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Clinical Characterization of Bronchial Asthma in Elderly and Non-Elderly Patients: the relevance of clinical phenotypes

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Dedicatória

Aos meus pais e avó por terem investido na minha educação e formação profissional e por me acompanharem ao longo deste longo percurso, incentivando-me a cada minuto, a fazer mais e melhor.

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Abstract

Background: Bronchial Asthma is a chronic inflammatory disease that affects about 300 million people worldwide. It is extremely important to compare clinical and functional features of asthma between elderly (EA) and non elderly (NEA) patients because several aspects of the diagnosis are different. Furthermore, in elderly asthmatic patients, late-onset (LOA) / adult-onset asthma (AOA) seems to be more frequent than long standing (LSA) / early-onset (EOA) / childhood-onset asthma (COA) and the former may be more frequently associated with more severe forms of asthma. In addition, in elderly patients, asthma frequently co-exists with other heart and lung diseases, particularly with chronic heart failure and chronic obstructive pulmonary disease (COPD). Thus, a thorough study of the clinical characteristics of bronchial asthma, taking into account the age of onset could help to clarify undervalued aspects of the clinical expression of the disease as well as different profiles of expression that are associated with clinical phenotypes. Such characterization may contribute towards better control of the disease as improvement in quality of life, once the appropriately tailored medication, taking into consideration phenotypic differences is given, particularly in the elderly.

Methods: Analytic and cross-sectional study in which the target population was composed of individuals with a confirmed diagnosis of asthma, who were either between 18-64 years or 65 years or older and were regularly followed up at an Immunoallergology or Pulmonology outpatient clinic of CHCB. All volunteers answered a questionnaire about personal and family history of respiratory disease, current and past occupational exposure, characterization of the place of residence, co-morbidities, usual medication, asthma triggers, number of acute crises and admittance to wards, principal symptoms and their frequency, asthma control medication, among other factor. Results were analyzed using the Software Package for Social Sciences (SPSS).

Results: Overall, 192 volunteers were included, with a median age of 59.1 years and predominantly of the female gender. Most patients were smokers, had a low level of schooling and social class and lived in urban areas. The predominant phenotype found was that of LSA/EOA/COA in association with atopic asthma, and mostly only partially or not controlled. For EA patients, the most prevalent and associated phenotypes were LOA/AOA with non-atopic asthma. In contrast, for NEA patients the most predominant phenotype was the combination of LSA/EOA/COA with atopic asthma. In terms of co-morbidities, rhinitis or a combination of rhinitis with dermatitis was significantly more common in the LSA/EOA/COA phenotype. In addition, a previous history of allergies was more frequently reported in EA patients with the LSA/EOA/COA phenotype. In terms of quality of life, NEA patients with

LOA/AOA phenotype were 4.48 times more likely to have limitation of activities caused by dyspnoea than NEA patients with the LSA/EOA/COA phenotype. On the other hand, the LOA/AOA phenotype was more frequently associated with limitation of activities caused by coughing and a higher frequency of wheezing manifestation (more than twice weekly) as well as having to use short-acting beta2-agonist (SABA) rescue medication. On the other hand, the beta2-agonists long-action (LABA) and anti-leukotrienes were more frequently associated with LOA/AOA.

Conclusion: LOA/AOA and LSA/EOA/COA phenotypes have significant differences in terms of manifestations of severity, family history of diseases and control medication. Nevertheless, these phenotypes may manifest to a similar extent, in different age groups.

Keywords

Bronchial Asthma; Clinical Characterization; Phenotypes; Elderly; Non-elderly;

Resumo

Introdução: A Asma brônquica é uma doença inflamatória crónica, que afeta cerca de 300 milhões de pessoas em todo o mundo. É extremamente importante comparar a asma nos idosos e nos não idosos, porque vários aspectos relativos ao diagnóstico são diferentes. Além disso, nos asmáticos idosos, a asma de início tardio (LOA) / asma com início na idade adulta (AOA) parece ser mais frequente do que a asma de longa duração (LSA) / Asma com início precoce (EOA) / Asma com início na infância (COA) e o primeiro fenótipo pode ser associado a formas mais severas da doença. Adicionalmente, a asma nos idosos coexiste com outras doenças respiratórias e pulmonares, particularmente a doença pulmonar obstrutiva crónica. Assim, o estudo mais aprofundado das características clínicas da asma brônquica, tendo em conta o início da manifestação dos sintomas poderá ajudar a clarificar aspetos subvalorizados na expressão clínica da doença, bem como diferentes perfis de expressão associados a fenótipos clínicos. Tal caracterização poderá contribuir para a melhoria da qualidade de vida e um melhor controlo da doença com a medicação adequada às diferenças fenotípicas, principalmente nos idosos.

