaanranta et al. 2017). Adult-onset asthma is the predominant phenotype in women by age 30-40 years and in men after age of 50 years (Honkamäki et al. 2019; Kankaanranta et al. 2017, Sood et al. 2013).

Adult-onset asthma has a poorer prognosis. Based on studies, remission is rare: about half of the patients have moderate to severe asthma, and about 66%–75% of the asthma is uncontrolled or only partially controlled (Almqvist et al. 2020;

Honkamäki et al. 2021; Price et al. 2014; Tuomisto et al. 2016; Tupper et al. 2021; Westerhof et al. 2018). The prevalence of severe asthma in Nordic countries is approximately 3.5%–5.4% (Hansen et al. 2023). Compared to childhood asthma, adult-onset asthma is associated with different risk factors such as lifestyles, more severe symptoms, and medication use, and is less associated with allergic conditions (Hisinger-Mölkänen et al. 2022; Ilmarinen et al. 2017; Kankaanranta et al. 2017; Pakkasela et al. 2020; Sood et al. 2013). Overall, adults with asthma have more diseases than those adults without (Honkamäki et al. 2023).

Previous studies have identified different phenotypes in adult-onset asthma to better understand the risk factors and course of the disease, based on which asthma treatment and monitoring could be tailored more individually (Ilmarinen et al. 2017; Ilmarinen et al. 2023; Khusial et al. 2017). A previous Finnish study identified five adult asthma clusters: non-rhinitic asthma, smoking asthma, female asthma, obesity-related asthma, and early-onset atopic adult asthma (Ilmarinen et al. 2017).

2.1.4 Diagnosis of asthma

Asthma diagnosis is based on a history of typical asthma symptoms and variable airflow limitation which should be confirmed by objective lung function measurements (Asthma: Current Care Guidelines 2022; GINA 2023; Porsbjerg et al. 2023). Asthma symptoms are often variable and occasional and may be provoked by, for example, respiratory virus infection, physical exertion, and exposure to allergens or other triggers (GINA 2023; Porsbjerg et al. 2023). A history of allergic rhinitis or eczema and a family history of asthma or allergy increase the probability that the respiratory symptoms are due to asthma (GINA 2023). When suspicion of asthma arises, carefully evaluating of preliminary data and assessing possible differential diagnostic tests should be considered, because similar symptom profiles occur also in other conditions such as heart diseases, gastroesophageal reflux, and other respiratory tract conditions (GINA 2023; Louis et al. 2022; Porsbjerg et al. 2018; Porsbjerg et al. 2023).

An asthma diagnosis is confirmed by showing reversible obstruction with pulmonary function tests (Asthma: Current Care Guidelines 2022; GINA 2023). In adults, diagnostically significant asthma findings in spirometry are considered at least 12 % and at least 200mL increase in forced expiratory volume in 1 second (FEV1) or forced vital capacity (FVC) after bronchodilatation (BD) compared with pre-bronchodilatation value (Asthma: Current Care Guidelines 2022; GINA 2023).

However, the sensitivity and specificity of the currently used bronchodilator response threshold for FEV_1 (≥12% and ≥200mL) is poor, thus, normal spirometry does not exclude asthma (Tuomisto et al. 2019; Tuomisto et al. 2021). If asthma suspicion is strong, spirometry should be repeated; moreover, other lung function tests should be considered to confirm the diagnosis (Louis et al. 2022; Porsbjerg et al. 2023; Tuomisto et al. 2019; Tuomisto et al. 2021). In two-week peak-flow (PEF) monitoring, diurnal variation of at least 20% and 60 L/min compared to a mean of morning and evening values at least three times, or a PEF value increase of at least 15% and 60 L/min in response to BD compared with the pre-bronchodilator value are diagnostic for asthma (Asthma: Current Care Guidelines 2022). A therapeutic trial with corticosteroids can also confirm asthma diagnosis. In a therapeutic trial, a FEV1 increase of at least 15% and 200mL or the mean PEF values during a several-day rise of at least 20% and 60 L/min are diagnostic for asthma (Asthma: Current Care Guidelines 2022; GINA 2023). Despite the guidelines' recommendations, lung function tests are not comprehensively used in asthma diagnostics and monitoring as previous studies show, with similar finding also in COPD (Aaron et al. 2017; Abrahamsen et al. 2020; Chapman et al. 2017; Gershon et al. 2012; Härtel et al. 2022; Kerr et al. 2023; To et al. 2015; Weidinger et al. 2009).

In addition to lung function, at the diagnostic phase, evaluating the blood eosinophil and neutrophil counts, together with serum immunoglobulin E (IgE) is essential; these provide important information on underlying inflammatory patterns (Asthma: Current Care Guidelines 2022; Flinkman et al. 2023; Lommatzsch et al. 2023; Louis et al. 2022; Porsbjerg et al. 2023). Symptoms indicating a possible respiratory allergy should be investigated, and potential allergic sensitization screened, for example, with allergen-specific IgE antibodies (Lommatzsch et al. 2023). The X-ray image of thorax is mainly used in differential diagnosis in adults (Asthma: Current Care Guidelines 2022). Sometimes, to confirm the suspicion of asthma, a bronchial provocation test or exercise test may be needed, which are usually performed in specialized medical care – similarly to measurement of FeNO, which can be used to obtain additional information about the degree of airway inflammation (American Thoracic Society & European Respiratory Society 2005; Asthma: Current Care Guidelines 2022; GINA 2023).

2.1.5 Treatment of asthma

The long-term goals of asthma management are to achieve good symptom control, maintain normal lung function, and prevent exacerbations (Asthma: Current Care Guidelines 2022; GINA 2023; Lommatzsch et al. 2023). The goal at the individual level is to prevent functional impairment, disability, and deaths from asthma (Asthma: Current Care Guidelines 2022; GINA 2023; Lommatzsch et al. 2023). Asthma treatment is guided by assessing and monitoring asthma control, which should be evaluated in all asthma-related health care contacts (Asthma: Current Care Guidelines 2022; GINA 2023). Section 2.2. discusses assessing asthma control in more detail.

Asthma treatment should be planned individually, considering the patient's symptoms, the underlying asthma phenotype, the risk for exacerbations, the prerequisites for implementing medication, the treatment's possible side effects, and the patient's own wishes (GINA 2023; Papi et al. 2018). Asthma medication commonly consists of the maintenance anti-inflammatory medication controlling the bronchial inflammation and symptom-relieving bronchodilator medication. Controller medication should be stepped up or down in line with the observed variations in the level of asthma control (Asthma: Current Care Guidelines 2022; GINA 2023). The inhaled corticosteroids (ICS) are the most used controllers, and the short-acting beta$_2$-agonists (SABA) are the most used relievers (GINA 2023; Larsson et al. 2020). The combination of ICS and a long-acting beta$_2$-agonist (LABA) inhaler can be used as the first choice of maintenance medication for most patients with moderate-to-severe asthma while for patients on ICS, LABA as an add-on medication effectively improves asthma control and prevents exacerbations (GINA 2023; O'Byrne et al. 2008). In Finland, entitlement to special asthma medication reimbursement requires an asthma diagnosis confirmed with objective tests. Reimbursement for asthma medication can be obtained after at least six months of regularly using ICS medication (Asthma: Current Care Guidelines 2022).

In addition to the above-mentioned medication, add-on therapies, such as leukotriene receptor antagonists (LTRA), long-acting muscarinic antagonists (LAMA), and theophylline can be considered for patients lacking asthma control with ICS and LABA use (Asthma: Current Care Guidelines 2022; GINA 2023). Severe asthma patients should be referred to specialised care where low-dose oral corticosteroids (OCS), azithromycin, or biological medications, such as anti-immunoglobulin E (anti-IgE), anti-interleukin 5 (anti-IL5), or anti-interleukin 4 (anti-IL4) can also be considered. Long-term use of OCS should be avoided due to

its side effects (Asthma: Current Care Guidelines 2022). Allergen-specific immunotherapy may also be considered if an allergy provokes asthma symptoms (Asthma: Current Care Guidelines 2022; GINA 2023).

As well as regular asthma medication, an essential part of asthma care in all patients are non-pharmacological aspects, such as smoking cessation, physical activity and exercise, weight management, and healthy diet, combined with self-management education, inhaler training, and a written asthma action plan (AAP) (GINA 2023; Larsson et al. 2020; Papi et al. 2018). If trigger factors, such as allergens, occupational exposures, or non-steroidal anti-inflammatory drugs (NSAIDs) provoke asthma, these should be avoided, and possible asthma-related comorbidities should be treated (GINA 2023; Larsson et al. 2020; Lommatzsch et al. 2023; Papi et al. 2018). Adult asthma patients should also take seasonal influenza and COVID-19 vaccines, and those over 65 are eligible to have a pneumococcal vaccine according to the current Finnish national vaccination programme (Asthma: Current Care Guidelines 2022; Finnish Institute for Health and Welfare 2023).

2.2 Asthma control

2.2.1 Definition

Asthma control refers to how much an asthma's manifestations can be observed in the patients or were reduced or removed by treatment (Taylor et al. 2008). Well-controlled asthma means a patient is free from respiratory symptoms day and night and can live a normal and active life with normal or the best possible lung function without a frequent need for SABA (not exceeding two puffs SABA/week) (GINA 2023).

Despite improvements in knowledge, evidence-based guidelines, and asthma medications, poor asthma control is still common and can occur in all treatment steps of asthma, highlighting the need for regular follow-up (Bosnic-Anticevich et al. 2018; Chipps et al. 2018; Hancock et al. 2022; Larsson et al. 2020; Price et al. 2014; Stridsman et al. 2021). Uncontrolled asthma reduces asthma- and general health-related quality of life and increases the risk of asthma exacerbations, mortality, and health care costs (Bosnic-Anticevih et al. 2018; Chipps et al. 2012; Ilmarinen et al. 2019; Mäkelä et al. 2013). Many factors have effect on asthma control, including

patient-, health care- and therapy-related issues, underscoring why assessing asthma should be comprehensive (Larsson et al. 2020).

2.2.2 Assessment

According to current guidelines, two domains of asthma control should be assessed: asthma symptom control and risk factors for poor asthma outcomes, such as exacerbations, persistent airflow limitation, and medication side effects (Table 1) (Asthma: Current Care Guidelines 2022; GINA 2023). Many risk factors for poor asthma outcomes and control are modifiable (Schatz 2012). Asthma control should be evaluated in all asthma-related health care contacts (Asthma: Current Care Guidelines 2022; GINA 2023). Previous studies have reported major gaps in asthma control assessment during asthma-related health care contacts in primary health care when it was not assessed in over 80% of patients (Price et al. 2019; Yawn et al. 2016). Considering how asthma control has been determined when comparing different studies is essential: for example, in the Finnish Seinäjoki Adult Asthma Study (SAAS) study population, 72% of the study patients had controlled asthma according to symptoms, but when considering strict criteria without exacerbations and with normal lung function, only 34% had controlled asthma (Ilmarinen et al. 2019).

Table 1. Assessment of asthma control in adults

A. ASTHMA SYMPTOM CONTROL
In the past 4 weeks, has the patient had: * • Daytime symptoms >2 times/week? • Any night waking due to asthma? • SABA use for symptoms >2 times/week? • Any activity limitation due to asthma?
B. RISK FACTORS FOR POOR ASTHMA CONTROL
Assess risk factors at diagnosis and periodically, particularly for patients experiencing exacerbations. Measure FEV_1 at start of the treatment, after 3-6 months of ICS-containing treatment to record the patient's personal best lung function, then periodically, e.g at least once every 1-2 years, more often in at-risk patients and those with severe asthma. **Examples of the factors that can increase the risk of exacerbations even if the patient has few symptoms** • **Medication issues:** high SABA use, poor adhrence to ICS medication, incorret inhaler technique • **Comorbidities:** e.g., obesity, rhinitis, chronic rhinosinusitis, gastroesophageal reflux, obstructive sleep apnea, depression, anxiety, food allergy, sensitivity to NSAIDs • **Exposures:** smoking, e-cigarettes, snuf, allergen exposure if sensitized, air pollution, occupational exposures • **Lung function:** low FEV_1, high bronchodilator responsiveness • **Type 2 inflammation markers:** high blood eosinophils, elevated FeNO • **Exacerbation history:** former severe exacerbation history, ≥1 exacerbation in last 12-months

Modified from Global Initiative for Asthma (GINA) 2023 guideline. SABA=short-acting $beta_2$-agonist, FEV_1=forced expiratory volume in first second, ICS=inhaled corticosteroid, NSAID=non-steroidal anti-inflammatory drug, FeNO=fraction of exhaled nitric oxide. *Asthma is considered well controlled if none of these occur, partly controlled if 1-2 of these occur and uncontrolled if ≥3 of these occur.

2.2.3 Determinants

Symptoms

Asthma symptoms vary in frequency and intensity over time and may have diurnal variation or occur episodically, as in the case of an upper respiratory tract infection, physical stress, or other irritants. Asthma symptoms are a considerable risk for adverse outcomes, but even if asthma is well-controlled, a patient may still be at risk of exacerbations (Asthma: Current Care Guidelines 2022; GINA 2023). Symptom

control should be assessed in every asthma-related contact, including prescription renewal (Asthma: Current Care Guidelines 2022; GINA 2023).

Asthma symptom control is assessed by evaluating the frequency of possible daytime symptoms, occurrence of night-time symptoms and night awakenings, potential activity limitations, and the frequency of SABA use (more than twice/week) in the past four weeks (GINA 2023). When no symptoms occur, asthma is considered well controlled; if one or two occur, asthma is partially controlled; three or more means uncontrolled asthma (Table 1) (GINA 2023). Specific validated symptom questionnaires, such as the asthma control test (ACT) and airway questionnaire (AQ20), should be used to evaluate asthma symptom control (Barley et al. 1998; GINA 2023; Nathan et al. 2004). However, previous studies show that physicians report seldomly using ACT (from 1% to 29%) (Chapman et al. 2017; Cloutier et al. 2018), whereas a more recent study based on register data from Sweden showed that ACT had been used in 44.2% of the patients (Stridsman et al. 2020). Assessing asthma symptom measures vary among professionals; primary care physicians perform these assessments more poorly than specialists (the results range for assessing different symptoms, 48%–56% vs. 71%–91%) (Cloutier et al. 2018).

Lung-function

Based on previous research, even 50%–70% of patients who report good asthma control are inaccurate in their perception (Bosnic-Anticevich et al. 2018; Kritikos et al. 2019). Solely relying on patient-reported clinical symptoms or symptom scores such as ACT can lead to overestimating true asthma control; thus, including spirometry with the bronchodilation test in the assessment guarantees more accurate monitoring of asthma (Cowie et al. 2007; Jain et al. 2014; Kaplan & Stanbrook 2010; Kritikos et al. 2019; Munoz-Cano et al. 2017; Park et al. 2015). Several asthma guidelines recommend that lung function tests should be used in asthma diagnostics and periodically after that to evaluate asthma control. However, no universal common consensus exists on how often they should be performed (Asthma: Current Care Guidelines 2022; Australian Asthma Handbook 2022; British guideline on the Management of Asthma 2019; GINA 2023; NAEPP 2020 guidelines). The GINA guideline recommends that FEV_1 should initially be measured after 3–6 months of regular ICS treatment to record the patient's best personal lung function and then periodically (Table 1) (GINA 2023). In adult-onset asthma, the level of FEV_1 reached during the first treatment year predicts later lung function (Kauppinen et al. 2020).

According to current Finnish asthma guidelines, a one-week PEF-monitoring with SABA is recommended to examine lung function; another possibility is to perform spirometry with SABA. Spirometry is recommended for all patients at least every 3–5 years and annually for those who have problems with treatment (Asthma: Current Care Guidelines 2022). Based on previous physicians' self-reports, in Germany, 57% of physicians used spirometry as a part of assessing asthma control; the proportion was 54% in China, 47% in Australia, 46% in France, 28% in Canada, 24% in Japan, and 11%–45% in the US, depending on whether GP or specialist was involved (Chapman et al. 2017; Cloutier et al. 2018). A more recent study from Germany showed that only 7% of asthma patients had spirometry performed, whereas 55% of patients with both asthma and COPD underwent spirometry at least once during the study period, suggesting spirometry was underused in primary health care (Härtel et al. 2022). According to the recent study from the US, over 80% of patients with newly diagnosed high-risk COPD had no recording of spirometry or peak-expiratory-flow assessment in the 12 months pre- or post-diagnosis, and the low recordings of spirometry were consistent irrespective of exacerbation history (Kerr et al. 2023). Weidinger et al. reported that approximately half the patients had a clinical evaluation, including spirometry or PEF-monitoring, in agreement with recommendations during a follow-up visit in primary health care in Sweden (Weidinger et al. 2009). In a more recent study from Sweden, Stridsman et al. showed similar results with adults with asthma (58%). This study also gathered data from specialized care, including new patient visits and follow-up contacts, so one might have expected the amount of performed spirometry to be larger (Stridsman et al. 2020).

Lung function decline in patients with asthma contribute to poorer outcomes and poorer asthma control; thus, promoting measures to improve lung health and regularly measuring lung function is essential. Among other things, overweight, obesity, asthma exacerbations, smoking with pack-years ≥10, and low physical activity are associated with lung function decline (Bermúdez Barón et al. 2022; Loponen et al. 2018; Munoz-Cano et al. 2017; Soremekun et al. 2023; Tommola et al. 2016).

Smoking

Smoking is a risk factor for adult-onset asthma (Sood et al. 2013; Jaakkola et al. 2019). Even if smoking is known to associate with reduced effectiveness of inhaled steroids, poorer asthma control, rapid lung function decline, higher health care costs, and all-

cause mortality in adults with asthma, smoking among this patient population is equally common as in the general adult population, varying from 10% to 26% between countries (Cerveri et al. 2012; Haughney et al. 2008; Hisinger-Mölkänen 2022; Ilmarinen et al. 2017; Kämpe et al. 2014; Lemmetyinen et al. 2018; Polosa et al. 2011; Selberg et al. 2019; Stridsman et al. 2020; Tan et al. 2020; Thomson et al. 2006; Thomson et al. 2022; Tommola et al. 2016; Tuomisto et al. 2016). Active and passive smoking leads to more severe asthma and triggers exacerbations (Thomson et al. 2022). The number of smoked pack-years correlates in a dose-dependent manner with frequent hospitalizations, more comorbidities and symptoms, and higher asthma severity (Polosa et al. 2011; Tommola et al. 2019). Smoking history over ≥10 pack-years is associated with poorly controlled asthma and accelerated lung function decline independently, regardless of whether the patient quit smoking (Kiljander et al. 2020; Tommola et al. 2016). Also, snuff and e-tobacco impair lung health and increase the risk of exacerbations, so actively avoiding these products should be encouraged (Bircan et al. 2021; Gudnadóttir et al. 2017; To et al. 2023).

The above results highlight the importance of interventions aimed at smoking cessation in the early phase among patients with adult-onset asthma. Moreover, above mentioned emphasize the importance of routinely screening and carefully assessing lifelong smoking history. Only modest numbers of successful smoking cessation have been reported in asthma (Jiménez-Ruiz et al. 2015; Polosa & Thomson 2013; Tommola et al. 2019). One possible explanation could be a poor evaluation of smoking history and provision of smoking cessation, which are suggested to be inadequately performed—not only regarding asthma but in other conditions too (Gräsbeck et al. 2020; Hirvonen et al. 2021; Kerr et al. 2023; Nelson et al. 2015; Self et al. 2010).

Comorbidities

Comorbidities, such as obesity, rhinitis, allergy, gastroesophageal reflux, depression, obstructive sleep apnea, bronchiectasis, and sensitivity to NSAIDs are common in people with asthma; these comorbidities are also associated with severe or difficult-to-treat asthma, poor symptom control, and higher health care costs via more frequent exacerbations and hospitalizations (Andersén et al. 2022; Backman et al. 2022; Hakola et al. 2011; Hirvonen et al. 2021; Honkamäki et al. 2021; Honkamäki et al. 2023; Ilmarinen et al. 2016; Ilmarinen et al. 2021; Kowalski et al. 2019; Porsbjerg et al. 2017; Ryan et al. 2021; Tay et al. 2016; Theodorescu et al. 2015; Wang et al. 2020). Comorbidities may contribute to poor disease control and cause similar

symptoms that occur in asthma, making distinguishing true severe asthma from difficult-to-treat asthma more difficult (Porsbjerg et al. 2017; Tay et al. 2016). Conversely, this may lead to over- or undertreatment with anti-asthmatic medication or misdiagnosis (Kaplan et al. 2020; Porsbjerg et al. 2017). Furthermore, comorbidities may be due to the side effects of treating severe asthma (Kankaanranta et al. 2023; Porsbjerg et al. 2017). The risk of multiple non-respiratory comorbidities is higher in late-onset and severe asthma (Bui et al. 2021; Honkamäki et al. 2023; Kankaanranta et al. 2023). A recent study showed that inhaled and/or oral corticosteroid use contributed to the risk of several comorbidities in severe asthma in a dose-dependent manner, particularly pneumonia, obesity, osteoporosis, heart failure, and atrial fibrillation (Kankaanranta et al. 2023). Therefore, optimizing the corticosteroid dose should be carefully evaluated in clinical practise (Asthma: Current Care Guidelines 2022; Kankaanranta et al. 2023). To the best of our knowledge, no data exist on how asthma-related comorbidities are assessed as a part of asthma control assessment, how this is applicated during long-term follow-up, and whether a patient receives treatment for possible comorbidities.

Allergic rhinitis is a predominant comorbid disease in asthma and is often associated with difficult-to-treat and uncontrolled asthma, similarly as chronic rhinosinusitis with nasal polyposis (CRSwNP) (Backer et al. 2023; Bosnic-Anticevich et al. 2018; Wang et al. 2020; Westerhof et al. 2018). A recent study based on expert interviews suggested that effective screening of combined upper and lower airway diseases (the concept of "global airways diseases") is still underperformed (Backer et al. 2023). In line with this, a previous cross-sectional study from Australia showed that undiagnosed and untreated rhinitis was prevalent among primary care asthma patients (Bosnic-Anticevich et al. 2018). Moreover, adherence to nasal corticosteroids among asthma patients was poor when over 65% of patients with moderate-severe rhinitis were not using the recommended intranasal medication (Bosnic-Anticevich et al. 2018). Objective long-term data does not exist on nasal symptom screening in asthma patients.

Obesity prevalence has increased in recent decades and continues to increase (Tolonen et al. 2022). Obesity in adults with asthma is a permanent problem in long-term follow-up, but little is known about whether body mass index (BMI) and possible overweight or obesity are assessed as a part of asthma management and whether asthma patients receive guidance on weight management (Ilmarinen et al. 2021). Obesity is associated with uncontrolled and severe asthma, lung function decline, poorer work ability, and higher health care costs (Backman et al. 2022; Bermúdez Barón et al. 2022; Hirvonen et al. 2021; Honkamäki et al. 2021; Ilmarinen

et al. 2021; Ryan et al. 2021; Tuomisto et al. 2016; Wang et al. 2020). Obesity is also an independent risk factor for asthma exacerbations, even in patients with few symptoms (GINA 2023). Obesity is a risk factor for asthma, but adult patients with asthma are also at higher risk of developing obesity (Moitra et al. 2023; Sood et al. 2013). Weight reduction in obese patients with asthma improves asthma control (Ulrik. 2016).

Physical activity, diet, and alcohol

Lifestyle factors can affect asthma control directly and indirectly, e.g., through lifestyle-associated comorbidities such as obesity. Physical activity, exercise habits, nutrition, and alcohol consumption also affect asthma control independently (Alwarith et al. 2020; Jaakkola et al. 2019; Loponen et al. 2018; Quintero & Guidot 2010; Stoodley et al. 2019). Regular exercise improves asthma control in adults (Jaakkola et al. 2019). A recent study demonstrated an association between long-term FEV_1 decline and daily physical activity in asthma when patients with a low physical activity level had a faster decline in lung function than patients with high physical activity, even if no significant difference existed between the groups in asthma control or symptoms (Loponen et al. 2018).

Regarding dietary matters, increased fat and decreased fibre intake relate to worsened lung function and airway inflammation (Berthon et al. 2013). Conversely, literature shows that fruit and vegetable intake has been associated with reduced asthma risk, particularly in children, and better asthma control (Alwarith et al. 2020; Garcia-Larsen et al. 2016). Alcohol's effects on asthma control may not be as well-known, and the results are somewhat controversial (Quintero & Guidot 2010; Sisson 2007). Excessive alcohol intake has been associated with increased bronchial hyper-reactivity and prevalence of airway obstruction (Quintero & Guidot 2010). Heavy drinking and smoking also often occur together and may create synergistic interactions on lung function (Frantz et al. 2014). The current asthma guidelines encourage healthy lifestyles, but the recommendations do not separately mention, for example, assessing alcohol use as part of an asthma patient's assessment (Asthma: Current Care Guidelines 2022; GINA 2023).

Medication adherence

Adherence can be defined as the patient's willingness to co-operate and follow the treatment recommendations agreed upon with the health care provider (George 2018). Many factors influence treatment adherence; thus, adherence may vary over time based on, for example, socio-economic, therapy-related, condition-related, healthcare system-related, and patient-related factors (George 2018). Health care professionals are central in promoting medication adherence. The major predictors of good adherence have been suggested to include regular asthma reviews and positive beliefs about the medication (Axelsson et al. 2015; Corsico et al. 2007). Good adherence to asthma therapy improves clinical outcomes and lessens health care costs (Mäkelä et al. 2013). It has been estimated that poor adherence may explain 24% of exacerbations and 60% of asthma-related hospital admissions (Bårnes & Ulrik 2015). In non-controlled asthma, long-term medication adherence <80% was associated with more rapid lung function decline, underscoring the importance of early detection of poor compliance with regular assessment and promoting medication adherence (Vähätalo et al. 2021).

Adherence to ICS medication varies among studies from 30% to 76% (Axelsson et al. 2015; Bosnic-Anticevich et al. 2018; Bårnes & Ulrik. 2015; Engelkes et al. 2015; Hussain et al. 2023; Reddel et al. 2015; Vähätalo et al. 2020; Vähätalo et al. 2021). Factors suggested to associate with poorer adherence are younger age, mild asthma, poor communication with health care providers and lower education level (Bårnes & Ulrik 2015; Kang et al. 2013; Mäkelä et al. 2013; Selberg et al. 2019). Axelsson et al. also showed that compliance with ICS medication was lower in patients who received asthma medication prescriptions when visiting a physician for reasons other than asthma (Axelsson et al. 2015). In the study of Cloutier et al., 91.7% of specialists reported assessing adherence, and almost 60% of primary care physicians (Cloutier et al. 2018). In studies evaluating documented patient data, evaluation of medication adherence was only found approximately 30% of patients (Yawn et al. 2016; von Bülow et al. 2017).

Inhalation technique

Using an inhaler is a skill that must be learned and maintained to effectively deliver medication in the bronchial system (GINA 2023). The patient must receive education on inhaler technique via a health care professional when asthma medication is initiated, and reassessment of inhaler technique should be conducted

regularly in planned asthma contacts (Asthma: Current Care Guidelines 2022; GINA 2023). Previous studies have suggested that poor inhalation technique is common, occurring in 50%–100% of patients (Bosnic-Anticevich et al. 2018; Munoz-Cano et al. 2017). A previous Australian study of 370 patients showed that every patient performed at least one inhalation error (Bosnic-Anticevich et al. 2018). The five most common errors included having their head in the wrong position during inhalation (the head was not tilted so that the chin would be slightly upward), not exhaling to empty the lungs before inhaling, not performing a sufficient breath-hold after inhalation, using an inappropriate inhalation technique, and taking the second dose within 30 seconds (Bosnic-Anticevich et al. 2018). Based on documented data in cross-sectional studies, inhalation technique was only assessed in 5%–19% of patients during the previous year, with no knowledge of how it was assessed as part of long-term asthma management (von Bülow et al. 2017; Yawn et al. 2016).

Patient self-care instructions

Self-management, including education and a personal written AAP is recommended as a key component of asthma care and it can improve asthma control and reduce unscheduled contacts, hospitalizations, and health care costs (Pinnock et al. 2017; Selroos et al. 2015). A personalized written AAP should provide clear instructions on what to do for worsening asthma, when and how the medication should be changed, and when to seek help. AAP can also be an educational tool for patients to understand asthma control (GINA 2023; Pinnock et al. 2017). Subjects with uncontrolled asthma utilize significantly more healthcare than those with controlled asthma; thus, these patients especially benefit from a personalized management plan (Stridsman et al. 2021). A recent study showed that self-management knowledge is associated with a higher educational level, physician continuity, written action plan, advanced treatment, and visiting an asthma nurse (Wireklint et al. 2021). Despite being recommended by asthma guidelines for three decades, self-management guidance is still sub-optimally implemented (Chapman et al. 2017; Cloutier et al. 2018; Pinnock et al. 2017; Stridsman et al. 2020; Tan et al. 2020; Wireklint et al. 2021; Yawn et al. 2016). A previous study reported inadequate non-pharmacological asthma management and showed that patients received AAPs verbally more often than by in writing (Tan et al. 2020).

Participation to follow-up and continuity of care

Regular asthma contact with a systematic approach improves asthma control; thus, it can be suggested that the lack of regular comprehensive assessment and follow-up can cause a risk of poor asthma control (Backer et al. 2012). The advantages of regular follow-ups have also been reported for other chronic conditions, such as type 2 diabetes (Kauppila et al. 2019). The importance of continuity of care and regular asthma follow-up visits are significant regarding medication adherence, knowledge of asthma, and self-care (Axelsson et al. 2015; Lautamatti et al. 2023; Stridsman et al. 2021; Wireklint et al. 2021). A recent review suggested that continuity of care also lowered premature mortality, unplanned health care contacts, and health care costs among asthma and COPD patients (Lytsy et al. 2022).

Factors underlying non-participation in follow-up may include patient- and healthcare system-related reasons such as attitudes, resources, personal ability, and asthma symptoms (Aine et al. 2017). Patients attending regular follow-up contacts may have more motivation to adhere to treatment and follow-up due to more symptomatic or severe disease (Pakkasela et al. 2023; Stridsman et al. 2021). Clinical features of less severe asthma and younger age have been suggested as risk factors for not only non-adherence to medication but a tendency to not participate in follow-up (Kang et al. 2013; Kaplan et al. 2020; Mäkelä et al. 2013). Similarly, older age, low socioeconomic status, and obesity have been suggested as risk factors for poor participation in follow-up (Backman et al. 2017). In other conditions, also alcohol consumption has shown negative impact in self-care behavior and treatment adherence (Engler et al. 2013; Rittmueller et al. 2015). It is suggested that overestimation of true asthma control is common, and the nature of asthma as a chronic disease is not sufficiently clear to the patients (Bosnic-Anticevich et al. 2018; Kritikos et al. 2019; Price et al. 2014; Tapanainen & Merivuori 2019). Thus, it could be assumed that the risk of not participate in follow-up is also higher among these patients, especially if the responsibility to arrange follow-up contact remains patient's own (Aine et al. 2017; Tapanainen & Merivuori 2019). Health care related issues such as poor availability of services due to lack of recourses can also affect realisation of follow-up (Aine et al. 2017).

Other determinants

When poorly managed, the determinants discussed above are also risk factors for exacerbations. Even if asthma is well-controlled, exacerbations may occur in every

treatment step, for example, being triggered by an upper respiratory tract infection (GINA 2023; Stridsman et al. 2021). Exacerbations of asthma are common occurring at least in every fifth patient annually (Hancock et al. 2022; Sandelowsky et al. 2022; Stridman et al. 2021). A previous history of exacerbation is a risk factor for new exacerbation, uncontrolled asthma, and lung function decline (Chipps et al. 2012; Hancock et al. 2022; Tupper et al. 2020). Exacerbation is a sign that there may be something to enhance in the treatment; thus, a follow-up visit should always be arranged for the patient (GINA 2023). A recent Swedish study showed that regardless of asthma severity, approximately 31% of patients had a post-exacerbation follow-up contact within 15 months after an exacerbation (Sandelowsky et al. 2022).

Indoor and outdoor inhaled allergens, air pollutants, and occupational exposures may induce severe asthma symptoms, even at low levels, and lead to poor asthma control (Abrahamsen et al. 2020; GINA 2023; Hisinger-Mölkänen et al. 2022). For example, mold, dust, strong scents, traffic exhaust, respiratory infections, and physical activities, along with passive tobacco smoke, may also be triggers (Backman et al. 2022; GINA 2023). In addition to the above-mentioned environmental, physical, and medical factors, socioeconomic factors affect asthma control and management; for example, low educational level and income are independently associated with uncontrolled asthma (Busby et al. 2021; Håkansson et al. 2021; Ilmarinen et al. 2022; Schatz et al. 2007; Selberg et al. 2019; Tan et al. 2020).

2.3 Asthma management

2.3.1 Assessing asthma control - regular follow-up contacts

Asthma control and management should be assessed regularly (GINA 2023). Recent systematic review found the term 'monitoring' being not widely used in the sense of long-term care (Falck et al. 2019). The 'monitoring' is frequently referred to periodic measurement that guides the management of a chronic condition (Falck et al. 2019; Glasziou et al. 2005). Glasziou et al. has defined that the aims of monitoring are to establish the response to treatment, detect the need to adjust the treatment, and to detect adverse effects (Glasziou et al. 2005). Since the long-term management of asthma is more than just measurable attributes, in this dissertation the term 'follow-up' is used instead of 'monitoring'.

National and international asthma guidelines, like the current Finnish care guideline in asthma, recommend that adults with asthma who regularly use medication should have an annual assessment (Asthma: Current Care Guidelines 2022; Australian Asthma Handbook 2022; British Guideline on the Management of Asthma 2019; GINA 2023). The Finnish Asthma guidelines recommend that if asthma control is good, regular contacts can be arranged for a nurse or physician according to the local practices; however, a physician should perform an assessment at least every 3–5 years (Asthma: Current Care Guidelines 2022). During the annual follow-up contacts, asthma control should be assessed, as well as exacerbations, possible OCS courses, emergency room visits, combined with risk factors for poor control and for future exacerbations, as described in section 2.2 (Asthma: Current Care Guidelines 2022; GINA 2023). Similarly, the inhaler technique should be regularly reassessed together with possible adherence obstacles and information needs considering asthma medication (Bosnic-Anticevich et al. 2018; GINA 2023). Regarding support for the self-care management of asthma, a patient's existing AAP should be reviewed and updated if needed, and the patient should be given a written copy. Figure 2 shows the content of follow-up visits according to recommendations of GINA 2023 and the Current Finnish Guidelines of Asthma (Asthma: Current Care Guidelines 2022; GINA 2023).

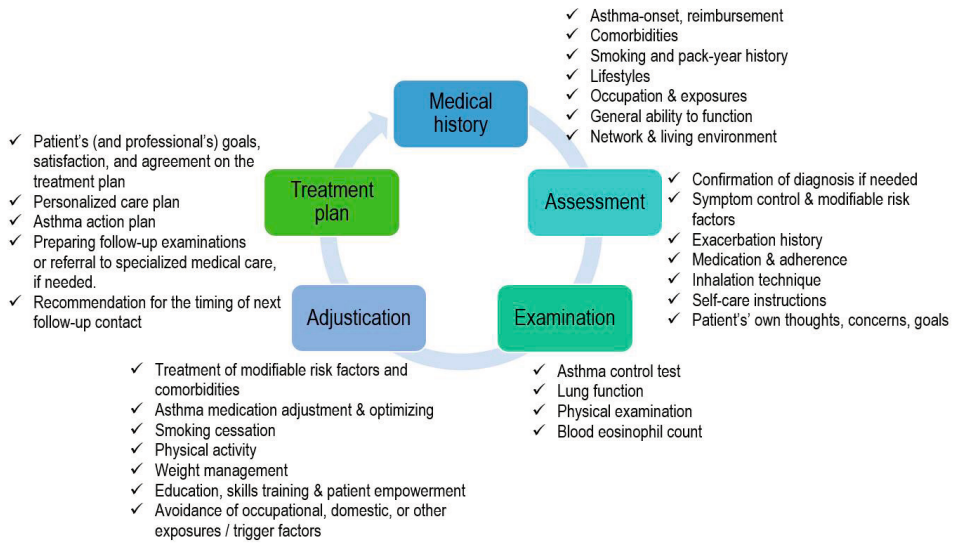

Figure 2. Content of asthma follow-up contact. Modified according to the Global Initiative for Asthma guideline and the Asthma Current Care Guidelines to also address key aspects of general medicine (Asthma Current Care Guidelines 2022; GINA 2023; Wonca Europe 2023 edition).

Despite recommendations of evidence-based guidelines, non-adherence to regular asthma follow-up is a worldwide problem; this lack of adherence is also reported for severe and childhood asthma (Kang et al. 2013; Larsson et al. 2018; Pakkasela et al. 2023; Reddel et al. 2015; Rönneberg et al. 2021; Stridsman et al. 2021; Tan et al. 2020; Yawn et al. 2016). The lack of annual reviews would not seem to be limited to primary health care (see Table 2) when studies assessing the total asthma population or patients from primary and specialized care have also suggested that even 50%–70% of patients do not have regular planned contacts (Table 2; Pakkasela et al. 2023; Reddel et al. 2015; Sandelowsky et al. 2022; Stridsman et al. 2021; Tan et al. 2020). According to previous research, the attendance rate for annual follow-up contacts in primary health care varies from 0% to 92.7% (Table 2). In a recent study, Chapman et. al. showed that according to patients' self-reports, 70.8% of the patients in Australia, 58.8% in Canada, 92.7% in China and 78.5% in the Philippines had seen a physician or other health care provider for routine asthma care during the past 12 months (Chapman et al. 2021). Notably, the population in the previous study does not necessarily characterize the typical asthma population due to the data collection methods used (Chapman et al. 2021). Another study in the United States showed the opposite, finding no planned contacts in any age group in primary health care; the

visits actualized due to asthma during the previous year were for assessing acute symptoms (Yawn et al. 2016).

A previous Finnish cross-sectional study showed that between 2001 and 2010, the number of scheduled asthma visits to physicians decreased from 73% to 69% and visits to a nurse from 28% to 23%, according to patients' self-reports; thus, the trend was decreasing, even if health care services had essentially remained unchanged (Kauppi et al. 2015). Based on a more recent study, the situation has further deteriorated because only 36% of patients had an annual scheduled asthma contact, according to questionnaire conducted in 2017 (Pakkasela et al. 2023). Both above-mentioned studies recruited patients based on a recently made medication purchase, or via pharmacies. Thus, more therapy- and follow-up-adherent patients may have been selected, and the study population may be incomparable to the total asthma population in primary health care. However, similar results to Pakkasela et al. have been reported based on the previous Swedish and Australian studies on primary health care (Axelsson et al. 2015; Larsson et al. 2018; Tan et al. 2020). The lack of regular contacts also occurs in severe asthma, which is suggested to be under-recognized in primary health care (Hansen et al. 2023; Larsson et al. 2018; Ryan et al. 2021; Rönnebjerg et al. 2021).

To the best of our knowledge, no previous studies assess how planned asthma follow-up contacts occur during long-term follow-up. Studies reporting insufficient frequency of regular review of asthma in primary health care are cross-sectional or based only on a short follow-up (≤2 years). Moreover, these studies often consist of register-based or patients' self-reported data. These studies have mainly aimed to assess the adherence to asthma guidelines, medication usage, asthma control or issues affecting it, or use of healthcare services among people with asthma. The limitation of previous studies assessing asthma follow-up in primary health care is that they do not give a longitudinal perspective of how asthma follow-up is conducted during a long-term period (Table 2). Another limitation that emerges in several studies dealing with adult-onset asthma is that the study population does not give a picture of the actual asthma population when, for example, patients with an ex- or current smoking history, multimorbidity, or co-existing COPD are often excluded (Table 2). Moreover, the study population may be a limited reflection of reality if only a group of patients receiving a certain type of treatment or who have asthma of a certain degree of severity is studied; therefore, the results are not directly comparable to the general asthma population. Organization of health care services, practices, and access to care may vary among countries and cultures; thus, directly comparing different practices can be difficult. Table 2 describes examples of studies

published since 2010 that have reported the annual frequency of asthma follow-up contacts in primary health care.