Métodos: Estudo analítico e transversal cuja população era constituída por pacientes com diagnóstico de Asma Brônquica confirmado, com idades entre os 18-64 anos e 65 anos ou mais velhos, regularmente seguidos nas consultas de Imunoalergologia ou Pneumologia do Centro Hospitalar Cova da Beira (CHCB). Todos os voluntários responderam a um questionário sobre a história pessoal e familiar de doença respiratória, exposição ocupacional actual e passada, caracterização da residência, comorbilidades associadas, hábitos medicamentosos, factores desencadeantes, número de crises agudas e internamentos, principais sintomas e a sua frequência, medicação de controlo da doença, entre outros. Os resultados foram analisados através do Pacote de Software para Ciências Sociais (SPSS).

Resultados: Foram incluídos 192 voluntários, com idade média de 59.1 anos e predominantemente do sexo feminino. A maioria era fumadora, tinha um baixo nível de escolaridade e classe social, e residiam predominantemente em meio urbano. A maior parte dos pacientes tinha LSA/EOA/COA e asma atópica e apenas controlo parcial ou não controlo da asma. Nos idosos, o fenótipo LOA/AOA foi associado à não atopia, enquanto que, para os não idosos, verificou-se a associação do fenótipo LSA/EOA com a atopia.
A presença de rinite ou da combinação da rinite e dermatite foi significativamente maior no fenótipo LSA, tal como a história de alergias nos pacientes idosos com este fenótipo. Um paciente jovem com LOA apresenta 4.48 vezes mais probabilidade de apresentar limitação das atividades causadas por dispneia. Também se observou que o fenótipo LOA estava mais frequentemente associado à limitação de actividades físicas, causada por tosse, e a uma maior frequência de manifestação da pieira (mais do que duas vezes por semana), tal como o

uso de agonistas beta2-ação curta. Por outro lado, os beta2-agonitas de ação longa e o uso de anti-leucotrienos associaram-se à LOA/AOA.

Conclusões: Os fenótipos LOA/AOA e LSA/EOA/COA apresentam diferenças significativas relativas à severidade das manifestações da asma, história familiar de doenças e medicação de controlo. De uma maneira geral, manifestam-se de igual modo nos diferentes grupos etários.

Palavras-chave

Asma Brônquica, Caraterização Clínica, Fenótipos, Idosos, Não Idosos.

Resumo Alargado

Introdução: A Asma brônquica é uma doença inflamatória crónica, que afeta cerca de 300 milhões de pessoas, em termos mundiais, e a sua prevalência tem vindo a aumentar em muitos países e a estabilizar noutros, em níveis relativamente elevados. É extremamente importante comparar a asma nos diferentes grupos etários, pelas diferenças associadas ao seu diagnóstico. Por exemplo, nos idosos pode coexistir com outras doenças pulmonares ou cardíacas, nomeadamente, a doença pulmonar obstrutiva crónica. Também neste grupo, as manifestações clínicas mais frequentemente associadas à asma brônquica – dispneia, tosse e sibilâncias intermitentes podem não ser tão aparentes e a sua importância é minimizada ao ser atribuída "à idade" ou serem mascaradas por co morbilidades. Assim, o estudo mais aprofundado das características clínicas da asma brônquica nos idosos, comparando-os com a população mais jovem, poderá ajudar a clarificar aspetos subvalorizados na expressão clínica da doença, bem como diferentes perfis de expressão dos sintomas, associados a diferentes fenótipos clínicos, tendo em conta a idade de início da manifestação dos sintomas. Tal caracterização poderá contribuir para a melhoria da qualidade de vida e um melhor controlo da doença com a medicação adequada nos asmáticos. Existem poucos estudos comparativos sobre a expressão clínica de asma brônquica nas duas faixas etárias, e particularmente nos idosos, o que, em Portugal e em outros países, será uma falha relevante dada a percentagem crescente de população envelhecida que apresentam.

Metodologia: Estudo analítico e transversal cuja população era constituída por pacientes com diagnóstico de Asma Brônquica confirmado, com idades entre os 18-64 anos e 65 anos ou mais velhos, regularmente seguidos nas consultas de Imunoalergologia ou Pneumologia do Centro Hospitalar Cova da Beira (CHCB), Covilhã. Alguns dos pacientes também foram contactados por via telefónica para comparecerem no Hospital. Todos os voluntários responderam a um questionário sobre a história pessoal/familiar, exposição actual/passada a fatores desencadeantes, caracterização da residência, comorbilidades associadas, hábitos medicamentosos, número de crises agudas e internamentos, principais sintomas e a sua frequência, medicação de controlo da doença, ACT, CARAT, entre outros. Os resultados foram analisados através do Pacote de Software para Ciências Sociais (SPSS),versão 23.0. Um valor-*p* inferior ou igual a 0,05 foi considerado significativo em todos os testes estatísticos.

Resultados: Foram incluídos 192 voluntários, com idade média de 59.1 anos e predominantemente do sexo feminino. A maioria era fumadora, tinha um baixo nível de escolaridade e classe social, e residiam predominantemente em meio urbano. A maioria da população em estudo tinha LSA/EOA/COA e asma atópica e tinha apenas controlo parcial ou não controlo da asma.

A presença de rinite ou da combinação da rinite e dermatite foi significativamente maior no fenótipo LSA/EOA/COA, tal como a história de alergias nos pacientes idosos com este fenótipo. Nos pacientes idosos, o fenótipo predominante foi a associação de LOA/AOA com asma não-atópica. Contrariamente, nos não idosos, foi a combinação do fenótipo LSA/EOA/COA com asma atópica. Em termos de qualidade de vida, um paciente jovem com AOA apresentava uma probabilidade 4.48 vezes maior de ter limitação das atividades causada por dispneia. Também se observou que o fenótipo LOA/AOA estava mais frequentemente associado à limitação da actividade causada por tosse e a uma maior frequência de manifestação da pieira (mais do que duas vezes por semana), tal como o uso de agonistas beta2 de ação curta (SABA). Por outro lado, o uso de agonistas beta2 de ação longa (LABA) associou-se preferencialmente à AOA, tal como o uso de anti-leucotrienos.

Conclusões: O fenótipo mais frequente na população geral foi o de asma com início na infância/adolescência, predominantemente atópica e surgindo no sexo feminino. Os fenótipos LOA/AOA e LSA/EOA/COA apresentaram diferenças significativas relativamente à severidade das manifestações da asma, história familiar de doenças e medicação de controlo. Contudo, de uma maneira geral, estes fenótipos manifestavam-se clinicamente de igual modo nos diferentes grupos etários.

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Lista de Acrónimos

ASA – acetylsalicylic acid
ACES CB – Cova da Beira Health Centre
ACT – The Asthma Control Test
BA – Bronchial Asthma
BB – beta blockers
CARAT – The Control of Allergic Rhinitis and Asthma Test
CES-D – Center for Epidemiologic Self-Report Depression Scale
CHCB – Cova da Beira Academic Hospital Centre
CHF – Congestive heart failure
COPD – Chronic Obstructive Pulmonary Disease
DM – Diabetes mellitus
FCS-UBI – Faculty of Health Sciences of the University of Beira Interior
GDS–15 – Geriatric Depression Scale
GERD - Gastro-esophageal Reflux Disease
HBP – High Blood Pressure
HrQoL – Health related Quality of Life
IC – Inhaled Corticosteroid
EA – Elderly asthmatic
NEA – Non- elderly asthmatic
LABA - Long-acting Beta2-Agonist
LOA - Late Onset Asthma
LSA – Long Standing Asthma
MMES – The Mini-Mental Examination State
NIA – Non-elderly asthmatic
NINA - Non-elderly non-asthmatic
OSA – Obstructive Sleep Apnea Syndrome
QoL – Quality of Life
SABA – Short-acting Beta2-Agonist
SF36 - Short Form Health Survey
SPSS - Software Package for Social Sciences
UBI – Universidade da Beira Interior
WHO – The World Health Organization

1. Introduction

Bronchial asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation (1).