Table 2. Examples of the studies published since 2010 reporting the occurrence of asthma follow-up visits in primary health care

Study	Subjects	Study description	Asthma diagnosis based on.	Limitations	% of asthma patients with ≥1 planned asthma contacts during last year	Oher important results
Axelsson et al. 2015 (Sweden)	165	Population-based study	Self-reported	Only patients with filled prescriptions were included. Self-reported data, only adherence calculated by objective data.	36%	Annual asthma contacts associated with higher adherence and beliefs that medication was necessary but not in asthma control.
Backer et al 2012 (Denmark)	1784	Intervention study	Physician diagnosed asthma.	Patients with concomitant COPD were excluded. The study layout was pre-defined and therefore could guide patients to apply for the offered follow-up visit more actively.	35%	Systematic assessment of asthma during planned contacts improved asthma management in those who attended in follow-up.
Chapman et al. 2021 (Multination al)	1216 patients & 803 PHC physician	Cross-sectional, multinational online-survey	Self-reported asthma diagnosed by physician.	Self-reported data. Selection bias due to the inclusion criteria: even if targeted, included physicians were not only GPs and patients did not represent the typical PHC population.	70.8% in Australia 58.8% in Canada 92.7% in China 78.5% in Philippines	Most physicians prioritized symptom control over exacerbation reduction.
Hussein et. al. 2023 (Malaysia)	1280 (85.3% adults; 14.7% children)	Cross-sectional study	Physician diagnosed asthma.	Recruitment was limited by convenience sampling of patients attending clinic for asthma follow-up, thus more therapy adherent patients may have been selected. COPD patients were excluded.	70.7% of adults 29.7% of children	Average frequency of follow-up contacts in the past 12 months was 4 in adults and 3 in children. Adherence to ICS medication was poor based on self-reports (42.2% vs. 29.8%).

Larsson et al. 2018 (Sweden)	18724	Observational cohort study (follow-up 1-2 years)	Physician diagnosed asthma	Patients with polymyalgia rheumatica or rheumatoid arthritis were excluded, thus the study population does not necessarily represent the total asthma population.	~ 29% visited PHC because of asthma ~22% visited GP and ~ 4.3% visited nurse because of asthma	In severe asthma only one-fifth of the patients had visited secondary care and one third had visited PHC because of asthma.
Lisspers et al. 2010 * (Sweden)	1477	Cross-sectional survey	Previously given asthma diagnosis (not able to determine more accurately).	The study population did not represent total PHC population when patients age >45 were excluded with the goal to exclude COPD patients.	33-49% 19.8-50.4% to nurse	Attendance rates to annual planned contacts was better if PHC centres had asthma clinic.* Patients who attended a planned visit in PHC centres with asthma clinics reported more knowledge on the disease. There was no difference on quality of life. Better asthma control was achieved if nurse was allocated more time.
Wireklint et al. 2021 (Sweden)	1442	Cross-sectional study	Physician diagnosed asthma	Self-reported data.	19% visited asthma/COPD nurse	Self-reported knowledge of self-management was associated with higher educational level, physician continuity, a written AAP, advanced treatment and in women, visiting asthma nurse.

Yawn et al. 2016 (United States)	1176	One-year retrospective study	Physician diagnosed asthma.	Study population does not represent total adult asthma-population in PHC; patients over >65 were excluded (inc. patients aged 5-65). All asthma-related contacts included.	0%	All asthma-related visits made by the patients (with ≥1 asthma-related visits during the previous year) were made for evaluation of acute symptoms, or with no planned visits found.

The inclusion criteria for the included studies were: 1) focused on primary care AND 2) reported the occurrence of annual follow-up contacts with GP, nurse or both AND/OR reported the effect of follow-up contacts in asthma AND 3) published since 2010. COPD=chronic obstructive pulmonary disease, GP=general practitioner, PHC=primary health care, ICS=inhaled corticosteroid, AAP=asthma action plan. *In the study of Lisspers et al. primary health care centres were compared based whether them had complete asthma clinic, incomplete asthma clinic or whether they were without asthma clinic. The criteria for complete asthma clinic were: trained asthma nurse; GP with responsibility for asthma care; access to spirometry, investigations and patient education according to guidelines; time allocated for the asthma nurse for this task at minimum of 0.5h/week per 1000 inhabitants (Lisspers et al. 2010).

2.3.2 Implementation of evidence-based guidelines in asthma follow-up

Asthma became a recognized public health problem in many countries in the mid-1980s and early 1990s, leading to the development of asthma guidelines and AAPs with the goal to reduce asthma deaths and morbidity (Bousquet et al. 2007; Haahtela et al. 2006). The first asthma treatment guidelines were based on expert opinions and published in areas where the asthma burden was the most severe—in Australia and New Zealand—and worldwide after that (Bousquet et al. 2007; Reddel et al. 2015). Developing the first evidence-based treatment recommendations began in the early 1990s with the co-operation of the World Health Organization (WHO) and the US National Heart, Lung, and Blood Institute (NHLBI), leading to the establishment of the Global Initiative for Asthma (Boulet et al. 2019; Bousquet et al. 2007). Evidence-based asthma guidelines aim to establish a consensus of scientific practices that should be implemented into daily clinical practice to improve patient care and decrease asthma burden (Asthma: Current Care Guidelines 2022; Bousquet et al. 2007; GINA 2023). The first Finnish Current Care Guidelines for Asthma was published in 2000 (Asthma: Current Care Guidelines 2000).

Even if evidence-based medicine and guidelines have improved the quality of health care, suboptimal adherence to care guidelines is a common worldwide problem with asthma and other common chronic conditions, such as diabetes, cardiovascular diseases, and COPD (Baldacci et al. 2019; Chapman et al. 2017; Cloutier et al. 2018; Eder et al. 2019; Ezeani 2016; Geary et al. 2019; Giezeman et al. 2017; Gyberg et al. 2015; Hill et al. 2010; Kerr et al. 2023; Pedersen et al. 2018; Sandelowsky et al. 2018). A previous study investigating the implementation of care guidelines found differences in the awareness of the recommendations, and also among professional groups in primary health care (Lehtomäki 2009). For example, nurses knew fewer care guidelines than physicians; conversely, treatment recommendations related to lifestyle factors were less known among physicians (Lehtomäki 2009). Although the perception of physicians was that they were familiar with the current care guidelines, it was more an increased awareness of recommendation's existence (Lehtomäki 2009). Previous reviews have suggested that also lack of knowledge, insufficient time, and resources are among the most common obstacles to the implementation of guidelines in primary health care (Ezeani 2016; Wang et al. 2023). The problem often is that when some model has

been implemented for use, the monitoring of the sustainability of the implementation remains almost nonexistent (Ahtiluoto et al. 2017).

Compliance with several guideline elements in assessing asthma control seems variable and weak in many previous studies, as Section 2.2. describes. Implementing current asthma guidelines has been hypothesized to remain a challenge—partly because they are long and complex; thus, more simplified guidelines are suggested (Lommatzsch et al. 2023; Rupasinghe et al. 2021). Previous studies evaluating the assessment of asthma in planned contacts in accordance with treatment recommendations consist mostly of cross-sectional studies or a short follow-up (≤2 years) (Table 3). Many of the studies assessing adherence to guidelines in primary health care are based on patients' and/or professionals' interviews (Table 3). Arguably, studies based on self-reported data can exaggerate or underestimate the reality, while information based on documented or register-derived data will likely be more reliable, giving a more realistic perspective. The problem with the latter is that if the documented data is poorly recorded or was not entered into the register, the interpretability of the results deteriorates. Table 3 shows examples of the studies reporting how asthma management details are assessed in primary health care during asthma contacts. To the best of our knowledge, no real-life longitudinal follow-up studies exist on how planned asthma follow-up is adopted in primary health care during a long-term period and how systematically assessment of asthma is conducted based on objective patient data recordings in planned asthma contacts.

Table 3. Examples of the studies reporting assessment of asthma management details in asthma contacts in primary health care

Study	Subjects	Study description	Limitations	Asthma assessment procedures % completed/year
Barton et al. 2009 (Australia)	247 GPs	Cross-sectional study	Study based on interviews, no objective data available. Some variables had missing data. Recall bias possible and risk of overestimation (Item was routinely completed if performed with ≥80% patients seen with moderate to severe asthma in last 12 months). Selection bias possible if more asthma-oriented GPs participated.	Out of the participated GPs: - 12% used spirometry - 13% reviewed written AAP - 30% reviewed inhalation technique - 24% assessed asthma severity - 29% assessed physical activity - 6.9% assessed nutrition - 11.3% assessed alcohol consumption - 50.2% assessed smoking
Bosnic-Anticevich et al. 2018 (Australia)	200 patients	Cross-sectional observational population-based study	Does not represent total PHC population with asthma (e.g. COPD patients and patients >40 years with history of smoking were excluded). Self-reported data, no objective data available.	-5% had inhalation technique reviewed
Chapman et al. 2017 (multinational)	1809 physicians	Cross-sectional survey (Canada, France, Germany, Australia, China, Japan)	Self-reported data, no objective data available. The results are not directly comparable to PHC practices based on the study's inclusion criteria. *	- 42% used spirometry (range by country 24-57%) -10% used ACT (range 1-29%) - 20-41 % assessed symptoms according to GINA criteria (depending on the symptom the variation could be large, e.g., range 8-95)
Cloutier et al. 2018 (United States)	1412 GPs and 233 specialists	National asthma survey	Self-reported data, no objective data available. The results are not directly comparable to PHC practices based on the study's inclusion criteria. *	Reported practices by specialists vs. GPs: -71-91% vs. 48-56% assessed asthma symptom control - 92% vs. 60% assessed medication adherence - 31% vs. 16% assessed written AAP - 13% vs. 11% used PEF-monitoring - 45% vs. 11% used spirometry - 40% vs. 17% assessed inhaler technique

Hussein et. al. 2023 (Malaysia)	1280	Cross-sectional study	Does not represent typical/total PHC asthma population, when more therapy adherent patients may have been selected, COPD excluded.	- 13.7% of adults and 27.7% of children had education and evaluation of AAP
Lisspers et al. 2010 (Sweden)	1477	Cross-sectional survey	The study population did not represent total PHC population when patients age >45 were excluded with the goal to exclude COPD patients.	- 21.5 - 33.2% of patients had PEF-monitoring performed depending on the type of PHC centers' asthma clinic type # - 87.2 – 93.3% of patients had received inhaler technique education - 54.6% – 68.1% of patients were aware how to adjust medication at variations of asthma
Price et al 2019 (Canada)	884	One-year prospective cohort study	Uncertainty of correct asthma diagnosis. Does not represent typical PHC asthma population when, e.g., COPD excluded (still not completely successfully). Included also unscheduled asthma contacts.	- 15.4% of patients had asthma control assessed; out of all contacts in 4.9% - no AAP was delivered
Yawn et al. 2016 (United States)	1176	One-year retrospective study	Study population does not represent total adult asthma-population in PHC when patients over >65 were excluded (inc. patients aged 5-65). Study assessed all-possible asthma-related contacts.	- 15% of patients had asthma control assessed (11.6% of adult patients) - 33.2% had medication adherence evaluated (34.1% of adult patients) - 7.6% had education on inhalation technique (2.8% of adults) - 1.3% had inhaler technique revised (0.7% of adults) - 3.1% had AAP assessed (1% of adults) - 81.3% of adult patients had exposure to tobacco documented

The inclusion criteria for the included study were 1) included primary health care patients OR primary health care professionals AND 2) the study either reported how asthma was evaluated during asthma contacts OR how treatment recommendations were followed. GP=general practitioner, AAP=asthma action plan, PHC=primary health care, COPD=chronic obstructive pulmonary disease, ACT=asthma control test, GINA=Global Initiative for Asthma, PEF=peak-flow. *The results may not be directly comparable to PHC practices based on the study's inclusion criteria as included both primary health care physicians but also specialists of which some could worked at specialized care. # In the study of Lisspers et al. primary health care centres were compared based whether they had complete asthma clinic, incomplete asthma clinic or whether they were without asthma clinic. The criteria for complete asthma clinic were: trained asthma nurse; GP with responsibility for asthma care; access to spirometry, investigations and patient education according to guidelines; time allocated for the asthma nurse for this task at minimum of 0.5h/week per 1000 inhabitants (Lisspers et al. 2010).

2.3.3 Organization of asthma care in the Finnish health care system

The Finnish health care system

The Finnish health care system is divided into primary and specialized health care. Since the 1st of January 2023, the 21 wellbeing services counties and the city of Helsinki have been responsible for organizing health and social services in Finland (Ministry of Social Affairs and Health 2023). Before this, the production of public health care services was legislated in 1972 as the responsibility of municipalities to provide the same access and standard of care for all patients, independent of socioeconomic status or geographical location (Primary Health Care Act 1972). Between 2000 and 2022, Finland had 21 hospital districts providing specialized care and approximately 130 to 160 health care centres (with a decreased number towards 2020s but some with multiple branches) providing primary care services for the residents in their own region. In addition to the municipal system, employers are obligated to offer and finance occupational preventive health care services for their employees (Occupational Health Care Act 2001). The employer can provide its employees general practitioner-level medical care and other healthcare services, but organizing medical care is voluntary. Financial incentive systems are not used in the public Finnish health care system, so they do not affect the type of care provided or, for example, the preparation of patient documentation entries. In addition, patients can seek for primary health care services through private health care, mainly financed at the patients' expense (Tynkkynen et al. 2016). Private health care services have been limited to bigger cities for a long time and are still concentrated in larger urban areas. The use of private health care services has increased over the past decade due to the challenges of accessing public healthcare services (Tynkkynen et al. 2016).

Finnish National Asthma Programme (1994–2004)

Finland was one of the first countries to implement a national asthma programme which has been an example for several other countries to develop their own (Flecher et al. 2020; Haahtela & Laitinen 1996; Haahtela et al. 2006). The National Asthma Programme, undertaken from 1994 to 2004, was successful, leading to a considerable decrease in asthma-related morbidity and health care costs (Burki 2019; Haahtela et al. 2006). The programme's primary goals were to improve national asthma management, prevent an increase in costs and decrease the burden of asthma on individuals and society (Haahtela & Laitinen 1996; Haahtela et al. 2006; Kauppi et al. 2015). Measures to achieve these goals included early detection of asthma and active treatment with regular ICS medication, guided self-management as the primary form of treatment, reduction of respiratory irritants such as smoking, implementation of individually planned patient education and rehabilitation, increased knowledge on asthma in key groups, and promotion of scientific research (Haahtela & Laitinen 1996; Haahtela et al. 2006). The asthma programme also emphasized measures to confirm the asthma diagnosis by objective lung function tests, follow patients regularly, and monitor lung function by objective lung function tests intermittently (Haahtela & Laitinen 1996; Haahtela et al. 2006). To promote this goal, the first national guidelines on measuring and assessing spirometry curves were published in 1995 (Sovijärvi et al. 1995).

The government oversaw the Finnish Asthma Programme but the Finnish Lung Health Association implemented it, by rolling out education campaigns focused especially on primary care because one of the main goals was to strengthen the role of primary health care in preventing, diagnosing, and managing asthma long-term (Burki 2019; Haahtela & Laitinen 1996; Haahtela et al. 2006; Kauppi et al. 2015). In 2004, 79% of the 21 hospital districts had regional adult asthma guidelines (Haahtela et al. 2006). However, the regional treatment programs did not have a common structure (Nuutinen et al. 2004). The regional treatment programs aimed to support the implementation of national recommendations, help strengthen the role of primary health care, clarify the division of labour, and unify the assessment and treatment of asthma patients regionally (Brander & Salinto 2009). The key to implementing national and regional asthma programmes was the network of local asthma coordinators in each Finnish health care centre (one responsible physician and at least one nurse) and specialists in regional hospitals, who, together, were responsible for local cooperation, including developing and updating the local

guidelines, referral, and treatment network (Haahtela & Laitinen 1996; Haahtela et al. 2006).

During and after the National Asthma Programme, the number of patients entitled to special reimbursement for asthma drug costs increased in Finland, reflecting improvement in diagnosing and treating asthma (Haahtela et al. 2017). As the prevalence of allergic diseases has grown in Finland, like many other Western countries, the Finnish Allergy Programme (2008–2018) was launched as a continuation to reduce the burden of allergies and asthma individually and societally (Haahtela et al. 2008; Haahtela et al. 2022). The development of the total asthma costs have steadily declined; however, the cost of outpatient care and asthma drugs have increased (Mattila et al. 2022). The average cost of asthma per patient decreased during the long-term follow-up (-60%), but the proportion of direct health care costs has remained relatively unchanged (Mattila et al. 2022).

Division of labour in asthma follow-up among primary care professionals

After conducting the Finnish National Asthma Programme, the main responsibility of asthma management shifted to primary health care, where most adult asthma patients are diagnosed and managed (Erhola et al. 2003; Haahtela et al 2006; Haahtela et al. 2017). The local asthma coordinators—one responsible physician and at least one nurse—were named in each health care center during the asthma programme. The responsible physician acted mainly as a consultant to the other GPs and coordinated the work with regional specialists, taking responsibility for educating colleagues and nurses on asthma (Erhola et al. 2003; Haahtela et al. 2006). From 2000 to 2001, respectively, 83% and 94% of health care centres had at least one GP or nurse nominated to work as the local asthma coordinator, and 73% of the adult asthma patients had a GP as their asthma physician (Erhola et al. 2003; Haahtela et al. 2006). Asthma nurses gave most of the patient education and served as a contact for patients (Haahtela et al. 2006). Nurses were also trained to perform spirometry and GPs to interpret the results (Haahtela et al. 2006). In 2001, spirometry was available in 95% of Finnish health care centres (Erhola et al. 2003).

Teamwork between physicians and nurses enhances healthcare delivery, also in asthma (Backer et al. 2012; Lisspers et al. 2010; Rupasinghe et al. 2021). A previous Danish study showed that asthma control improved when the nurse and physician both participated in a planned contact using a systematic approach (Backer et al. 2012). In health care centres with asthma nurse and GP responsible for the asthma clinic, patients were shown to have medication at higher step, and more knowledge

of asthma and self-management (Lisspers et al. 2010). According to a previous review, no significant difference was found between nurse-led vs physician-led asthma care, but this review's limitation was quite small number of studies and the included population cannot be directly compared to the common primary health care population (Kuethe et al. 2013). Another systematic review assessing the quality of primary care by advanced practice nurses found that nurse groups demonstrated equal or better outcomes than physician groups for physiologic measures, patient satisfaction, and costs (Swan et al. 2015). In the previous review, only one study included asthma patients, limiting conclusions about whether this applies to asthma (Swan et al. 2015).

In the Finnish healthcare system, assessing the asthma management, medication, and follow-up treatment plan have largely been the physician's responsibility, while a nurse's duties included performing lung function tests, guiding inhalation technique, lifestyle, and dispensing general patient guidance (Erhola et al. 2003). After the Finnish Asthma Programme, it was considered that the role of asthma nurses should further be strengthened so that educated nurses could take care of majority of asthma follow-up contacts (Haahtela et al. 2006). However, no long-term data exist on how this has been actualized. In recent decade, the job description of an asthma nurse in primary health care may have partly begun to be abandoned, and the job description based on special areas of expertise may have increasingly moved to a model where nurses treat all patient groups and sub-areas, although the scientific evidence for this is weak (Aine et al. 2017).

Table 4 describes the current division of responsibilities between primary and specialized care in diagnosing and treating of asthma.

Table 4. The division of responsibilities between primary and specialised care in adult-onset asthma in Finland

PRIMARY HEALTH CARE Main responsibility for asthma diagnostics, treatment, follow-up, and reimbursement statements for medication. Available tests: peak flow monitoring, spirometry, thorax X-rays, allergy investigations, blood eosinophils, serum immunoglobulin E, and other laboratory tests.
SPECIALISED CARE CONSULTATION IS NEEDED IF ✓ The diagnosis of asthma cannot be confirmed in primary care. ✓ The symptoms do not respond to treatment as expected, even if possible factors affecting asthma control have been taken into account. ✓ Poor control of asthma during pregnancy. ✓ Occupational asthma suspicion, or the need for long-term work capacity assessment. ✓ Consideration for allegen-spesific immunotherapy. ✓ Asthma is not adequately controlled with low/medium dose inhaled corticosteroid medication combined with ≥1 add-on-drug (e.g., long-acting β_2-agonist, long-acting muscrarinic agonist, leucotriene receptor antagonist). ✓ Frequent exacerbations with need of oral corticosteroid courses.

Modified according to Current Care Guidelines 2022 (Asthma: Current Care Guidelines 2022).

2.3.4 The role of primary care

Primary care providers are at the frontline of asthma diagnosis and management; they also play a key role in identifying and managing uncontrolled and severe asthma. They can significantly contribute to asthma control by performing objective lung function measurements, optimizing therapy, and addressing risk factors such as non-adherence, smoking, and comorbidities.

As discussed, the first Finnish National Asthma guidelines were introduced in 2000, during the Finnish National Asthma Programme (Asthma: Current Care Guidelines 2000). During the effective implementation of Finland's national asthma program, there were significant improvements in asthma management, so it could also be assumed that the first national asthma guidelines were well adopted. To support this, Pakkasela et al. suggested recently that asthma treatment guidelines and clinical practise were well aligned in Finland, and the self-reported achieved asthma control among adults was good, indicating the guidelines were well implemented (Pakkasela et al. 2023). In previous study asthma control was determined by ACT scores; however, it can overestimate the true situation, as Section 2.2.3 describes,

and more accurate information could be enabled by including objective lung function measurements and evaluating possible exacerbation history, as was demonstrated in another Finnish asthma population previously (Ilmarinen et al. 2019). Furthermore, due to the study's cross-sectional setting, it does not provide longitudinal data on how asthma management is obtained. The study population consisted of people with asthma who had purchased medication for obstructive lung diseases during the previous 12 months, so it may exclude those patients who were less adherent to their medication and does not give true picture of the total asthma population. Also, recall bias are possible in self-reported data.

Remission of adult-onset asthma is rare; in many patients, the disease is only partially controlled or uncontrolled (Honkamäki et al. 2021; Tuomisto et al. 2016; Tupper et al. 2021; Westerhof et al. 2018). Based on previous studies, inadequate adherence to ICS medication may not be the reason for suboptimal asthma control in Finland (Pakkasela et al. 2023; Vähätalo et al. 2020). Therefore, it is reasonable to assume that there are other issues behind, possibly both patient-related and healthcare-related. Problems with accessing care have been increasing in previous decades which raises concerns about whether asthma control will deteriorate, especially if there are deficiencies in adherence to treatment recommendations regarding the follow-up and assessment of asthma (Aine et al. 2017; Lautamatti et al. 2022; Raivio et al. 2014; Tynkkynen et al. 2016). In the previous study Aine et al. reported large variations in the conduction of follow-up and treatment of asthma in Finland due to, among other things, lack of resources, staff turnover, and deficiencies in continuing education. These altogether affected in the quality and availability of care (Aine et al. 2017). Moreover, job descriptions of asthma nurses included other tasks, and other nurses, who did not necessarily have similar familiarity with lung diseases, also participated in the guidance of asthma patients (Aine et al. 2017).

It is likely that the treatment and follow-up of asthma is largely carried out during visits for other conditions or for other reason (Aine et al. 2017, Tapanainen & Merivuori 2019). An Australian study also suggested the focus is on treating acute asthma over controlling asthma (Rupasinghe et al. 2021). In visits where asthma is not the only issue of attention, it could be assumed there are no similar possibilities for comprehensively assessing asthma than those in planned contacts. For example, comorbid conditions may shift the primary focus, and the assessment of asthma remains secondary, which could also be supported by the fact that asthma patients with comorbidities have poorer asthma self-management knowledge (Tapanainen & Merivuori 2019; Wireklint et al. 2021). Similarly, it is likely that asthma medication renewals are largely made in other contexts without paying attention to evaluating

asthma control, inhaler technique, or medication adherence without direct contact with the patient, as previous studies also suggested (Larsson et al. 2018; Sandelowsky et al. 2022).

Based on the literature review presented above, assessing and monitoring asthma in primary health care in Finland must be more accurately assessed, especially when gaps between evidence-based recommendations and practice are suggested to cause poor health outcomes in asthma (Flecher et al. 2020; Price et al. 2019). Exploring the long-term adherence to evidence-based asthma guidelines, how planned asthma contacts occur, and how the factors affecting asthma control are evaluated during planned contacts is important. Such enables identifying the possible healthcare-related reasons for poor asthma control that should be corrected. In addition, knowing what kind of patients undergo follow-up and which patients should be paid more attention to during the follow-up is also important. As healthcare resources are limited, optimally allocating resources, and delivering care is essential.

3 AIMS OF THE STUDY

1. To assess the occurrence of planned asthma follow-up contacts in primary health care and whether they are carried out according to guidelines. (I, III, IV)

2. To assess the use of objective lung function measurements in the long-term follow-up of asthma patients in primary health care. (I)

3. To assess how smoking and pack-years are documented during planned asthma contacts and how often patients are advised in smoking cessation. (III)

4. To assess how comorbidities, lifestyle factors, asthma symptoms, medication data, inhalation technique, and self-care guidance are considered during planned contacts. (IV)

5. To explore if the assessment of asthma differs depending on the professional (GP, nurse, or both) responsible for the contact. (I, III, IV)

6. To assess the occurrence of planned asthma contacts and treatment adherence in primary health care versus specialised care and identify the factors associated with non-participation in planned follow-up contacts. (II)

4 MATERIAL AND METHODS

4.1 SAAS study design

The present study is a part of the Seinäjoki Adult Asthma Study (SAAS), which is a real-life single-centre 12-year follow-up study of patients with adult-onset asthma (Kankaanranta et al. 2015). The study was divided into two parts: a diagnostic visit at the study baseline from 1999 to 2002 and a 12-year follow-up visit from 2012 to 2013 (Figure 3). The original study cohort consisted of 256 adult patients (age ≥15 years) diagnosed with new-onset asthma in Seinäjoki Central Hospital, Finland. Patients recruited to the study were referred to specialised medical care by primary care physicians due to asthma suspicion. Written informed consent to participate in the study was obtained at the diagnostic visit. The exclusion criteria were a previous diagnosis of asthma in childhood or an inability or unwillingness to give informed consent (Table 5). Smokers and patients with comorbidities or other lung diseases were not excluded from the study. A respiratory physician diagnosed asthma based on typical asthma symptoms, and diagnosis was confirmed by objective lung function measurements showing significant bronchial reversibility or variability (Kankaanranta et al. 2015). An exercise provocation test was performed on some of the patients to confirm the diagnosis. The ICS medication was started immediately after the diagnosis (Kankaanranta et. al. 2015). After the diagnosis was confirmed and medication was initiated, the patients were treated and monitored by physicians, mostly in primary health care according to the Finnish National Asthma Programme and the Finnish Current Care Guidelines for Asthma, unless asthma severity or other respiratory diseases required monitoring in specialised care (Asthma: Current Care Guidelines 2000 and 2006; Haahtela & Laitinen 1996; Kankaanranta et al. 2015).

After a 12-year follow-up, 203 patients completed a follow-up visit in respiratory department (Figure 4), where lung function was measured, laboratory samples collected, asthma status and disease control were evaluated using structured questionnaires (ACT, AQ20, CAT), and comorbidities were assessed (Barley et al. 1998; Jones et al. 2009; Kankaanranta et al. 2015; Nathan et al. 2004). A structured questionnaire asked patients for their background information and medication use. In addition to data collected at the diagnostic visit and the follow-up in 2013, all data

on health care contacts, hospitalizations, and emergency department visits during the 12-year follow-up were retrospectively collected from patient records from primary care, occupational care, private health care, and public hospitals. All data gathered during these contacts was analyzed. Figure 3 schematically shows the course of the SAAS follow-up study.

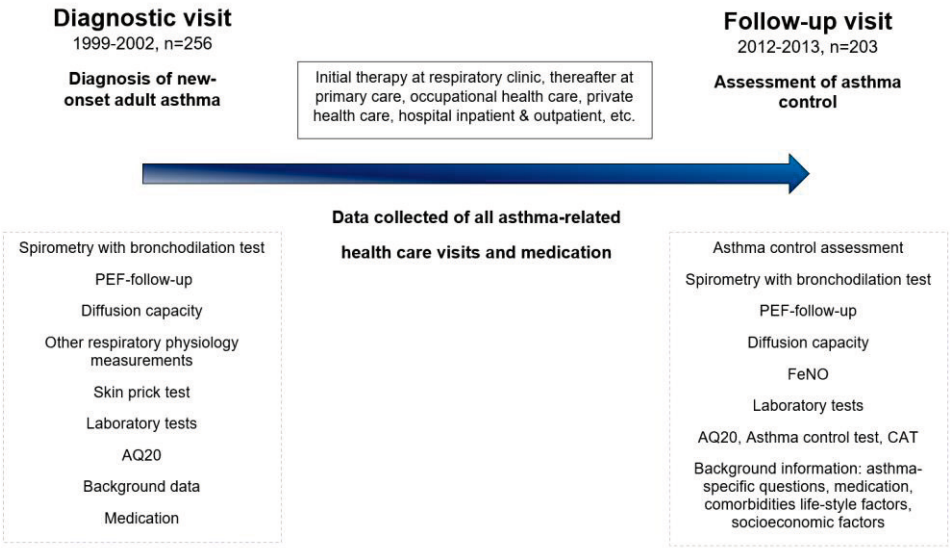

Figure 3. A schematic presentation of the Seinäjoki Adult Asthma Study (SAAS) (modified from Kankaanranta et al. 2015). PEF=peak-flow, AQ20=Airway Questionnaire 20, FeNO=Fraction of exhaled nitric oxide, CAT=COPD Assessment Test.

Table 5. Inclusions and exclusions criteria used in the SAAS study

Inclusion criteria ✓ A diagnosis of new-onset asthma made by a respiratory specialist ✓ Diagnosis confirmed by at least one of the following objective lung function measurements* o FEV_1 reversibility in spirometry of at least 15 % and 200 mL o Diurnal variability (⩾20%) or repeated reversibility (⩾15%/60 L/min) in PEF follow-up o A significant decrease in FEV_1 (15%) or PEF (20%) in response to exercise or allergen o A significant reversibility in FEV_1 (at least 15% and 200 mL) or significant mean PEF change in response to a trial with oral or inhaled glucocorticosteroids ✓ Symptoms of asthma ✓ Age ≥ 15 years
Exclusion criteria ✓ Physical or mental inability to provide signed informed consent ✓ Diagnosis of asthma below the age of 15 years

Modified from Kankaanranta et al. 2015. FEV_1=Forced expiratory volume in one second, PEF=peak expiratory flow. *The objective lung function criteria reflect those of National and International Guidelines valid in 1999–2002 (Kankaanranta et al. 2015).

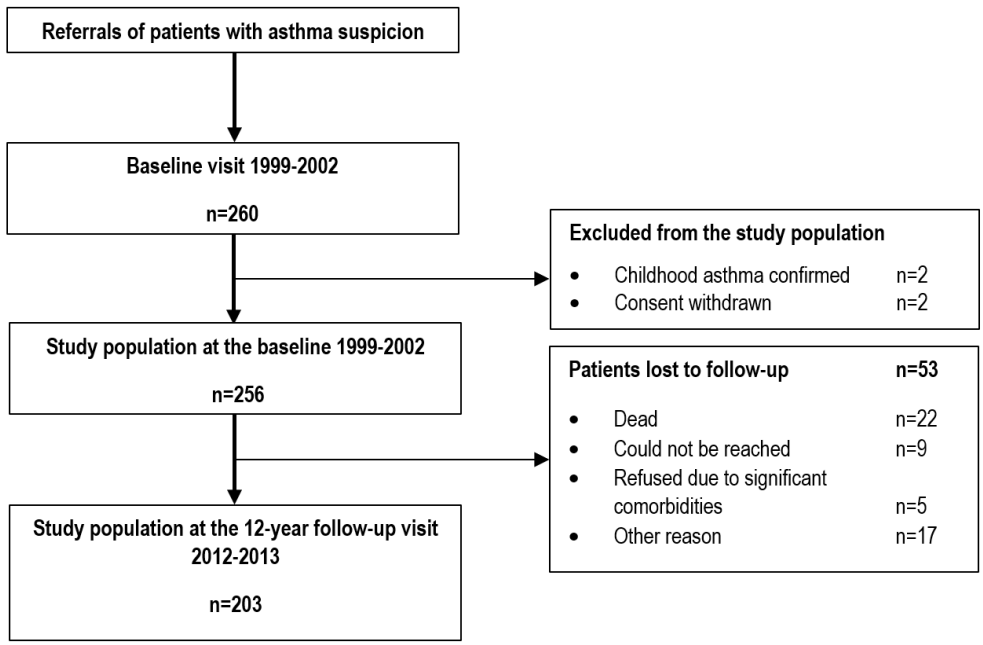

Figure 4. The SAAS study flowchart (modified from Tuomisto et al. 2016).

4.1.1 Lung function measurements

According to international recommendations, lung function measurements were performed with a spirometer (Miller et al. 2005). The Finnish reference values were used (Viljanen et al. 1982). At the diagnostic visit, a bronchodilator test with 200μg of salbutamol was performed, and at least 200 mL and a 15% increase in FEV_1 or FVC was considered significant. At the study baseline, PEF-monitoring was performed for two weeks and the response to bronchodilator medication was measured simultaneously. At the 12-year follow-up visit, bronchodilator test was performed with 400μg of salbutamol.

During the 12-year follow-up, PEF-monitoring and spirometry were used in monitoring asthma. All data was collected from planned asthma contacts in primary care to evaluate whether spirometry or peak flow monitoring was used in the asthma follow-up. Only a complete two-week peak flow monitoring was included when evaluating the use of PEF-monitoring.

The lung function measurements at baseline (1999–2002) and at follow-up visit (2012–2013) were analysed. The annual FEV_1 decline was calculated by measuring the change between the highest FEV_1 measurement available during the first 2.5 years after the diagnosis and start of ICS therapy and FEV_1 at the follow-up and by dividing the elapsed time in years.

4.1.2 Blood samples

Venous blood samples were systematically collected at the 12-year follow-up visit. Laboratory assays were performed in an accredited laboratory (SFS-EN ISO/IEC 17025:2005 and ISO 15189:2007) of Seinäjoki Central Hospital. White blood cell differential counts were determined, and IgE-levels were measured using ImmunoCap (Termo Scientific, Uppsala, Sweden). At the 12-year follow-up visit, serum levels for carbohydrate-deficient transferrin (CDT) and plasma γ-glutamyltransferase (GT) concentration were also determined. CDT was measured by a turbidimetric immunoassay (TIA) after ion exchange chromatography (%CDT, Axis-Shield, Oslo, Norway), and GT concentration was measured using enzymatic colorimetric assay, as standardized against IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) (Hietala et al. 2006).

4.1.3 FeNO

The FeNO was measured with a portable rapid-response chemiluminescent analyzer (flow rate 50mL/s; NIOX System Aerocrine, Solna, Sweden) according to American Thoracic Society standards (American Thoracic Society/European Respiratory Society 2005).

4.1.4 Allergy testing

Atopy was tested by skin-prick tests towards common allergens at the baseline visit; if at least one positive reaction was found, the patient was considered atopic.

4.1.5 Background data, symptoms, asthma control, and severity

Background data was collected using a structured questionnaire, and data on symptoms were collected by using the ACT, AQ20, and CAT (Barley et al. 1998; Jones et al. 2009; Nathan et al. 2004). An assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report, and assessment of severe asthma was performed according to the ERS/ATS severe asthma guidelines (Chung et al. 2014; GINA 2010).

4.1.6 Assessment of smoking and alcohol consumption

Smoking status was determined at the diagnostic visit and the 12-year follow-up visit in specialized care. The detailed, lifelong smoking history of every patient was assessed based on the questionnaire on background information and the interviews made by respiratory nurse at the baseline and at the follow-up visit. Lifelong cumulative exposure to smoking was evaluated by assessing smoked pack-years (20 cigarettes per day for one year). The participants were categorized into never smokers, ex-smokers, or current smokers according to their current and past smoking behavior at the study baseline and the 12-year follow-up visit. All documented smoking data from planned contacts was collected and analyzed.

Information on alcohol consumption was assessed at the 12-year follow-up visit using detailed structured questionnaires. Heavy alcohol consumption was evaluated by self-report, by combined index based on γ-glutamyltransferase and carbohydrate-

deficient transferrin measurements (GT-CDT-index), or by both. Assessing alcohol consumption was performed according to US definitions for alcohol consumption by portion/week (National Institute on Alcohol Abuse and Alcoholism, NIAAA). For men, heavy drinking was defined as 14 portions or more per week, and for women, consuming 7 portions or more per week (portion indicates 14g alcohol).

4.1.7 Comorbidities and lifestyle factors

The overall presence of comorbidities was based on patients' self-reported comorbidities or on medication use. Conditions considered comorbidities included hypertension, diabetes, coronary heart disease, stroke and transient ischemic attack, chronic kidney disease, atrial fibrillation and other cardiac arrhythmias, peripheral vascular disease, heart failure, depression, painful condition (daily use of analgesic medication), treated dyspepsia, thyroid disorders, diverticular disease of the intestine, rheumatoid arthritis and other inflammatory polyarthritis and systematic connective disorders, anxiety and other stress-related and somatoform disorders, irritable bowel syndrome, cancer, treated constipation, prostate disorders, glaucoma, epilepsy, dementia, schizophrenia/non-organic psychosis or bipolar disorder, psoriasis, inflammatory bowel disease, migraine, bronchiectasis, Parkinson's disease, multiple sclerosis, viral hepatitis, and chronic liver disease. Unclear cases were confirmed from the patient records (Ilmarinen et al. 2016).

Additional data was collected from planned asthma contacts retrospectively on how comorbidities commonly associated with asthma (obesity, nasal conditions, gastroesophageal reflux, obstructive sleep apnea, and intolerance to NSAIDs) were documented in patient records. Similarly documented information from lifestyle factors, including exercise habits, dietary matters, and alcohol use, were analyzed.

4.1.8 Data on medication and calculation of medication adherence

Patients reported their medication use during the follow-up on the questionnaire, and documented data on medication was collected from patient records. The prescribed dose for each patient was calculated based on medical records. The dispensed doses for SABA, purchased corticosteroids, and antibiotics were obtained from the Finnish Social Insurance Institution, which records all medication purchased from all Finnish pharmacies (Vähätalo et al. 2018; Vähätalo et al. 2020). All prescribed and dispensed ICS doses were converted to beclomethasone

dipropionate equivalents for calculation (Vähätalo et al. 2018; Vähätalo et al. 2020). The 12-year adherence and annual adherence for each patient were calculated by using specific formulas considering aspects such as medication possession ratio (MPR) and proportion of days covered (PDC) (Vähätalo et al. 2020).

$$12-year\ adherence\ (\%) = \frac{12-year\ cumulative\ dispenced\ dose\ of\ ICS\ (\mu g)}{12-year\ cumulative\ prescribed\ dose\ of\ ICS\ (\mu g)} * 100$$

$$Annual\ adherence\ (\%) = \frac{yearly\ dispenced\ dose\ of\ ICS\ (\mu g)}{yearly\ prescribed\ dose\ of\ ICS\ \ (\mu g)} * 100$$

Counting all dispensed SABA canisters during the 12-years together and dividing the sum by 150 puffs [SABA canisters (150 puffs/canister) during the 12-year period] determined SABA use (Vähätalo et al. 2022).

4.1.9 Ethical permission and study registration

The participants of the 12-year follow-up contact gave written informed consent to the study protocol approved by the Ethics committee of Tampere University Hospital, Tampere, Finland (R12122). Institutional permission (Seinäjoki Central Hospital, Seinäjoki, Finland) was obtained. The SAAS study is registered on ClinicalTrials.gov with the identifier number NCT02733016.

4.2 Methods used in assessing the asthma follow-up contacts

4.2.1 Definitions

All asthma-related health care contacts of the 203 patients participating in the SAAS study during the 12-year follow-up were assessed. The following definitions distinguish the different asthma contact types:

Planned asthma contacts: contacts where the only reason for the visit was a planned asthma follow-up contact.

Primary health care contacts: contacts in health care centres and occupational health care.

Specialized care contacts: contacts in specialised care in the respiratory department.

Private health care contacts: contacts in private health care.

GP contact: contact with the GP/occupational health physician participating in the assessment of asthma.

Nurse contact: contact with the nurse participating in the assessment of asthma.

Both GP and nurse contact: contact with both professionals participating in the assessment of asthma.

Office-based contact: contact in which the patient encountered the professional face-to-face in the asthma follow-up visit.

GP telephone contact: planned contacts via a GP's phone call to a patient.

Unscheduled contacts: contacts made due to asthma exacerbation or infection.

All asthma-related health care contacts: contacts include planned asthma contacts, and those made for infection, exacerbation, or for asthma and other

reasons.

Unclear type of contact: the exact type was undeterminable.

4.2.2 Planned asthma follow-up contacts in primary health care

Planned asthma follow-up contacts in public health care centres and occupational health care were considered the primary health care planned asthma follow-up contacts. Of the 203 patients in the SAAS study, 152 had planned asthma contacts in primary health care, the total number of planned asthma contacts being 603 (Figure 5) (I, III). Of these 603, 414 were conducted in primary health care centres and 189 in occupational health care.

The included population varied somewhat in the original communications: compared to studies I and III the number of planned asthma contacts in primary care (n=603) increased by four (n=607) and patients with asthma contacts by two (n=154) in our fourth study (IV). This was due to a data coding error during the initial data recording phase which was found when collecting additional data for the fourth study. All data documented and gathered during these contacts were assessed and analyzed to evaluate the content of planned asthma contacts in primary health care.

Of the 51 patients who did not have planned asthma contacts in primary health care, 22 had follow-up visits only in specialised or private health care, and the remaining 29 did not have any follow-up contacts between diagnostic visits and the 2013 follow-up visit.

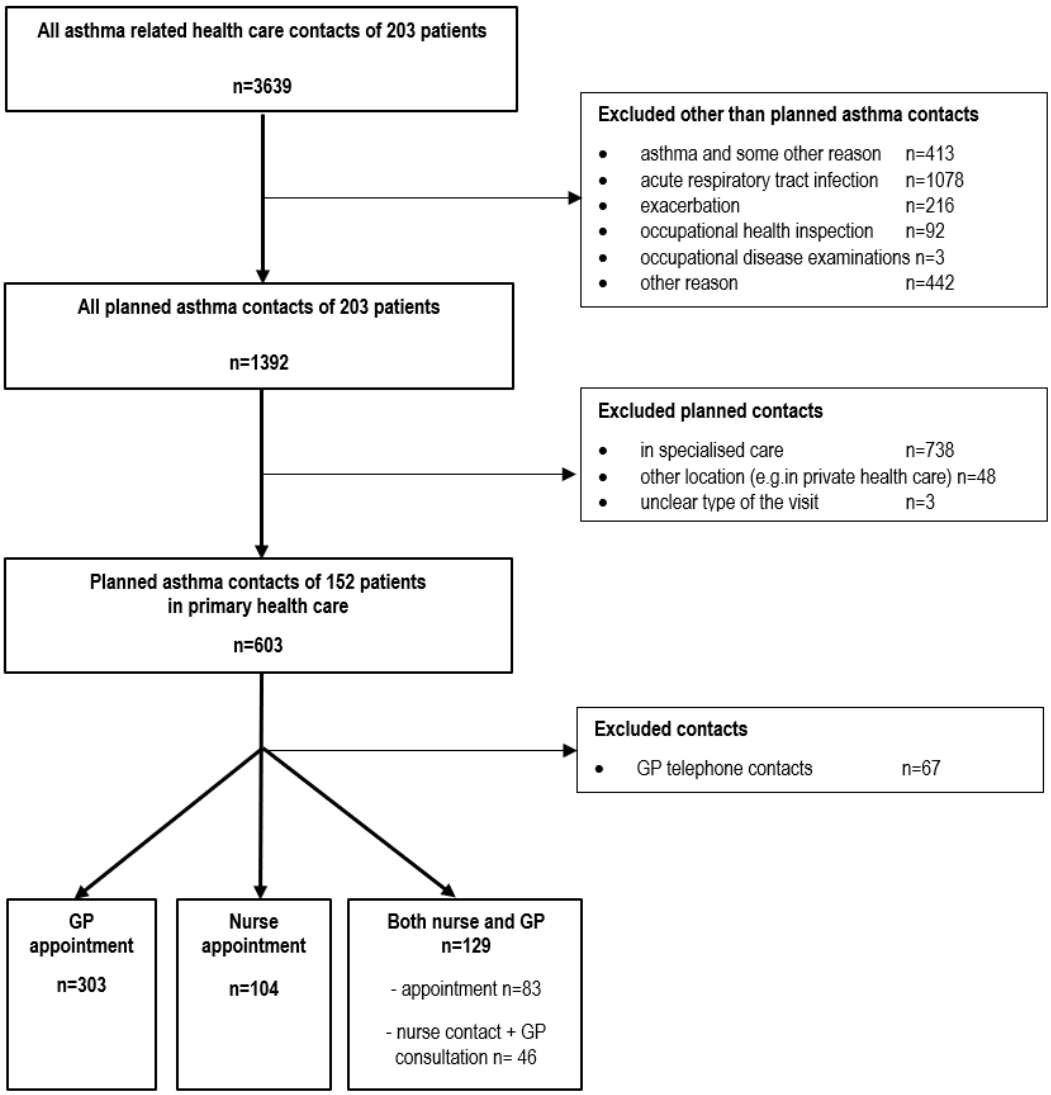

Figure 5. The flow diagram of the distribution of follow-up visits in primary health care. GP=general practitioner.

4.3 Statistical analyses

Statistical analyses were performed using SPSS software, versions 25–27 (IBM SPSS Armonk, NY). Two-sided p-values were used and a p-value <0.05 was considered statistically significant. The Shapiro–Wilk test was used to assess normality and by visual evaluation of distribution. Two-group comparisons were performed using Student's t-test for continuous variables with normal distribution, Mann–Whitney test for continuous variables with skewed distributions, and Pearson chi-square or Fisher's exact tests for categorized variables.

Annual adherence was plotted against time for individual patients, and mean area under curve (AUC) values were compared using independent samples from the Mann–Whitney U test to analyze differences in annual adherence over the 12-year period between patients having planned contacts, mainly in primary health care or specialized care. Multivariable binary logistic regression determined the association between alcohol consumption and poor participation in planned asthma follow-up, adjusting for age, sex, pack-years, BMI, and form of residency (original communication II).

5 SUMMARY OF RESULTS

5.1 Description of the study population

Of the 203 patients in the SAAS-study, 152 had planned asthma contacts in primary health care (Figure 5). This population formed the main sample in original publications I, III, and IV. At the 12-year follow-up visit, the mean age of the patients with planned follow-up contacts in primary health care was 59; most of them were women (63.2%), and 50.0% were either ex- or current smokers. The population was also characterized as overweight (BMI 28.5 kg/m^2): 37.2 % of them were atopic, 71.7% had rhinitis, and 30.3% had uncontrolled asthma according to GINA 2010 guideline (GINA 2010). Out of the adults with asthma 12.6% also had co-existing COPD, and the overall median number of comorbidities was one (IQR 0–2). ICS medication was in use in 82.2% of patients based on self-reports. At follow-up visit, the mean pre-BD FEV_1 was 87%, mean post-BD FEV_1 91%, and post-BD FEV_1/FVC 0.76 (Table 6).

In publication IV, the included population (n=145) varied somewhat numerically from the total population with primary health care asthma contacts when only patients with office-based planned visits were included in this study. In general, the characteristics of the study population were still very similar to those in original communications I and III. The original communications detailed the characteristics of the study population included in each study (I, III, IV). Study II's population (n=198) was quite similar to the total SAAS study population (n=203) that has been previously characterized (Tuomisto et al. 2016).

Table 6. Characteristics of the 152 patients with planned follow-up contacts in primary health care at the 12-year follow-up visit.

	Patients (n=152) with planned asthma follow-up contacts in primary health care
BASIC CHARACTERISTICS	
Female *n (%)*	96 (63.2)
Age (y) *mean (SD)*	59 (13)
BMI (kg/m^2) *mean (SD)*	28.5 (5.9)
Smokers (ex or current) *n (%)*	76 (50.0)
Atopic *n (%)* [a]	51 (37.2)
ASTHMA CONTROL AND SEVERITY	
ACT score *median (IQR)*	21 (19-24)
Uncontrolled asthma *n (%)* [b]	46 (30.3)
Severe asthma *n (%)* [c]	9 (5.9)
LUNG FUNCTION & INFLAMMATORY PARAMETERS	
Pre-BD FEV_1 (%) *mean (SD)*	87 (17)
Post-BD FEV_1 (%) *mean (SD)*	91 (17)
Pre-BD FEV_1/FVC *median (IQR)*	0.74 (0.67-0.79)
Post-BD FEV_1/FVC *median (IQR)*	0.76 (0.70-0.80)
Blood eosinophils (x10^9/l) *median (IQR)*	0.15 (0.10-0.27)
Total IgE (kU/l) *median (IQR)*	61 (23-154)
FeNO (ppb) *median (IQR)*	11 (5-19)
MEDICATION	
Daily ICS in use *n (%)*	125 (82.2)
Daily SABA in use *n (%)*	21 (13.8)
Daily LABA in use *n (%)*	78 (51.3)
Daily add-on drug in use *n (%)*	85 (55.9)
≥1 OCS course during 12-y follow-up *n (%)*	50 (33.6)
Total adherence to ICS over 12 years *median (IQR)*	81.0 (47.2-98.5)
COMORBIDITIES	
Obesity (BMI ≥ 30kg/m^2) *n (%)*	51 (33.6)
Rhinitis *n (%)*	109 (71.7)
Co-existing COPD (Post FEV_1/FVC <0.7 and pack-y ≥10) *n (%)*	19 (12.6)
Diabetes *n (%)*	19 (12.5)
Hypertension *n (%)*	49 (32.2)
Ischemic heart disease *n (%)*	18 (11.8)
Any psychiatric disease *n (%)*	20 (13.2)
Treated dyspepsia *n (%)*	13 (8.6)
Number of comorbidities *median (IQR)*	1 (0-2)
HEALTH CARE USE	
All-asthma related healthcare contacts during 12-y *median (IQR)*	17 (11-24)
≥1 hospitalization during 12-y *n (%)*	39 (25.7)

BMI=Body Mass Index, ACT=asthma control test, BD=bronchodilation, FEV_1=forced expiratory volume in one second, FVC=forced vital capacity, IgE=immunoglobulin E, FeNO=fraction of nitric oxide in exhaled air, ICS=inhaled corticosteroid, SABA=short-acting β_2-agonist, LABA=long-acting β_2-agonist. Add-on drug=long-acting β_2-agonist, leukotriene receptor antagonist, theophylline and/or tiotropium in daily use. OCS=oral corticosteroid, COPD=chronic obstructive pulmonary disease. [a] At least one positive skin prick test of common allergens. [b] Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report. [c] Assessment of severe asthma was performed according to the ERS/ATS severe asthma guideline 2014 (Chung et al. 2014).

5.2 Planned asthma contacts in primary health care

The number of planned asthma follow-up contacts in primary health care was 603. Thus, on average, each patient (n=152) had four planned contacts during the 12-year follow-up. The annual average of planned asthma contacts in primary health care was 50, i.e., every third patient attended a planned visit each year. When the patients were divided into two groups according to the number of planned contacts (<4 vs. ≥4), 84 patients had <4 [median 1 (IQR 1–2)], and 68 had ≥4 [median 6 (IQR 4–8)] planned contacts in primary health care during the 12-year follow-up. Thus, most of the patients had planned follow-up contacts in primary health care less often than every third year. The annual number of planned asthma contacts varied between 21 and 67, with being the weakest during first two years (Figure 6). This could be explained by the fact that during the first two years after diagnosis, many patients were still being monitored by specialized care before the follow-up was transferred to primary health care.

The 603 planned asthma contacts in primary health care consisted of 303 GP contacts, 104 nurse contacts, 129 combined GP and nurse contacts, and 67 GP telephone contacts. Of the 129 combined GP and nurse contacts, in 83, the patient met nurse and GP thereafter; in 46 contacts, the patient met nurse, and GP was only consulted (Figure 5). Thus, after excluding GP telephone contacts, 536 were office-based visits where the patient encountered a GP, nurse, or both. (I)

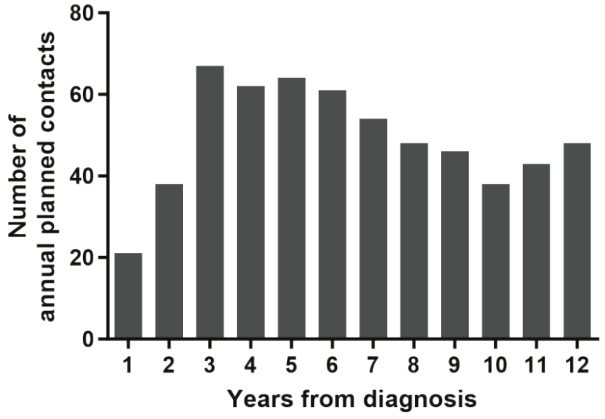

Figure 6. The number of annual planned asthma contacts in primary health care during the 12-year period. The total number of patients was 152 and the number of planned contacts 603.

5.2.1 Evaluation of symptoms and performed lung function tests

We excluded the GP telephone contacts to assess the content of office-based planned asthma contacts in primary health care because these were often short phone calls and were basically not intended to replace a more comprehensive face-to-face assessment. Of the 536 planned office-based asthma contacts, occurrence of possible respiratory symptoms was recorded in 79.0% of visits and in 86.8% if both professionals were involved. Lung function tests (spirometry, PEF-monitoring, or both) were performed in 87.5% of contacts and in 98.4% if both professionals participated in the contact. Spirometry was done more often than peak flow monitoring throughout the whole follow-up, and there was no sign of a decrease in the performance of the lung function test during the 12-year follow-up (Figure 7). During the 12-year follow-up, peak flow monitoring was conducted in 51.7% of the contacts and spirometry in 76.1%. Data on ACT was seldom found—only in 6.3% of contacts but more often if both professionals participated in assessing the patient (15.5%). Pulmonary auscultation was registered in 72.9% of GPs' contacts. (I, IV)

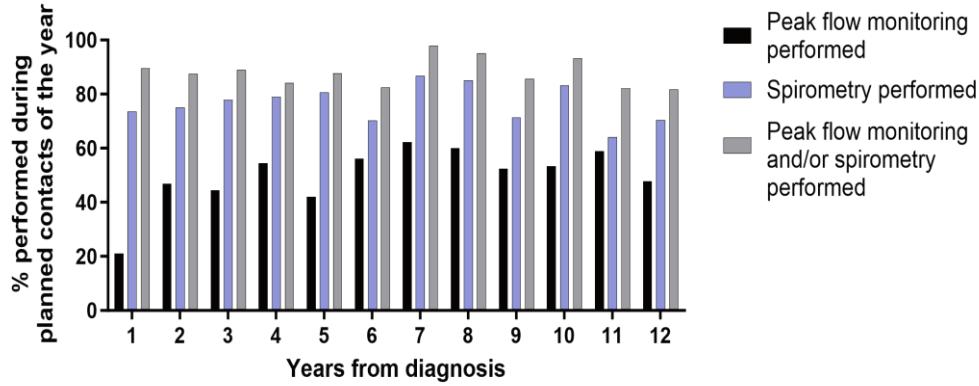

Figure 7. Percentage of lung function tests performed in planned office-based follow-up contacts in primary health care during the 12-year period. The data is presented as percentage of all annual office-based contacts (total number of contacts n=536).

5.2.2 Evaluation of smoking and smoking cessation

In assessing asthma, knowledge of the smoking status and pack-years can be considered paramount, especially if the patient is an ex- or current smoker (Polosa et al. 2011; Porsbjerg et al. 2018; Tommola et al. 2016; Tommola et al. 2019). We assessed all 603 planned asthma contacts to evaluate the assessment of smoking in planned asthma contacts in primary health care. Of the 152 patients with planned asthma contacts, the smoking status was not reported even once for 95 (62.5%), and smoked pack-years were not calculated even once for 125 patients (82.2%). When assessing the smoking habits of this population in more detail, in the study baseline, 52.0% were never smokers, 33.5% were ex-smokers, and 14.5% were current smokers. At the 12-year follow-up, 96% of never smokers could still be classified as never smokers; among ex-smokers, 6% had changed their status to active smokers. After diagnosis, 32% of the smokers had quit smoking (Figure 8); thus, active smoking in this population dropped from 14.5% to 12.5% during the 12-year follow-up.

When exploring smoking status, smoking status was not recorded even once in 70.9% of never smokers, in 64.7% of ex-smokers, and in 27.3% of current smokers. Of all 603 planned contacts, smoking status was only recorded in 104 contacts (17.2%), and pack-years were calculated and recorded in 39 (6.5%). Pack-years were documented in 0.8% of contacts when the patient was an ex- or current smoker. Of the 104 contacts in which smoking status was recorded, the proportion of recorded data was almost equal among never smokers (n=36), ex-smokers (n=32) and current smokers (n=36). Figure 9 presents how the recording of smoking data was conducted in primary health care.

We analyzed the 69 planned asthma contacts of the 22 patients who were current smokers at the study baseline to assess how smoking habits were screened and if smoking cessation was recommended for current smokers in primary health care. During the 12-year follow-up, smoking status was recorded in 49.3% of annual contacts for current smokers, but pack-years were calculated only in 6.3%. The number of cigarettes currently smoked was more often mentioned, in 35.4% of annual contacts. Smoking cessation was rarely recommended: only 15 times during a 12-year follow-up, and out of all current smokers, for nine patients only. Thus, 59.1% of current smokers had not received smoking cessation advice during planned contacts. After asthma was diagnosed, 32% of the smokers had succeeded quitting smoking; of these, 43% had received smoking cessation during planned contacts.

Compared to ex-smokers, current smokers used more antibiotics and had more unscheduled health care contacts during the follow-up.

We explored the 536 planned office-based asthma contacts in primary health care (GP, nurse, or both) to evaluate whether differences exist between professionals in documenting smoking or in smoking cessation advising. Smoking status was mentioned in 13.5% of GP contacts, 27.9% of nurse contacts, and 25.6% of contacts when the nurse and GP participated. Pack-years were mentioned in only 2.4% of GP contacts, 13.5% of nurse contacts, and 14.0% of contacts when both professionals were involved. Thus, smoking data was more often documented if the nurse participated in the follow-up visit. (III)

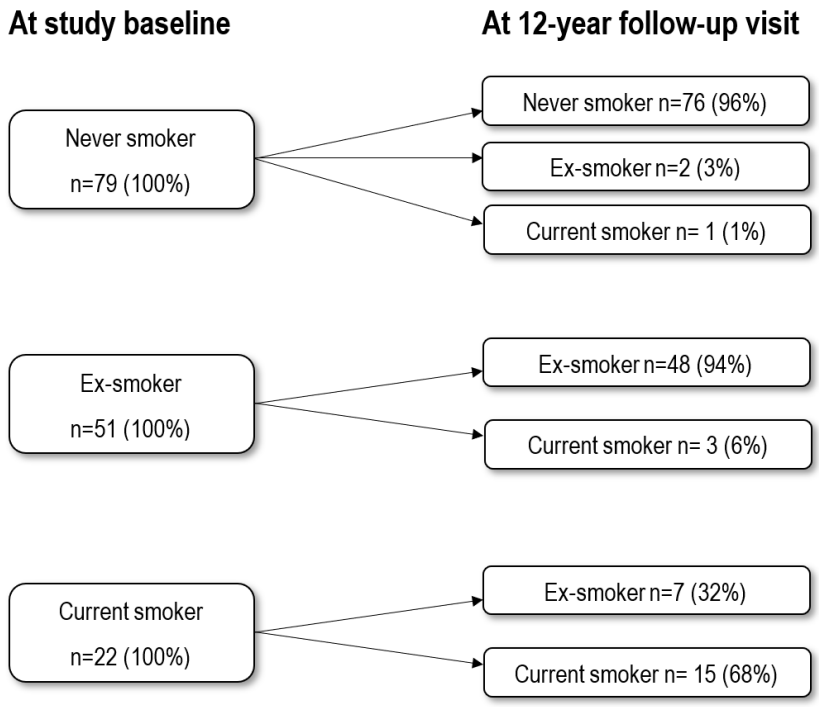

Figure 8. Smoking status changes during the 12-year follow-up among 152 patients with planned asthma follow-up contacts in primary health care.

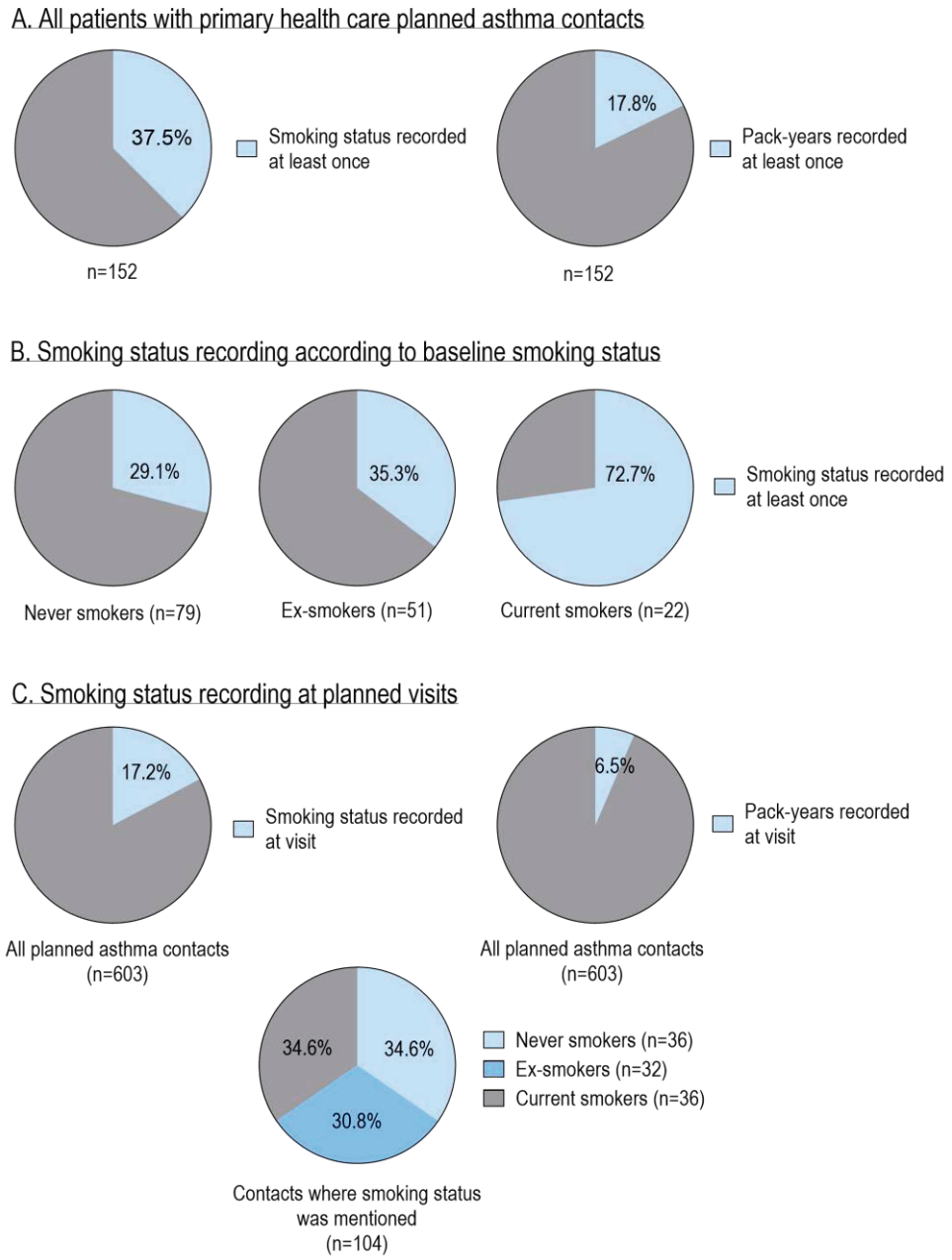

Figure 9. Recording of smoking and pack-years in planned asthma contacts during the 12-year follow-up in primary health care.

5.2.3 Evaluation of comorbidities and lifestyle factors

Assessing comorbidities is important during planned asthma follow-up contacts as they are associated with the risk for poor asthma control and exacerbation (GINA 2023; Porsbjerg & Menzies-Gow 2017). All recorded patient data was collected and analyzed from the full 12-year follow-up to evaluate the assessment of comorbidities and lifestyle factors in office-based contacts (n=542) in primary health care (IV).

Documentation of comorbidities often associated with asthma, such as obesity, rhinitis, obstructive sleep apnea, reflux symptoms, and intolerance to NSAIDs, was seldom done in the planned asthma contacts in primary health care. Occurrence of chronic or allergic rhinitis was recorded most often but still in only 8.9% of contacts and mentioned in 24.1% of subjects. Overall, evaluating possible nasal symptoms was registered in 15.5% of contacts and at least once in 52 patients (35.9%) with office-based contacts. Of all planned office-based asthma contacts, obesity or overweight were documented in 0.9% to 1.3% of contacts. BMI information was mentioned in 1.5% of contacts. Information on BMI, overweight, obesity, or both BMI and information on overweight/obesity were found in health records of 15 patients (10.3%). Reflux symptoms, obstructive sleep apnea, and intolerance to NSAIDs were seldom documented (in ≤ 1.1% of contacts).

No significant differences were found in the recording of comorbidities among professionals. Out of lifestyle factors, exercise habits were more often mentioned if the nurse participated in the planned contacts (from 21.7% to 29.1%). Exercise habits were the most frequently documented lifestyle factor, found in 16.2% of contacts and 33.8% of the patients at least once, while dietary-related issues and alcohol consumption were mentioned in <1% of contacts. (IV)

5.2.4 Asthma management details and the guidance given at follow-up

All documented patient data considering medication, inhalation technique, and patient guidance from the 12-year follow-up was collected and analyzed to assess how other asthma management details were conducted during the planned asthma contacts (IV). The brand names of all asthma medications were recorded in 70.3% of all office-based planned contacts (n=542), while complete dosage and inhaler names were recorded only in 13.5% and 11.4%. Asthma medication data was more commonly only partially documented and more frequently found if both professionals participated in the contact. Revision of inhalation technique was only documented in 2.2% of all contacts and in 7.8% of nurse contacts. Of all patients

with office-based planned contacts, inhalation technique was revised for 6.9% of patients during the 12-year follow-up. Medication for reflux or nasal symptoms was rarely mentioned or initiated at the follow-up.

Of all planned office-based asthma contacts, the timing for the next follow-up contact was recommended in 62.5% of contacts and more often when the GP or both professionals participated. An AAP was recorded in 5.0% of contacts; of all patients, only 16.6% had documented information on AAP in planned contacts. If the AAP was updated, it was more frequently given only verbally to the patient, based on documented information. Guidance to lose weight, increase exercise or reduce alcohol intake was rarely documented—in <1% of contacts. (IV)

Figure 10 summarizes the methods used to assess asthma during planned office-based follow-up contacts. Table 7 summarizes the assessed and documented asthma management details in planned office-based asthma follow-up contacts and how these were performed according to professionals participating in the visit.

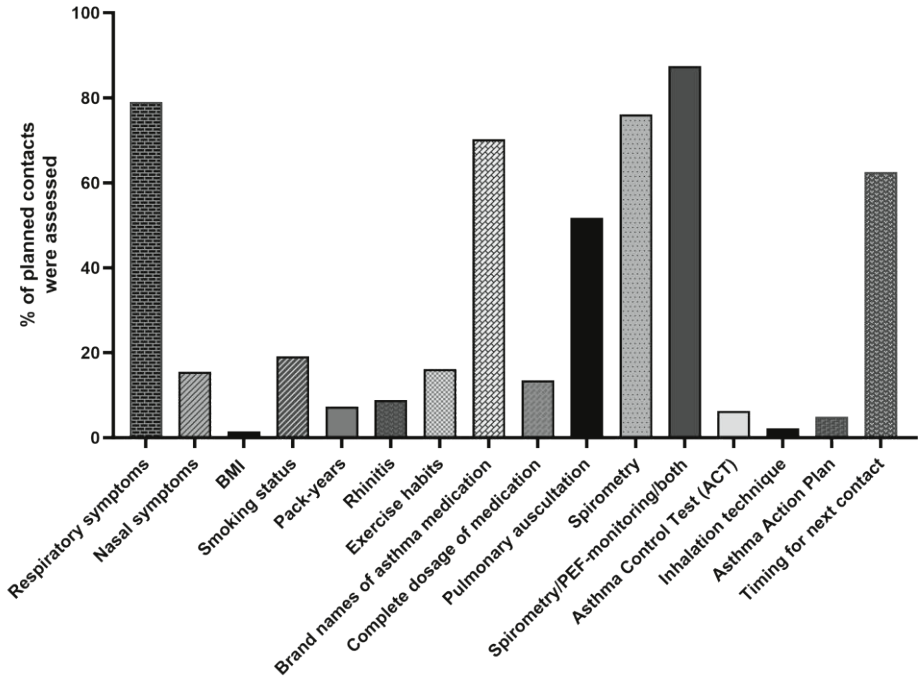

Figure 10. Assessments conducted during the office-based planned asthma visits (n=542) in primary health care. Data from original communications I, III and IV.

Table 7. Assessment and documentation of asthma management details according to professionals in planned office-based asthma follow-up visits in primary health care during 12-years.

	All planned office-based asthma contacts	GP contacts	Nurse contacts	Both GP and nurse contacts	P-value
ASSESSMENT OF SYMPTOMS (IV) [a]					
Respiratory symptoms n (%)	428 (79.0)	237 (76.5)	79 (76.7)	112 (86.8) * ∞	**0.043**
Nasal symptoms n (%)	84 (15.5)	54 (17.4)	13 (12.6)	17 (13.2)	0.358
ASSESSMENT OF SMOKING DATA (III) [b]					
Smoking status n (%)	103 (19.2)	41 (13.5)	29 (27.9) *	33 (25.6) *	**<0.001**
Pack-years n (%)					
- yes	5 (0.9)	2 (0.7)	1 (1.0)	2 (1.6)	**<0.001**
- mentioned nonsmoker	34 (6.3)	5 (1.7)	13 (12.5) *	16 (12.4) *	
ASSESSMENT OF LUNG FUNCTION (I) [b]					
Spirometry/PEF-monitoring or both n (%)	469 (87.5)	255 (84.2)	87 (83.7)	127 (98.4) * ∞	**<0.001**
ASSESSMENT OF COMORBIDITIES (IV) [a]					
BMI n (%)	8 (1.5)	3 (1.0)	3 (2.9)	2 (1.6)	0.365
Chronic/allergic rhinitis or its symptoms n (%)	48 (8.9)	30 (9.7)	6 (5.8)	12 (9.3)	0.481
MEDICATION DATA (IV) [a]					
Asthma medication drug/brand names n (%)	381 (70.3)	198 (63.9)	77 (74.8) *	106 (82.2) *	**<0.001**
Inhalation technique revised n (%)	12 (2.2)	1(0.3)	8 (7.8) *	3 (2.4)	**<0.001**
PATIENT GUIDANCE (IV) [a]					
Asthma action plan (verbal, written, or both) n (%)	27 (5.0)	14 (4.5)	5 (4.9)	8 (6.2)	0.759
Recommendation for the timing of the next planned contact n (%)	339 (62.5)	198 (63.9)	53 (51.5)	88 (68.2) ∞	**0.025**

Data from original communications I, III and IV. Statistically significant p-values are presented bold. *Indicates p<0.05 compared to group 'GP contacts. ∞Indicates p<0.05 compared to group "Nurse contacts". GP=general practitioner, PEF=peak expiratory flow, BMI=body mass index. [a] In the original publication IV the total number of assessed office-based planned asthma follow-up contacts was 542. Out of the 542 contacts, 310 were GP contacts, 103 nurse contacts, and in 129 contacts both GP and nurse took part in assessing asthma. [b] In the original publications I and III the total number of assessed office-based planned asthma follow-up contacts was 536. Out of the 536 planned contacts, 303 were GP contacts, 104 nurse contacts, and in 129 contacts both nurse and GP took part assessing asthma.

5.3 Overall participation in planned asthma contacts

The patients were categorized based on the number of planned contacts during the study period to assess the overall occurrence of planned asthma follow-up in the SAAS study population (0–1 contact vs ≥2 contacts) (II). Because the follow-up during the first 1–2 years after diagnosis was mainly performed at the respiratory department in specialized care, categorizing the patients was based on the number of planned asthma contacts after 2002.

Patients with ≥2 planned contacts (n=146) had a median of 5 (IQR 3–8) follow-up visits, resulting in approximately one planned contact every second year. In the study population, 141 patients had ≥2 planned asthma contacts after 2002, whether mainly in primary health care (n=111) or mainly in specialised care (n=30). Five patients could not be directly classified into either of the above categories, when four had two separate contacts in primary health care and specialised care, and one patient had three separate follow-up contacts in primary health care, private health care, and specialised care during the follow-up.

Of the 203 patients in the SAAS study, 57 had only 0–1 planned asthma contacts, and of these patients, 29 patients had none during the 12-year period. Risk factors for non-participation in follow-up were assessed by characterizing the patients with 0–1 planned contacts during the follow-up in more detail. Patients with 0–1 planned asthma follow-up contacts were more often found to be heavy alcohol consumers and had higher levels of alcohol use biomarkers GT and GT-CDT. In multivariable binary logistic regression analyses heavy alcohol consumption also predicted poorer participation in planned follow-up after adjusting for age, sex, pack years, BMI, and form of residency (II).

5.4 The effect of follow-up on asthma control

The patients were divided into two groups based on the number of planned asthma contacts during the follow-up to assess the association of the number of follow-up contacts—among other things—on asthma control and treatment adherence. The patients (n=198) with 0–1 planned contacts vs ≥2 planned contacts were compared to evaluate if participation in follow-ups was associated with asthma control in the SAAS study population (II). Differences were not found in asthma control as defined

according to the GINA 2010 guideline, but patients with ≥2 planned contacts seemed to have more symptoms according to ACT and AQ20 questionnaires; they also used more medication for asthma (needed more OCS courses and collected more SABA canisters, LABA, and add-on-drugs) and had more hospitalizations due to asthma as well as other asthma-related healthcare visits (Barley et al. 1998; GINA 2010; Nathan et al. 2004). Significant differences were not found between the groups in lung function or inflammatory parameters. (II)

We divided the primary health care study population (n=152) into two groups according to the number of planned asthma contacts (<4 vs ≥4) in primary health care during the 12-year period to assess how the number of follow-up contacts is associated with asthma control (I). In both groups approximately every third patient had uncontrolled asthma according to GINA 2010 criteria (GINA 2010). Patients with ≥4 planned contacts had more often ICS medication based on self-reports and had a higher total adherence to ICS medication. These patients had more other asthma-related health care visits and were more often in working life. These groups did not significantly differ according to basic characteristics, lung function, or asthma severity. (I)

5.5 Comparison of the patients with follow-up mainly in primary health care versus specialised care

Further analysis was performed by categorizing the 141 patients with ≥2 planned asthma contacts into two groups according to the main site of follow-up to assess the differences between patients with planned contacts mainly in primary health care versus specialised care (II). In both groups, the median number of planned contacts during the follow-up was four (with IQR 3-7 in primary health care and IQR 2-5 in the specialised care group). Patients with follow-up contacts mainly in primary health care had better and more stable adherence to ICS medication-(annual means between 74.3% and 84.7%) during the whole 12-year follow-up period than those with follow-up contacts mainly in specialised care (annual means between 45.1% and 67.7%) as Figure 11 shows. Patients who were mainly monitored in specialised care had higher daily prescribed ICS doses (budesonide eq), but no significant differences were found in the average dispensed doses between the groups. When investigating the underlying reasons for lower adherence, most of the patients (80.0%) having planned contacts mainly in specialised care seemed to discontinue their regular follow-ups when the asthma monitoring was transferred to primary health care,

where patients should have arranged the follow-up themselves. These patients also had the lowest total adherence to ICS medication (37.0%). (II)

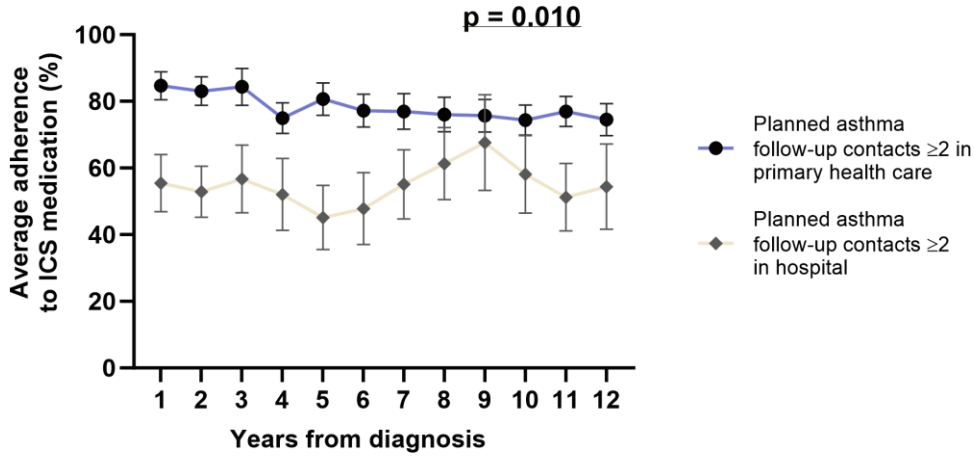

Figure 11. The annual changes in adherence to ICS medication over 12-years. Annual adherences shown as mean ± SEM (determinated to patients with medication purchased; n=104 patients mainly asthma follow-up contacts in primary health care and n=25 mainly in hospital). P-value defined by area under the curve method and independent-samples Mann-Whitney U test.

6 DISCUSSION

6.1 Compliance with asthma guidelines in asthma follow-up in primary health care

This thesis aimed to assess the long-term conduction of planned asthma follow-up in primary health care and how several factors affecting asthma control are assessed during the follow-up contacts. According to national and international asthma guidelines, a healthcare provider should regularly assess and review asthma patients (Asthma: Current Care Guidelines 2022; Australian Asthma Handbook 2022; British Guideline on the Management of Asthma 2019; GINA 2023). Regular follow-up of asthma is essential due to the variability of the disease, but also as remission of adult-onset asthma is rare, and the possible reasons and risk factors for poor asthma control are complex (Almqvist et al. 2020; GINA 2023; Honkamäki et al. 2021; Larsson et al. 2020; Porsbjerg et al. 2018; Tuomisto et al. 2016; Westerhof et al. 2018). Results of this thesis supported the previous studies showing that one of the Finnish Asthma Programme's main goals in directing the responsibility of asthma management and monitoring to primary care has succeeded when most of the patients' asthma follow-up was mainly carried out during the long-term period in the primary healthcare setting (Erhola et al. 2003; Haahtela et al. 2006; Tuomisto et al. 2010). However, this 12-year real-life follow-up showed that regular follow-up of asthma did not occur according to evidence-based guidelines in the Hospital District of South Ostrobothnia in Finland, when almost 30% of all asthma patients seemed to be lost to follow-up, and regular contacts were not actualized. Although the occurrence of possible asthma symptoms and the performance of lung function tests were well documented as part of evaluating asthma, the comprehensive assessment and self-management guidance of patients in planned asthma contacts remained insufficient based on documented data. The results support the previous studies showing gaps between evidence-based recommendations and practice in primary health care (Flecher et al. 2020; Price et al. 2019).

To the best of our knowledge this thesis is the first study to present the real-life long-term occurrence of planned asthma follow-up contacts and how asthma management details are assessed based on objective documented patient data. The

results of this thesis are valuable because long-term real-life follow-up studies of adult-onset asthma are rare (Tuomisto et al. 2015). In several previous studies reporting asthma follow-up or evaluations, the assessed asthma visits have consisted of all asthma-related contacts, and the studies have not necessarily focused on evaluating the conduction of planned follow-up contacts. Moreover, previous studies have mainly used register-derived or self-reported information and have chiefly been cross-sectional or based on short follow-up, among other things (Tables 2 & 3).

This thesis suggests that implementing evidence-based asthma guidelines has been only partially successful in primary health care, and improving the systematic assessment and follow-up of asthma is needed. These results are in line with those in the recent Finnish study, reporting similar proportion of patients with annual follow-up (Pakkasela et al. 2023). However, Pakkasela et al. showed 78% of patients reporting to have an asthma self-management plan, and 97% reporting that they had been taught how to use their inhaler (Pakkasela et al. 2023). The inhaler technique and AAP were seldom assessed during planned asthma follow-up contacts in primary health care based on this thesis. Pakkasela et al. study's results may reflect the application of asthma treatment guidelines on a more general level, such as what kind of guidance the patient has received based on self-reported data at least once during or after the diagnosis of asthma. Thus, the difference in these two studies may indicate that after the patient receives the initial guidance and education of asthma, the guidance decreases thereafter. The assessment of inhaler technique and AAP may also have improved since the current study's follow-up as the previous survey of Pakkasela et al. was carried out more recently.

During the 2010s, awareness and knowledge of severe asthma has increased; similarly, using ready-made phrase templates has become more common in primary health care. These may have improved systematic assessment of asthma. However, no national common asthma templates are in use in Finland. Moreover, the increase in the challenges of availability of services may have negatively affected asthma follow-up, even though the number of primary care outpatient visits due to asthma seems to have remained unchanged during the 2010s (Aine et al. 2017; Jantunen et al. 2021). Aine et al.'s study reported that due to the lack of GPs in some health care centres, only patients with uncontrolled asthma symptoms could visit the GP (Aine et al. 2017). The systematic assessment of asthma cannot be assumed to be possible if patients are only offered short acute appointments. One could also speculate whether assessing asthma is considered as important as, for example, diabetes and cardiovascular diseases. Arguably, there is a risk in visits where asthma is not the only

issue, that other long-term conditions may take attention away from asthma. More research is needed to discover the current situation and how asthma assessment and follow-up are carried out in primary health care in the 2020s.

6.1.1 Occurrence of planned asthma contacts

The current Finnish asthma guidelines recommend annual contacts (Asthma: Current Care Guidelines 2022). The results in this long-term follow-up study showed that the regular yearly contacts were not actualized when approximately only every third patient attended a planned asthma contact each year in primary health care; therefore, each patient had, on average, four planned contacts during the 12-year period. These results align with previous studies containing similar findings with approximately 30%–37% of patients having annual contact (Axelsson et al. 2015; Larsson et al. 2018; Pakkasela et al. 2023; Sandelowsky et al. 2023; Stridsman et al. 2021). When the population was divided according to the number of follow-up contacts (≥4 vs <4 planned contacts), the patients who had at least four follow-up contacts in primary health care during the 12-year study, formed a minority, showing that with most of the patients, the follow-up contacts occur more infrequently.