The prevalence of asthma is increasing in many areas of the globe and affects about 300 million people worldwide, having substantially the same prevalence in both sexes (1,2). Asthma is the 14th most important disorder in the world in terms of extent and duration of disability, often causing a reduced quality of life (3). Furthermore, although, over time, deaths from asthma have globally decreased, they tend to occur most often in the elderly (3).

In Portugal, around 10.5% of the residents are asthmatic (4, 36). According to the *4º Inquérito Nacional de Saúde*, from 2005/06, 7.2% of the elderly have asthma, most of whom are women (65.9%) (2). Nevertheless, data concerning the elderly may underestimate the true prevalence of asthma since several studies have suggested that Asthma in this age group remains poorly perceived, poorly recognized and sub-optimally treated (3, 4).

Given these facts and knowing that disease can vary individually (6), it is increasingly important to study the possible phenotypes to find similarities and differences between them. A precise definition of asthma phenotypes may further improve our understanding of underlying genetic basis, pathophysiologic mechanisms, treatment response and prognosis (28). Currently, asthma phenotypes are defined as the integration of different characteristics that are the product of the interaction of the patient's genes with the environment (27), based on a variety of clinical presentations, physiological characteristics, and responses to therapy. This classification could be based on age of onset of manifestations, the presence of atopy, inflammatory markers, among other (7, 27).

Previous studies suggest that factors such atopy, age of onset, duration of illness and comorbid conditions are possible determinants of different phenotypes observed in severe persistent asthma (7) as well as in other forms of asthma (1).

Asthma more frequently begins in childhood, with an incidence peak at around 3 years of age (3). Nevertheless, many cases begin later in life, namely in adulthood. According to the age of onset and duration of asthma it is possible to divide asthmatics into those with early-onset, long-standing asthma (LSA), and those with late-onset asthma (LOA). However, there are discrepant definitions of the specific threshold age that discriminates between these two subtypes (8), with some studies stating that LOA is the subtype that arises after 40 years of age (9), whereas other studies define the threshold at as early as 12 years of age (8). Generally, LSA begins in childhood or adolescence and LOA begins in adulthood (10). An

additional, related possibility is to define onset-related phenotypes according to 16 or 18 years of age, with asthma beginning earlier than that period being defined as early-onset or childhood-onset asthma (EOA / COA), and asthma that begins later than that being defined as late-onset or adult-onset asthma (AOA) (8). In the current study, asthma that had begun before 18 years was regarded as EOA/COA and asthma that had begun later than that being labelled as AOA (9). Thus, in our study, AOA is generally equivalent to LOA and EOA/COA is generally superimposable upon LSA.

Some studies have shown that AOA / LOA is more common in the female gender, has a low remission rate and is less often associated with allergy and atopic diseases (10). In fact, it has been reported that AOA / LOA patients are a mixed group of patients and different sub-phenotypes may be identified (39). Some studies were able to subdivide LOA/AOA into five different subtypes, based upon cluster analysis: eosinophilic inflammation predominant asthma, mild-to-moderate-well controlled asthma, obese-noneosinophilic asthma, smoking asthma and severe obstructive asthma (20). Although LSA/COA/EOA patients may represent a relatively more homogeneous group of patients, often with a strong allergic history and family history of asthma (7), there are also different clinical sub-phenotypes that have been reported (1).

Thus, LSA/COA/EOA and LOA/AOA may have different clinical presentation, disease course and response to treatment (2, 10, 39). Although they share some common features, they may have different causes and very different prognoses.

It is also advantageous to characterize asthma in terms of atopy, in order to optimize management of disease. Atopic/extrinsic asthma is characterized by the manifestation of symptoms when patients are exposed to allergenic triggers and is generally associated with rhinitis, atopic dermatitis or other allergies. It generally begins in childhood and is therefore more likely to be associated with EOA/COA/LSA whereas non-atopic/intrinsic asthma generally begins in adulthood, may be preferentially associated with occupational or viral exposures and is more likely observed in LOA/AOA patients (11,12).