Of the 203 patients in the SAAS study population, 57 (28%) only had 0–1 planned contacts during the long-term follow-up and, overall, 29 patients had none. Some of these patients may have overestimated the actual control of asthma or did not perceive asthma as a chronic disease requiring regular reviews as shown also in previous studies (Bosnic-Anticevich et al. 2018; Kritikos et al. 2019). Asthma control did not differ between patients with 0–1 planned asthma contacts compared to patients with ≥2 contacts, according to GINA 2010 criteria (GINA 2010). Overall, in the SAAS study population, asthma remission was rare (3%), suggesting this did not result in less frequent asthma follow-up visits (Tuomisto et al. 2016). In multivariable binary logistic regression, heavy alcohol consumption predicted poorer participation in follow-ups among patients with fewer planned asthma contacts. This finding supports the results of a previous Finnish study, which reported on healthcare personnel's thoughts on the possible patient-related factors that could lead to a patient not attending a follow-up: health care professionals considered the risk of non-participation higher with older people and in men who are heavy drinkers and smokers (Aine et al. 2017). Almost half of this study's current smokers were heavy alcohol users. In statistical analyses, the male sex showed a trend for being a risk factor for poor participation in asthma follow-ups, but age or smoked pack-years

were not associated with missing follow-up contacts, as previous studies suggested (Aine et al. 2017; Backman et al. 2017; Kang et al. 2013; Mäkelä et al. 2013).

6.1.2 Assessment of factors affecting asthma control

This thesis showed how the various areas of asthma treatment guidelines have been adopted in long-term asthma follow-up in primary health care; Figure 12 summarizes the results. Adherence to lung function tests was excellent when spirometry, peak flow monitoring, or both were performed in over 87% of contacts during the follow-up and in almost all contacts (>98%) if both professionals were involved in the asthma contact. Primary health care has excellently adopted measuring objective lung function tests as part of assessing asthma control in addition to evaluating occurrence of respiratory symptoms. These findings support adherence to the Finnish National Asthma Programme, evidence-based asthma guidelines, and to the regional asthma programme in the study area—all emphasizing the importance of assessing asthma symptoms and objective lung function tests (Asthma: Current Care Guidelines 2022; GINA 2023; Haahtela & Laitinen 1996; Haahtela et al. 2006; Somppi et al. 1997). Previous studies have reported the underuse of objective lung function measurements in asthma diagnostics and monitoring in many countries as Section 2.2.3 discussed in more detail (Chapman et al. 2017; Gershon et al. 2012, Härtel et al. 2022; Kerr et al. 2023; To et al. 2015; Weidinger et al. 2009). In this study, the occurrence of asthma symptoms was recorded in almost 80% of all contacts and approximately 87% of contacts when both nurse and GP participated in assessing asthma. The extent of evaluating symptoms and the true symptom burden of the patients was not assessed in the present study; thus, more research is needed regarding this issue in the future. Documentation of ACT was rarely found, which may be because it was not yet widely used in Finland during the SAAS study follow-up period.

To the best of our knowledge, this is the first long-term study to report how asthma medication information is documented during planned asthma contacts. Most of the previous studies considering asthma medication information have described the prevalence in using different types of medication, for example, ICS alone or combination, or how professionals prescribed them. In this study, asthma medication brand names were found in over 70% of contacts but in less than 14% of contacts complete dosage or inhalers. Patients with follow-up contacts mainly in primary health care had higher and more stable mean adherence (>80%) to ICS

medication during the 12-year follow-up period than those who were mainly followed in specialised care. Observed adherence was good as several previous studies have reported a lower proportion varying between 30% and 70% (Axelsson et al. 2015; Bosnic-Anticevich et al. 2018; Bårnes & Ulrik 2015; Engelkes et al. 2015; Hussain et al. 2022; Reddel et al. 2015). In the study of Vähätalo et al. was found that overall adherence to ICS medication in the SAAS-study population was 69% (Vähätalo et al. 2020). The present thesis showed that adherence to ICS medication was even better if the patient had at least two planned asthma contacts during the follow-up period. Conversely, adherence to ICS medication was poorer in patients who participated less in the asthma follow-up contacts or discontinued the follow-up. These findings can be considered to support previous studies that regular follow-up supports asthma medication adherence (Axelsson et al. 2015; Corsico et al. 2007; Stridsman et al. 2021).

In the present series of studies, one could not assess how medication adherence was discussed among planned asthma contacts in primary health care. Based on the results, the primary health care professionals may have been good at promoting the importance of regularly maintaining medication. Since the names of the medications were recorded well, compliance in medication treatment may have been discussed to some extent. A recently published Finnish study showed that continuity of treatment with the same physician was connected to better medication adherence, also in asthma (Lautamatti et al. 2023). Continuity of care and emphasizing the importance of follow-up during the contacts could be one explaining factor for the good adherence in the present study; a recommendation for timing of the next planned contact was found in over 62% of primary health care contacts and almost 70% if both professionals participated.

Results suggest that the most urgent needs for improvement in managing asthma patients are assessment of smoking, comorbidities, lifestyle factors, and medication inhalation technique—similarly as smoking cessation and patient self-care guidance. According to the documented data, these potential causes for poor asthma control were poorly evaluated during planned asthma contacts, indicating that application of these areas of asthma guidelines were weakest (Asthma: Current Care Guidelines 2022; GINA 2023). Asthma control might improve if more attention was paid to these issues (Larsson et al. 2020; Porsbjerg et al. 2018). A recent Swedish study aligns with these results, showing that adherence to guidelines must improve, particularly in smoking cessation, patient education, and the use of written action plan (Stridsman et al. 2020).

What was surprising in the present series of studies was how poorly the documentation of, for example, inhalation technique, asthma self-care instructions, and smoking had been done because all these issues had been emphasized during the national asthma programme and in evidence-based asthma guidelines (Asthma: Current Care Guidelines 2000; GINA 2002; Haahtela & Laitinen 1996; Haahtela et al. 2006). The poor recording of smoking data among asthma patients can also be considered confusing because smoking harms the lungs and strongly relates to overall morbidity and mortality (GBD 2019 Risk Factors Collaborators 2019; GOLD 2023; Wolf et al. 2023). Finland has also had a national smoking cessation guideline since 2002 (Winell et al. 2018). Based on this thesis and previous Finnish studies, one could argue that smoking cessation activities in primary health care in Finland have remained inadequate despite guidelines (Aine et al. 2017; Erhola et al. 2003; Gräsbeck et al. 2020; Tuomisto et al. 2007).

Apart from smoking and physical activity, the role of other lifestyle factors in asthma management has not been emphasized as such in the asthma treatment guidelines. However, the importance of weight management was already mentioned in the 2000 Current Care Guidelines, and diet, physical activity, and alcohol consumption plays a key role in this (Asthma: Current Care Guidelines 2000). Our results align with previous Norwegian study showing that guidance of physical activity, dietary issues and alcohol use was seldom recorded also for stroke patients during their follow-up in primary health care (Pedersen et al. 2018).

Based on these results, one could question whether connection of comorbidities to asthma control and management are understood in primary health care because comorbidities were poorly screened. As an example, although about 70% of patients had chronic rhinitis, it was undertreated based on the recorded medical data. One could speculate, whether the significance of comorbidities in asthma control was perhaps not as well understood in the 2000s as it is today; this association probably became better understood at the end of the 2000s and during the 2010s, as the research on severe asthma and its related risk factors increased (Boulet & Boulay 2011). Obesity, nasal conditions (e.g., rhinitis, sinusitis, and polyposis), and gastroesophageal reflux were mentioned in 2002 in a GINA guideline as factors that may exacerbate asthma (GINA 2002). Also, except for obstructive sleep apnea, all the comorbidities in this study and their possible effects on asthma control were mentioned already in the Finnish guideline in 2000. Thus, one could consider that the practices this study reported reflect the best practices in 2002 and onward because evidence-based guidelines were available in primary health care during the SAAS study period.

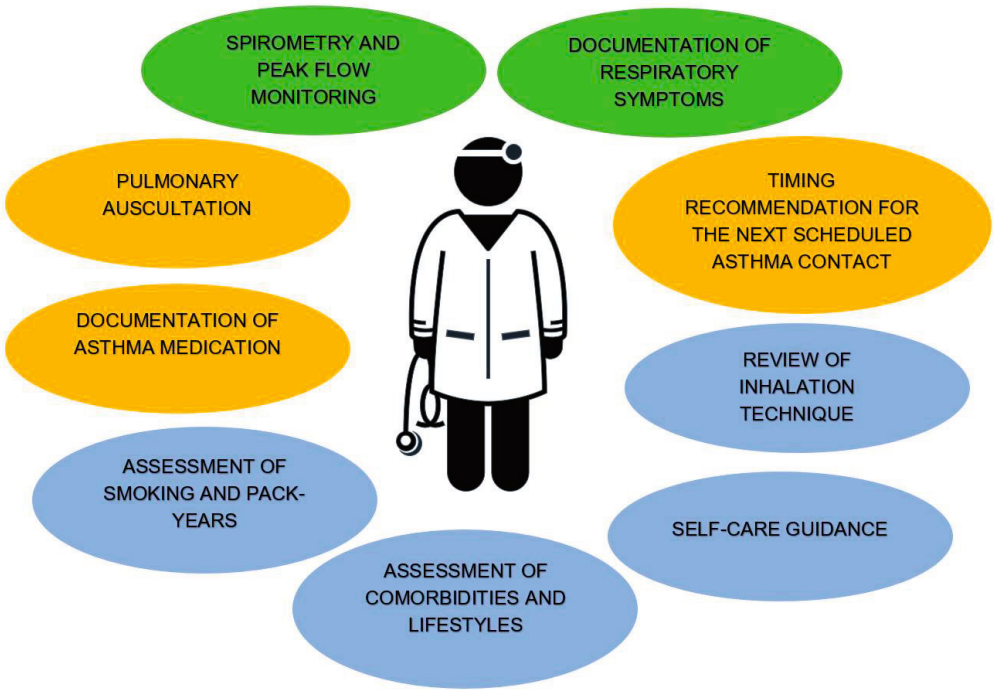

Figure 12. The content of asthma follow-up contacts (n=603) in primary health care. The asthma assessment details that were conducted well are marked in green, moderately conducted are marked in yellow and poorly conducted in blue.

6.1.3 Assessment of asthma according to professionals

A GP conducted over half the planned asthma contacts in primary health care, while a nurse only conducted 17%. Thus, these findings suggest the aim to strengthen an asthma nurse's role in the asthma follow-up was not reached to the extent aimed in the national asthma programme during current study's follow-up period (Haahtela et al. 2006). Approximately every fifth contact was performed with the co-operation of the nurse and GP during the follow-up period. In general, evaluating lifestyle factors, patient guidance, lung function test performance, and revision of inhalation technique have largely been the nurse's responsibility, while the GP's task has been more to interpret lung function tests, assess asthma control, medication, and the patient's treatment recommendations (Erhola et al. 2003; Haahtela et al. 2006). The differences that emerged in this study according to whether the patient met the GP, nurse, or both partially adapted to this division of labour, but it seemed that in many contexts, cooperation between the nurse and GP could produce the best result, as

also previous studies have suggested (Backer et al. 2012; Lisspers et al. 2010; Rupasinghe et al. 2021). In many respects, significant differences between professionals did not emerge; instead, the results emphasized that both professional groups should improve asthma assessment.

6.1.4 The effect of follow-up contacts on asthma

Previous studies have suggested that patients whose disease is not properly controlled are likelier to seek follow-up (Pakkasela et al. 2023; Stridsman et al. 2021; Tan et al. 2020). Conversely, there are also evidence-based data that by regularly and systematically assessing asthma, increasing the level of asthma control is possible (Backer et al. 2012). The findings in this thesis can be considered to support both abovementioned. Patients with ≥2 planned asthma contacts had more difficult-to-treat asthma since they used more medication for asthma but still had more symptoms, exacerbations, and other asthma-related health care contacts. However, no differences in lung function or asthma control (according to GINA 2010) existed compared to patients with 0–1 contact. Thus, it could be hypothesized that with planned asthma contacts, more severe asthma can be treated at the same level as milder and less-symptomatic asthma. Results also suggest that some of the patients could have benefited from more phenotype-adjusted treatment.

6.2 Methodological considerations of the study

The present thesis was based on the clinical real-life adult-onset asthma cohort of the SAAS study. A respiratory physician made the asthma diagnosis based on typical asthma symptoms with objective lung function measurements, showing the reversibility of airway obstruction (Kankaanranta et al. 2015). Therefore, an asthma diagnosis can be considered reliable. Overall, over 94% of the patients diagnosed with novel asthma at the study site were recruited to the study (Kankaanranta et al. 2015). In 2001, the study population represented > 38% of all novel adult-asthma diagnoses in the whole geographical area (Ilmarinen et al. 2019). Moreover, the study population reflects well the typical primary health care asthma population when smokers, patients with concomitant COPD, or other comorbidities were not excluded (Honkamäki et al. 2019; Kankaanranta et al. 2015). Compared to previous

population-based studies (Finland Estonia Sweden study FinEsS) from the same geographical area, the prevalence of smoking and rhinitis was quite similar in the present study population, while the incidence of COPD was lower in the FinEsS study, which may be explained by excluding patients over 70 and patients' underreporting COPD in the previous study (Honkamäki et al. 2019; Pakkasela et al. 2020).

This thesis included the nurse and GP contacts. Overall, this real-life study had 603 planned contacts, which may be expected to yield a representative sample of real-life adult asthma management. Since this thesis focused purely on planned asthma visits, these contacts can be estimated to give a good picture of how asthma guideline elements have been implemented and adopted in the planned follow-up and assessment of asthma. It could be assumed that in visits where asthma is not the only issue of attention or if the visit has been made, for example, due to exacerbation or infection, no similar opportunities for comprehensive and systematic assessment of asthma exist; thus, the results might be expected to be poorer. When comparing assessment of asthma in planned contacts, GP telephone contacts were excluded when these were often short phone calls basically unintended to replace comprehensive face-to-face assessment.

Methodological limitations exist, considering the current study. The results do not represent all of Finland. Regional variations may occur between hospital districts in asthma care similarly as suggested recently with diabetes (Winell et al. 2023). Regional variations may exist due to, for example, different local operating practices, electronic patient information systems or health care resources (Aine et al. 2017; Winell et al. 2023).

Another limitation is that the results may not reflect the current situation as the data was collected from 2002 to 2013. The problem with long-term follow-up studies is that practices and knowledge may have changed during the follow-up period. However, follow-up studies help to evaluate the persistence or occurrence of the results in the long-term period better than, for example, cross-sectional studies, which usually provide information from a certain period or situation during the study; thus, the results in cross-sectional studies can be considered more hypothetical.

One limitation acknowledged to the current thesis is that implementing the systematic assessment of asthma was evaluated based on documented patient data. For example, smoking, comorbidities, or other asthma-related details may have been evaluated or discussed during the contacts or assessed earlier in other contexts (such as in visits for asthma and other reason, or in contacts made because of acute

exacerbation). Smoking information and BMI may also have been recorded in a separate spirometry template. However, if this data was not recorded in patient document entries during the planned asthma contacts, this can lead to the intervention being underestimated. According to good clinical practice, measures taken shall be recorded; otherwise, it can be interpreted that it has not been done or that the existence of the matter and its possible effect on asthma has not been considered. Also, regarding continuity of care, patient document entries must be done well.

Another limitation is that the assessed visits were limited to focus purely on planned asthma follow-up contacts. For example, lifestyle factors or comorbidities may have been better evaluated during visits where asthma was not the only reason for the visit. Asthma assessment and follow-up may also be carried out in connection with other visits. This is why in the future it is important to study asthma assessment with more extensive data, including, for example, asthma follow-up visits where the reason for contact has also been some other underlying disease or symptom of the patient.

The present study did not assess more precisely what kind of conclusions were made based on the evaluated variables during the contact and how these conclusions affected patients' therapy and asthma control. For example, the skills of GPs to interpret spirometry or nurses to assess the inhalation technique were not estimated. Since it was a retrospective observational cohort study, it was not possible to evaluate whether interventions in poorly assessed factors, for example comorbidities or smoking, would have changed the situation in those patients whose asthma was not properly controlled and who visited more frequently. Other aspects of asthma care, such as the evaluation of asthma exacerbations, were unexplored in the present study. More research is needed to evaluate the abovementioned topics.

Adherence to ICS treatment was objectively evaluated by comparing the patient's dispensed doses to prescribed doses for the 12-year follow-up period (Vähätalo et al. 2020). A possible limitation considering adherence calculation was that when the medical records were not always complete (e.g., shortage of physicians' notes or missing information) prescribed medication was calculated based on previously confirmed information (Vähätalo et al. 2020). Also, even if medication was dispensed, whether it was used as prescribed was not guaranteed (Vähätalo et al. 2020). Asthma control was defined according to GINA 2010 criteria at the 12-year follow-up visit, and asthma severity was classified according to the ERS/ATS 2014 guideline (Chung et al. 2014; GINA 2010). Even if asthma control and asthma severity criteria have changed since then, we consider it correct to use the data as it

was collected and evaluated at the clinical visit on asthma control and used in the original SAAS study material.

The SAAS study cohort consisted of patients who had been originally referred to Respiratory Department due to respiratory symptoms with asthma suspicion (Kankaanranta et al. 2015). One might argue that therefore the population may differ in some characteristics from the entire asthma population, if, for example, patients with more severe symptoms were more easily referred to specialised medical care for diagnostic examinations. We cannot fully exclude this bias. Moreover, the number of patients with follow-up contacts, mainly in specialised care (II), was low—as well as the number of current smokers at the 12-year follow-up (III)—which may have led to low statistical power in analyses; thus, clinical studies with larger cohorts are needed.

6.3 Clinical implications

The present thesis demonstrated how planned follow-up and assessment of asthma has been adopted in the primary health care system in the Hospital District of South Ostrobothnia in Finland. The results of this thesis confirm that with well-planned and coordinated training and collaboration of different parties is possible to change clinical practice permanently: the Finnish National Asthma Programme successfully transferred the main responsibility of asthma management and monitoring to primary health care. At the same time, monitoring of lung function tests together with symptom assessment was well adopted in primary health care. However, several areas still need improvement.

This series of studies may help identify possible health care practice-related causes for uncontrolled and difficult-to-treat asthma and which areas in assessment and follow-up of asthma require more urgent attention. Based on the results above, the entire healthcare system must pay more attention to the occurrence of asthma follow-up as the frequency of planned contacts was insufficient, and many patients chose not to participate in the follow-up. Comprehensively assessing asthma should be improved during planned asthma contacts. Although the study was conducted regionally in South Ostrobothnia in Finland, one can argue this study's results may indicate the situation at the level of the entire country. This hypothesis is supported by several previous studies, including those published from the Nordic countries, that have found correspondingly shortcomings in occurrence of asthma follow-up

and assessment in primary health care (Table 2; Table 3; Hansen et al. 2023; Reddel et al 2015; Rönnebjerg et al. 2021; Sandelowsky et al. 2022; Stridsman et al. 2020; Stridsman et al. 2021; Tan et al. 2020). To conclude how well the results of this thesis apply entire primary health care in Finland, we would need a comprehensive nationwide study on the conduction of asthma assessment during follow-up visits. Based on our results, more attention should also be paid to the quality of patient documentation entries, as also another previous Finnish study have suggested (Vainiomäki et al. 2008).

6.3.1 Organization of asthma follow-up contacts

The organization and timing for the future follow-up should be planned during the asthma diagnosis and planned contacts and in connection with exacerbations, emergency room visits, and prescription renewals (GINA 2023). A nurse can largely perform regular asthma follow-up, as every patient does not need an annual physician's assessment if the asthma is well controlled. According to current Finnish asthma guidelines, patients should visit a physician at least every third to fifth year (Asthma: Current Care Guidelines 2022). Based on the results of this thesis, the follow-up cannot be completely omitted in the years between physician visits, even if the asthma control was described as stable; the disease is heterogenic, and many patients' asthma is not well controlled, highlighting the need for regular contacts. Patients with difficult-to-treat and severe asthma should have regular check-ups and, if necessary, also more frequently (GINA 2023; Larsson et al. 2018; Rönnebjerg et al. 2021). Attention should also be paid to identifying severe asthma in primary care because it is under-recognized (Hansen et al. 2023; Ryan et al. 2021). Asthma management might be improved if known which phenotypes require more frequent assessment (Khusial et al. 2017). More research is needed to determine the optimal follow-up interval for different asthma phenotypes to design more personalized asthma management and follow-up.

Based on the results of this thesis, the patients' awareness of asthma as a long-term disease requiring regular follow-up, whose management is significantly influenced by numerous factors, including comorbidities and lifestyles, should be emphasized. Healthcare professionals and patient organizations promoting respiratory health are central in this work. Transitioning from specialized medical care to primary health care is important phase to support the continuity of follow-up; at this point, the patient must get information about the importance of follow-

up. Similarly, the patient needs to receive a recommendation on when, where, and how to continue follow-up because, in the Finnish primary healthcare system, the responsibility to arrange planned contact lies with oneself. Continuity of care is especially important to adult asthmatics, as shown also in this study. Continuity should be promoted in the asthma management, not only due to commonly existing comorbidities and chronic, complex nature of disease but as there is also evidence that it improves medication adherence and self-care skills (Axelsson et al. 2015; Lautamatti et al. 2023; Wireklint et al. 2021).

6.3.2 Performing comprehensive assessment of asthma

Is achieving better asthma control possible? If so, how could asthma treatment be improved with the available resources and availability of services in primary care? Based on the results, several guideline elements could be better applicated in asthma follow-up to improve asthma control and patients' asthma-related quality of life. Primary healthcare practitioners should increasingly pay attention to evaluating possible risk factors for poor asthma control. The importance of screening and treating asthma-related comorbidities in primary health care should be given more attention. Comorbidities may mimic asthma symptoms and lie behind difficult-to-treat disease (Porsbjerg & Menzies-Gow 2017; Tay et al. 2016). If not identified, this can lead to wrong diagnoses or, for example, unnecessary healthcare costs. If the connection between comorbidities and asthma is not recognized, such can also lead to unnecessary enhancing asthma medication with a higher risk of side effects or other comorbidities caused by cortisone treatment (Kankaanranta et al. 2023). One could argue whether asthma patients have sufficient knowledge about how comorbidities can affect disease management. This may be an area where patients would need more information and training, but also a topic for further research.

Healthy lifestyle is a key part of the non-pharmacological treatment of asthma. According to our results, there is much room for improvement in assessing lifestyle factors. Notably, the morbidity indices of the area where the current study was conducted are among the highest in Finland, including lung diseases (Koponen et al. 2023). Arguably, this study's results may reflect the general habits in the overall assessment of lifestyle factors, suggesting that more attention should also be paid to these issues in other diseases. Documentation and follow-up of BMI with guidance for weight management should be more emphasized in asthma guidelines as part of routine management. Although weight management has been mentioned already in

the 2000 Current Care Guidelines, it has not been sufficiently adopted in asthma management (Asthma: Current Care Guidelines 2000).

Based on the known dose-dependent harms of smoking for people with asthma, it is essential to evaluate smoking status and pack-year history when asthma is diagnosed and during each asthma contact (Kiljander et al. 2020; Tommola et al. 2019). Moreover, patients who use snuff and e-tobacco should be screened. Patients should be given guidance and support for quitting smoking, e-tobacco and snuff. (Bircan et al. 2021; Gudnadóttir et al. 2017; To et al. 2023). Screening of alcohol use should also be performed for asthma patients because excessive alcohol consumption harms lung health; as this study shows, alcohol may also be associated with a higher risk of non-participation in the follow-up (Quintero & Guidot 2010). As it is a modifiable risk factor, more research is needed on alcohol's effect on asthma.

A recent study showed that patients with follow-up visits had higher ICS collection and lower OCS collection from pharmacy than patients without regular visits (Sandelowsky et al. 2022). That and the possible harms associated with long-term high doses of corticosteroids support why the patients receiving regular asthma medication should have annual planned contacts to help assess optimal ICS doses (Asthma: Current Care Guidelines 2022; Kankaanranta et al. 2023). Moreover, the inhalation technique should be reviewed regularly. According to the results, this is one of the central areas needing improvement in asthma management.

Guided self-management improves asthma patients' quality of life and reduces emergency room visits, hospital days and healthcare costs (Pinnock et al. 2017). A Finnish study has shown that professionals expect guided self-care to bring savings (Aine et al. 2017). Based on this study, asthma patients' self-care guidance should be improved in the primary health care system. An AAP should be assessed and updated in every asthma contact, but this was not actualized based on results. Because asthma is a long-term condition requiring a holistic approach, asthma patients would benefit from written personalized care plans, which include written AAP instructions. Evidence exists of the positive effect of the personalized care plan, e.g., for depression, COPD, and type 2 diabetes management (Coulter et al. 2015; Lenferink et al. 2017; Mikkola et al. 2022). For example, in type 2 diabetes, a personalized care plan positively contributed to disease control, monitoring, and reducing unplanned healthcare use (Mikkola et al. 2020; Mikkola et al. 2022). Overall, this plan is considered to support treatment for all long-term illnesses, but its degree of usage in Finland varies (Coulter et al. 2015; Winell et al. 2019).

6.3.3 Clinical implications of the study for allocating resources

The load on primary care is large, and the resources are insufficient (Koskela & Auvinen 2022). One could assume, due to the lack of resources, asthma follow-up is increasingly carried out by nurses, and that it is more challenging to get to GPs' office just because of asthma than was during the follow-up period of this study. Due to the complexity of asthma care, and for the self-care and lifestyle guidance to succeed, adequate time and resources should be guaranteed in assessing asthma. Presumably, when the assessment is done systematically according to the treatment recommendations, some additional healthcare visits and costs would be saved.

Although containing comprehensive information, quickly finding the needed information in long evidence-based guidelines can be difficult (Lommatzsch et al. 2023). Therefore, as suggested, shorter and more clearly structured guidelines could be easier to implement in primary health care (Lommatzsch et al. 2023). Based on our results, the content of asthma guidelines could need to be reviewed and supplemented with regard asthma follow-up; for example, the importance of assessing risk factors for poor asthma control, and lifestyle factors should be more emphasized. One could also speculate whether renewing the asthma program is needed for the 2020s, as national and regional asthma programs have been suggested as being better at improving asthma care than conventional guidelines (Selroos et al. 2015).

The multi-professional co-operation in assessing asthma in primary health care could be further strengthened, for example with pharmacists. During the Finnish Asthma Programme, pharmacies were included in the program; however, one could speculate whether this cooperation has decreased since then and could it be used more, for example, in assessing asthma control, inhalation technique, and patient guidance (Erhola et al. 2003; Haahtela et al. 2006). With pharmacists' help, the nursing resources could be freed for other work because, for example, a pharmacist could handle the medication advice related to asthma. Previously was shown the interventions of pharmacists positively affected the percentage of asthma-controlled patients, asthma symptoms, and severity (Garcia-Cardenas et al. 2016). In general, as a part of the multi-professional team in primary health care, pharmacists would presumably give benefits, also to other patient groups, because primary care patients often have multiple illnesses, and polypharmacy is common. Moreover, physiotherapists could be more utilized with asthma patients, for example, in support of rehabilitation and exercise guidance (Aine et al. 2017).

Although previous Finnish studies have shown that between 2015 and 2019 73%–83% of health care centres still had a nurse designated as an asthma nurse, there were also indications that the job description of asthma nurses has been abandoned to some extent (Aine et al. 2017; Tapanainen & Merivuori 2019). Asthma nurses often had only limited time for their work while taking care of several other tasks (Aine et al. 2017; Tapanainen & Merivuori 2019). Other nurses may participate more in asthma monitoring; concerns have also been raised about insufficient access to asthma education (Aine et al. 2017; Tapanainen & Merivuori 2019). Based on this thesis, healthcare personnel obviously need continuous training in asthma management because asthma is a heterogenic disease, and evidence-based knowledge is increasing. This research also shows that a comprehensive knowledge of asthma is important for the professional performing the assessment. These results emphasize that trained respiratory nurses are crucial in primary care in the present and future. With their extensive knowledge, they can largely be responsible for comprehensively assessing asthma patients if a physician's consultation support is available.

From the beginning of 2023, establishing 21 wellbeing services counties to replace former hospital districts has provided a new basis for developing uniform healthcare services covering larger regions. In this context, developing and updating uniform asthma treatment programs covering entire regions could be possible, including implementing national asthma templates and educating professionals in systematically assessing asthma. Evidence-based electronic medical record interventions have shown they can improve documentation and care provision, also in asthma; these should be promoted further in Finland (Falck et al. 2020; Landeo-Gutierrez et al. 2023; McClatchey et al. 2023). Digital reporting of PEF results has already been used to some extent in Finland (Tapanainen & Merivuori 2019). Going forward, using digital preliminary information data prepared by the patient could be more utilized in planned asthma contacts. As digital services develop, not all patients are able to use them, and these are not always appropriate. Therefore, an opportunity for a traditional follow-up contact must also exist.

More research is needed to evaluate the overall asthma care obtained in all asthma-related contacts in primary health care, and with larger populations. Similarly, further studies are needed to evaluate the status of current asthma follow-up and how the situation has changed since this study follow-up period to further develop the personalized follow-up and management of asthma.

7 CONCLUSIONS

This 12-year real-life follow-up study showed that implementation of evidence-based asthma guidelines has only partially succeeded in primary health care in the Hospital District of South Ostrobothnia in Finland, and there is need to improve systematic assessment and follow-up of asthma patients.

The present thesis main findings were:

1. Regular follow-up of asthma did not occur according to evidence-based guidelines at primary health care when only every third patient had planned asthma follow-up contact annually.
2. Primary health care professionals' adherence to lung function measurements, especially to spirometry, as a part of assessing asthma control is good.
3. Smoking and pack-years were poorly documented during planned asthma contacts, and smoking cessation was rarely recommended to current smokers during their planned asthma contacts. Based on the results, the assessment of asthma patients' smoking habits and smoking cessation guidance require significant improvement.
4. Documentation of possible respiratory symptoms, asthma medication names, and recommendations for timing the next contact were reasonably well recorded. Contrarily, comorbidities, lifestyle factors, inhalation technique, and AAP were poorly considered during planned asthma contacts in primary care. According to recorded patient data, these aspects should be given greater attention.
5. This thesis showed that a GP conducted over half of the planned asthma contacts in primary health care, while a nurse performed only 17%. The differences in asthma assessment depending on whether the patient met a GP, a nurse, or both during the visits could be explained by the usual division of labour between the nurse and GP. In many respects, significant differences between professionals did not emerge; rather, the results emphasized that both professional groups should improve asthma

assessment. The results of this thesis indicated that cooperation between the nurse and GP could produce the best result.

6. The patients with at least two follow-up contacts used more medication and health care and had more asthma symptoms and exacerbations, but there were no significant differences in lung function or asthma control according to GINA 2010 when compared to patients with 0–1 contact. The patients mainly monitored in primary health care had higher and more stable adherence to ICS medication during the study period. Most of the patients with follow-up contacts mainly in specialised care seemed to discontinue their regular follow-up when they should have arranged follow-up contacts with primary health care. Overall, of all patients, almost one-third only had 0–1 planned asthma contact during the study period. Heavy alcohol consumption was associated with poorer participation in planned contacts.

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PUBLICATIONS

PUBLICATION I

Planned primary health care asthma contacts during 12-year follow-up after Finnish National Asthma Programme: focus on spirometry

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ARTICLE OPEN

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Planned primary health care asthma contacts during 12-year follow-up after Finnish National Asthma Programme: focus on spirometry

Jaana Takala[1,2✉], Pinja Ilmarinen[2], Leena E. Tuomisto[2], Iida Vähätalo[2], Onni Niemelä[3,4] and Hannu Kankaanranta[2,5]

Primary health care (PHC) providers are at the front line of asthma management. To evaluate how planned asthma follow-up occurred in PHC and whether lung function tests were used, 203 patients were followed for 12 years as part of a real-life asthma cohort Seinäjoki Adult Asthma Study (SAAS). A total of 152 patients had visits in PHC attending on average to four planned contacts during 12-year follow-up corresponding to one visit every third year. National guideline recommends annual visits. Patients with ≥4 contacts seemed to have more difficult asthma and better adherence to inhaled corticosteroid medication. Lung function tests were performed on average in 87.5% of annual planned follow-up contacts. Spirometry was performed in 70%, 71% and 97% of all contacts depending on whether it was a contact to GP, nurse or both. Overall, the frequency of follow-up contacts was insufficient but PHC adherence to lung function testing was excellent.

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INTRODUCTION

Asthma is a common, heterogeneous disease, causing considerable morbidity affecting all age groups[1]. Adherence to international and national guidelines in asthma seems to be highly variable[2–5]. It is logical to assume that if clinical guidelines were better adopted it would also lead to better patient outcomes.

Asthma prevalence is still increasing also in Finland[1,6], and the most of asthma cases are diagnosed at adult age[7,8]. Remission of adult-onset asthma is rare[9,10]. There are many possible reasons for poor asthma control and high symptom burden such as allergic or chronic rhinitis, smoking, comorbidities, obesity and low initial lung function as well as problems in inhalation techniques and adherence to asthma medication[1,11,12]. Patients with both systemic inflammation and comorbidity have been shown to have the poorest outcome in asthma[13]. To improve asthma control and outcomes, it is crucial that the routine follow-up contacts in primary health care (PHC) are performed according to a high standard, and there is a need to pay attention to the quality of these contacts[2,14].

Finland was one of the first countries to implement a national asthma programme[15]. The main goals of the Finnish Asthma Programme (1994–2004) were to improve national asthma management, prevent an increase in costs and decrease the burden of asthma to individuals and society[16,17]. One of the main objectives of the programme was to strengthen the role of PHC in the prevention, diagnosis and long-term therapy of asthma[15–19]. The Finnish Asthma Programme emphasized measures to confirm asthma diagnosis by lung function tests, to follow patients regularly and to monitor asthma control also by lung function tests intermittently[15,16]. To achieve these objectives, nurses in the PHC were trained to perform spirometry and general practitioners (GP) to interpret the result. In 2001, spirometry was available in 95% of Finnish health care centres[20].

To our knowledge, no previous long-term follow-up studies exist on the occurrence of planned asthma follow-up contacts in PHC and use of lung function tests during the long-term follow-up of asthma. Thus the main aim of this study was to describe how planned asthma follow-up contacts occurred in PHC and to evaluate the use of objective lung function tests (spirometry and peak flow monitoring) in the long-term follow-up of asthma patients. The second aim was to evaluate the use of lung function tests depending on who encounters the patient: GP, nurse, or both.

RESULTS

Characteristics of the study population

The current study is a part of the real-life adult asthma cohort, Seinäjoki Adult Asthma Study (SAAS), in which 203 patients were followed for 12 years (1999–2013) after diagnosis of new-onset adult asthma[21]. The exclusion and inclusion criteria of the SAAS study are shown in eTable 1. Out of the total of 203 patients, 152 participated in planned PHC asthma follow-up contacts. Forty-nine patients were excluded because of not having planned follow-ups in PHC or having them only in private health care or in respiratory department (Fig. 1). Most of the patients with planned PHC asthma follow-up contacts were females (Table 1). At follow-up visit, mean age was 59 years and every second patient had smoking history. Approximately one third of the patients had uncontrolled asthma according to Global Initiative for Asthma (GINA) 2010[22]. The main characteristics of the study population at follow-up visit are shown in Table 1.

The distribution of the planned follow-up contacts in primary care

The number of all planned asthma follow-up contacts in PHC was 603. Thus, on average, each patient ($n = 152$) had approximately four planned contacts during the 12-year follow-up period. During

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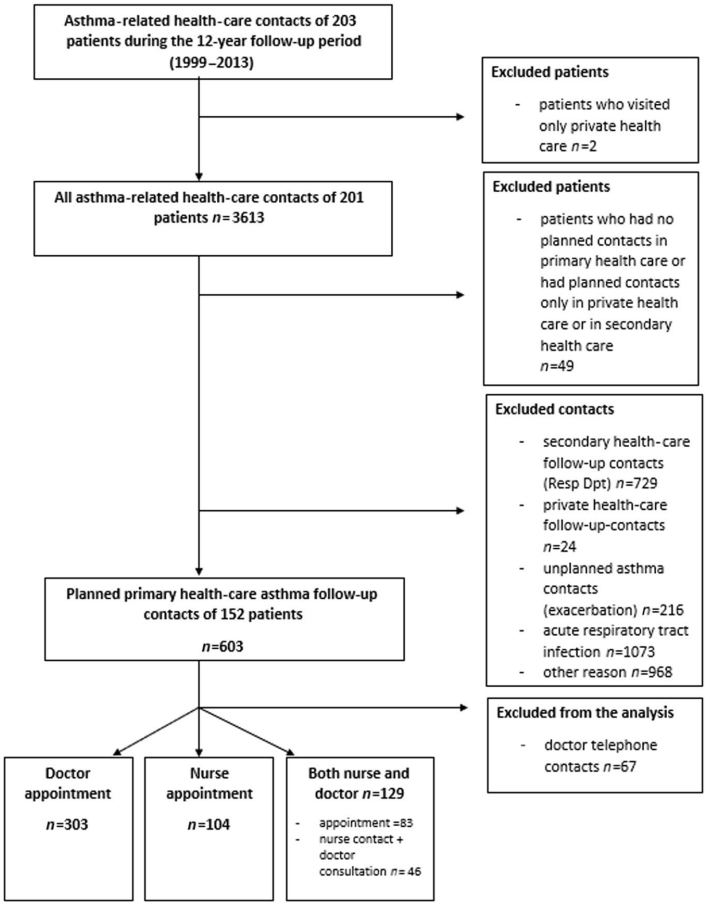

Fig. 1 Study profile. The flowchart of the study.

the years 1–12 after diagnosis, annual number of planned contacts varied from 21 to 67 (Fig. 2). The annual average of planned contacts was 50, i.e. every third patient attended a planned visit each year.

Differences between patients having <4 or ≥4 planned contacts

The patients participating in planned follow-ups ($n = 152$) were divided into two groups according to the number of planned asthma follow-up contacts in PHC (<4 vs. ≥4 follow-up contacts): 84 patients had <4 [median 1 (interquartile range (IQR) 1–2)] and 68 patients had at least 4 [median 6 (IQR 4–8)] planned follow-up contacts during the 12-year follow-up period. The groups with <4 vs. ≥4 follow-up visits showed no difference regarding gender, age, smoking, lung function, markers of inflammation [blood eosinophils, neutrophils, immunoglobulin E (IgE) or fraction of NO in exhaled air (FeNO)] or proportion of severe asthma according to ERS/ATS 2014[23] (Table 2). Approximately one third of the patients in both groups had uncontrolled asthma according to GINA 2010 (Table 2)[22]. Patients with higher number of planned follow-up visits (≥4) had more often inhaled corticosteroid (ICS) medication in daily use and their adherence to ICS medication over 12 years was higher. This group had also higher number of all asthma-related health care visits and were more often in working life (Table 2). No significant differences were found in lung function or other parameters at the baseline (eTable 2).

Lung function tests in planned follow-up contacts

To evaluate whether spirometry or peak flow monitoring were used in the follow-up of asthma as suggested by the guidelines, we collected information from the planned follow-up visits ($n = 603$). We excluded 67 follow-up contacts related to planned GP telephone contacts only. Thus, out of the total 603 contacts, we included 536 planned PHC follow-up contacts where patient encountered GP, nurse or both. Spirometry, peak flow monitoring or both were performed in 87.5% of these contacts. During the 12-year follow-up, peak flow monitoring was carried out in 51.7% of the contacts and spirometry in 76.1% of the contacts. Incomplete peak flow monitoring was excluded. The annual percentages of performed lung function tests in planned follow-up contacts ($n = 536$) are shown in Fig. 3. There was no sign of a decrease in performance of lung function testing during the 12-year follow-up.

Table 1. Basic characteristics of patients having planned asthma follow-up contacts in primary care at 12-year follow-up visit.