Independently of the phenotypes in question, investigation of clinical features of asthma in the elderly may be difficult. In fact, a diagnosis of asthma in the elderly may be harder to confirm due to several diseases that may also cause breathlessness, and may be confounding factors, such as chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) (16). Furthermore, elderly patients tend to assume that breathlessness is due to advanced age, which may have implications such as poor management of asthma and a negative impact on quality of life (3). Many studies demonstrated efficacy of adequate asthma treatment in reducing symptoms and exacerbations, thereby improving health-related quality of life and lung function, achieving asthma control, controlling airway inflammation, and reducing mortality rates (35). Recent evidence has further suggested that treatment tailored to specific asthma phenotypes may be quite advantageous in terms of outcomes. However, clinical trials in elderly patients are very scarce, since this type of patients is

generally excluded from such studies. Nevertheless, a thorough phenotypic characterization of elderly asthmatic patients is warranted so that treatments may also be tailored to different subgroups of asthmatics in that period of life.

Thus, the goal of this study was to compare the different phenotypes (LOA/AOA and EOA/COA/LSA) in elderly and non-elderly patients, to analyze whether there was a tendency for the presence of different triggers, risk factors and disease manifestations in different phenotypes in different age groups.

2. Material and Methods

2.1. Study Design and Sample Selection

This was an observational and descriptive study. The target population consisted of individuals with a confirmed diagnosis of Bronchial Asthma (BA), who were regularly seen at Pulmonology or Immunoallergology hospital outpatient clinics.

The volunteers were separated into two age groups: non-elderly (at least 18 years of age but below 65) and elderly (at least 65 years of age). For each patient, the data were collected in one single moment.

The exclusion criteria were co-morbidity with Chronic Pulmonary Obstructive Disease (COPD) or Restrictive Pulmonary Disease and low Mini-Mental State Examination (MMSE) score.

This study was approved by the Ethics Committee of the Faculty of Health Sciences of the University of Beira Interior (FCS), Covilhã, Portugal and the Ethics Committee of Cova da Beira Hospital (CHCB).

2.2. Patient Recruitment

Patients were invited to participate in the study by being sequentially recruited at the hospital clinics or via a telephone call. All volunteers that accepted to participate signed a written informed consent that had been approved by the Ethics Committee of the CHCB (Appendix II).

2.3. Questionnaire

The standardized and detailed questionnaire was filled out by the patients in the presence of the investigators. Data collection was performed by a group of trained researchers who also participated in the planning of the study, thereby ensuring maximal homogeneity. Data about personal and family history of diseases, current and past occupational exposure, characterization of place of residence, personal hobbies and educational qualifications, drug and personal habits, the main asthma triggers, number of acute crises and admittances to wards, principal symptoms and their frequency, and co-morbidities associated with asthma were obtained.

Standardized questionnaires, validated for the Portuguese population were used: Geriatric Depression Scale (GDS-15), the Center of Epidemiologic Study Depression Scale (CES-D), Mini-Mental Examination State (MMES) (Appendix IV), Short Form Health Survey (SF-36) and Asthma Quality of Life questionnaire (AQLQ).

The GDS-15 and the CES-D were used as instruments for the assessment of depression-specific symptoms in the elderly and non-elderly patients, respectively (13, 14). The MMSE was employed for the screening of cognitive deterioration, taking into consideration the

interviewee's degree of schooling (15).

SF-36 was used to assess the health related quality of life in all volunteers (18, 19). AQLQ was applied for the assessment of QoL in all asthmatic patients (15, 19).

The Asthma Control Test (ACT) and the Control of Allergic Rhinitis and Asthma Test (CARAT) were applied to assess the level of asthma control either on its own (ACT) or in association with rhinitis control (CARAT).

2.4. Definitions

For this study, we defined Long Standing Asthma (LSA) as equivalent to the Dutch definition of Early Onset Asthma (EOA) or Childhood Onset Asthma (COA), and involving the development of asthma symptoms and confirmed bronchial asthma before 18 years of age (8). We also defined Late Onset Asthma (LOA) as equivalent to Adult Onset Asthma (AOA), when symptoms of asthma developed after that age (8).

We also defined atopy as the presence of at least one positive cutaneous response (> 3 mm) to aeroallergens and/or a positive serum test for screening aeroallergen-specific IgE (> 0.35 kUA/L. The *in vitro* test for determination of serum values of IgE specific for the standard screening battery of aeroallergens (Phadiatop aeroallergens) was performed using a fluorometric methodology (Unicap 100 Phadia Diagnosis®, Phadia, Sweden),

2.5. Spirometry with Bronchodilation

Spirometry was performed in volunteers without episodes of respiratory infections in the previous four weeks, with the patients sitting down, using the EasyOne spirometer (ndd Medical Technologies, Andover, MA, USA) before and 15 minutes after inhalation of 200 μg of a short-acting beta2-agonist (salbutamol), via a metered dose inhaler and a spacer chamber. Only spirometric tests which met the American Thoracic Society (ATS) / European Respiratory Society (ERS) criteria were used for analysis (40). When bronchial obstruction was detected, bronchodilation was carried out and a positive response was recorded in the presence of an increase in FEv1 of at least 200 ml and 12% (40).