	Patients having asthma follow-up contacts in primary care
Number of patients	152
Female, *n* (%)	96 (63.2)
Age	59 (13)
BMI	28.5 (5.9)
Smokers (ex or current), *n* (%)	76 (50.0)
Atopic, *n* (%)[a]	51 (37.2)
Rhinitis, *n* (%)	107 (71.8)
Uncontrolled asthma, *n* (%)[b]	46 (30.3)
Daily LABA in use, *n* (%)	78 (51.3)
Daily add-on drug in use, *n* (%)	85 (83.3)
Daily ICS in use, *n* (%)	125 (81.2)
Daily SABA in use, *n* (%)	21 (13.8)
≥1 oral corticosteroid course during 12-year follow-up, *n* (%)	50 (33.6)
Pre-BD FEV_1 (%)	87 (17)
Post-BD FEV_1 (%)	91 (17)
Pre-BD FEV_1/FVC	0.74 (0.67–0.79)
Post-BD FEV_1/FVC	0.76 (0.70–0.80)
FeNO (ppb)	11 (5–19)
Blood neutrophils ($\times 10^9$/l)	3.7 (2.8–4.7)
Blood eosinophils ($\times 10^9$/l)	0.15 (0.10–0.27)
Total IgE (kU/l)	61 (23–154)
ACO (post-FEV_1/FVC < 0.7 and pack-years ≥10), *n* (%)	19 (12.6)
ACT score	21 (19–24)

If not otherwise mentioned, data shown are mean (SD) or median (25th–75th percentiles).
BMI Body Mass Index, *LABA* long-acting β2-agonist, *Add-on drug* long-acting β2-agonist, leukotriene receptor antagonist, theophylline and/or tiotropium in daily use, *ICS* inhaled corticosteroid, *SABA* short-acting β2-agonist, *BD* bronchodilator, *FEV_1* forced expiratory volume in 1 s, *FVC* forced vital capacity, *FeNO* fraction of NO in exhaled air, *ACO* asthma–COPD overlap, *ACT* asthma control test.
[a]At least one positive skin prick test of common allergens.
[b]Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report.

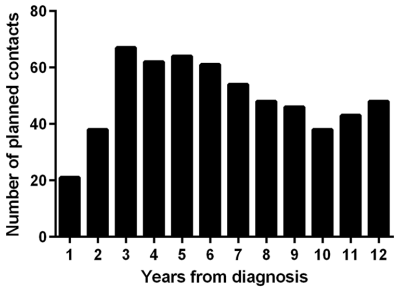

Fig. 2 The distribution of planned contacts in primary care during 12-year follow-up. Total number of planned contacts was 603.

Table 2. Characteristics of the study groups at 12-year follow-up visit.

	Planned PHC follow-up contacts ≥4	Planned PHC follow-up contacts <4	*P* value
Number of patients	68	84	
Female, *n* (%)	43 (63.2)	53 (63.1)	0.986
Age	59 (12.8)	60 (13.4)	0.641
BMI	27.3 (23.6–30.9)	28.1 (25.1–31.7)	0.152
Smokers (ex/current), *n* (%)	30 (44.1)	46 (54.8)	0.192
Pack-years	19 (9–32)	15 (4–28)	0.233
Rhinitis, *n* (%)	48 (72.7)	59 (71.1)	0.825
Uncontrolled asthma, *n* (%)[a]	21 (30.9)	25 (29.8)	0.510
Severe asthma, *n* (%)[b]	5 (7.4)	4 (4.8)	0.501
Daily ICS in use, *n* (%)	63 (92.6)	62 (73.8)	**0.003**
ICS dose of daily users (budesonide eq. μg)	800 (400–1000)	800 (400–1000)	1.000
ICS, *n* (%)			
At high dose	23 (39.7)	18 (25.0)	0.074
At medium dose	16 (27.6)	13 (18.1)	0.194
Total adherence in ICS medication during 12 years	82.1 (34.7)	68.1 (37.3)	**0.025**
Daily LABA in use, *n* (%)	40 (58.8)	38 (45.2)	0.096
Daily SABA in use, *n* (%)	9 (13.2)	12 (14.3)	0.852
Daily add-on drug in use, *n* (%)	43 (63.2)	42 (50.0)	0.102
≥1 oral corticosteroid course for asthma during 12-year follow-up, *n* (%)	24 (35.8)	26 (31.7)	0.597
Hospitalizations ≥1, *n* (%)	17 (25.0)	22 (26.2)	0.867
ACO (post-FEV_1/FVC < 0.7 and pack-years ≥10), *n* (%)	7 (10.4)	12 (14.3)	0.480
ACT score	21 (19–24)	22 (20–24)	0.726
Blood eosinophils ($\times 10^9$/l)	0.15 (0.09–0.27)	0.16 (0.10–0.29)	0.429
Blood neutrophils ($\times 10^9$/l)	3.9 (2.7–4.7)	3.6 (2.8–4.7)	0.564
Total IgE (kU/l)	71 (26–161)	52 (22–150)	0.485
FeNO (ppb)	11 (5–19)	12 (5–19)	0.467
Pre-BD FVC (%)	97.5 (14.7)	99.6 (14.3)	0.388
Pre-BD FEV_1 (%)	85.5 (18.0)	88.8 (16.3)	0.240
Post-BD FVC (%)	98.4 (15.0)	101.2 (14.6)	0.243
Post-BD FEV_1 (%)	88.5 (17.9)	92.5 (15.8)	0.149
Post-BD FEV_1/FVC	0.74 (0.69–0.80)	0.77 (0.71–0.81)	0.197
Annual change in lung function from $Max_{0-2.5}$ to follow-up			
FEV_1 (ml/year)	−45.6 (37.2)	−46.0 (29.1)	0.939
FEV_1 %/year	−0.53 (1.09)	−0.44 (0.89)	0.565
Comorbidities	1.0 (0–2.0)	1.0 (0–3.0)	0.103
In working life, *n* (%)	36 (52.9)	30 (35.7)	**0.033**
Time of education ≥12 years, *n* (%)	23 (33.8)	17 (20.2)	0.059
All asthma-related health care visits during 12-year follow-up	19 (13–26)	14 (9–20)	**0.001**
Unplanned visits	3.5 (1–11)	4.0 (1–10)	0.945

If not otherwise mentioned, data shown are mean (SD) or median (25th–75th) percentiles. Statistically significant *P* values are presented in bold. Annual change in FEV_1 or FVC from point of maximal lung function within 2.5 years after start of therapy to the 12-year follow-up visit.
PHC primary health care, *BMI* Body Mass Index, *ICS* inhaled corticosteroid, *LABA* long-acting β2-agonist, *SABA* short-acting β2-agonist, *Add-on drug* long-acting β2-agonist, leukotriene receptor antagonist, theophylline and/or tiotropium in daily use, *ACO* asthma–COPD overlap, *ACT* asthma control test, *FeNO* fraction of NO in exhaled air, *BD* bronchodilator, *FVC* forced vital capacity, *FEV_1* forced expiratory volume in 1 s.
[a]Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report.
[b]Assessment of asthma severity was performed according to the ERS/ATS severe asthma guideline 2014.

Lung function tests in planned follow-up contacts according to the health care professional

To evaluate whether differences exist in the use of lung function tests according to who encounters the patient in the follow-up contact, we divided the total amount of the follow-up contacts ($n = 536$) into three groups (Fig. 1). Out of all the planned follow-up contacts, 303 were GP contacts, 104 were asthma-nurse contacts and in 83 contacts patient met first nurse and GP thereafter. In 46 contacts, nurse met patient and then consulted GP, and these contacts were included to the last group (total number of combined GP and nurse contacts $n = 129$).

We found that peak flow monitoring, spirometry or both were done in 98.4% of all planned asthma contacts if patient encountered both nurse and GP. Spirometry was done more often than peak flow monitoring through the whole follow-up period irrespective of who encountered the patient in the planned follow-up contact. Lung function tests were performed more often if patient met both doctor and nurse when compared to encountering either alone (Fig. 4).

DISCUSSION

To the best of our knowledge, no previous long-term follow-up studies exist on the occurrence of planned asthma follow-up contacts in PHC and use of lung function tests during the long-term follow-up of asthma. In this 12-year real-life follow-up study, we found that each patient had on average 4 planned asthma contacts in PHC during the follow-up period corresponding to a frequency of 1 visit every third year while the national guideline recommended annual contacts with nurse or GP. Adherence to lung function tests, especially to spirometry, as a part of assessing asthma control was excellent. Spirometry, peak flow monitoring or both were performed in 87.5% of all planned contacts, spirometry in 76.1% and peak flow monitoring in 51.7% of contacts. If both professionals were involved in follow-up visit, lung function tests were done in almost every planned asthma contact. These results suggest that in Finland the frequency of asthma follow-up contacts is insufficient but the PHC adherence to lung function test performance is at high level.

According to Finnish guidelines[16,24] and current GINA report, asthma patient should have regular review by health care provider[1]. In many studies, it has been suggested that adherence to recommended regular follow-up is insufficient[5,17,25], and many patients are lost to follow-up[26]. In these studies, conclusions have mostly been made based on relatively short follow-up or based on asthma-related visits or planned contacts in PHC during the previous year. The recommendation of the Finnish Asthma Programme[15,16] was that patients should continue visits with health care professionals yearly even if asthma is controlled. We found that the given recommendation on asthma follow-up contact frequency was not followed even if patients were informed about the importance to continue long-term visits in PHC. In our study, 49 out of 203 patients were excluded because of not having planned follow-ups in PHC and 29 of these patients did not have any follow-up contacts during the 12-year follow-up period. Total of 152 patients participated in planned asthma contacts mostly in PHC but it is possible that some of the patients had also additional asthma contacts in respiratory department or in private health care. The first two follow-up contacts after asthma diagnosis were mainly done in the respiratory department explaining why there were fewer planned contacts in PHC during the first 2 years of the follow-up period. After the first 2 years, the number of planned asthma contacts increased and slightly decreased in the middle of the follow-up period until new increase towards the end of the 12-year follow-up. The patients who had planned follow-up contacts in PHC had on average four contacts, but when using this amount as a threshold value we found that most patients ($n = 84$) had less than four planned contacts during the 12-year follow-up period showing that most of the asthma patients are not regularly visiting a doctor or nurse. Our finding is supported by the previous Swedish observational cohort study[25] where on average every third patient visited primary care doctor because of asthma irrespective of disease severity. Previous Finnish cross-sectional study showed that in 2010 69% of asthma patients reported a scheduled visit to a physician compared to 73% in 2001[17]. Scheduled appointments to nurse reduced similarly from 28% in 2001 to 23% in 2010 while health care services had essentially remained the same[17]. However, study consisted of patients visiting pharmacies[17], indicating that more therapy and planned follow-up adherent patients might have been selected. Recent American study showed that across all age groups 22.2% of the patients had no asthma-related visits to the primary care in the previous year. The visits that were actualized due to asthma were made for evaluation of acute symptoms, but planned asthma care visits were not found[5]. The previous and our results suggest that nonadherence to follow-up is a worldwide phenomenon. Because remission of adult-onset asthma is rare unlike in childhood asthma[9,10,27,28], missing regular follow-up cannot be assumed to be harmless. It can be claimed that even four planned contacts during a 12-year follow-up period is too few.

Planned asthma management with systematic approach in general practice has been shown to improve asthma control[29]. We were not able to find studies considering occurrence of long-term planned follow-up in PHC and how planned contacts affect asthma control in long-term period. It is logical to assume that patients with more planned asthma contacts are having better asthma control and that regular long-term follow-up improves outcome. In our study, one third of the patients in both groups (<4 or ≥4 planned contacts) had uncontrolled asthma according to GINA 2010[22], and there was no difference in the proportion of severe asthma according to ERS/ATS 2014[23] and no differences in asthma control according to asthma control test (ACT) scores or lung function. These findings suggest that the frequency of asthma contacts had no effect on the level of asthma control. The group with four or more planned contacts had also more other asthma-related health care contacts. This result combined with tendency to increased use of high ICS dose and add-on drugs suggests that these patients had more persistent and difficult disease. They also had better adherence to ICS medication. Thus our results suggest that patients with more difficult asthma are more likely to participate regularly in planned follow-up contacts and they also have better adherence to medication. One could also speculate that with more regular follow-up it is possible to treat more persistent asthma to the same level with milder ones because the two contact groups did not have any significant differences in lung function, markers of inflammation or asthma control at the end of the follow-up. To support this, a Danish study showed that systematic approach in planned follow-up contacts increased the level of well-controlled asthma by 20% and reduced uncontrolled asthma by 14%[29]. Advantages of more frequent contacts were also reported recently with type 2 diabetes patients who had stopped to attend to follow-up in diabetes clinics as prescribed: with more frequent contacts, they succeeded to improve their glycaemic control in primary diabetes health care[30]. Previous results support the assumption that with regular follow-up it is possible to improve control of a persistent disease. However, we were not able to assess whether medically correct actions were taken in planned asthma follow-up contacts or whether the good adherence to ICS medication was due to more regular follow-up or more difficult asthma or both of them. Previous study of the SAAS cohort showed that cumulative dose of ICS increased during the 12-year follow-up period and prescription discontinuation was rare[31]. Good adherence to

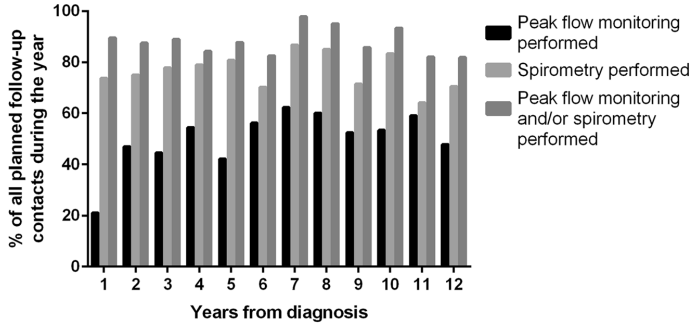

Fig. 3 Percentage of lung function tests performed in planned follow-up contacts in primary health care. The data are presented as percentage of all annual planned contacts. Total amount of planned contacts during 12-year follow-up was 536.

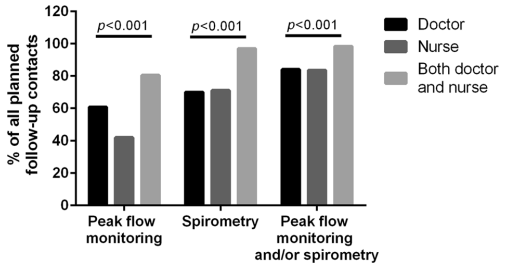

Fig. 4 Percentage of lung function tests performed according to the health care professional encountering the patient in primary health care. Percentage of performed lung function tests in planned contacts according to professionals during the 12-year follow-up period. Number of contacts with GP was 303, 104 with nurse and 129 with both doctor and nurse.

asthma therapy has been suggested to improve the clinical outcomes and to lessen health care costs[32].

Access to asthma follow-up visits has shown significant regional variation in Finland depending for example on the municipal service system and resources[33]. In our study, patients with four or more planned contacts were more often in working life even though the mean age of the two groups was similar. One explanation may be that employees may have had better access to PHC services in Finland, as previously suggested[34,35], because of the ability to use both occupational and PHC services. There are probably many patient-related issues affecting adherence to asthma follow-up including attitudes, personal resources, ability and asthma symptoms. Many patients with asthma do not regard themselves as sick and are not concerned about their condition[36], and it could also be one reason to miss follow-up in our study. In previous studies, patients lost to follow-up have been younger and have had clinical features of less severe asthma at the time of diagnosis, with similar findings also in studies concerning adherence to asthma medications[26,32,37]. In our study, age, sex or lung function at baseline was not associated with less frequent follow-up. In the group of less than four planned contacts, almost 74% of the patients reported daily ICS use but the median daily ICS dose was 800 µg indicating that most of the patients using ICS were treated with moderate-to-high doses.

Guidelines recommend that assessment of asthma should include evaluation of symptom control, future risk of adverse outcomes, treatment issues such as inhaler technique and adherence, side effects, smoking and comorbidities[1,24]. There is no universal common consensus about all aspects and contents of asthma control visits for example for lung function testing. Current GINA report recommends objective lung function measurements as necessary for initial diagnosis of asthma as well as long-term monitoring of asthma[1]. Previous studies have shown that reliance on patient-reported clinical symptoms[38–41] or ACT score can lead to overestimation of asthma control[41,42]. Inclusion of spirometry in the assessment guarantees more accurate monitoring of asthma control[38–41] without input from secondary care[43]. Objective lung function measurements are not comprehensively used in asthma diagnostics[44] and monitoring[2,3,45], despite several studies[38–41] and guidelines[1] supporting their use. A Swedish study showed that one third of the patients with asthma visiting PHC during initial visits and approximately half of the patients during follow-up visits had a clinical evaluation, including spirometry or peak flow monitoring, in agreement with recommendations[2]. In Germany, 57% of physicians used spirometry as a part of assessing asthma control when proportion was 46% in France, 47% in Australia, 28% in Canada, 54% in China and 24% in Japan[3]. In contrast, our results show that in Finland spirometry was performed in >76% of all scheduled contacts.

To the best of our knowledge, there are no previous studies investigating the longitudinal lung function follow-up of adult asthma patients in PHC. We found that spirometry, peak flow monitoring or both were performed in almost 88% of all planned follow-up contacts. When both professionals took part in the visit, lung function tests were carried out in almost every planned contact. Utilization of spirometry was higher compared with peak flow monitoring during the entire follow-up. In Finland due to the law of special reimbursement for chronic asthma medication, it has been crucial for decades to confirm asthma diagnosis by objective lung function tests, but continuous follow-up of lung function tests has not been required for the reimbursement. In the PHC, the use of spirometry increased significantly after introduction of both the national programmes of asthma (1994–2004) and chronic obstructive pulmonary disease (COPD; 1997–2007) and the current asthma care guideline (2000–)[46]. To enhance the implementation of the asthma programme, regional guidance was also available in 79% of the Finnish health care centres in 2001[20,47]. The quality of the Finnish PHC spirometry curves has been found good in 78–80% of cases[48]. As shown also in the previous study of pre-diagnostic lung function tests in the same area[49], the current study of the post-diagnostic use of lung function tests support adherence to the national and regional asthma guidelines.

The Current Finnish Guideline recommends that asthma patient should have an annual planned contact with nurse or GP if asthma control is otherwise good and that the appointment with GP should be at least every third or fifth year[24]. Based on the evaluation of the results of the Finnish Asthma Programme, it was

recommended that the role of asthma nurses should be further strengthened so that educated nurses could perform most of the annual asthma follow-up contacts[16]. Our study showed that this was not reached while only approximately 17% ($n = 104$) of all planned contacts were nurses' and most of the patients had overall less than four planned contacts during the follow-up period. Similarly, in previous studies most of the planned visits of asthma patients were doctor appointments[17,25]. According to a previous Finnish study, respiratory nurses in PHC tend to lack appropriate time in relation to number of respiratory patients when they also take care of other patients and tasks[33]. In our study, spirometry, peak flow monitoring or both was performed in almost every planned contact if patient encountered both nurse and GP. This suggests that planned asthma follow-up contact may benefit from the involvement of both professionals[50]. In a Danish study[29], planned asthma management by both nurse and doctor participating with systematic approach improved asthma control. In a previous review, nurse-led care did not have any differences when compared to physician-led management of asthma[51], but because the review included only one study with uncontrolled patients and was based on relatively small number of studies that the results cannot be directly applied to primary care practice where patients are often multimorbid and have often uncontrolled disease.

Our study has several strengths. The diagnosis of asthma was made by a respiratory physician and the diagnosis was based on typical symptoms and objective lung function measurements showing reversibility of airway obstruction. Smokers and patients with comorbidities were not excluded. Therefore, this study population well represents a typical PHC population with asthma[21]. Possible weakness of our study is that our results may not represent entire Finland. There may be regional imbalance for example in the frequency of spirometry or planned follow-up contacts. We were not able to assess what kind of conclusions were made based on the lung function tests and how these conclusions affected on therapy and asthma control. Also, skills of GPs to interpret spirometry were not estimated. We were not able to assess how often spirometry revealed a clinical issue that was not emerged by measuring asthma control with ACT because in Finland ACT was gradually introduced around 2010.

Evidence-based medicine and guidelines have improved the quality of health care, but still suboptimal adherence to care guidelines is a common worldwide problem seen not only with asthma[2–5] and chronic obstructive pulmonary disease[52–54] but also with other common chronic conditions, such as cardiovascular diseases and diabetes[55–59]. GPs generally deal with multimorbid patients. It could be argued that asthma may lack appropriate attention and follow-up with patients with multimorbidity, as recently found with COPD[54]. Based on our results, it is essential to pay more attention to asthma follow-up not only when the frequency of planned contacts is insufficient but also when many patients choose not to participate in follow-up. In the Finnish health care system, arranging the follow-up contact is primarily the patients' responsibility as most often no recall systems are used in PHC. It is essential to pay more attention to occurrence of planned follow-up contacts during the routine prescribing or dispensing. Adequate resources, including respiratory nurses, in PHC should be guaranteed because it has influence both on management of regular follow-up of asthma and other chronic conditions and on availability of health care services. The role of respiratory nurses should be strengthened so that they could focus more on respiratory patients and their follow-up. It can be argued whether every patient needs an annual asthma follow-up contact if asthma is mild and otherwise in control. In the future, identification of asthma phenotype may enable to determine the optimal follow-up frequency for different patients[12]. More research is needed to evaluate how other essential factors such as smoking and comorbidities associated with asthma control are managed in follow-up contacts in long-term period.

In conclusion, we showed that PHC adherence to lung function measurements, especially to spirometry, as a part of assessing asthma control is good in Finland. The frequency of asthma follow-up contacts in PHC is insufficient when only every third patient was attending a planned visit each year. We showed that adherence to therapy may be better if patients have more planned contacts. In the future, it is necessary to pay more attention to asthma follow-up and characterize the population who is at a risk to drop out of asthma follow-up.

METHODS

Study design, inclusion and exclusion criteria

The present study was a part of SAAS, which is a single-centre (Department of Respiratory Medicine, Seinäjoki Central Hospital, Seinäjoki, Finland) 12-year real-life follow-up study of patients with new-onset asthma diagnosed at adult age (≥15 years). The details of the SAAS study protocol with specific diagnostic criteria has been published separately previously[21]. This study is registered at www.ClinicalTrials.gov with identifier number NCT02733016.

In the original study, cohort patients ($n = 257$) were recruited between October 1999 and April 2002 from the diagnostic visit in Seinäjoki Central Hospital respiratory department. Diagnosis of new-onset asthma was made by a respiratory physician based on typical symptoms and was confirmed by objective lung function measurements[9,12,21]. Smokers and patients with concomitant COPD or other comorbidities were not excluded (Supplementary Table 1). After the diagnosis was confirmed and the medication started, the patients were treated and monitored by their personal physicians mostly in PHC according to the Finnish National Asthma Programme[15,16].

After 12 years (mean 12.2, range 10.8–13.9), a total of 203 patients completed a follow-up visit in respiratory department. Asthma status, disease control, comorbidities and medication were evaluated using structured questionnaires (Airways Questionnaire 20 (AQ20) and ATC), and lung function was measured. The participants of the follow-up visit gave written informed consent to the study protocol approved by the Ethics committee of Tampere University Hospital, Tampere, Finland (R12122). In addition to the data gathered at these visits, all data of asthma-related health care contacts during 12-year period was collected from PHC, occupational health care, private clinics and hospitals as previously prescribed[9,12,21]. The flowchart of the study is shown in Supplementary Fig. 1.

In the present study, all asthma-related health care contacts of the 203 patients during the 12-year follow-up period were explored. Two of the patients were excluded in the beginning because they visited only in private health care. The rest 201 patients had 3616 asthma-related health care contacts. Of those, we included planned PHC (public health care centres and occupational health care) asthma follow-up contacts of 152 patients, the total number of contacts being 603 (Fig. 1). Out of the rest 49 patients, 20 arranged their follow-up in private health care and 29 patients did not have any planned follow-up between the diagnostic visit and the year 2013 follow-up visit in the respiratory department. The data of 152 patients and the data gathered from their planned asthma contacts in PHC were evaluated. During the SAAS study period, all health care centres in our region had respiratory nurses and coordinator–GP responsible for the asthma management in the health care centre, yet every GP managed their own asthma patients.

Lung function, computation of adherence, inflammatory parameters and other clinical measurements

Lung function measurements were performed with a spirometer according to international recommendations[60]. Only complete 2-week peak flow monitoring was included when evaluating the use of lung function tests. Prescribed medications and dose calculations were carried out based on the data obtained from planned asthma contacts and the dispensed ICS doses were obtained from the Finnish Social Insurance Institution that records all purchased medication from any Finnish pharmacy. Adherence to ICS medication was evaluated by comparing the patient's dispensed doses to the prescribed doses for the whole 12-year period. Shortly, we converted all prescribed and dispensed ICS doses to budesonide

equivalents and based on that information calculated annual and total 12-year adherence for each patient[61]. FeNO was measured with a portable rapid-response chemiluminescent analyser according to American Thoracic Society standards[62] (flow rate 50 mL/s; NIOX System, Aerocrine, Solna, Sweden). Venous blood was collected, and white blood cell differential counts were determined. Total IgE levels were measured by using ImmunoCAP (Thermo Scientific, Uppsala, Sweden). Laboratory assays were performed in an accredited laboratory (SFS-EN ISO/IEC 17025:2005 and ISO 15189:2007) of Seinäjoki Central Hospital. Patients completed AQ20[63] and ACT. Assessment of asthma control was performed according to the GINA 2010 report[22].

Definition of PHC

In Finland health care services are divided into PHC and specialized medical care. The country is divided into 21 hospital districts, which provide specialist medical care for the population in their area. Finland has approximately 160 health care centres and many of these consist of several branches, especially in cities. In addition, employers have an obligation to provide occupational health care for their employees. The primary aim of occupational health care is to maintain and improve work ability[64]. For example, an adult working person who has a new-onset asthma diagnosed at specialized medical care may have the ability to use either PHC services or occupational health care. In this study, we considered both planned follow-up contacts in health care centres and in occupational health care as the PHC follow-up contacts.

Statistical analysis

Continuous data are expressed as mean (SD) for variables with normal distribution and, if skewed distribution, shown as median and 25th–75th percentiles. Shapiro–Wilk test was used to assess normality. Two-group comparisons were performed by using Student's *t* test for continuous variables with normal distribution, Mann–Whitney test for continuous variables with skewed distribution or Pearson Chi-square test for categorized variables. Statistical analyses were performed using the SPSS software, version 25 (IBM SPSS, Armonk, NY). A P value < 0.05 was regarded as statistically significant. Two-sided P values were used.

Reporting summary

Further information on research design is available in the Nature Research Reporting Summary linked to this article.

DATA AVAILABILITY

All data generated or analysed during this study are included in this published article (and its Supplementary Information File). According to ethical permission and patient data protection laws of Finland, single patient data cannot be made available.

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AUTHOR CONTRIBUTIONS

This study is a part of the Seinäjoki Adult Asthma Study. J.T. analysed and interpreted the data with help of P.I., wrote the manuscript and contributed to the study design. L.E.T. and H.K. designed the study and guided the work. P.I. contributed to the study design, interpretation of the data and provided statistical advice. P.I. also helped with drawing pictures to this article. I.V. contributed to the computation of adherence. O. N. contributed to the laboratory analyses. All authors accept full conduct of the study and critically revised the manuscript and accepted the final version.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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PUBLICATION II

Participation in scheduled asthma follow-up contacts and adherence to treatment during 12-year follow-up in patients with adult-onset asthma

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RESEARCH ARTICLE Open Access

Participation in scheduled asthma follow-up contacts and adherence to treatment during 12-year follow-up in patients with adult-onset asthma

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Abstract

Background: Poor treatment compliance is a common problem in the treatment of asthma. To our knowledge, no previous long-term follow-up studies exist on how scheduled asthma follow-up contacts occur in primary health care (PHC) versus secondary care and how these contacts relate to adherence to medication and in participation to further scheduled asthma contacts. The aim of this study was to evaluate occurrence of scheduled asthma contacts and treatment compliance in PHC versus secondary care, and to identify the factors associated with non-participation to scheduled contacts.

Methods: Patients with new adult-onset asthma (n = 203) were followed for 12 years in a real-life asthma cohort of the Seinäjoki Adult Asthma Study (SAAS). The first contacts were mainly carried out in secondary care and therefore the actual follow-up time including PHC visits was 10 years.

Results: A majority (71%) of the patients had ≥ 2 scheduled asthma contacts during 10-year follow-up and most of them (79%) mainly in PHC. Patients with follow-up contacts mainly in PHC had better adherence to inhaled corticosteroid (ICS) medication during the whole 12-year period compared to patients in secondary care. In the study population, 29% of the patients had only 0–1 scheduled asthma contacts during the follow-up. Heavy alcohol consumption predicted poor participation in scheduled contacts.

Conclusions: Patients with mainly PHC scheduled asthma contacts were more adherent to ICS medication than patients in the secondary care. Based on our results it is necessary to pay more attention to actualization of asthma follow-up visits and systematic assessment of asthma patients including evaluation of alcohol consumption.

Trial registration Seinäjoki Adult Asthma Study is retrospectively registered at www.ClinicalTrials.gov with identifier number NCT02733016. Registered 11 April 2016.

Keywords: Asthma, Adherence, Scheduled follow-up, Primary care, Secondary care, Inhaled corticosteroids, Alcohol

Background

Asthma is a chronic inflammatory airway disease with different phenotypes [1]. A large proportion of asthma cases are diagnosed at adult age [2, 3]. Remission of adult-onset asthma is rare [4, 5] and poor asthma control is a common problem despite improvements in

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understanding, evidence-based guidelines and asthma medications [6, 7]. Uncontrolled asthma has been shown to reduce both asthma- and general health-related quality of life (HRQoL) [8, 9], increase health care costs, the risk of asthma exacerbations and mortality [10]. Many factors may lead to poor asthma control including allergy, rhinitis, gastroesophageal reflux, smoking, obesity, problems in inhalation technique and poor adherence to asthma medication [1, 11–14]. One possible reason to adverse treatment outcome is non-participation to asthma follow-up visits and it seems to be a problem in many countries [15–18]. Issues affecting the adherence to treatment and occurrence to asthma follow-up visits may include both patient-related and health care system-related factors [19, 20].

To our knowledge, there are no previous long-term real-life follow-up studies on how scheduled asthma follow-up contacts occur in primary health care (PHC) versus secondary care and how these contacts relate to adherence to medication and in participation to further scheduled asthma contacts. Thus, the main aim of this study was to assess how scheduled asthma contacts occur, and possible differences in adherence to medication and participation to further follow-up depending on whether patients have follow-up contacts mainly in PHC versus secondary care. The second aim of this study was to identify the factors associated with non-participation to asthma follow-up visits.

Methods

Study design, inclusion and exclusion criteria

This real-life study was a part of Seinäjoki Adult Asthma Study [SAAS (www.ClinicalTrials.gov; NCT02733016)] which is a single-center 12-year follow-up study of 257 patients with new-onset adult asthma diagnosed between October 1999 and April 2002 in Seinäjoki Central Hospital respiratory department. [21] More than 94% of the patients diagnosed with novel asthma in the study site were recruited to the study and in 2001, the study population represented > 38% of novel diagnoses of asthma made to adults in the whole geographical area. [21] Smokers, patients with allergies or with concomitant COPD or other comorbidities were not excluded. [21] After asthma diagnosis was confirmed and medication initiated the patients were managed by their personal physicians mostly in PHC according to the Finnish National Asthma Programme [22] unless asthma severity or other respiratory diseases required monitoring in specialized care. As described previously[2, 4, 15, 21], after 12 years (mean 12.2, range 10.8–13.9) a total of 203 patients completed a follow-up visit where the participants gave written informed consent to the study protocol approved by the Ethics committee of Tampere University Hospital, Tampere, Finland (R12122). In addition to the data gathered at the diagnostic and follow-up visits, all data on asthma-related health care contacts during 12-year period was collected from PHC, occupational health care, private clinics and secondary care [2, 4, 15, 21]. The SAAS-study protocol has been published previously [21].

In the present study all asthma-related health care contacts after asthma diagnosis of the 203 patients were explored and the data on planned asthma contacts was evaluated. Because scheduled asthma contacts during the two first years were mainly done in respiratory department, we categorized patients based on the amount of scheduled asthma contacts after 2002: 0–1 contacts vs. ≥ 2 contacts. Five patients were excluded because of classification difficulties (Fig. 1). Further analysis was performed by categorizing patients with ≥ 2 contacts into two groups according to the main location of scheduled asthma follow-up contacts (visits mainly in PHC versus mainly in secondary care) (Fig. 1). Planned follow-up contacts both in health care centres and occupational health care were considered as PHC contacts [15].

Computation of adherence, evaluation of alcohol consumption and other clinical measurements

As described in our previous studies, adherence to inhaled corticosteroid (ICS) medication was evaluated by comparing the dispensed doses to the prescribed doses for the whole 12-year period. [23, 24] The prescribed dose in each patient was calculated based on medical records, and the dispensed ICS, short-acting β_2-agonist (SABA) and oral corticosteroids were obtained from the Finnish Social Insurance Institution, which records all purchased medication from all Finnish pharmacies. [23, 24] The 12-year adherence and annual adherence for each patient was calculated by using specific formulas as previously described taking into account aspects from Medication possession ratio (MPR) and proportion of days covered (PDC). [23] Heavy alcohol consumption was evaluated by self-reports (according to the US definitions for alcohol consumption by portions/week), laboratory analyses [(gammaglutamyltransferase (GT) and gammaglutamyltransferase-carbohydrate-deficient transferrin-index (GT-CDT)] or by both [25, 26]. Detailed information on the assessment of asthma control and severity, lung function measurements and other clinical measurements are described separately in Additional file 1: Appendix E1.

Statistical analysis

Continuous data is expressed as mean (SD) for variables with normal distribution. If skewed distribution, median and 25–75 percentiles are shown. The Shapiro–Wilk-test

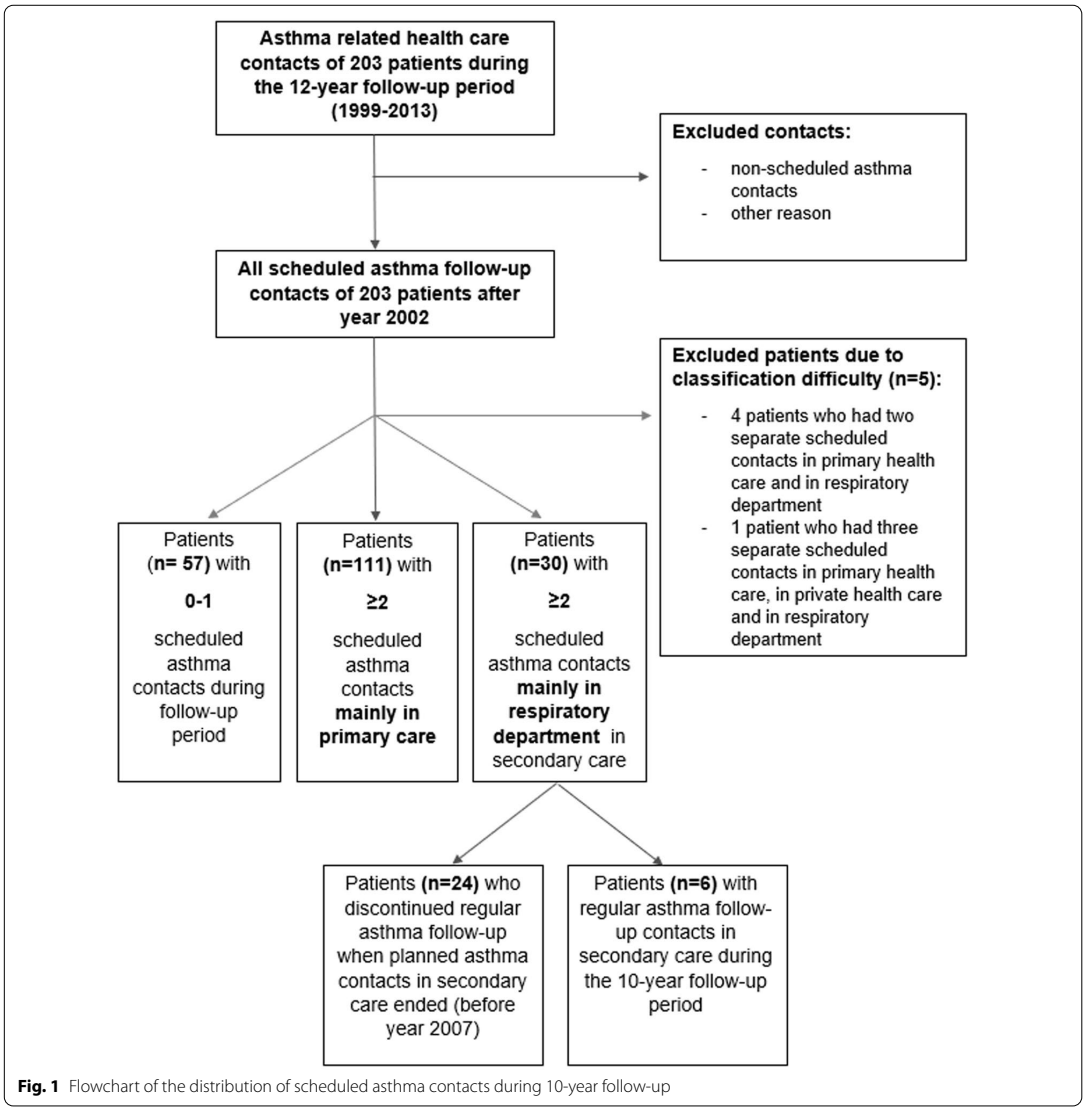

Fig. 1 Flowchart of the distribution of scheduled asthma contacts during 10-year follow-up

was used to assess normality. Two group comparisons were performed by using Student's t test for continuous variables with normal distribution, Mann–Whitney test for continuous variables with skewed distribution and Pearson Chi-square test or Fisher's exact test for categorized variables. Two-sided p-values were used. To analyse differences in annual adherence over the 12-year period between patients having scheduled contacts mainly in PHC or secondary care, annual adherence was plotted against time for individual patients and mean area under curve (AUC) values were compared by using independent-samples Mann–Whitney U test. A P value < 0.05 was regarded as statistically significant. Multivariable binary logistic regression was performed to determine the association between alcohol consumption and poor participation in planned asthma follow-up, adjusting for age, sex, pack-years, BMI and form of residency. Statistical analyses were performed using SPSS software, versions 25–26

(IBM SPSS, Armonk, NY) and GraphPad Prism software, version 9.0. (GraphPad, La Jolla, CA, USA).

Results

Characteristics of the study population

The included 198 patients were divided into two groups according to the number of scheduled follow-up contacts (0–1 vs. ≥ 2) during the 10-year follow-up period. After the year 2002, 141 (71.2%) patients had at least two scheduled contacts either mainly in PHC or in secondary care (respiratory department). However, 57 (28.8%) patients had only 0–1 scheduled contacts (Fig. 1).

To evaluate if differences exist in patient characteristics according to the number of scheduled contacts, we compared the patients with ≥ 2 [median 5 (interquartile range (IQR) 3–8)] scheduled contacts to those with 0–1 scheduled contacts (Table 1). At follow-up visit, mean age in both groups was 58 years. No differences were found in sex, smoking status, asthma control defined according to GINA 2010 [27] or asthma therapy steps according to GINA 2019 [28]. Patients with ≥ 2 scheduled follow-up contacts used more medication for asthma and were more often symptomatic as measured by ACT [29] and AQ20 scores. [30] The patients with ≥ 2 scheduled contacts needed more oral corticosteroid courses, collected more SABA-canisters, had a higher number of hospitalizations due to asthma and more health care visits. Patients with 0–1 scheduled asthma follow-up contacts were more often heavy users of alcohol and had higher levels of alcohol use biomarkers GT and GT-CDT (Table 1). No significant differences were found between the groups in lung function or inflammatory parameters (Additional file 1:Table E2).

To assess whether alcohol consumption associates with poor participation (0–1 visits) in scheduled asthma follow-up contacts after adjusting for age, sex pack years, BMI and form of residency we carried out multivariable binary logistic regression analysis (Table 2). After adjustments, heavy alcohol use remained a significant risk factor for poorer participation in follow-up. Male sex showed a trend for being a risk factor for poor participation to asthma follow-up visits (Table 2).

Comparison of patients with ≥ 2 scheduled asthma contacts mainly in PHC or in secondary care

To evaluate differences between scheduled asthma contacts carried out mainly in PHC or secondary care, the 141 patients having ≥ 2 scheduled asthma contacts were divided into groups according to the main site of asthma contacts: 111 (78.7%) patients had ≥ 2 scheduled follow-up contacts [median 4 (interquartile range (IQR) 3–7)] mainly in PHC and 30 (21.3%) patients had ≥ 2 scheduled contacts [median 4 (interquartile range (IQR) 2–5)] mainly in secondary care after year 2002 (Table 3). Scheduled contacts to private health care were rare in these groups (median 0 visits in both groups). Patients having follow-up contacts mainly in secondary care were younger, had lower FEV_1 and FVC, higher FEV_1 reversibility and steeper annual decline in lung function. No significant differences were found in sex, smoking status, asthma control, comorbidities, socioeconomics or health care use as shown in Table 3 and in Additional file 1: Table E3.

Changes in medication adherence over 12 years

Patients with ≥ 2 scheduled asthma follow-up contacts mainly in secondary care reported less often daily ICS in use and their total adherence to ICS medication was lower during the 12-year follow-up (Table 4). To explore the variation in long-term adherence, we determined annual adherence to ICS for each patient. The annual adherence was overall lower in patients with ≥ 2 scheduled asthma follow-up contacts mainly in secondary care vs. in PHC ($p = 0.010$) (Fig. 2). Furthermore, adherence was more stable in the group with ≥ 2 scheduled contacts mainly in PHC (annual means between 74 and 85%) and fluctuated more in the group with contacts mainly in secondary care (between 45 and 68%) (Fig. 2). In the secondary care-group the daily prescribed ICS dose (budesonide eq) was higher but no significant differences were found in average dispensed daily doses between the groups among 12-year follow-up (Table 4).

To explore reasons for the poorer adherence in patients with follow-up contacts mainly in secondary care ($n = 30$), we analyzed their scheduled follow-up contacts in more detail and found that 6 (20%) had continuous follow-up in respiratory department in secondary care during the whole follow-up period and 24 (80%) had most of their follow-up visits before the year 2007 (Fig. 1). In the latter group, only few had separate scheduled contacts in PHC, private health care or in secondary care during 2008–2013. These patients had the weakest total adherence to ICS medication (Table 5). Patients with continuous follow-up in secondary care ($n = 6$) had better adherence to ICS medication, more symptoms according to ACT scores, had higher therapy step according to GINA 2019, needed more SABA and had more other respiratory-related health care visits. None of them were in the working life. No significant differences were found in alcohol consumption, co-morbidities or socioeconomics (Additional file 1: Table E4).

Discussion

In this real-life long-term follow-up study we evaluated how scheduled asthma contacts occur, assessed differences in adherence to medication and treatment

Table 1 Characteristics of the study groups at 12-year follow-up visit

	Scheduled asthma follow-up contacts 0–1 n = 57	Scheduled asthma follow-up contacts ≥ 2 n = 141	P-value
Female n (%)	29 (50.9)	86 (61.0)	0.206
Age (y)	58 (14)	58 (14)	0.718
BMI (kg/m^2)	27.7 (25.0–30.8)	28.1 (24.3–31.3)	0.998
Smoking history n (%)			
Ex/current	32 (56.1)	74 (52.5)	0.753
Pack-years of smokers	15 (4–31)	15 (6–28)	0.968
Chronic or allergic rhinitis n (%)	37 (64.9)	102 (72.3)	0.308
Atopic n (%) [a]	20 (37.7)	47 (37.3)	> 0.999
Blood eosinophils (× 10^9/l)	0.19 (0.10–0.27)	0.16 (0.10–0.28)	0.708
Uncontrolled asthma n (%) [b]	13 (22.8)	44 (31.2)	0.477
Severe asthma (ATS/ERS 2014) n (%) [c]	1 (1.8)	11 (7.8)	0.185
Asthma therapy steps (GINA 2019) n (%) [d]			
Step 1–2	13 (22.8)	24 (17.0)	0.384
Step 3	11 (19.3)	33 (23.4)	
Step 4	6 (10.5)	28 (19.9)	
Step 5	9 (15.8)	30 (21.3)	
ACT score	23 (21–25)	21 (19–24)	**0.012**
AQ20 score	3 (1–6)	4 (2–7)	**0.019**
Self-reported daily ICS n (%)	34 (59.6)	117 (83.0)	**0.001**
Average prescribed daily ICS dose during 12-year follow-up (µg budesonide eq)	921 (781–1018)	1140 (944–1604)	0.308
Total adherence to ICS medication during 12-y (%)	66 (26–93)	76 (45–98)	0.259
Daily LABA in use n (%)	19 (33.3)	74 (52.5)	**0.018**
Daily SABA in use n (%)	3 (5.3)	20 (14.2)	0.089
SABA canisters (150puff/canister) during 12-y	4 (1–12)	9 (4–17)	**0.004**
Daily add-on drug in use n (%)	19 (33.3)	80 (56.7)	**0.004**
≥ 1 oral corticosteroid course for asthma during 12-year follow-up n (%)	13 (22.8)	52 (37.7)	**0.047**
Co-existing COPD (Post FEV$_1$/FVC < 0.7 and pack-y ≥ 10) n (%)	13 (23.2)	20 (14.3)	0.143
Alcohol use markers above normal range n (%)			
GT	21 (37.5)	34 (24.1)	0.078
GT-CDT	15 (27.3)	20 (14.2)	**0.039**
GT-CDT	3.5 (3.2–3.9)	3.3 (3.0–3.7)	**0.021**
GT (U/l)	35.5 (28.2–67.8)	28.8 (22.1–45.5)	**0.006**
Heavy alcohol consumption (evaluated by self-report, GT-CDT index or by both) n (%) [e]	16 (29.1)	23 (16.3)	**0.049**
≥ 1 hospitalization due to asthma n (%)	6 (10.5)	33 (23.4)	**0.048**
All asthma-related health care visits during 12-year follow-up	9 (5–16)	17 (11–24)	**< 0.001**
Scheduled asthma contacts	0 (0–1)	5 (3–8)	**< 0.001**
Unscheduled contacts [f]	3 (0–8)	3(1–10)	0.247

Significant *p*-value shown as bold

If not otherwise mentioned shown are mean (SD) or median (25th–75th percentiles). BMI = Body Mass Index, ACT = Asthma control test, AQ20 = Airway questionnaire, ICS = inhaled corticosteroid, LABA = long-acting β_2-agonist, SABA = short-acting β_2-agonist, Add-on drug = long-acting β_2-agonist, leukotriene receptor antagonist, theophylline and/or tiotropium in daily use. GT = γ-glutamyltransferase, CDT = carbohydrate-deficient transferrin, GT-CDT = combined index based on γ-glutamyltransferase (GT) and carbohydrate-deficient transferrin (CDT). [a] At least one positive skin prick test of common allergens. [b]Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report. [c]Assessment of severe asthma was performed according to the ERS/ATS severe asthma guideline 2014. [d]Classification of asthma therapy steps was made based on daily medication regimen according to the GINA 2019 guideline. The GINA step could not be determined in 44 patients because of the lack of medication purchased. [e]Assessment of alcohol consumption was performed according to the US definitions for alcohol consumption by portions/week. [f]Unscheduled contacts include visits due to respiratory infections or exacerbations

compliance in PHC versus secondary care, and identified the factors associated with non-participation to scheduled contacts. We showed that 71.2% of the patients had ≥ 2 (median 5) scheduled asthma follow-up contacts during 10-year follow-up. Patients with ≥ 2 scheduled contacts used more medication for asthma, had

Table 2 Association of various factors with poor participation in asthma follow-up (0–1 scheduled contacts) in multivariable binary logistic regression analysis

Variable	OR	95% Confidence interval	p value
Age	0.99	0.97–1.02	0.609
Male sex	1.99	0.98–4.05	0.058
BMI ≤ 24.99 (ref)	1		0.211
BMI ≥ 25–29.99	1.09	0.45–2.67	0.846
BMI ≥ 30	1.91	0.86–4.24	0.111
Pack-years ≥ 10yrs	0.79	0.74–3.52	0.228
Alcohol heavy user	**2.51**	**1.11–5.70**	**0.027**
Living alone	1.07	0.45–2.57	0.881

Significant *p*-value shown as bold

n = 192. BMI = Body Mass Index. Assessment of alcohol consumption was performed according to the US definitions for alcohol consumption by portions/week. Heavy alcohol consumption was evaluated by self-reports, GT-CDT index or by both. For men, heavy drinking is defined as consuming 14 portions or more per week. For women, heavy drinking is defined as consuming 7 portions or more per week. Portion indicates 14 g alcohol

more severe asthma symptoms and exacerbations than patients with 0–1 scheduled contacts. Patients with 0–1 scheduled contacts (28.8%) were more often individuals with heavy alcohol consumption, which also predicted poorer participation in scheduled asthma follow-up contacts in adjusted analysis. Of those with ≥ 2 scheduled asthma contacts, 78.7% had their asthma follow-up mainly in PHC. Patients with follow-up contacts mainly in secondary care (21.3%) were younger, had poorer lung function, showed more FEV_1 reversibility and had weaker long-term adherence to ICS medication, and most of them seemed to discontinue the regular asthma follow-up when they should have arranged follow-up contacts in PHC.

According to guidelines asthma patients should have regular reviews by health care providers [1, 22, 31]. Non-adherence to regular asthma follow-up has been a common problem worldwide [15–18]. Our previous results from SAAS 12-year follow-up confirmed that only every third asthma patient attended a planned contact with health care professional in PHC each year [15]. In this study the patients with ≥ 2 scheduled asthma contacts had median 5 (IQR 3–8) scheduled contacts during 10-year follow-up resulting in approximately one scheduled contact every second year. Our results suggest that these patients may have had more difficult-to-treat asthma since they used more medication for asthma but still had more symptoms, exacerbations, and other asthma-related health care contacts. This suggests also that some of them could have benefited from more asthma phenotype-adjusted treatment. Our results are in line with previous studies [9, 16, 32, 33], showing that frequent scheduled contacts were not associated with asthma control and that patients with more symptomatic asthma participated more regularly in follow-up and used more health care services. Patients with severe asthma symptoms should be systematically reviewed to find out if they have true severe asthma or difficult-to-treat asthma [7, 34]. Based on our results it could be hypothesized that with scheduled asthma follow-up contacts more severe asthma can be treated to the same level with milder and less-symptomatic asthma.

Younger age [10, 17] and clinical features of less severe asthma [14, 17] have been suggested as risk factors for not only non-adherence to medication but also for a tendency for such patients to be lost during follow-up [17]. Also older age, low socio-economic status, obesity and ischemic heart disease are considered to be risk factors to non-participation in asthma follow-up. [35] In this study, out of 198 patients with new-onset adult asthma, 29% had only 0–1 scheduled asthma contacts during the 10-year follow-up period after the first follow-up visits in respiratory department. Alarmingly, 29 out of 203 patients did not have any scheduled contacts. [15] Asthma remission was rare (3%) in SAAS-study population [4] suggesting that it did not explain less frequent follow-up visits. It could be argued that these patients may have over-estimated their asthma control [36]. We found that patients with 0–1 scheduled contacts were more often heavy alcohol drinkers and heavy alcohol consumption associated with poorer participation in scheduled asthma follow-up contacts in multivariable binary logistic regression analysis. Assessment of alcohol consumption is not included in current asthma guidelines [1, 31] though alcohol is known to have negative impact also on respiratory health [37], treatment adherence and self-care-behavior [38, 39].

One of the main objectives of the Finnish National Asthma Programme (1994–2004) was to strengthen the role of PHC in the prevention, diagnosis and long-term therapy of asthma. [22] Our results are in line with previous study [40] showing that after implementation of the National Asthma Programme most of the adult-asthma patients were managed in PHC. Patients (21%) with ≥ 2 scheduled asthma follow-up contacts mainly in secondary care had poorer lung function, showed more FEV_1 reversibility and the prescribed ICS doses were higher than in patients having follow-up contacts in PHC. The annual decline in lung function was also steeper. These findings suggest that patients with mainly secondary care contacts had more difficult asthma needing respiratory specialist consultation [1, 31].

It has been suggested that the major predictors of good adherence include regular asthma reviews by health care professionals and positive beliefs about the medication. [32] Adherence to medication varies in

Table 3 Characteristics of the asthma patients with follow-up contacts mainly in primary health care versus secondary care

	Scheduled asthma follow-up contacts ≥ 2 mainly in PHC n = 111	Scheduled asthma follow-up contacts ≥ 2 mainly in secondary care n = 30	P-value
Female n (%)	70 (63.1)	16 (53.3)	0.400
Age (y)	60 (13)	52 (14)	**0.002**
BMI (kg/m^2)	27.8 (23.9–31.2)	29.0 (26.3–33.5)	0.096
Smoking history n (%)			
Ex/current	57 (51.4)	17 (56.7)	0.682
Pack-years of smokers	18 (7–30)	11(4–19)	0.114
Chronic or allergic rhinitis n (%)	79 (71.2)	23 (76.7)	0.649
Atopic n (%) [a]	34 (33.7)	13 (52.0)	0.108
Uncontrolled asthma n (%) [b]	32 (28.8)	12 (40.0)	0.376
Severe asthma (ATS/ERS 2014) n (%)[c]	7 (6.3)	4 (13.3)	0.247
Asthma therapy steps (GINA 2019) n (%) [d]			
Step 1–2	18 (16.2)	6 (20.0)	0.441
Step 3	30 (27.0)	(10.0)	
Step 4	23 (20.7)	5 (16.7)	
Step 5	24 (21.6)	6 (20.0)	
Co-existing COPD (Post FEV_1/FVC < 0.7 and pack-y ≥ 10) n (%)	14 (12.7)	6 (20.0)	0.377
Number of comorbidities	1 (0–2)	1 (0–2)	0.803
Metabolic syndrome n (%)	10 (9.1)	7 (23.3)	0.054
ACT score	21 (19–24)	21 (16–23)	0.438
AQ20 score	4 (2–7)	4 (2–8)	0.783
Blood eosinophils (× 10^9/l)	0.15 (0.09–0.26)	0.19 (0.11–0.33)	0.130
Blood neutrophils (× 10^9/l)	3.8 (2.8–4.7)	3.5 (3.1–4.7)	0.720
Total IgE (kU/l)	57.0 (24.0–147.0)	74.5 (23.5–383.0)	0.388
FeNO (ppb)	10.0 (5.0–17.5)	10.0 (5.0–30.0)	0.863
Pre-BD FVC (%)	99.0(14.7)	91.4 (15.5)	**0.015**
Pre-BD FEV_1 (%)	88.0 (17.5)	79.9(12.1)	**0.018**
Post-BD FVC (%)	99.9 (15.2)	93.6 (15.0)	**0.045**
Post-BD FEV_1 (%)	91.0 (17.2)	84.4 (12.3)	0.053
Pre-BD FEV_1/FVC	0.74 (0.68–0.79)	0.75 (0.66–0.80)	0.952
Post-BD FEV_1/FVC	0.75 (0.70–0.81)	0.76 (0.68–0.80)	0.950
FEV_1 reversibility (ml)	80 (10–150)	130 (55–213)	**0.013**
FEV_1 reversibility (%)	2.89 (0.38–5.41)	4.14 (2.15 – 6.84)	0.073
Annual change in lung function from Max0–2,5 to follow-up [e]			
FEV_1 (ml/y)	− 39 (− 60 to − 22)	− 46 (− 76 to − 26)	0.091
FEV_1%/y	− 0.38 (− 0.96 to 0.37)	− 0.70 (− 1.35 to − 0.15)	**0.022**

Significant *p*-value shown as bold

If not otherwise mentioned shown are mean (SD) or median (25th–75th percentiles). BMI = Body Mass Index, ACT = Asthma control test, AQ20 = Airway questionnaire, FeNO = fraction of NO in exhaled air, BD = bronchodilator, FVC = forced vital capacity, FEV_1 = forced expiratory volume in 1 s. [a]At least one positive skin prick test of common allergens. [b]Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report. [c] Assessment of asthma severity was performed according to the ERS/ATS severe asthma guideline 2014. [d]Classification of asthma therapy steps was made based on daily medication regimen according to the GINA 2019 guideline. The GINA step could not be determined in 26 patients because of the lack of medication purchased. [e]Annual change in FEV_1 during 12 years of follow-up (ΔFEV_1 from point of maximal lung function within 2.5 years after start of therapy to the 12-year follow-up visit)

many studies between 30 and 70%. [41] Previously, we have shown that the mean 12-year adherence to ICS medication in SAAS-cohort was 69%. [23] In this study the mean 12-year adherence was 76% if patient had ≥ 2 scheduled asthma contacts and 66% in patients having only 0–1 scheduled contacts. Patients with mainly PHC follow-up contacts had better adherence (82%) to ICS medication during the whole 12-year follow-up period than those with mainly secondary care contacts (52%). In SAAS-study population adherence to ICS decreased

Table 4 Medication and adherence to ICS treatment in patients followed in primary health care or in secondary care

	Scheduled asthma follow-up contact ≥ 2 mainly in PHC n = 111	Scheduled asthma follow-up contact ≥ 2 mainly in secondary care n = 30	P-value
Self-reported daily ICS n (%)	98 (88.3)	19 (63.3)	**0.004**
Average prescribed daily ICS dose among 12-years (µg budesonide equivalents)	800 (591–1000)	967 (825–1098)	**0.008**
Average dispensed daily ICS dose among 12-years (µg budesonide equivalents)	597 (331–838)	485 (67–870)	0.197
Total adherence to ICS medication during 12-y (%)	82 (50–99)	52 (8–80)	**0.007**
Average adherence ≥ 80% during 12-years (µg dispensed / µg prescribed × 100) n (%)	54 (51.9%)	7 (28.0%)	**0.026**
Daily LABA in use n (%)	59 (53.2)	15 (50.0)	0.838
Daily SABA in use n (%)	15 (13.5)	5 (16.7)	0.768
SABA canisters (150puff/can.) during 12-y	9 (4–17)	7 (3–15)	0.322
Daily add-on drug in use n (%)	64 (57.7)	16 (53.3)	0.683
Systemic steroid in daily use (for asthma or other indication) n (%)	1 (0.9)	2 (6.7)	0.114
≥ 1 oral corticosteroid course for asthma during 12-year follow-up n (%)	39 (35.5)	13 (46.4)	0.282
≥ 2 oral corticosteroid course for asthma/2 years n (%)	20 (18.2)	3 (10.7)	0.411
Purchased oral corticosteroids prednisolone mg/year	53.6 (0–154)	63.8 (0–271)	0.498

Significant *p*-value shown as bold

If not otherwise mentioned shown are mean (SD) or median (25th–75th percentiles). ICS = inhaled corticosteroid, LABA = long-acting β_2-agonist, SABA = short-acting β_2-agonist. Add-on drug = long-acting β_2-agonist, leukotriene receptor antagonist, theophylline and/or tiotropium in daily use

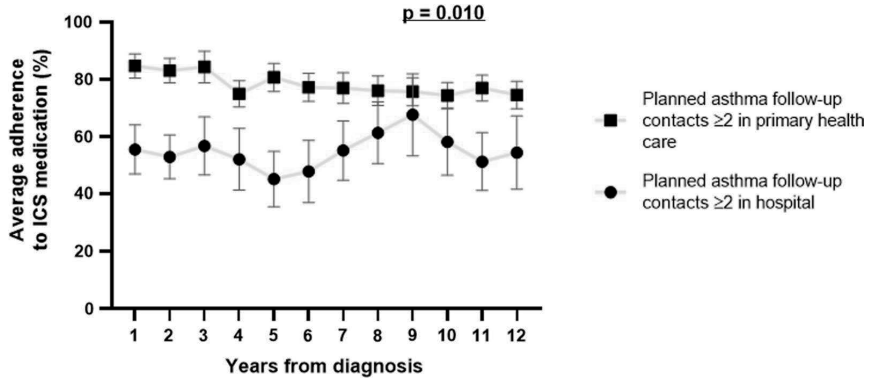

Fig. 2 Changes in adherence over 12-years. Annual adherences shown as mean ± SEM (determined to n = 104 patients mainly in primary health care and n = 25 mainly in hospital). P-value defined by area under the curve method and independent-samples Mann–Whitney U test

most rapidly during the first 4 years of follow-up. [23] In the current analysis, we showed that, surprisingly, the decrease in adherence was most prominent in those being followed in secondary care. It could be suggested that PHC is more able to promote compliance in asthma treatment than secondary care. It was found that most of the patients (80%) having scheduled contacts mainly in secondary care seemed to discontinue the regular asthma follow-up when asthma was brought to control and monitoring was transferred to PHC where patients should have arranged follow-up contacts by themselves. These patients had low total adherence to ICS medication (37%). These results suggest that a proportion of patients followed in secondary care may have suffered from a more general difficulty to adhere to therapy and follow-up and may have some challenges in life management that we were not able to identify. Not only physical but also various mental

Table 5 Characteristics of the patient groups with ≥ 2 scheduled asthma contacts mainly in hospital

	Scheduled asthma follow-up contacts mainly before year 2007 n = 24	Continuous asthma follow-up contacts in secondary care during the whole period n = 6	P-value
Female n (%)	13 (54.2)	3 (50.0)	> 0.999
Age (y)	49.7 (14.7)	58.8 (11.1)	0.127
BMI (kg/m^2)	30.4 (26.8–34.6)	28.2 (19.3–28.9)	0.073
Smoking history n (%)			
Ex/current	15 (62.5)	2 (33.3)	0.360
Pack-years of smokers	13 (11)	9 (8)	0.662
ACT score	22 (18–23)	14 (10–21)	**0.033**
AQ20 score	4 (2–8)	8 (2–12)	0.321
Uncontrolled asthma n (%) [a]	8 (33.3)	4 (66.7)	0.318
Severe asthma (ATS/ERS 2014) n (%) [b]	2 (8.3)	2 (33.3)	0.169
Asthma therapy steps (GINA 2019) n (%) [c]			
Step 1–2	6 (25.0)	0	**0.005**
Step 3	2 (8.3)	(16.7)	
Step 4	5 (20.8)	0	
Step 5	1 (4.2)	5 (83.3)	
Daily ICS in use n (%)	14 (58.3)	5 (83.3)	0.372
Average daily prescribed ICS dose among 12-years (µg budesonide equivalents)	921 (781–1018)	1140 (944–1604)	0.060
Average daily dispensed ICS dose among 12-years (µg budesonide equivalents)	268 (47–702)	998 (820–1714)	**0.003**
Total adherence to ICS medication during 12-y	37 (6–66)	81 (78–132)	**0.006**
Daily LABA in use n (%)	10 (41.7)	5 (83.3)	0.169
SABA canisters (150puff/canister) during 12-y	4 (2–12)	16 (12–64)	**0.009**
Pre-BD FEV_1 (%)	79.3 (11.55)	82.3 (14.90)	0.656
Post-BD FEV_1 (%)	83.7 (10.75)	87.3 (18.17)	0.656
Pre-BD FEV_1/FVC	0.75 (0.68–0.79)	0.67 (0.64–0.80)	0.347
Post-BD FEV_1/FVC	0.76 (0.68–0.81)	0.75 (0.67–0.79)	0.494
Annual change in lung function from $Max_{0-2.5}$ to follow-up [d]			
FEV_1 (ml/y)	− 46 (− 86 to − 26)	− 48 (− 62 to − 25)	0.527
FEV_1%/y	− 0.83 (− 1.5 to − 0.19)	− 0.63 (− 0.90 to − 0.45)	0.527
In working life n (%)	13 (54.2)	0 (0)	**0.024**
All asthma-related health care visits during 12-year follow-up	14 (10–22)	36 (25–55)	**0.004**

Significant *p*-value shown as bold

If not otherwise mentioned shown are mean (SD) or median (25th–75th percentiles). BMI = Body Mass Index, ACT = Asthma control test, AQ20 = Airway questionnaire, ICS = inhaled corticosteroid, LABA = long-acting β_2-agonist, SABA = short-acting β_2-agonist, BD = bronchodilator, FEV_1 = forced expiratory volume in 1 s, FVC = forced vital capacity. [a]Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report. [b]Assessment of severe asthma was performed according to the ERS/ATS severe asthma guideline 2014.[c] Classification of asthma therapy steps was made based on daily medication regimen according to the GINA 2019 guideline. The GINA step could not be determined to 10 patients because of the lack of medication purchased. [d]Annual change in FEV_1 during 12 years of follow-up (ΔFEV1 from point of maximal lung function within 2.5 years after start of therapy to the 12-year follow-up visit)

health factors can interact and affect asthma outcomes. [13] Thus, it could be suggested that some of the psychological or behavioral characteristics or comorbidities of the patients monitored mainly in secondary care may both be the original reason for choosing secondary care follow-up but also the reason for non-compliance with treatment and follow-up.

Our study has several strengths. The diagnosis of asthma was made by respiratory physician and the diagnosis was based on typical symptoms and objective lung function measurements showing reversibility of airway obstruction. [21] Smokers and patients with concomitant COPD or other comorbidities were not excluded [21]. Prevalence of rhinitis and smoking among the present

population was shown to be quite similar to that in a previous population-based study (FinEsS) from the same geographical area [42, 43] while the incidence of COPD was lower in the FinEsS study (9.7%) when compared to our study (16.7%). [42] This may be explained by the exclusion of patients over 70 years of age and patients´ underreporting of COPD in the previous study based on self-reports. [42] In the present study, COPD was defined by objective criteria (≥ 10 pack years and post-BD $FEV_1/FVC < 0.7$). The prevalence rates of high-risk alcohol consumption in the present study population (19.6%) were also well in line with the statistics in the general population. [44, 45] Therefore, this study population well represents a typical population with asthma [21, 42]. Adherence to ICS treatment was evaluated objectively by comparing the patient´s dispensed doses to the prescribed doses for the whole 12-year period. [23] Possible limitations considering adherence calculation has been described in our previous study. [23] Weakness of our study is that results may not represent entire Finland. [20] In this study we were not able to assess more precisely the content of the follow-up contacts and how systematically patients were evaluated or advised and how these factors affected asthma control, adherence to ICS medication and participation to further follow-up contacts. Possible weakness is that alcohol markers were counted only in the follow-up visit, thus we were not able to assess whether alcohol consumption changed over time. It could be assumed that tendency to use alcohol is somewhat constant habit. [44] The number of patients in the scheduled asthma follow-up contacts mainly in secondary care was low which has led to low statistical power in analyses, thus clinical studies with larger study cohorts are needed.

Based on our results it is essential to pay more attention to participation in asthma follow-up since almost one third of all asthma patients seem to be lost-to-follow-up and regular follow-up contacts are not actualized. Particularly when asthma patients are referred to PHC from secondary care further emphasis should be placed on possible recall-systems and guidance of the patient to take care of scheduling further asthma follow-up contacts. Patients with asthma should be systematically reviewed. Alcohol consumption should be assessed in asthma patients as part of routine clinical practice and this recommendation should also be included in asthma guidelines. Further studies are needed to evaluate how other essential factors affecting asthma control are taken into account in scheduled contacts.

Conclusion

In this 12-year real-life follow-up study we showed that patients with mainly PHC scheduled asthma contacts were more adherent to ICS medication than patients in the secondary care. Patients with ≥ 2 scheduled follow-up contacts used more medication but still had more asthma symptoms, exacerbations and health care use. Almost one third of all patients were having only 0–1 scheduled asthma contact during the long-term follow-up-period. Heavy alcohol consumption was associated with poorer participation in scheduled contacts. Thus, in the future it is necessary to pay more attention to actualization of asthma follow-up visits as well as to systematic assessment of asthma patients also including evaluation of possible alcohol consumption.

Abbreviations

PHC: Primary health care; ICS: Inhaled corticosteroid; SABA: Short-acting β_2-agonist.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-022-01850-1.

Additional file 1. Participation in scheduled asthma follow-up contacts and adherence to treatment during 12-year follow-up in patients with adult-onset asthma. An additional data file containing more study statistics and methodology.

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Authors' contributions

This study is a part of Seinäjoki Adult Asthma Study. JT contributed to the study design, analyzed and interpreted the data, draw the pictures to this article with help of PI and wrote the manuscript. IV contributed to the computation of adherence and SABA use. LET and HK designed the study and guided the work. PI contributed to the study design and provided statistical advice. ON contributed to the laboratory analyses and provided guidance on alcohol markers. All authors accept full conduct of the study and critically revised the manuscript. All authors have read and approved the final version of the manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article (and its Additional file 1). According to ethical permission and patient data-protection laws of Finland, single patient data cannot be made available. The corresponding author will answer more detailed inquiries.

Declarations

Ethics approval and consent to participate
Institutional permissions (TU1114 and LET) were obtained and all enrolled patients in SAAS-study cohort signed informed consent to the study protocol approved by the Ethics committee of Tampere University Hospital, Tampere, Finland (R12122). Permission for use and the data concerning dispensed medication for was granted by the Finnish Social Insurance Institution.

Consent for publication
Not applicable.

Competing interests
None of the authors declares any competing interests concerning this article. Dr. Takala reports personal fees from Novartis, personal fees and non-financial support from NovoNordisk and non-financial support from GSK, outside the submitted work. Dr. Vähätalo reports personal fees from AstraZeneca, outside the submitted work. Dr. Tuomisto reports personal fees from AstraZeneca, Boehringer-Ingelheim, and GlaxoSmithKline, outside the submitted work. Dr. Niemelä has nothing to disclose. Dr. Ilmarinen is an employee of GlaxoSmithKline. Dr. Ilmarinen reports personal fees from GlaxoSmithKline, Novartis, AstraZeneca and Mundipharma, outside the submitted work. Dr. Kankaanranta reports personal fees and non-financial support from AstraZeneca, Boehringer-Ingelheim, and Orion Pharma, personal fees from Chiesi, Novartis, MSD, Mundipharma, SanofiGenzyme, and GlaxoSmithKline, outside the submitted work.

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Publisher's Note

PUBLICATION III

Documentation of smoking in scheduled asthma contacts in primary health care: a 12-year follow-up study

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ARTICLE OPEN

Check for updates

Documentation of smoking in scheduled asthma contacts in primary health care: a 12-year follow-up study

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Smoking among asthmatics is common and associates with poorer asthma control, more rapid lung function decline and higher health care costs in dose-dependent manner. No previous real-life studies exist, however, on how smoking status and pack-years are documented in scheduled asthma contacts in primary health care (PHC) during long-term follow-up, and how often patients are advised to quit smoking. In this real-life 12-year follow-up study, we showed that out of all scheduled PHC asthma contacts ($n = 603$) smoking was mentioned only in 17.2% and pack-years only in 6.5%. Smoking data was not recorded even once in 70.9% of never smokers, 64.7% of ex-smokers and 27.3% of current smokers. Smoking including pack-years were mentioned more often if nurse took part on the scheduled contact. For current smokers, smoking cessation was recommended only in 21.7% of their scheduled contacts. Current smokers used more antibiotics and had more unscheduled health care contacts during follow-up.

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INTRODUCTION

Worldwide, asthma is a common heterogenic disease consisting of multiple different phenotypes[1–3]. Adult-onset asthma is often associated with lifestyle or environmental factors such as smoking and obesity[1,3]. These factors may contribute to suboptimal asthma control alongside allergy, rhinitis, gastroesophageal reflux, comorbidities, problems in inhalation technique, and poor adherence to asthma medication[1,2,4,5]. Smoking is known to associate with reduced effectiveness of inhaled steroids[6], poorer asthma control[5,7–9], rapid decline in lung function[4,10], and higher health care costs[3]. Patients with asthma may become vulnerable to the adverse effects of smoking on lung function already before asthma is diagnosed[10]. The number of smoked pack-years correlate with frequent hospitalizations, higher number of comorbidities, symptoms and asthma severity in a dose-dependent manner[9,11]. Among patients with adult-onset asthma smoking history of ≥10 pack-years is associated with accelerated lung function decline independently of whether the patient has stopped smoking or not[4]. Patients with smoking history of ≥10 pack-years often present with poorly controlled asthma[7,9]. These results not only highlight the importance of interventions aimed at smoking cessation in early phase among patients with adult-onset asthma but also underscore the importance of routine screening and careful assessment of lifelong smoking history during follow-up.

Smoking poses an enormous threat to public health worldwide, killing more than eight million people every year although the prevalence of smoking has been declining at global level by 23% over the past 12 years[12]. Smoking among asthma patients varies between countries approximately from 10 to 26%[13,14], and it is usually equally common in general adult population[15]. Patients with respiratory disease have a greater and more urgent need to stop smoking[16] due to the obvious benefits of smoking cessation for the decreased prevalence of chronic obstructive pulmonary disease (COPD)[17] and better symptom control in asthma[15]. Unfortunately only modest smoking cessation rates have been reported in asthma[18,19]. Asking about smoking and encouraging smoking cessation varies greatly between general practitioners (GP) in different countries in Europe and U.S., and is often not implemented as recommended[20,21].

According to current guidelines, smoking status and history should be evaluated in asthma[1,22] and in COPD[23] and recorded systematically in medical records[23]. It can be argued that if patients' smoking status or a discussion about smoking cessation was not documented during the planned patient contacts, it was not done. To the best of our knowledge no previous long-term real-life studies exists on how smoking status including pack-years are documented in real-life scheduled asthma contacts in primary health care (PHC). Thus, the main aim of this study was to assess how smoking and pack-years were documented during scheduled asthma contacts in PHC and if differences exist between contacts with GP, nurse, or both. The second aim was to evaluate how often patients were advised in smoking cessation and to assess how smoking status affected their asthma control and health care use.

METHODS

Study design and population

The present study was a part of Seinäjoki Adult Asthma Study (SAAS), which is a single-center (Department of Respiratory Medicine, Seinäjoki Central Hospital, Seinäjoki, Finland) 12-year real-life follow-up study of 203 patients with new-onset asthma diagnosed at adult age (≥15 years). The details of the SAAS study protocol with inclusion, exclusion and specific diagnostic criteria have been published previously (eTable 1)[24]. More than 94% of the patients diagnosed with novel asthma in the study site were recruited to the SAAS study[24]. Diagnosis of new-onset asthma was made by a respiratory physician based on typical symptoms and was confirmed by objective lung function measurements[24,25].

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Smokers and patients with concomitant COPD or other comorbidities were not excluded[24]. After the diagnosis was confirmed and the medication started the patients were treated and monitored by their personal physicians mostly in PHC according to the Finnish National Asthma Programme[24–26]. After 12 years (mean 12.2, range 10.8–13.9 years) a total of 203 patients completed a follow-up visit in respiratory department in secondary health care where asthma status, disease control, comorbidities and medication were evaluated using structured questionnaires and lung function was measured[24]. The participants of the follow-up visit gave written informed consent to the study protocol approved by the Ethics committee of Tampere University Hospital, Tampere, Finland. In addition to the data gathered at diagnostic and follow-up visits, all data of asthma-related health care contacts during 12-year period was collected from PHC, occupational health care, hospital, and private clinics as previously prescribed[24,25]. The flowchart of the SAAS study is shown in Supplementary Fig. 1. The SAAS study is registered at www.ClinicalTrials.gov with identifier number NCT02733016.

In the present study, all asthma-related health care contacts ($n = 3639$) of the 203 patients during the 12-year follow-up period were assessed (Fig. 1). Of those, we included scheduled PHC asthma follow-up contacts of 152 patients, the total number of scheduled contacts in PHC being 603 (Fig. 1). The excluded 51 patients did not have any scheduled asthma contacts in PHC[25]. In this study, we considered both scheduled follow-up contacts in health care centers and in occupational health care as PHC follow-up contacts. Out of the 603 scheduled asthma contacts, 303 were doctor appointments, 104 nurse appointments, 129 were contacts when both nurse and GP were involved in the asthma follow-up visit and 67 consisted of planned GP telephone contacts (Fig. 1). The occurrence of not only these PHC contacts ($n = 603$) but also the overall participation of the 203 patients in scheduled asthma

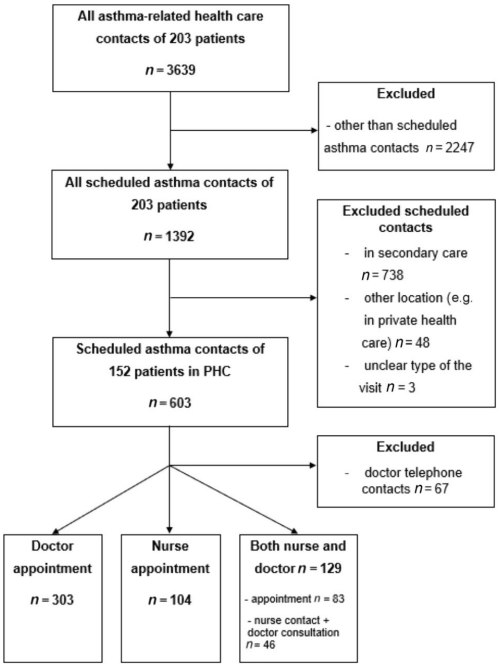

Fig. 1 The flowchart of the study. The distribution of scheduled asthma contacts.

contacts during SAAS study period are described in our previous studies[25,27] as well as the definition of Finnish PHC and the organization of asthma management in the health care centers[25].

Assessment of smoking

Smoking status was determined at the diagnostic visit and at the 12-year follow-up visit in secondary health care. The patients were categorized to never smokers, ex-smokers, or current smokers according to their current and past smoking behavior. Those who reported having never smoked regularly were considered never smokers. Those who had smoked regularly but had quitted smoking before the clinical visit were considered ex-smokers. Those who smoked currently were classified as current smokers. Lifelong cumulative exposure to tobacco was evaluated by assessing smoked pack-years (20 cigarettes per day for 1 year). All documented smoking data collected at scheduled asthma contacts during 12-year follow-up period in PHC were evaluated and analyzed.

Lung function, inflammatory parameters, computation of adherence, and other clinical measurements

Lung function measurements were performed with a spirometer according to international recommendations[28]. The annual FEV_1 decline was calculated by measuring the change between the highest FEV_1 measurement available during the first 2.5 years after the diagnosis and start of inhaled corticosteroid (ICS) therapy ($Max_{0–2.5}$) and FEV_1 at the follow-up, and by dividing the sum with elapsed time. Fraction of exhaled nitric oxide (FeNO) was measured with a portable rapid-response chemiluminescent analyzer according to American Thoracic Society standards[29] (flow rate 50 mL s^{-1}; NIOX System, Aerocrine, Solna, Sweden). Venous blood was collected, and white blood cell differential counts were determined. Total immunoglobulin E (IgE) levels were measured by using ImmunoCAP (Thermo Scientific, Uppsala, Sweden). Laboratory assays were performed in an accredited laboratory (SFS-EN ISO/IEC 17025:2005 and ISO 15189:2007) of Seinäjoki Central Hospital. Patients completed Airways Questionnaire 20 (AQ20)[30], Asthma Control Test (ACT)[31] and COPD Assessment Test (CAT)[32]. Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report[33]. Classification of asthma therapy steps was assessed by daily medication regimen according to the Global Initiative for Asthma (GINA) 2019 guideline [Step 1 and 2: >0–400 µg ICS as budesonide equivalents OR daily LTRA OR low-dose ICS-formoterol; Step 3: >400 µg ICS as budesonide equivalents OR low-dose ICS + LABA OR low-dose ICS + LTRA; Step 4: >800 µg ICS as budesonide equivalents OR medium dose ICS and at least one second controller (LABA, LAMA, LTRA, xanthine, chromones); Step 5: >800 µg ICS as budesonide equivalents and at least one second controller (LABA, LAMA, LTRA, xanthine, chromones) OR biologics][34].Assessment of severe asthma was performed according to the ERS/ATS severe asthma guideline 2014[35].

Adherence to ICS medication was evaluated by comparing the dispensed doses to the prescribed doses for the whole 12-year period as described in our previous studies[36,37]. The prescribed dose in each patient was calculated based on medical records, and the dispensed ICS, short-acting β_2-agonist (SABA) and oral corticosteroids were obtained from the Finnish Social Insurance Institution, which records all purchased medication from all Finnish pharmacies[36,37]. The 12-year adherence and annual adherence for each patient was calculated by using specific formulas as previously described taking into account aspects from Medication possession ratio (MPR) and proportion of days covered (PDC)[36]. SABA usage was determined by counting all dispensed SABA canisters during 12-year follow-up together and

dividing the sum by 150 puffs [SABA canisters (150 puff/canister) during 12 years].

Information on alcohol consumption was assessed by detailed structured questionnaires. Heavy alcohol consumption was evaluated by self-report, GT-CDT index or by both. Assessment of alcohol consumption was performed according to the US definitions for alcohol consumption by portions/week (portion indicates 14 g alcohol)[38]. Serum levels for carbohydrate-deficient transferrin (CDT) were measured by a turbidimetric immunoassay (TIA) after ion exchange chromatography (%CDT, Axis-Shield, Oslo, Norway) and plasma γ-glutamyltransferase (GT) concentration was measured using enzymatic colorimetric assay, as standardized against IFCC (International Federation of Clinical Chemistry and Laboratory Medicine). More detailed information on GT and CDT measurements and on calculating the GT-CDT index have been previously reported[39].

Statistical analysis

Continuous data is expressed as mean (SD) for variables with normal distribution and for parameters with skewed distributions, medians and 25–75 percentiles are shown. The Shapiro–Wilk test was used to assess normality. Two group comparisons were performed by using Student's t test for continuous variables with normal distribution, Mann–Whitney test for continuous variables with skewed distribution and Pearson Chi-square test or Fisher's exact test for categorized variables. Two-sided p-values were used. A p value <0.05 was regarded as statistically significant. Statistical analyses were performed using the SPSS software, version 27.0.1.0 (IBM SPSS, Armonk, NY).

Reporting summary

Further information on research design is available in the Nature Research Reporting Summary linked to this article.

RESULTS

Characteristics of the study population

Out of the total number of 203 patients in SAAS study population, 152 participated in scheduled asthma follow-up visits in PHC. In total, these patients had 603 scheduled asthma contacts in PHC, thus, each patient had approximately four planned contacts during the 12-year follow-up period as described previously[25]. Most of the patients with scheduled PHC asthma follow-up contacts were women. At follow-up visit, mean age was 59 years and every second patient had a history of smoking. Approximately one-third of the patients had uncontrolled asthma according to GINA 2010[33]. The main characteristics of the study population ($n = 152$) at follow-up visit are shown in Table 1.