2.6. Statistical Analysis

Results were analyzed with the *Software Package for Social Sciences* (SPSS®), version 23.0 software. Descriptive analysis was used for the characterization of the sample.

Comparative analysis of quantitative variables between two groups was performed using Student's t test or Mann-Whitney U test, depending on the type of distribution of variables.

Chi-Square test and Fischer's exact test were used in the case of nominal variables. Descriptive analysis was used for the characterization of the sample. Normality of the distribution of variables was analyzed using K-S Lilliefors or Shapiro-Wilk Tests.

3. Results

3.1. Recruitment

For the present study, 112 elderly asthmatic (EA) patients and 104 non-elderly (NEA) patients with diagnosis of Bronchial Asthma followed up at CHCB outpatient clinics were identified as possible volunteers for this study (Figure 1). Of the EA, 4 refused to participate and 11 could not be contacted. Of the 97 remaining EA patients, a further 5 patients had to be excluded: 1 had a low MMSE score, 2 had COPD co-morbidity and 2 had their questionnaires lost. The remaining 92 EA were interviewed. The NEA sample came from a list of 104 patients. We could not contact 4 of them, leaving us with 100 NEA participants, and a total of 192 asthmatic patients (EA + NEA).

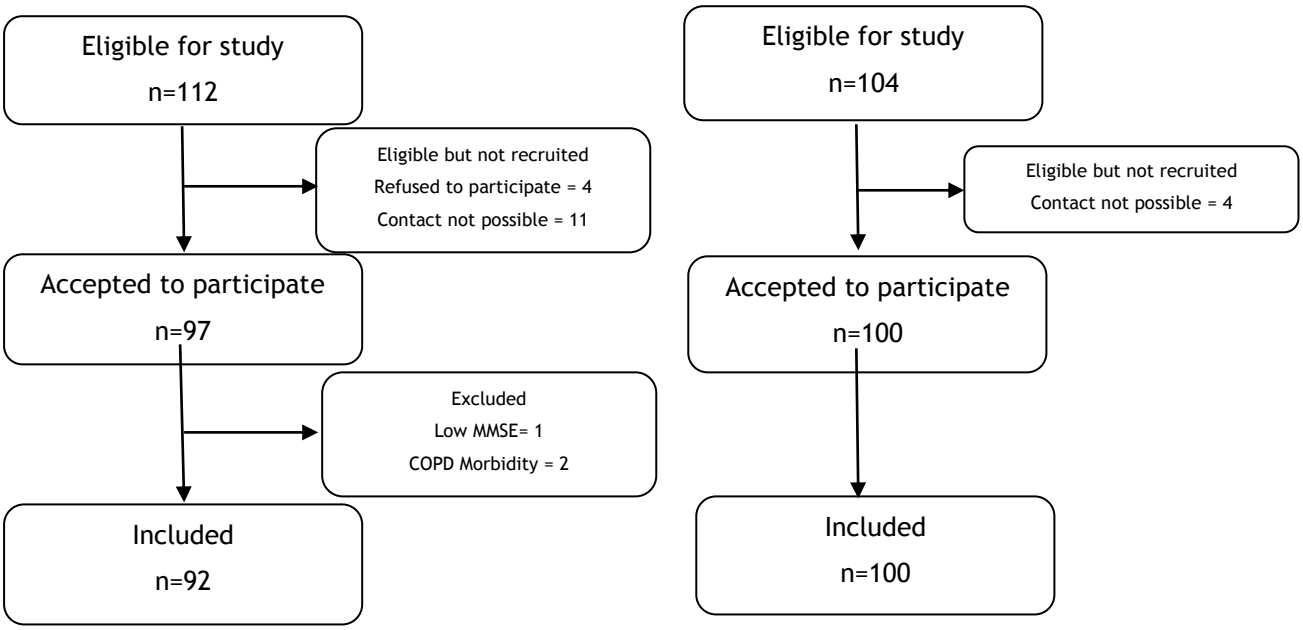

Figure 1 – Representative flowchart of the selection sample

3.2. Demographic characterization of the study population

Of the 192 subjects evaluated, 157 (81.8%) were female and 35 (18.2%) were male with a mean age of 59.1 years (18 – 86 years). There were no significant gender differences between elderly and non-elderly asthmatics. Most patients had a low (4 years) degree of schooling [45.8% (n=192)] and belonged to class III [38.5% (n=74)] and class IV [40.1% (n=77)] of the Graffar Scale, with the elderly asthmatic patients having a significantly lower mean number of schooling years. Most patients lived in an urban setting (63% of NEA and 53.3% of EA), without significant differences between groups. Professionally, 10% of NEA and all EA patients were retired. Only 5% of EA were working in the textile industry and 14% of them

were working in agriculture. However, of all the retired elderly asthmatics, 47.9% had worked in the textile industry for several years

Sociodemographic features of the asthmatic patients, such as schooling, socioeconomic level, area of residence and occupation prior to retirement, are shown in Table 1.

Table 1. Demographic characteristics of the sample

		All (n=192)	NEA (n=100)	EA (n=92)	*p*-value[a]
Age (years)	Mean ± SD Median Range	59.1±18,1 64 18 – 86	45.2± 13.2 46 19-64	72.9± 5.5 71 65 - 86	-
Gender	Female Male	157 (81.8%) 35 (18.2%)	81 (81.0%) 19 (19.0%)	76 (82.6%) 16 (17.4%)	0.773
Schooling	None 4 years 4-9 years 9-12 years ≥ 12 years	7 (7.6%) 88 (45.8%) 33 (17.2%) 34 (17.7%) 30 (15.6%)	2 (2.0%) 21 (21.0%) 23 (23.0%) 28 (28.0%) 26 (26.0%)	5 (5.4%) 67 (72.8%) 10 (10.9%) 6 (6.5%) 4 (4.3%)	<0.001
Residence	Rural Urban	80 (41.7%) 111 (58.3%)	37 (37.0%) 63 (63.0%)	43 (46.7%) 49 (53.3%)	0.759
Occupational exposure	Professions without relevant exposure Textile industry Agriculture Mining Retired -from textile industry	70 (36.5%) 5 (2.6%) 14 (7.3%) 1 (0.5%) 102 (53.1%)	70 (70%) 5 (5%) 14 (14%) 1 (1%) 0 (0%)	0 (0%) 0 (0%) 0 (0%) 0 (0%) 92 (100%) 45 (48.9%)	-
Graffar Scale	Class I Class II Class III Class IV Class V	11 (5.7%) 30 (15.6%) 74 (38.5%) 77 (40.1%) 0 (0%)	11 (11%) 25 (25%) 50 (50%) 14 (14%) 0 (0%)	0 (0%) 5 (5.4%) 24 (26.1%) 63 (68.5%) 0 (0%)	<0.001
MMSE	No cognitive defect Cognitive defect	392(100%) 0 (0%)	100 (100%) 0 (0%)	92 (100%) 0 (0%)	-
CES-D	Normal Depressive	157 (78.5%) 43 (21.5%)	73 (73.0%) 27 (27.0%)	---	-
GDS	Normal Slightly Depressive Severely Depressive	137 (71.4%) 47 (24.5%) 8 (4.2%)	---	65 (70.7%) 24 (26.1%) 3 (3.3%)	-

It should be stressed that although the tests assessing depression in elderly and non-elderly asthmatic patients were different, most patients were not depressed and only a low, but similar proportion of patients in each group was severely depressed.

3.3 Clinical characterization of the population

From the clinical assessment of the asthmatic patients, more volunteers had long-standing or early-/childhood-onset asthma – LSA/EOA/COA (73.7% of NEA, 53.3% of EA). Although there was a trend for more elderly patients having LOA/AOA, this did not reach statistical significance (Table 2). In contrast, there was a clear difference between both groups, in terms of atopy, with clearly a higher proportion of NEA than EA being atopic (80% versus 18%, respectively). Very similar results were also quite apparent in terms of family history of allergic diseases. Most of the patients were still current smokers, without significant differences between groups of asthmatics. More than half of the patients had previously smoked (51% of NIA, 55.4% of IA).