Table 1. Characteristics of the patients ($n = 152$) with scheduled follow-up contacts in primary health care at 12-year follow-up visit.

	Patients with scheduled asthma follow-up contacts in primary health care
Number of patients	152
Female *n* (%)	96 (63.2)
Age (years)	59 (13)
BMI (kg/m^2)	28.5 (5.9)
Smokers (ex or current) *n* (%)	76 (50.0)
Atopic *n* (%)[a]	51 (37.2)
Rhinitis *n* (%)	109 (71.7)
Uncontrolled asthma *n* (%)[b]	46 (30.3)
Daily ICS in use *n* (%)	125 (82.2)
Daily SABA in use *n* (%)	21 (13.8)
Daily LABA in use *n* (%)	78 (51.3)
Daily add-on drug in use *n* (%)	85 (55.9)
≥1 oral corticosteroid course during 12-year follow-up *n* (%)	50 (33.6)
Pre-BD FEV_1 (%)	87 (17)
Post-BD FEV_1 (%)	91 (17)
Pre-BD FEV_1/FVC	0.74 (0.67–0.79)
Post-BD FEV_1/FVC	0.76 (0.70–0.80)
FeNO (ppb)	11 (5–19)
Blood eosinophils (×10^9/l)	0.15 (0.10–0.27)
Total IgE (kU/l)	61 (23–154)
Co-existing COPD (post FEV_1/FVC < 0.7 and pack-year ≥10) *n* (%)	19 (12.6)
ACT score	21 (19–24)

If not otherwise mentioned, shown are mean (SD) or median (25th–75th percentiles). Add-on drug = long-acting β_2-agonist, leukotriene receptor antagonist, theophylline, and/or tiotropium in daily use.
BMI Body Mass Index, *ICS* inhaled corticosteroid, *SABA* short-acting β2-agonist, *LABA* long-acting β2-agonist, *BD* bronchodilator, *FEV_1* forced expiratory volume in 1 s, *FVC* forced vital capacity, *FeNO* fraction of nitric oxide in exhaled air, *ACT* asthma control test.
[a]At least one positive skin prick test of common allergens.
[b]Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report.

Changes in smoking habits during the 12-year follow-up

The patients having scheduled contacts in PHC were divided into three groups according to their smoking status at the study baseline (never smoker, ex-smoker, and current smoker). Out of 152 patients, 52.0% ($n = 79$) were never smokers, 33.5% ($n = 51$) were ex-smokers and 14.5% ($n = 22$) were current smokers at the time of the asthma diagnosis (Fig. 2). Out of the 79 patients representing never smokers, 96% could still be classified as never smokers at the 12-year follow-up visit. Among ex-smokers 6% had changed their status into active smokers. After the diagnosis, 32% of smokers had managed to quit smoking (Fig. 2). In this study population, active smoking reduced from the 14.5 to 12.5% during the 12-year follow-up after asthma diagnosis.

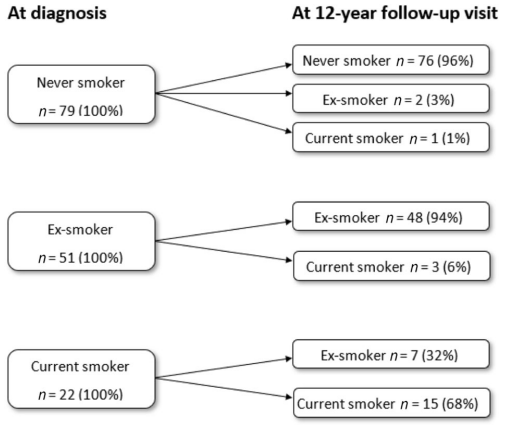

Fig. 2 Smoking status changes. Smoking habit changes during the 12-year follow-up.

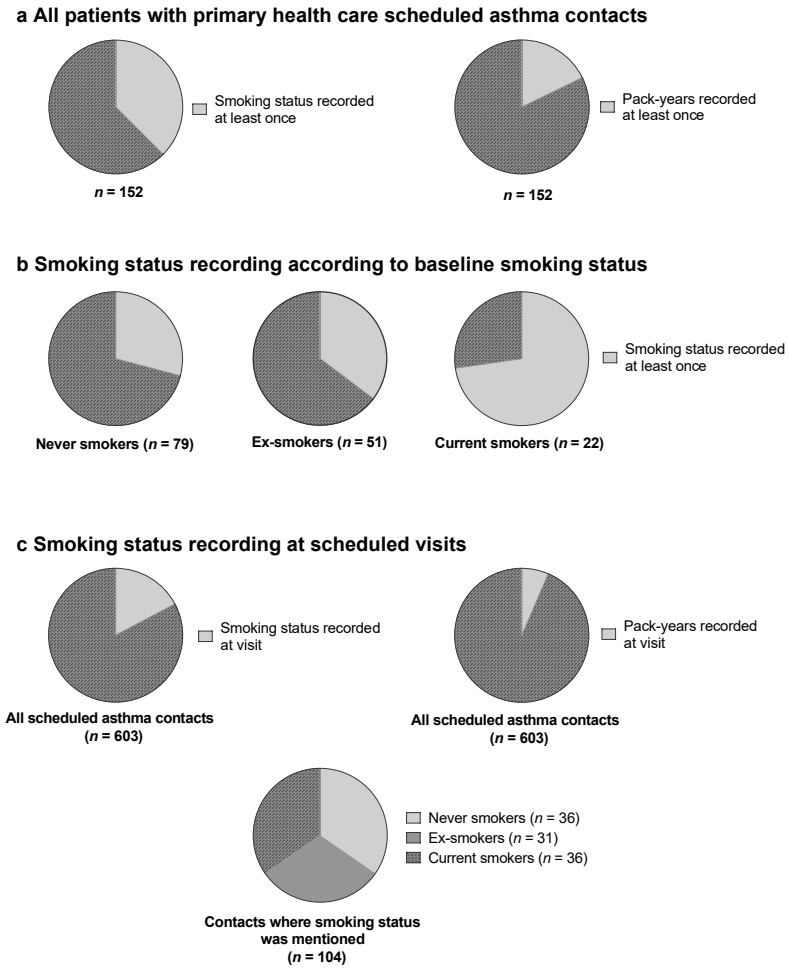

Fig. 3 Distributions of smoking data recordings in scheduled asthma contacts. Distributions of smoking data recordings according to **a** study population, **b** baseline smoking status, and **c** number of scheduled contacts.

Recording of smoking data in scheduled asthma contacts

To evaluate the assessment of smoking in the scheduled asthma contacts ($n = 603$), all documented smoking-related data were collected and analyzed from the follow-up period. Out of the 152 patients having scheduled contacts in PHC, smoking status was not reported even once for 95 patients (62.5%) and smoked pack-years were not calculated even once for 125 patients (82.2%) (Fig. 3a). Smoking status was not recorded even once in 56 (70.9%) never smokers, in 33 (64.7%) ex-smokers and in 6 (27.3%) current smokers (Fig. 3b). Out of all 603 scheduled asthma contacts, smoking status was recorded only in 104 contacts (17.2%) and pack-years were calculated in 39 contacts (6.5%) (Fig. 3c). In most visits where pack-years had been mentioned (34 contacts, 5.6%), it was stated that patient was never smoker (i.e., 0 pack-years) and in only 5 visits (0.8%) pack-years were evaluated in a current or ex-smoker. Of the 104 contacts in which smoking status was recorded, 36 visits were done by never smokers, 32 visits by ex-smokers and 36 visits by current smokers (Fig. 3c).

The occurrence of the scheduled asthma contacts ($n = 603$) of this study population ($n = 152$) during 12-year follow-up in PHC is described more precisely in our previous study[25]. During the years 1–12 after diagnosis, the annual number of scheduled contacts among 152 patients varied from 21 to 67[25]. At the same time recording of smoking status varied annually from 4.8 to 34.9% (on average 16.8%) being the weakest during the first two years (Fig. 4). The annual average of calculation of pack-years was 6.5%.

Documentation of smoking data in patients with ex-smoking or current smoking history

In the assessment of asthma, the knowledge on the smoking status can be considered highly important especially if the patient is ex-smoker or current smoker[40]. Out of all 603 scheduled contacts, 45.9% ($n = 277$) were contacts in which the patient was either current or ex-smoker. Among these patients ($n = 73$), smoking was not mentioned even once with 39 patients (53.4%) and pack-years were not calculated even once with 68 patients

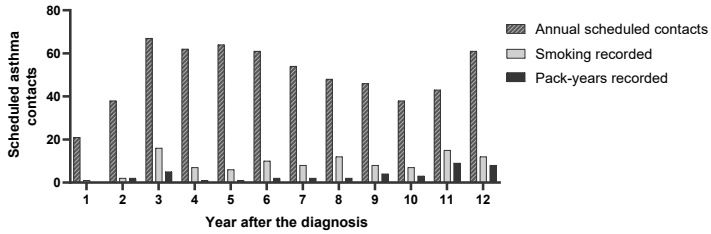

Fig. 4 Recording of smoking data during annual scheduled asthma contacts. Smoking data recording in all scheduled asthma contacts ($n = 603$) in primary health care during 12-year follow-up among 152 patients with adult-onset asthma.

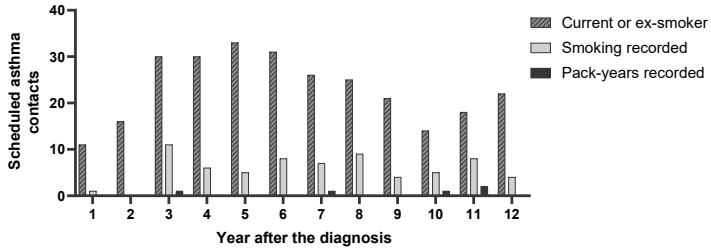

Fig. 5 Recording of smoking data during annual scheduled asthma contacts among ex- or current smokers. Recording of smoking status and pack-years in scheduled asthma contacts over a period of 12 years in patients being either current or ex-smoker.

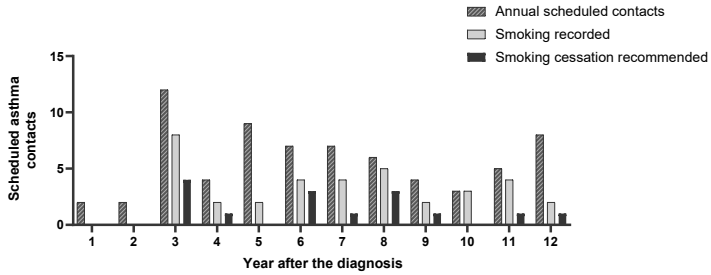

Fig. 6 Smoking data recording and smoking cessation advising during 12-year follow-up for patients being current smokers at the study baseline. The total number of all scheduled asthma contacts of current smokers ($n = 22$) in primary health care was 69.

(93.2%). During these contacts, smoking was recorded on average in 23.9% and pack-years in 2.1% of the annual contacts (Fig. 5).

Recording of smoking habits and smoking cessation advising among current smokers

To explore how smoking habits were screened and if smoking cessation was recommended for current smokers in PHC, we analyzed the 69 scheduled asthma contacts of the patients who were current smokers ($n = 22$) at the study baseline (Fig. 6). The annual number of scheduled asthma contacts among current smokers varied between 2 and 12 during the follow-up period. During these contacts, smoking was recorded on average in 49.3% of annual contacts. Pack-years were poorly recorded, and number of currently smoked cigarettes was more often mentioned than pack-years (35.4 vs. 6.3%) (eFig. 2). Smoking cessation was rarely recommended, a total of 15 times during 12-year period corresponding to 21.7% of visits in which the patient was an active smoker. Out of all current smokers, 13 (59%) had not had smoking cessation advise during scheduled asthma follow-up contacts. As shown in Fig. 2, 32% of smokers ($n = 7$) managed to quit smoking during the follow-up, and out of these 43% ($n = 3$) had received smoking cessation advise during scheduled contacts.

Documentation of smoking data according to the health care professional

To evaluate if differences exist in the recording of smoking according to who is responsible for the patient in the office-based asthma follow-up contact, we divided the follow-up contacts ($n = 603$) in PHC into three groups (Fig. 1). Out of all planned follow-up contacts, 303 were GP contacts, 104 were asthma-nurse contacts, and in 83 contacts patient met first nurse and GP thereafter. In 46 contacts, nurse met patient and then consulted GP, and these contacts were included to the last group (total number of combined GP and nurse contacts $n = 129$). We excluded 67 follow-up contacts related to planned GP telephone contacts only (Fig. 1). Smoking status was mentioned in 13.5% of doctor contacts, in 27.9% of nurse contacts and in 25.6% of contacts when both nurse and GP took part in the contact. Pack-years were mentioned only in 2.4% of scheduled contacts when patient met only GP. Smoking and pack-years were mentioned

Table 2. Recording of smoking in scheduled primary health care office-based visits ($n = 536$) according to the health care professional encountering the patient.

	Doctor contact ($n = 303$)	Nurse contact ($n = 104$)	Both doctor and nurse contact ($n = 129$)	p-value
Smoking status mentioned *n* (%)	41 (13.5)	29 (27.9)	33 (25.6)	<0.001
Pack-years mentioned *n* (%)				
No	296 (97.7)	90 (86.5)	111 (86.0)	<0.001
Yes	2 (0.7)	1 (1.0)	2 (1.6)	
Mentioned, that non-smoker	5 (1.7)	13 (12.5)	16 (12.4)	

more often if nurse participated in the scheduled contact (Table 2).

Characteristics of the patient groups according to the study baseline smoking history

The above results show that smoking status and pack-year history were infrequently recorded in scheduled asthma follow-up contacts. To evaluate the importance of smoking status to the outcome of asthma, we divided the patients ($n = 152$) into two groups according to smoking status at the study baseline: 79 patients were never smokers, and 73 patients were ex-smokers or current smokers. At the 12-year follow-up, most of the patients having positive smoking status were men (54.8%) and had median 17.0 (6.3–29.3) pack-years smoking history. They had more partially and uncontrolled asthma, had lower FEV_1 and FEV_1/FVC ratio, steeper annual decline in lung function, and more symptoms according to CODP Assessment test (CAT)[32] when 26.0% of them had also co-existing COPD (Table 3). Never smokers had more allergy and asthma medications in use. Every fourth ex-smoker or current smoker (25.0%) were also heavy users of alcohol. No significant differences were found in health care use or in comorbidities (eTable 2).

Characteristics of the ex-smokers and current smokers at 12-year follow-up visit

We subsequently explored how ex-smoking or current smoking affected the disease characteristics at the end of the follow-up. For this purpose, we divided the patients into two groups according to smoking status at 12-year follow-up visit: ex-smokers ($n = 57$) and current smokers ($n = 19$). At the end of the follow-up period, most of the current smokers were women, they were younger [mean age 53.2 (10.1)] and had a median of 22.2 pack-years (from 15.6 to 33.5) smoking history. Current smokers had more unscheduled contacts in health care and used more antibiotic courses during the follow-up. Out of all current smokers ($n = 19$), smoking status had been recorded at least once with 14 patients (73.7%) but more often only with 8 patients (42.1%) during the 12-year follow-up. Almost half of current smokers (47.7%) were heavy users of alcohol and none of them had education over 12 years (Table 4). Current smokers had lower fraction of NO in exhaled air (FeNO) and 26.3% of them had also thyroid disease, but no significant differences were found in other comorbidities, asthma control, asthma severity, lung function, or other laboratory parameters (Table 4 and eTable 3).

DISCUSSION

In this real-life 12-year follow-up study, we showed that smoking was infrequently addressed in PHC in a regionally representative sample of asthma patients in Finland. Out of all 603 scheduled asthma contacts in PHC, smoking status was mentioned only in 17.2% and pack-years in 6.5% of contacts. Out of the total of 152 patients having visits in PHC, smoking status was not reported even once for 62.5% of the patients and smoked pack-years were not calculated even once for 82.2%. Smoking data were not recorded even once in 70.9% of never smokers, 64.7% of ex-smokers, and 27.3% of current smokers. We found that smoking and pack-years were mentioned more often if nurse took part on the scheduled contact. Among the population representing current smokers at baseline, 32% succeeded to quit smoking during the 12-year follow-up. For current smokers, smoking cessation was recommended only approximately in every fifth (21.7%) follow-up visit, and 59% of these patients had not received smoking cessation advise during scheduled asthma contacts. As expected, patients with smoking history showed poorer outcomes in asthma.

One of the main goals of the Finnish National Asthma Programme was reduction in respiratory irritants, such as smoking and environmental smoking[26]. Previously, it has been shown that smoking reduced from 24% to 18% among asthmatics in Finland during 2001–2010[41]. In our study, half of the asthma patients in PHC were ex-smokers or current smokers. In this study population, active smoking declined from the 14.5% to 12.5% during the follow-up. In 2018, 15% of working aged men and 13.0% of women were daily smokers in Finland[42]. Thus our study population did not differ significantly from general population or from typical population with asthma[42,43].

To the best of our knowledge, no previous real-life studies exist on how smoking status and the quantities of pack-years are documented in scheduled asthma contacts in PHC in long-term follow-up, and how often during the follow-up the patients are advised to quit smoking. Studies assessing documentation of smoking often include, also, patients with COPD or other chronic diseases[13,21,44–47]. A previous review reported that failure to adequately document smoking history is common in asthma but also in other conditions[44]. On the other hand, a single study from U.S. focusing on treatment recommendations in asthma has indicated high percentages of smoking-related reports in patient records[48]. In our study, out of the total of 152 patients, smoking status was assessed and documented only in 37.5% of adult asthmatics. Among ex-smokers and current smokers ($n = 73$), smoking was documented in less than half (47%) and pack-years less than in 7% of the patients. Recent registry-based study from Finnish secondary care showed that among asthmatics smoking status was documented in 61% of patients and that clinicians documented smoking more actively in years 2016–2018 than in years 2010–2012[47]. The patients included in the previous study were either diagnosed for the first time with disease or they were referred to secondary care for treatment optimization[47]. Thus, it could be argued that due to this fact smoking was more likely to be documented and, on the other hand, use of preliminary information forms is more common in secondary care in Finland, which may have made smoking information more visible. During SAAS-study, general background information forms, which would contain, e.g., smoking and pack-year information, were not in use in PHC in the study region. Our results, suggesting that smoking was recorded in less than every fifth scheduled asthma contact and pack-years in <7% of contacts, may reflect the possible national neglecting attitudes toward smoking habits in PHC in

Table 3. The characteristics of the study groups according to the baseline smoking status at 12-year follow-up visit.

	Never smoker $n = 79$	Ex-smoker or current smoker $n = 73$	p-value
Male n (%)	16 (20.3)	40 (54.8)	**<0.001**
Age (years)	58.8 (13.9)	60.2 (12.3)	0.486
BMI (kg/m^2)	27.8 (4.4)	29.2 (7.1)	0.123
Smoking status mentioned *n* (%)	23 (29.1)	34 (46.6)	**0.030**
Mentioned ≥2 times	7 (8.9)	14 (19.2)	0.061
Pack-years mentioned *n* (%)	22 (27.8)	5 (6.8)	**<0.001**
Pack-years of smokers	–	17.0 (6.3–29.3)	–
Asthma control GINA 2010[a] *n* (%)			
Well controlled	39 (49.4)	15 (20.5)	
Partially controlled	19 (24.1)	33 (45.2)	<**0.001**
Uncontrolled	21 (26.6)	25 (34.2)	
ACT score	22 (19–24)	21 (19–23)	0.549
CAT score	10 (5–17)	13 (8–19)	**0.041**
Average daily prescribed ICS dose among 12 years (µg budesonide equivalents)	800 (507–934)	841 (696–1054)	**0.019**
Average daily dispensed ICS dose among 12 years (µg budesonide equivalents)	474 (319–788)	712 (386–898)	0.098
Total adherence in ICS medication during 12 years (%)	78.5 (46.4–100.5)	81.5 (47.4–93.7)	0.720
Add-on drug in daily use *n* (%)	44 (55.7)	41 (56.2)	>0.999
SABA puffs/week	1.6 (0.97–3.67)	2.4 (0.99–4.47)	0.247
Number of asthma or/and allergy medication in use	3 (2–3)	2 (2–3)	**0.046**
Pre-BD FEV_1 (%)	91.9 (15.2)	82.4 (17.7)	**<0.001**
Post-BD FEV_1/FVC	0.78 (0.71–0.82)	0.73 (0.68–0.79)	**0.004**
Annual change in lung function from $Max_{0–2.5}$ to follow-up[b]			
FEV_1 (ml/year)	−32.6 (−54.2–19.7)	−52.5 (−66.2–25.9)	**0.005**
FEV_1 %/year	−0.26 (−0.80–0.39)	−0.70 (−1.18–0.09)	**0.004**
Co-existing COPD (Post FEV_1/FVC < 0.7 and pack-year ≥10) *n* (%)	0	19 (26.4)	**<0.001**
Heavy alcohol consumption (evaluated by self-reports, GT-CDT index or by both) *n* (%)[c]	9 (11.4)	18 (25.0)	**0.035**

If not otherwise mentioned shown are mean (SD) or median (25th–75th percentiles). Bold values indicates statistically significant p-values. Add-on drug = long-acting β_2-agonist, leukotriene receptor antagonist, theophylline, and/or tiotropium in daily use.
BMI Body Mass Index, *ACT* asthma control test, *CAT* COPD assessment test, *ICS* inhaled corticosteroid, *SABA* short-acting β_2-agonist, *BD* bronchodilator, *FEV_1* forced expiratory volume in 1 s, *FVC* forced vital capacity, *GT-CDT* gammaglutamyltransferase-carbohydrate-deficient transferrin-index.
[a]Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report.
[b]Annual change in FEV_1 during 12 years of follow-up (ΔFEV_1 from point of maximal lung function within 2.5 years after start of therapy to the 12-year follow-up visit).
[c]Assessment of alcohol consumption was performed according to the US definitions for alcohol consumption by portions/week. For men, heavy drinking is defined as consuming 14 portions or more per week. For women, heavy drinking is defined as consuming 7 portions or more per week. Portion indicates 14 g alcohol.

accordance with previous study showing that smoking habits was mentioned only in 42% of asthma referral letters sent to respiratory department[49]. In addition, in more recent Finnish study, recording of smoking status was visible in 14.2% of the PHC referrals to operative care and very little attention was paid to the need for preoperative smoking cessation in PHC[50]. During the Finnish National COPD program written information on smoking habits in records increased from 16.6% of all patients with respiratory symptoms in 1997 to 53.2% in 2002 and in COPD group from 45.0 to 84.3%[51]. However, duration and amount of smoking were also poorly documented[51]. Based on our results, overall amount of current tobacco use was more often mentioned than pack-years among smoking asthmatics.

Many of the studies are conducted from the perspective of what has been done by the GP, but less is known whether differences exist according to the professional that meets the patient (GP, nurse of both). Swedish study showed that documentation of smoking habits was more frequently carried out in asthma nurse consultations compared to GP contacts (78 vs. 28%)[45]. Our results are similar, but although smoking data was recorded more often when asthma nurse participated in the scheduled contact, still smoking was mentioned only in <70% and pack-years in <15% of these contacts.

According to current guidelines patients with asthma should strongly be encouraged to quit smoking[1,22]. Cessation support and treatment should be provided in all health care settings and by all health care providers[12]. Study based on self-reports showed that 41% of the patients with lung conditions reported receiving information from doctor or nurse about the health effects of smoking both before and after their diagnosis, while 13% reported that they had received guidance only before diagnosis, 31% after diagnosis and 15% of patients not at all[46]. It is suggested that even if smoking is screened it is less likely that smoking patients are advised to quit[52]. In addition, diagnosis of respiratory disease does not seem to motivate people to quit smoking[53]. In our study smoking cessation was rarely recommended to asthmatics, a total

Table 4. Characteristics of ex-smokers and current smokers at the 12-year follow-up visit.

	Ex-smoker $n = 57$	Current smoker $n = 19$	p-value
Male *n* (%)	35 (61.4)	6 (31.6)	**0.034**
Age (years)	61.8 (12.6)	53.2 (10.1)	**0.008**
BMI (kg/m^2)	29.1 (6.8)	29.0 (7.7)	0.987
Pack-years of smokers	12.8 (3.5–24.0)	22.2 (15.6–33.5)	**0.011**
Heavy alcohol consumption (evaluated by self-reports, GT-CDT index or by both) *n* (%)[a]	9 (16.1)	9 (47.4)	**0.011**
In working life *n* (%)	21 (36.8)	12 (63.2)	0.062
Length of education ≥12 years *n* (%)	7 (12.3)	0	**0.004**
Smoking status mentioned *n* (%)	21 (36.8)	14 (73.7)	**0.008**
≥2 during 12-year follow-up	6 (10.5)	8 (42.1)	**0.003**
Pack-years mentioned during 12-year follow-up *n* (%)	2 (3.5)	3 (15.8)	0.096
FeNO (ppb)	12.0 (7.0–23.0)	5 (2.5–8.0)	**<0.001**
Uncontrolled asthma *n* (%)[b]	22 (38.6)	5 (26.3)	0.145
Severe asthma *n* (%)[c]	3 (5.3)	3 (15.8)	0.161
ACT score	21 (19–24)	21 (19–22)	0.266
CAT score	13 (7–18)	14 (9–19)	0.580
Average daily dispensed ICS dose among 12 years (μg budesonide equivalents)	609 (331–838)	770 (490–958)	0.231
Total adherence in ICS medication during 12 years (%)	76.7 (46.7–93.2)	85.7 (41.1–98.3)	0.686
Purchased antibiotic courses during the follow-up *n* (%)	8 (2–13)	12 (5–19)	**0.040**
≥2 OCS course for asthma during 2 years before follow-up *n* (%)	13 (22.8)	1 (5.6)	0.165
Purchased OCS courses during the follow-up (mg/year)	80 (0–188)	92 (0–217)	0.990
≥1 hospitalization due to any respiratory related reason *n* (%)	13 (22.8)	6 (31.6)	0.543
Unscheduled contacts	4 (1–10)	9 (3–17)	**0.012**
Co-existing COPD (post $FEV_1/FVC < 0.7$ and pack-year ≥10) *n* (%)	15 (26.8)	4 (21.1)	0.765
Thyroid disease *n* (%)	3 (5.3)	5 (26.3)	**0.020**

If not otherwise mentioned, shown are mean (SD) or median (25th–75th percentiles). Bold values indicates statistically significant p-values.
BMI Body Mass Index, *GT-CDT* gamma*glutamyltransferase*-carbohydrate-deficient transferrin-index, *FeNO* fraction of NO in exhaled air, *ACT* asthma control test, *CAT* COPD assessment test, *ICS* inhaled corticosteroid, *OCS* oral corticosteroid, FEV_1 forced expiratory volume in 1 s, *FVC* forced vital capacity.
[a]Assessment of alcohol consumption was performed according to the US definitions for alcohol consumption by portions/week. For men, heavy drinking is defined as consuming 14 portions or more per week. For women, heavy drinking is defined as consuming 7 portions or more per week. Portion indicates 14 g alcohol.
[b]Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report.
[c]Assessment of severe asthma was performed according to the ERS/ATS severe asthma guideline 2014.

of 15 times during 12-year period corresponding to 21.7% of visits in which the patient was an active smoker. Out of all current smokers, 32% succeeded to quit smoking but at the same time over half of the patients did not receive cessation advice, and few of the non-smokers and ex-smokers began to smoke. The proportion of patients who received guidance to quit smoking (41%) was in line with found by Stridman et al. (38%)[13]. In our study, out of the patients who succeeded to quit smoking, 43% had received smoking cessation advise during scheduled asthma contacts in PHC. Recent Finnish study showed that smoking cessation was discussed with 55.4% of current smoker asthmatics in secondary care, but still these patients were seldom referred to nurse-managed smoking cessation program[47].

Our results raise doubts whether PHC professionals are truly aware of the importance of evaluation of smoking and smoked pack-years among asthma patients, and whether these are better screened with COPD patients as smoking is a well-known risk factor for the disease[23]. Recent study from Finland showed that smoking status was documented more frequently in COPD and sleep apnea patients in secondary care, and that smoking cessation was discussed more frequently in COPD (59.5%) and type I diabetes (61.0%) than in asthma (55.4%)[47]. In U.S. was also found that PHC physicians provided counseling more frequently to smokers with COPD than smokers without chronic diseases (46% vs 25%) or with asthma (31%)[21]. In Sweden, smoking cessation support was offered to 27% of 12–17 year old adolescent asthmatics, to 38% of adult-asthmatics and to 51% of the patients with COPD[13]. Based on our study and previous studies[49,50,54,55] it could be argued that smoking cessation activities in PHC in Finland have remained inadequate despite asthma guidelines[1,22] and national smoking cessation guidelines since 2002[56]. Although there is strong evidence for the benefits of quitting smoking, its implementation is shown to be poor not only in respiratory diseases but also in many other conditions[21,44,53,57]. A previous study from U.S. suggested that among smokers with chronic smoking-sensitive diseases, 50–72% of the patients received no counseling about smoking cessation[21]. Study from Finland reported inadequate smoking cessation counseling when number of smokers who had been advised by at least one health care professional during the preceding year varied from 24% to 26% for men and 22% to 26% for women[58]. In more recent study Hirvonen et. al. showed that in Finnish secondary care encouragement to smoking cessation varied between seven common chronic disease from 41% to 61%[47]. Several factors may influence in physicians' engagement in smoking cessation including physician-related, patient-related, and health care organization-related factors[20,52,59]. Among pregnant asthmatics smoking may be better screened and the benefits of smoking cessation more thoroughly advised[60]. It is also suggested that smoking cessation counseling is more frequently provided to young patients and,

overall, if more time is available for the contact[21]. The probability for quitting smoking is shown to be more likely with higher levels of education and fewer years of smoking[53].

Our results further showed that patients with ex-smoking or current smoking history had poorer outcome in asthma. In line with previous studies[7,9] they had more symptoms, poorer lung function and more partially controlled and uncontrolled asthma. One quarter of them had also co-existing COPD. In our study almost every second current smoker was also heavy alcohol drinker. It could be argued that this may increase the risk that smoking is not actively addressed while heavy alcohol consumption is shown to associate with poorer participation in asthma follow-up[27]. Alcohol and smoking may also create adverse synergistic interactions on lung function[61]. At the end of the study period, out of all current smokers almost 70% were female, they were younger, had lower education level, more unscheduled health care contacts and used more antibiotics. There were no differences between ex-smokers and current smokers in lung function, in hospitalizations or in use of oral corticosteroids. Current smokers had lower FeNO and more thyroid disease which both have shown to associate with smoking[62,63]. The above results indicate that among smoking asthmatics the assessment of smoking and pack-year history and active advising of smoking cessation is crucial and should be done more actively in every health care contact.

Our study has several strengths. The diagnosis of asthma was made by a respiratory physician and the diagnosis was based on typical symptoms and objective lung function measurements showing reversibility of airway obstruction. The study population well represents a typical PHC population with asthma when smokers or patients with co-morbidities were not excluded[24,43]. In this study all scheduled asthma contacts in PHC were evaluated including both nurse and GP contacts. Thus, documentation of smoking habits could be accurately assessed. Overall, in this real-life study we had 603 scheduled contacts, which may be expected to yield a representative sample of real-life adult asthma population. Possible weakness of our study is that our results may not represent entire Finland. It is, however, more likely that similar neglecting attitudes towards smoking habits in asthma care are also prevailing throughout the world. Differences may occur, for example, in the use of structured preliminary information forms, that could make tobacco use status more identifiable for clinicians. Possible limitation is also that smoking habits may have been screened and smoking cessation advised but it has not been documented to the patient records. On the other hand, according to the good clinical practice, measures taken shall be recorded in medical records or otherwise it can be interpreted that it has not been carried out. It should also be noted that the number of current smokers at the follow-up ($n = 19$) was low, which might lead to loss of power in statistical analyses.

Based on our results and the known facts of dose-dependent harms of smoking to asthmatics, it appears that PHC practitioners should pay increasing attention to the evaluation of smoking habits among asthmatics, including quantitative estimates of the number of pack-years. This should be done already at the time of asthma diagnosis and followed during each subsequent asthma contact. The importance of assessment and recording of smoking and pack-years as well as smoking cessation should be increasingly emphasized in asthma treatment guidelines. In addition to smoking, the possible use of snuff and e-tobacco should be screened, as they have also been suggested to impair lung health[64,65].The use of ready-made phrase templates could help to collect smoking data more efficiently during asthma follow-up contacts. According to recent national tobacco statistics decline in the number of smoking adults seems to have stopped in Finland[42]. The PHC has the main responsibility in counseling and managing smoking cessation. The first component of brief patient counseling for tobacco cessation starts with asking about the smoking status[12,56]. Based on our findings, smoking cessation should be provided more actively to asthmatics by ensuring adequate resource, guidance, support, and time for this work. Group counseling would provide the opportunity for peer support to the patients and enable effective use of health care resources but also virtual support systems for smoking cessation should be developed and effectively utilized. The presence of an electronic medical record reminder has suggested to be valuable tool in efforts to promote smoking cessation[66] and its use should be further assessed in existing patient information systems. Further studies are needed to evaluate how other essential factors affecting asthma control are considered in scheduled asthma contacts in PHC.

As a conclusion, in this real-life 12-year follow-up study we showed that smoking and pack-years were poorly addressed in PHC in Finland. Out of all scheduled asthma contacts ($n = 603$), smoking status was recorded only in 17.2% and pack-years only in 6.5%. Smoking data were not recorded even once to 70.9% of never smokers, to 64.7% of ex-smokers, and to 27.3% of current smokers. Smoking and pack-years were documented more often if nurse took part on the scheduled contact. Smoking cessation was rarely recommended. In the future, it is essential that PHC practitioners pay more attention to evaluation of smoking habits and the number of pack-years among asthmatics.

DATA AVAILABILITY

All data generated or analyzed during this study are included in this published article and its Supplementary Information File. According to ethical permission and patient data-protection laws of Finland, single patient data cannot be made available.

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AUTHOR CONTRIBUTIONS

This study is a part of Seinäjoki Adult Asthma Study. J.T. contributed to the study design, analyzed, and interpreted the data, draw the pictures to this article and wrote the manuscript. L.E.T. and H.K. designed the study and guided the work. P.I. contributed to the study design and guided the work. I.V. contributed to the computation of adherence and SABA use and provided statistical advice. O.N. contributed to the laboratory analyses. All authors accept full conduct of the study and critically revised the manuscript. All authors have read and approved the final version of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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PUBLICATION IV

Documentation of comorbidities, lifestyle factors, and asthma management during primary care scheduled asthma contacts

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ARTICLE OPEN

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Documentation of comorbidities, lifestyle factors, and asthma management during primary care scheduled asthma contacts

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Systematically assessing asthma during follow-up contacts is important to accomplish comprehensive treatment. No previous long-term studies exist on how comorbidities, lifestyle factors, and asthma management details are documented in scheduled asthma contacts in primary health care (PHC). We showed comorbidities and lifestyle factors were poorly documented in PHC in this real-life, 12-year, follow-up study. Documented information on rhinitis was found in 8.9% and BMI, overweight, or obesity in ≤1.5% of the 542 scheduled asthma contacts. Of the 145 patients with scheduled asthma contacts, 6.9% had undergone revision of their inhalation technique; 16.6% had documentation of their asthma action plan. Screening of respiratory symptoms was recorded in 79% but nasal symptoms in only 15.5% of contacts. Lifestyle guidance interventions were found in <1% of contacts. These results, based on documented patient data, indicate a need exists to further improve the assessment and guidance of asthma patients in PHC.

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INTRODUCTION

Asthma is a long-term variable respiratory disease[1] with low remission rates if diagnosed at adult age[2–4]. The reasons for poor asthma control are complex and may include patient-, healthcare-, and therapy-related issues[5]. Comorbidities such as obesity, allergy, rhinitis, gastroesophageal reflux, psychiatric disorders, obstructive sleep apnea, bronchiectasis, and sensitivity to non-steroidal anti-inflammatory drugs (NSAIDs) are common in asthmatics[6–13]. Asthma-related comorbidities may contribute to poor disease control by aggravating or mimicking symptoms, thus making it more difficult to distinguish true, severe asthma from difficult-to-treat asthma[7,9]. This, in turn, may lead to overtreatment or undertreatment with anti-asthma medication or lead to misdiagnosis[6,7]. The risk of multiple, non-respiratory comorbidities has been shown to be higher in late-onset asthma[11,14]. Socioeconomic factors[15,16], poor adherence to inhaled corticosteroids (ICS)[1,5], problems in inhalation technique[1,5] and lifestyle factors such as smoking[17] and low physical activity[18], are also, in addition to comorbidities, associated with poorer asthma control. Self-management, including education, personal action plan, and structured follow-up, are strongly recommended as key components of asthma care and are shown to improve asthma control and reduce patients' use of health-care resources and costs[19,20].

The aforementioned aspects underscore why regular holistic assessment and guidance of asthma patients is important[1]. Annual follow-up reviews do not, unfortunately, occur often according to guidelines[21–24], even in severe asthma[25,26], that is shown to be underdiagnosed in primary health care (PHC)[27]. The lack of regular follow-up is not limited only to primary care[21,22], when studies with patients from both primary and specialised care have also suggested that ~50–70% of patients[23,24] and over 30% in severe asthma[26] had no annual planned contacts. Moreover, adherence to asthma guidelines has been reported to be suboptimal among health-care practitioners[21,28–30]. Based on those factors, one might assume asthma evaluation is largely carried out, e.g., during visits made for other conditions or for acute exacerbations. However, in visits where asthma is not the only issue of attention, or if the visit has been made, e.g., due to acute exacerbation, no similar possibility for a comprehensive asthma assessment exists, arguably, except in planned follow-up contacts. Thus, it can be considered important to discover how systematically asthma assessments are performed in visits that focus purely on asthma to evaluate how guidelines are implemented in asthma monitoring.

The main responsibility for asthma treatment was shifted to PHC within the Finnish National Asthma Programme[31]. Important programme goals, were, e.g., active asthma treatment, use of lung function tests as part of control assessment, patient education together with guided self-management, and possible trigger evaluation[31]. Our previous long-term study showed that adherence to lung function measurements, especially to spirometry, in assessing asthma control was high in PHC[22]. Conversely, the frequency of asthma follow-up contacts was insufficient[22], as was smoking data and smoking cessation documentation[32]. Previous studies, mainly based on self-reports or short-term follow-ups, have suggested several shortcomings in asthma management in PHC, including asthma control assessment[30,33,34], self-care guidance[33,34], rhinitis screening and treatment[35,36], inhaler technique review[30,34] and physical activity, nutrition and alcohol consumption assessment[34].

To the best of our knowledge, no previous long-term real-life studies exist on how comorbidities, lifestyle factors, and asthma management details, such as inhalation technique and medication data, are screened and documented in scheduled asthma contacts during long-term follow-up in PHC, being the current study's aim. Our additional aim was to assess whether there are differences

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according to who encountered the patient at the follow-up visit (GP, nurse, or both).

METHODS

Setting of the SAAS study

The study was part of the Seinäjoki Adult Asthma Study (SAAS), a real-life, single-centre, 12-year follow-up study of 203 patients with new-onset asthma diagnosed at adult age (≥15 years). The details of the SAAS study protocol with inclusion, exclusion and specific diagnostic criteria were published separately (eTable 1)[37]. The original study cohort comprised 256 patients with new-onset asthma diagnosed between 1999 and 2002 in Seinäjoki Central Hospital's respiratory department by a respiratory physician based on typical symptoms and was confirmed by objective lung function measurements. Smokers and patients with concomitant COPD or other comorbidities were also included[37]. The patients were treated and monitored by their personal physicians after the diagnosis was confirmed and the medication started, mostly in PHC, according to the Finnish National Asthma Programme[31] as described previously[22,37]. The patients were invited to follow-up visit in the respiratory department after 12 years (mean 12.2, range 10.8–13.9 years). Of the original study population, 53 patients were lost to follow-up (Supplementary Figure 1) and 203 patients completed a follow-up visit, where asthma status, disease control, comorbidities, and medication were evaluated using structured questionnaires and lung function was measured[37,38]. The participants in the follow-up visit gave written informed consent to the study protocol approved by the Ethics Committee of Tampere University Hospital, Tampere, Finland[37]. All data of the asthma-related health-care contacts ($n = 3639$) during the 12-year period were collected from PHC, occupational health care, private clinics, and hospitals in addition to the data gathered at diagnostic and follow-up visits, as previously described[22,37]. Each patient, on average, had 4 [interquartile range (IQR) 1–6] scheduled asthma contacts and, overall, 15 (IQR 9–23) asthma-related health-care contacts during the follow-up period. The SAAS study flowchart and schematic presentation are shown in the supplementary material (eFig. 1; eFig. 2). The SAAS study is registered at www.ClinicalTrials.gov with identifier number NCT02733016[37].

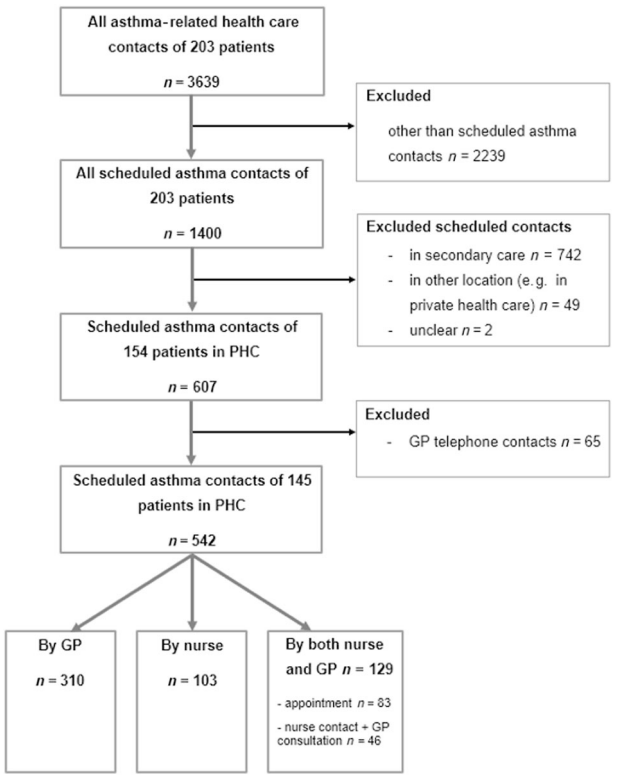

Fig. 1 The flowchart of the study.

Study design and population

All asthma-related health-care contacts ($n = 3639$) of the 203 patients during the 12-year follow-up period were retrospectively assessed in the present study (Fig. 1). The following definitions were used to categorise different asthma contact types:

- *Primary health care (PHC) contact*: contact made in primary health care centre or in occupational health care.
- *Secondary care contact*: contact in specialised care in respiratory department.
- *Private health care contact*: contact in private health care.
- *Doctor/GP contact*: contact with only GP participating in the asthma assessment.
- *Nurse contact*: contact with only nurse participating in the asthma assessment.
- *Both doctor/GP and nurse contact*: contact with both professionals participating in the asthma assessment.
- *Scheduled asthma contact*: planned monitoring contact that purely focused on asthma.
- *Office-based contact*: patient encountered the professional face-to-face.
- *GP telephone contact*: a doctor phone call to a patient regarding asthma.
- *Other than scheduled asthma contact*: includes other asthma-related health-care contacts, excluding planned asthma contacts.
- *Unclear type of contact*: the exact type for the contact could not be determined.
- *All asthma-related health-care contacts*: includes scheduled asthma contacts and contacts made for infection, exacerbation, or for asthma and other reason.

We excluded contacts made for infection, exacerbation or for asthma and other reason of all the asthma-related contacts ($n = 3639$) (Fig. 1). Of the total 203 patients, 154 had scheduled asthma contacts ($n = 607$) in PHC, while 20 patients' follow-up was arranged in secondary care or in private health care, and 29 patients had no planned follow-up contacts between the diagnostic visit and the 12-year follow-up visit as our previous study described[22]. Overall, of all scheduled asthma contacts during the 12-year follow-up, 742 occurred in secondary care, 49 in other locations, and two contacts' locations were unclear. Our previous studies described the occurrence of scheduled asthma contacts in PHC and the overall occurrence of asthma follow-up contacts in the SAAS study population[22,23].

We included all office-based, scheduled asthma contacts ($n = 542$) in PHC in this study. GP telephone contacts ($n = 65$) were excluded because these were often short phone calls, e.g., due to a previously made medication change, discussion of current test results, or the need for specific medical certificates, and were basically not intended to replace a more comprehensive face-to-face assessment. Nine patients had only telephone contacts of the total population of 154 patients with scheduled asthma contacts in PHC. Thus, after exclusion of GP telephone contacts, the total population in this study with office-based, scheduled asthma contacts was 145 (Fig. 1). The data of 145 patients and the data gathered from their office-based, scheduled asthma contacts in PHC were manually collected and evaluated.

Evaluation of the content of asthma contacts according to professional

We divided the 542 scheduled contacts into three groups (GP, nurse, or both) to evaluate whether differences exist in how

comorbidities and other asthma-related data were documented. The contacts were evaluated according to who was responsible for the patient in the office-based asthma follow-up contact: 310 were GP contacts,103 were nurse contacts, and 129 were combined GP and nurse contacts (Fig. 1). Of 129 combined GP and nurse contacts, the patient first met the nurse and the GP thereafter at the same visit in 83 contacts; the patient met the nurse and the GP was only consulted in 46 contacts.

Collection of data on comorbidities, lifestyles, symptoms, and asthma management

We collected information on the comorbidities associated with asthma, including obesity, nasal conditions, gastroesophageal reflux, obstructive sleep apnea (OSA) and intolerance to NSAIDs. The evaluated nasal conditions included chronic/allergic rhinitis, sinus infections and nasal polyps. We also collected information on documentation of obesity-related lifestyle factors (including exercise habits, diet, and alcohol use), asthma symptoms, and patient guidance. All documented medication and data considering inhalation technique were manually collected from patient records and evaluated. Our previous studies described performance of lung function tests, documentation of smoking data and smoking cessation activities in scheduled asthma contacts in PHC[22,32].

Assessment of lung function, asthma control, severity, and other clinical parameters

The lung function measurements were performed with a spirometer according to international recommendations at the diagnostic visit and at the 12-year follow-up visit[37,38]. The fraction of exhaled nitric oxide (FeNO) was measured with a portable rapid-response chemiluminescent analyser according to American Thoracic Society standards[39] (flow rate 50 mL·s^{-1}; NIOX System, Aerocrine, Solna, Sweden). Venous blood was collected, and white blood cell differential counts were determined. Total immunoglobulin (Ig)E levels were measured by using ImmunoCAP (Thermo Scientific, Waltham, USA). Laboratory assays were performed in an accredited laboratory (SFS-EN ISO15189:2013) of Seinäjoki Central Hospital.

Patients completed the Asthma Control Test (ACT) and Airways Questionnaire 20 (AQ20) in the 12-year follow-up visit[40,41]. An asthma control assessment was performed according to the Global Initiative for Asthma (GINA) 2010 report[42]. Severe asthma assessment was performed according to the ERS/ATS severe asthma guideline 2014[43]. Adherence to inhaled corticosteroid (ICS) medication was evaluated by comparing the dispensed doses to the prescribed doses for the whole 12-year period as our previous studies described[44,45]. The prescribed dose in each patient was calculated based on medical records, and the dispensed ICS, short-acting β_2-agonist (SABA) and oral corticosteroids were obtained from the Finnish Social Insurance Institution, which records all purchased medication from all Finnish pharmacies[44,45]. The 12-year adherence and annual adherence for each patient were calculated using specific formulas previously described, considering aspects from the medication possession ratio (MPR) and proportion of days covered (PDC)[44].

Information on alcohol consumption was assessed by detailed structured questionnaires at the 12-year follow-up visit. Heavy alcohol consumption was evaluated by self-report, GT-CDT index or both. An alcohol consumption assessment was performed according to the US definitions for alcohol consumption by portions/week (portion indicates 14 g alcohol)[46]. Serum levels for carbohydrate-deficient transferrin (CDT) were measured by a turbidimetric immunoassay (TIA) after ion exchange chromatography (%CDT, Axis-Shield, Oslo, Norway); plasma γ-glutamyltransferase (GT) concentration was measured using enzymatic colorimetric assay, as standardised against IFCC (International Federation of Clinical Chemistry and Laboratory Medicine). More detailed information on GT and CDT measurements and on calculating the GT-CDT index has been previously reported[47].

The Finnish health-care system during the study

The production of public health care services was the municipalities' responsibility during the study follow-up period[48]. Finland was divided into 21 hospital districts that provided specialised medical care for the population in their own areas, and approximately 160 health-care centres provided the primary health-care services described previously[22]. Employers were obligated to offer occupational health-care services for their employees in addition to the municipal system[48]. Financial incentive systems affecting what will be recorded were not in use in public or occupational health care. Primary health-care services could also be sought from private health care mainly financed by the patients' own expence[48]. However, the availability of private health-care services during the study period was very limited in the study region compared to bigger cities. Consequently, most patients could use only public health-care services. Thus, in this and in our previous studies[22,23,32], planned asthma follow-up contacts in health-care centres and in occupational health care were considered scheduled PHC contacts. All health-care centres in the region had respiratory nurses and a coordinator GP responsible for asthma management in the health-care centre, yet all GPs managed their own asthma patients during the study period. A common electronic patient record system was not yet used in the region, and professionals could use different and separate software in primary health-care centres, hospitals, and private health care. Our previous study also discussed the Finnish health-care system[22].

Statistical analysis

Continuous data are expressed as mean (SD) for variables with normal distribution and for parameters with skewed distributions medians, and 25–75 percentiles are shown. Group comparisons were performed by using Pearson Chi-square test for categorised variables. Two-sided p-values were used. A P-value < 0.05 was regarded as statistically significant. Statistical analyses were performed using SPSS software, version 27.0.1 (IBM SPSS, Armonk, NY).

Reporting summary

Further information on research design is available in the Nature Research Reporting Summary linked to this article.

RESULTS

Characteristics of the study population

Of the 203 total patients in SAAS study, 145 had scheduled office-based asthma contacts in PHC with a GP, nurse, or both. Most patients with PHC follow-up visits were female (63.4%). The mean age was 59.3 and BMI 28.4 at 12-year follow-up visit; thus, the study population was characterised with overweight. Half of the patients were ex- or current smokers, 37.4% were atopic (at least one positive skin prick test of common allergens), 69.7% had rhinitis, 8.3% had treated dyspepsia, and 31.0% of the patients had uncontrolled asthma according to GINA 2010[42]. The total adherence to ICS medication (ug budesonide equivalent dispensed/ug budesonide equivalent prescribed *100) during the 12 years was 81.3% among patients with scheduled office-based asthma contacts in PHC. Table 1 shows the characteristics of the study population at the 12-year follow-up visit. The Supplementary Material (eTable 2) shows the baseline characteristics of the 145 patients.

Documentation of comorbidities and lifestyle factors in scheduled asthma contacts

All documented data was collected and analysed from the full 12-year follow-up period to evaluate the comorbidities and lifestyle factors assessments in scheduled asthma contacts in PHC. Documentation was seldom done for comorbidities such as obesity, overweight, rhinitis, sleep apnea, reflux symptoms, and intolerance to NSAIDs in the 542 scheduled asthma contacts in PHC. The occurrence of possible chronic or allergic rhinitis was documented in 8.9% of contacts and reflux symptoms in 1.1% of contacts (Table 2). Chronic or allergic rhinitis was mentioned in 35 subjects (24.1%) of the 145 patients with scheduled asthma contacts in PHC (eTable 3). Obesity or overweight were documented only in 0.9% to 1.3% of contacts, and the information on BMI was found in 1.5% of the contacts of the total 542 scheduled, office-based asthma contacts (Table 2). Recorded information on BMI was found in 8 patients (5.5%) out of 145 patients with scheduled asthma contacts in PHC. Overall, BMI and/or possible overweight or obesity were mentioned in 15 patients' (10.3%) health records (eTable 3). Exercise habits were the most-often documented lifestyle factor, in 16.2% of the contacts (Table 2) and in 49 (33.8%) of the patients at least once (eTable 3). Dietary matters and alcohol consumption were rarely mentioned (Table 2).

We evaluated whether differences exist in the documentation of comorbidities or lifestyle factors according to who is responsible for the patient in the office-based asthma contacts; the GP, nurse, or both. However, no significant differences were found in recording comorbidities, but out of lifestyle factors, exercise habits were more-often mentioned (from 21.7% to 29.1%) if the nurse participated in the scheduled contact (Table 2).

Documentation of asthma symptoms, medication, and patient guidance

Data on asthma management details (asthma symptoms, including ACT, medication, inhalation technique, patient guidance, etc.) during the follow-up period were collected and analysed. Figure 2 shows the documentation of collected asthma management details during scheduled asthma contacts (=542) in PHC. The occurrence of possible respiratory symptoms was recorded in 79.0% of visits and in 86.8% if both nurse and GP took part in the scheduled contact of the 542 scheduled PHC asthma contacts (Table 3). Nasal symptoms were mentioned in only 15.5% of the contacts (Table 3) and, overall, at least once in 52 patients (35.9%) (eTable 3). Data on the Asthma Control Test (ACT)[40] was seldom found, in only 6.3% of contacts, but it was documented more often if both the nurse and GP participated in the contact (15.5%). Pulmonary auscultation data were registered in 72.9% of the physicians' contacts.

The brand names of the entire asthma medication were recorded in 70.3% of all contacts ($n = 542$), while complete dosage of the medication and inhaler names or types were recorded less often in only 13.5% and 11.4% of all contacts. Overall, asthma medication data were mostly only partially documented and were more frequently mentioned if both professionals attended in the contact (Table 3). Changes in asthma medication were made in 26.8% of visits and more often during contacts when the GP was involved (36.1%). The information on inhalation technique revision was documented in only 2.2% of contacts (Table 3) and more by nurse (8.7%), but out of all 145 patients, it was revised in only 10 (6.9%) patients during 12-year follow-up (eTable 3). Regarding medication for comorbidities, medication for the nose was started or changed 23 times and twice for reflux symptoms in scheduled asthma contacts during the 12-year follow-up (Table 3). Nasal medication was documented at least once in 46 patients (31.7%) and reflux medication in 8 patients (5.5%) out of 145 patients (eTable 3).

Table 1. Characteristics of the 145 patients with scheduled follow-up contacts in primary health care at 12-year follow-up visit.

	Patients ($n = 145$) with scheduled asthma follow-up contacts in primary health care
Basic characteristics	
Female *n (%)*	92 (63.4)
Age (y), *mean (SD)*	59.3 (13.2)
BMI (kg/m^2), *mean (SD)*	28.4 (5.9)
Atopic *n (%)*[a]	49 (37.4)
Smokers (ex or current) *n (%)*	72 (49.7)
Alcohol heavy user *n (%)*	24 (16.6)
Asthma severity n (%)	
ACT score, *median (IQR)*	22 (19–24)
Uncontrolled asthma *n (%)*[b]	45 (31.0)
Severe asthma according to ERS/ATS criteria *n (%)*[c]	10 (6.9)
Lung function & inflammation parameters	
Pre-BD FEV_1 (%), *mean (SD)*	87 (17)
Post-BD FEV_1 (%), *mean (SD)*	90 (17)
Pre-BD FEV_1/FVC, *median (IQR)*	0.73 (0.67–0.79)
Post-BD FEV_1/FVC, *median (IQR)*	0.75 (0.69–0.80)
FeNO (ppb), *median (IQR)*	11 (5–19)
Blood eosinophils (×10^9/l), *median (IQR)*	0.16 (0.10–0.27)
Total IgE (kU/l), *median (IQR)*	61 (23–153)
Medication	
Daily ICS in use *n (%)*	122 (84.1)
Daily SABA in use *n (%)*	21 (14.5)
Daily LABA in use *n (%)*	76 (52.4)
Daily add-on drug in use *n (%)*	82 (56.6)
Total adherence to ICS over 12 years, *median (IQR)*	81.3 (49.7–98.9)
≥1 oral corticosteroid course during 12-yr follow-up *n (%)*	49 (34.5)
Comorbidities	
Obesity (BMI ≥ 30 kg/m^2) *n (%)*	47 (32.4)
Rhinitis *n (%)*	101 (69.7)
COPD *n (%)*	21 (14.6)
Diabetes *n (%)*	18 (12.4)
Hypertension *n (%)*	47 (32.4)
Ischemic heart disease *n (%)*	16 (11.0)
Any psychiatric disease *n (%)*	18 (12.4)
Treated dyspepsia *n (%)*	12 (8.3)
Number of comorbidities (COPD included), *median (IQR)*	1 (0–2)
Health care use	
Scheduled asthma contacts in PHC, *median (IQR)*	3 (1–6)
All-asthma-related health care contacts, *median (IQR)*	17 (11–24)
≥1 hospitalisation during 12-y *n (%)*	39 (26.9)

BMI body mass index, *ACT* asthma control test, *IQR* interquartile range, *BD* bronchodilator, *FEV_1* forced expiratory volume in 1 s, *FVC* forced vital capacity, *FeNO* fraction of nitric oxide in exhaled air, *ICS* inhaled corticosteroid, *SABA* short-acting β_2-agonist, *LABA* long-acting β_2-agonist. *Add-on drug* long-acting β_2-agonist, leukotriene receptor antagonist, theophylline and/or tiotropium in daily use. *PHC* primary health care.
[a]At least one positive skin prick test of common allergens.
[b]Assessment of asthma control was performed according to the Global Initiative for Asthma (GINA) 2010 report.
[c]Assessment of severe asthma was performed according to the ERS/ATS severe asthma guideline 2014.

Table 2. Documentation of comorbidities and lifestyle factors in scheduled asthma contacts ($n = 542$) and according to professional encountering the patient at follow-up contact.

	All scheduled PHC asthma contacts $n = 542$	GP contact $N = 310$	Nurse contact $N = 103$	Both GP and nurse $N = 129$	*P*-Value
Comorbidity-related information recorded n (%)					
BMI	8 (1.5)	3 (1.0)	3 (2.9)	2 (1.6)	0.365
Overweight	7 (1.3)	5 (1.6)	0	2 (1.6)	0.435
Obesity	5 (0.9)	4 (1.3)	0	1 (0.8)	0.485
Sleep apnea					
- suspected, not diagnosed	2 (0.4)	0	1 (1.0)	1 (0.8)	**0.019**
- diagnosed	4 (0.7)	0	3 (2.9)*	1 (0.8)	
Chronic/allergic rhinitis or its symptoms	48 (8.9)	30 (9.7)	6 (5.8)	12 (9.3)	0.481
Sinus infections or nasal polyps	29 (5.4)	19 (6.1)	3 (2.9)	7 (5.4)	0.450
Recurrent sinus infections	5 (0.9)	5 (1.6)	0	0	0.151
Reflux symptoms	6 (1.1)	5 (1.6)	1 (1.0)	0	0.335
NSAID intolerance	3 (0.6)	1 (0.3)	1 (1.0)	1 (0.8)	0.690
Lifestyle-related factors recorded n (%)					
Exercise habits	88 (16.2)	30 (9.7)	30 (29.1)*	28 (21.7)*	**<0.001**
Diet	5 (0.9)	1 (0.3)	1 (1.0)	3 (2.3)	0.135
Alcohol consumption	1 (0.2)	0	0	1 (0.8)	0.201

Statistically significant *p*-values are presented in bold.
*$p < 0.05$ compared to group doctor contacts.

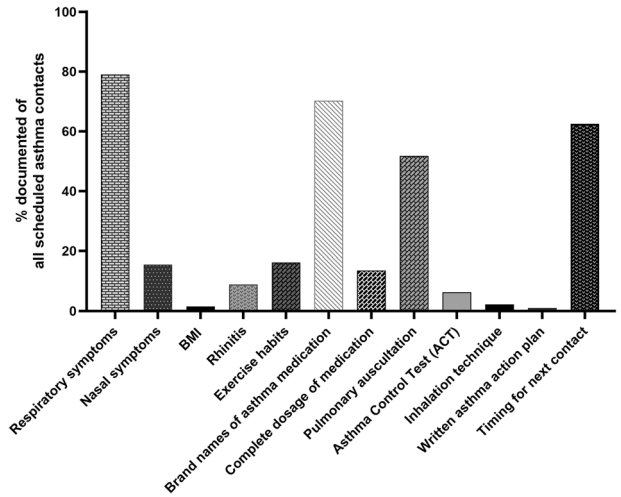

Fig. 2 Documentation of asthma management details in scheduled asthma contacts in PHC during 12-year follow-up. The total number of contacts was 542.

Of all scheduled asthma contacts, the timing for the next scheduled follow-up contact was recommended in 62.5% of contacts and more often when the GP or both professionals were involved. In contrast, an asthma action plan (AAP) was recorded in only 5.0% of contacts (Table 3), and of all patients, only 24 (16.6%) had an AAP documented during the 12-year follow-up (eTable 3). Guidance on lifestyles (to lose weight, to increase exercise, or to reduce alcohol intake) was also rarely documented (Table 3).

DISCUSSION

In this 12-year, real-life, follow-up study we showed that comorbidities, lifestyle factors, inhalation technique, and asthma action plan were poorly documented during scheduled asthma contacts ($n = 542$) in PHC in Finland. The most frequently recorded asthma details were respiratory symptoms (79%), asthma medication brand names (70%), and the recommendation for the timing of the next follow-up contact (62.5%). All these details were found even more often if the nurse and GP both participated in the contact. Rhinitis was the most-often documented comorbidity, but it was registered only in 8.9% of all contacts. Recorded information on possible lifestyle guidance interventions given to the patients was found in <1% of contacts. Results from this longitudinal study may help to identify potential health-care practice-related causes of uncontrolled and difficult-to-treat asthma, and which areas require more urgent training and attention.

Obesity has been shown to be associated with uncontrolled and severe asthma[1–3,27,49–51], poorer work ability[12], lower lung function, more dispensed oral corticosteroids with higher doses, and higher health-care costs[50], and it is a risk factor for asthma exacerbations even in patients with few symptoms[1]. Adult patients with asthma are at a higher risk of developing obesity[52]. Moreover, obesity has been shown to be a permanent problem in more than 85% of adult patients with asthma in long-term follow-up[50]. Weigh reduction in obese adults, also after bariatric surgery[53], has shown to lead to overall improvement in asthma control, including airway hyper-responsiveness and inflammation[54]. We showed in this study that professionals rarely documented information about a patient's BMI, overweight, or obesity. According to documented information, patients received no guidance in relation to obesity-related lifestyle factors during long-term follow-up, even though these factors are also shown to contribute to asthma independently. For example, low physical activity is associated with faster lung function decline[18], dietary components are suggested to affect immune pathways in asthma[55], and prolonged and heavy alcohol exposure may impair mucociliary clearance and may complicate asthma management[56]. A previous study based on physicians' self-reports regarding clinical practice indicated that, overall, very few GPs assessed asthma patients' lifestyle factors[34], which is in line with our results. Overall, based on documented patient data, lifestyle

Table 3. Documentation of asthma management details during scheduled asthma contacts ($n = 542$) and according to professional encountering the patient at follow-up contact.

	All scheduled contacts $N = 542$	GP contact $N = 310$	Nurse contact $N = 103$	Both GP and nurse $N = 129$	*P*-Value
Asthma assessment performed					
Respiratory symptoms *n* (%)	428 (79.0)	237 (76.5)	79 (76.7)	112 (86.8)*‡	**0.043**
Nasal symptoms *n* (%)	84 (15.5)	54 (17.4)	13 (12.6)	17 (13.2)	0.358
Work effect on symptoms assessed *n* (%)	53 (9.8)	37 (11.9)	5 (4.9)	11 (8.5)	0.096
Pulmonary auscultation *n* (%)	281 (51.8)	226 (72.9)‡∞	0	55 (42.6)‡	**<0.001**
ACT *n* (%)	34 (6.3)	5 (1.6)	9 (8.7)*	20 (15.5)*	**<0.001**
Medication recorded					
Asthma medication *n* (%)					
- Drug/brand names	381 (70.3)	198 (63.9)	77 (74.8)*	106 (82.2)*	**<0.001**
- Drug/brand names at least partially	483 (89.1)	273 (88.1)	88 (85.4)	122 (94.6)	0.056
- Complete dosage of asthma medication	73 (13.5)	49 (15.8)‡	8 (7.8)	16 (12.4)‡	**0.028**
- Dosage of asthma medication at least partially	350 (64.6)	207 (66.8)‡	54 (52.4)	89 (69.0)‡	**0.015**
- Inhalers	62 (11.4)	37 (11.9)	8 (7.8)	17 (13.2)	0.199
- At least some of the inhalers	183 (33.8)	114 (36.8)	25 (24.3)	44 (34.1)	0.067
Asthma medication changed in some way	145 (26.8)	112 (36.1)‡∞	5 (4.9)	28 (21.7)‡	**<0.001**
Possible side-effects evaluated	31 (5.7)	19 (6.1)	2 (1.9)	10 (7.8)	0.149
Inhalation technique *n* (%)					
- Mentioned	12 (2.2)	1 (0.3)	9 (8.7)*∞	2 (1.6)	**<0.001**
- Revised	12 (2.2)	1(0.3)	8 (7.8)*	3 (2.4)	**<0.001**
Nasal medication *n* (%)					
Started or changed	23 (4.2)	17 (5.5)‡	0	6 (4.7)	**0.024**
Already in use, no changes	75 (13.8)	34 (11.0)	16 (15.5)	25 (19.4)	
Medication for reflux symptoms *n* (%)					
Started	2 (0.4)	2 (0.6)	0	0	0.528
Already in use	7 (1.3)	5 (1.6)	0	2 (1.6)	
Patient guidance recorded					
Lifestyle factors *n* (%)					
- Recommendation to lose weight	5 (0.9)	4 (1.3)	0	1 (0.8)	0.485
- Recommendation to increase exercise	3 (0.6)	2 (0.6)	1(1.0)	0	0.579
- Recommendation to reduce alcohol use	1 (0.2)	0	1 (1.0)	0	0.118
Asthma action plan mentioned *n* (%)[a]	27 (5.0)	14 (4.5)	5 (4.9)	8 (6.2)	0.759
- Verbal AAP	22 (4.1)	14 (4.5)	3(2.9)	5 (3.9)	0.055
- Written AAP	2 (0.4)	0	0	2 (1.6)	
- Both verbal and written AAP	3 (0.6)	0	2 (1.9)	1 (0.8)	
Recommendation for the timing of the next scheduled contact *n* (%)	339 (62.5)	198 (63.9)	53 (51.5)	88 (68.2)‡	**0.025**

Statistically significant *p*-values are presented in bold.
ACT asthma control test, *AAP* asthma action plan.
*$p < 0.05$ compared to group doctor contacts.
‡$p < 0.05$ as compared to group nurse contacts.
∞$p < 0.05$ as compared to group both GP and nurse contact.
[a]Asthma action plan (AAP) = Written and/or verbally given description of how an individual should manage asthma, including advice for changes in medication, if necessary, and a plan for contact with the healthcare system.

factors were poorly registered; however, nurses mentioned exercise habits in almost every third contact. Lifestyle guidance was more the nurse's responsibility in previous national and local asthma programmes, which may explain this result.

Allergic rhinitis is known as a predominant comorbid disease in difficult-to-treat asthma[36,49]. Chronic rhinosinusitis is known to be an independent predictor of asthma exacerbation among patients with difficult asthma[9,57]. Considering the unity of the upper and lower respiratory tract, the concept called 'united airways', screening and treating of rhinitis and other nasal conditions in asthma is important[57,58]. Thus, evaluating possible nasal symptoms and adherence to nasal medication should be assessed in every asthma contact. Medications treating nasal diseases have also been shown to be useful in improving control of asthma and reducing bronchial hyper-responsiveness[58]. A recent study showed that approximately 67% of the patients with moderate-severe rhinitis were not using the recommended intranasal corticosteroid therapy[36]. Aligning with previous studies[35,36], our results showed that even though rhinitis is highly prevalent[49], its screening and treatment in patients with asthma was suboptimal

in PHC. In our study 70% of patients had rhinitis but it was recorded in less than every tenth and, overall, nasal symptoms less than in every fifth contact. The initiation of rhinitis treatment was rare. Based on recorded nasal medication data, over half of the patients with rhinitis may have been undertreated when medication for chronic rhinitis has been available only with a doctor's prescription. Documentation of reflux symptoms, OSA and intolerance to NSAIDs was similarly underperformed, despite all these conditions being associated with severe asthma, poor symptom control, and more frequent exacerbations and hospitalisations[8,10,51,59,60]. NSAIDs (including aspirin) may exacerbate asthma symptoms in patients with N-ERD (NSAID-exacerbated respiratory disease), a chronic eosinophilic inflammatory disorder of the respiratory tract occurring in patients with asthma and/or rhinosinusitis with nasal polyps[10]. A recent study showed that the prevalence of N-ERD was 6.9% among asthmatics[60], while the prevalence of gastroesophageal reflux varies between 17–74%[7,9] and the prevalence of OSA ~39–50%[6,9]. Reflux disease and OSA may arguably have been underdiagnosed in our study population, considering a majority have a BMI > 25. OSA was probably not yet well known in PHC during the current study's time period, and recognition improved after the national sleep apnea programme in Finland (2002–2010)[61].

The results in this and our previous studies[22,32] suggest that implementation of the Finnish National Asthma Programme's[31] main objectives has been partially successful in PHC, but room still exists for improvement (Fig. 3). We found in this study that screening of asthma symptoms as a part of asthma control assessment has been managed well in PHC. Cloutier et al.'s previous study[30] showed that physicians monitor selected symptoms depending on the symptom, from 48.4% to 56.0%. We were unable in this study to assess more precisely the extent of the symptoms' evaluation and of the patients' true symptom burden; thus, more research regarding this issue is needed in the future. Patients have been shown to overestimate their asthma control[36], which supports assessing asthma control using objective methods such as lung function tests together with symptom questionnaires. ACT documentation was rarely found in our study, similar to previous studies in which validated patient-reported questionnaires were rarely used to monitor asthma control[28,30]. ACT was not yet in wide use in Finland during the SAAS study period, which probably explains our results to some extent. Pulmonary auscultation was recorded in almost 3 of 4 physicians' contacts but never in nurses' contacts, which is explained by the fact that pulmonary auscultation is usually performed only by a doctor in Finland.

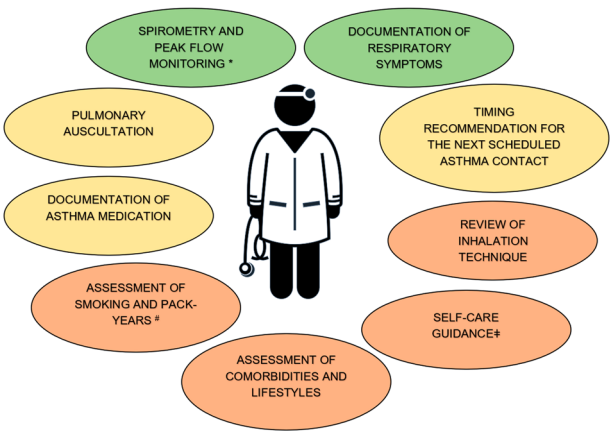

Fig. 3 The content of the asthma follow-up contacts in PHC. Green colour describes the performed assessment that were implemented well, yellow colour describes moderate implementation, and the orange describes the measures that are poorly implemented. *Takala et al.[22]. #Takala et al.[32]. ‡Self-care guidance includes patient asthma action plan instructions and lifestyle guidance.

It is essential that the complete asthma medication information, including names, doses and inhalers, is documented in patient records for continuity of care, because the professional responsible for patient care may change. The common electronic patient record system was not yet in use in our region during the SAAS study period, and some patients still had handwritten paper prescriptions in addition to those that were prescribed through the electronic patient health record system. As a result, the patient health record system did not necessarily have an up-to-date medication list or information about possible changes to medication made elsewhere, which also advocates for the importance of recording medication information. Asthma medication brand names were mentioned in 70% of scheduled contacts in our study, but dosage and inhalers were documented in only <14% of contacts. Only doctors had the right to prescribe medicines during the study period, which explains why medication changes were more common in visits when a GP was involved. This study and our previous studies[22,23], show that patients with ≥2 scheduled contacts in PHC had high mean adherence to ICS medication (>80%), and their adherence level was higher compared to patients who had mainly follow-up contacts in secondary care (82% vs. 52%)[23]. Higher adherence was associated with non-controlled disease in SAAS-study population, while total adherence <80% was associated with more rapid lung function decline in not-controlled disease[62]. Our results suggest that professionals in PHC are good at promoting adherence to asthma medication. We were unable in this study, unfortunately, to assess in more detail how medication adherence was evaluated and if discussion supporting adherence to treatment, occurred at the contacts. The names of the medications in use were recorded well and adherence was high, so it can be assumed that treatment compliance in medication was discussed in the follow-up contacts to some extent. It could be speculated that continuity of care may be one reason for the good adherence when it was also shown that the recommendation for the timing of the next scheduled contact was documented in over 62% of contacts and in almost 70% if both professionals were attending.

Incorrect inhaler technique is common and can lead to poor asthma control[1]. Previous studies from Sweden and Finland showed that 87–97% of patients reported that they had received education about inhalation technique[24,63]. Another study from Australia revealed that patients overestimated the true success of their own inhalation technique when 73% of patients believed they did well, whereas an objective assessment showed that all patients had at least two errors and over 70% exhibited five or more errors[36]. In studies from the U.S. and Australia, 17–30% of PHC clinicians reported assessing inhaler technique[30,34], but based on documented and reported patient data, only 1–5% of patients had their inhaler technique checked[21,36], which is in line with our results. Checking the inhalation technique is usually the nurses' task in the Finnish health care system, but still, according to recorded patient data, this was performed in approximately only 8% of nurse contacts, which is alarming.

AAP is a description of how an individual should manage asthma, including advice for medication changes, if necessary, and a plan for contact with the health-care system[20]. Use of written action plans is suggested to be poor both in PCH and in secondary care[33] and shown to vary from 0 to 50%[21,28,30,33,34]. A previous study from Finland showed that over 78% of adult asthmatics reported having an asthma self-management plan[24], but based on our results, AAP was not assessed or updated during planned contacts according to documented data. Recorded information on AAP was found in only 5% and written action plan in 1% of contacts, which can be considered surprising when one of the Finnish Asthma Programme's most important goals was patients' self-care guidance, including provision of both written and verbal

asthma action plans[31]. Every patient in the SAAS study population received both verbal and literal asthma guidance, usually immediately upon asthma diagnosis confirmation in the respiratory department. Thus, could be argued whether the existence of an AAP was considered self-evident in PHC; however, it does not justify the omission of an AAP assessment. Chapman et al. suggested that physicians tend to rely upon advances in pharmacological intervention to improve the quality of asthma care rather than the non-pharmacological aspects of asthma management[28]. Our results showing that AAP and lifestyle interventions were poorly implemented in scheduled follow-ups in PHC support that. A recent UK study showed that many factors, such as poor attendance at asthma clinics, lack of time, demarcation of roles, limited access to a range of resources and competing agendas in consultations that are often due to multimorbidity, may increase the risk that self-care guidance is not provided during contacts[64]. These potential barriers are important to recognise when developing asthma monitoring and treatment guidance in the future.

This study's major strength is its use of a real-life, unselected, adult-asthma population when patients with smoking or comorbidities were not excluded. Thus, our study population represents a typical PHC population with asthma[37,65]. Their asthma diagnosis was originally made by a respiratory physician based on typical symptoms and objective lung function measurements showing reversibility of airway obstruction[37]. All scheduled asthma contacts in PHC were evaluated in this study, including both nurse and GP visits, and the overall number of scheduled contacts may be expected to yield a representative sample of a real-life, adult-asthma population. We acknowledge that the significance of comorbidities in asthma control was perhaps not as well understood in 2002 compared to today. However, all the comorbidities with the exception of OSA, as well as other asthma management details evaluated in this study, have already been discussed in the first Finnish asthma guideline in 2000 and also e.g., in the GINA 2002 recommendation[66,67]. Therefore, it can be estimated that PHC has had opportunities to apply the best evidence-based practices during the study's period. This study's results are valuable because long-term, real-life, follow-up studies of adult-onset asthma in PHC are rare. Our results help to understand the possible health-care-related causes behind uncontrolled and difficult-to-treat asthma, e.g., which areas in assessing asthma require more specific training and attention.

A possible weakness of our study is that, e.g., comorbidities and other asthma-related details evaluated may have been screened and discussed during scheduled contacts or assessed earlier in other contexts, but these data have not been recorded. However, according to good clinical practice, the measures taken shall be recorded; otherwise, it can be interpreted that this has not been performed, or that the existence of the matter and its possible connection has not been considered. Additionally, regarding continuity of care, it is important that patient document entries are done well. We were unable in this study to assess more precisely either the extent of symptoms' evaluation or the content of AAP instructions. Other important aspects of asthma care were not assessed in this study, such as exacerbations and trigger avoidance. More research is needed to evaluate these topics. Another limitation of our study is that our results may not represent Finland entirely, and it may not reflect the current situation, because the data were collected between 2002–2013. No common national asthma template is in use, and the recording practices may also differ regionally, e.g., due to different electronic health record systems. The use of ready-made phrase templates has become more common since the SAAS study period, which may have improved screening and assessment of asthma control-related issues. However, problems with accessibility to PHC have been increasing[48,68], and it is very likely that asthma treatment and follow-up is largely carried out during visits for other conditions or for other reasons. A new, long-term follow-up study from the 2010s to 2020s would be needed to assess the current situation and whether asthma assessment has improved since the follow-up period in this study. Asthma control was defined according to GINA 2010 criteria at the 12-year follow-up visit, and asthma severity was classified according to the ERS/ATS 2014 guideline[42,43]. We consider it correct to use the data as they were collected and evaluated at the clinical visit on asthma control and as used in the original SAAS study material, even if asthma control and asthma severity criteria have change since then.

Regular monitoring is important when adult-onset asthma is often in non-remission[2–4]. The causes of poor asthma control can be complex[1,5], and as shown in this study, based on documented patient data, the systematic assessment of asthma should be further improved in scheduled asthma contacts. However, our results also suggest that need exists to pay more attention to the quality of patient document entries in PHC in Finland[69]. Based on this study, the importance of screening and treating asthma-related comorbidities in PHC should be given more attention, especially those associated with uncontrolled and severe asthma. Documentation and follow-up of BMI data, together with guidance on healthy lifestyles and weight management, should be emphasised more in asthma guidelines as part of routine management. Reviewing asthma inhaler technique and patient self-care guidance are also central areas needing improvement. Based on these results, it is obvious that health-care personnel need continuous training in asthma management. In general, evaluation of lifestyle factors, patient guidance, lung function test performance, and revision of inhalation techniques have largely been the nurse's responsibility, while the doctor's task has been more to assess asthma control, medication, and patients' personal treatment recommendation. The regular asthma follow-up could be carried out largely by the nurses, because not every patient needs a doctor's assessment every year if their asthma is well controlled. Nevertheless, the nurse can gather information to assess asthma control and consult the doctor if needed. Asthma is one of our most common chronic diseases, but one could speculate whether its assessment is considered as important as, e.g., cardiovascular diseases, and whether possible multimorbidities[11,14] divert attention from asthma itself. The establishment of 21 well-being services counties to replace the former hospital districts since the beginning of 2023 in Finland has provided a new basis for developing uniform health-care services covering larger regions. It would be possible in this context to develop and update uniform asthma treatment chains covering entire regions and even to implement national asthma templates and educate professionals in systematic asthma assessment. This could improve asthma management. Further promoting the use of structured phrase templates could support asthma assessment in scheduled contacts, because it has been shown that evidence-based EMR interventions improve the asthma documentation and provision of asthma care[70]. In addition, shorter and clearly structured guidelines could be easier to implement in PHC[71]. Given the complexity of asthma care, sufficient time and resources for asthma assessment must be guaranteed for comprehensive evaluation and patient guidance to be successful. More research is needed to evaluate the overall asthma care that is currently obtained in all asthma-related contacts in PHC and to guide health-care personnel education regarding asthma monitoring in the future.

In conclusion, we showed in this real-life, 12-year, follow-up study that comorbidities, lifestyle factors, inhalation techniques, and asthma action plans were poorly documented in scheduled asthma contacts in PHC. Our results, based on documented patient data, suggest that the comprehensive assessment and guidance of asthma patients still needs to be improved in PHC.

DATA AVAILABILITY

All data generated or analysed during this study are included in this published article and its Supplementary Information File. According to ethical permission and patient data-protection laws of Finland, single patient data cannot be made available.

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AUTHOR CONTRIBUTIONS

This study is a part of Seinäjoki Adult Asthma Study. J.T. contributed to the study design, analysed, and interpreted the data, draw the pictures to this article and wrote the manuscript. L.E.T., PI., and H.K. contributed to the study design and guided the work. I.V. contributed to the computation of adherence and SABA use and provided statistical advice. O.N. contributed to the laboratory analyses. All authors accept full conduct of the study and critically revised the manuscript. All authors have read and approved the final version of the manuscript.

COMPETING INTERESTS

None of the authors declares any competing interests concerning this article. J.T. reports personal fees from NovoNordisk, Novartis, AstraZeneca, and Sanofi outside the current work. I.V. reports personal fees from AstraZeneca outside the current work. L.E.T. reports personal fees from GSK and Boehringer-Ingelheim outside the current work. P.I. is employed by GSK as scientific advisor. H.K. reports fees for consultancies and lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi Pharma, Covis Pharma, GSK, Medscape, MSD, Novartis, Orion Pharma and SanofiGenzyme outside the current work. O.N. declares that he has no relevant conflicts of interest.

ADDITIONAL INFORMATION

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