In terms of co-morbidities, most patients had rhinitis and this co-morbidity was significantly more frequent in NEA than in EA (76% versus 59.8%, respectively; $p<0.001$). In contrast, chronic heart failure (CHF) and high blood pressure (HBP) were significantly more frequently observed in elderly asthmatics.

The current medication more frequently used by asthmatics was inhaled corticosteroids (92.2 of the target population), without significant differences between elderly and non-elderly asthmatics. Short-acting beta-2 agonists (SABA) were only used as rescue medication by 75% of NEA and 55.4% of EA), with a trend for fewer elderly asthmatics using them. In contrast, significantly more elderly than non-elderly asthmatics were using long acting beta-2 agonists (LABA) (65.2% versus 41%, respectively; $p=0.024$). It should also be stressed that more than half of all asthmatic patients were on anti-histamines, because of their associated rhinitis, but these drugs were much more frequently used by NEA than EA (80% versus 28.3%, respectively; $p<0.0001$).

Finally, no significant differences, in terms of inhalational technique were detected between elderly and non-elderly asthmatics, although it should be stressed that around one quarter to one third of patients had a totally incorrect technique.

Table 2. Background clinical characterization of elderly and non-elderly asthmatic patients

		All (n=192)	**NEA (n=100)**	**EA (n=92)**	***p*-value**
Age of onset of asthma	COA/EOA/LSA AOA/LOA	122 (63.5%) 70 (36.5%)	73 (73%) 27 (27%)	49 (53.3) 43 (46.7%)	0.089
Atopy	Atopic Non-Atopic	98 (51%) 94 (49%)	80 (80%) 20 (20%)	18 (19.6%) 74 (80.4%)	**0.009**[c]
Tobacco smoking history	Smoker Never smoker	102 (53.1%) 90 (46.9%)	51 (51%) 49 (49%)	51 (55.4%) 41 (44.6%)	0.984
Co-morbidities	Rhinitis	131 (68.2%)	76 (76%)	55 (55,4%)	**<0.001**[c]
	Dermatitis	43 (22.4%)	27 (27%)	16 (17.4%)	0.637
	OSA	5 (2.6%)	1 (1%)	4 (4.4%)	-
	CHF	7 (3.6%)	0 (0%)	7 (7.8%)	**0.003**
	DM	22 (11.5%)	7 (7%)	15 (16.7%)	0.394
	GERD	19 (9.9%)	9 (9%)	10 (11.1%)	0.996
	HBP	77 (40.1%)	21 (21%)	56 (62.2%)	**<0.001**

Family history of diseases	Respiratory disease	92 (47.9%)	48 (48%)	44 (47.8%)	0.896[c]
	Allergies	62 (32.8%)	43 (43%)	20 (21.7%)	**<0.001**[c]
Current Medication	SABA	126 (65.6%)	75 (75%)	51 (55.4%)	0.087
	LABA	101 (52.6%)	41 (41%)	60 (65.2%)	**0.024**
	IC	177 (92.2%)	91 (91%)	86 (93.5%)	0.982
	Anti-leucotrienes	73 (38%)	49 (49%)	24 (26.1%)	**0.030**
	Theophylline	9 (4.7%)	3 (3%)	6 (6.5%)	0.856
	Oral CS	11 (5.7%)	6 (6%)	5 (5.4%)	0.999
	Anti-IgE	2 (1%)	0 (0%)	2 (2.2%)	-
	Anti-histamines	106 (55.2%)	80 (80%)	26 (28.3%)	<0.0001
	Beta-blockers	9 (4.7%)	4 (4%)	5 (5.4%)	0.994
	ASA	14 (7.3%)	4 (4%)	10 (10.9%)	0.501
	Other	121 (63%)	45 (45%)	76 (82.6%)	<0.0001
Inhalational technique	Correct Acceptable Incorrect	36 (14.5%) 144 (58.1%) 68% (27.4%)	20 (15.4%) 72 (55.4%) 38 (29.2%)	16 (13.6%) 72 (61%) 30 (25.4%)	0.501[c]

In terms of further characterization of the features of asthma in these patients, most had mild or moderate, persistent asthma but there was a trend for more elderly asthmatics than non-elderly asthmatics having moderate persistent asthma (Table 3). In addition, significantly more EA than NEA had had hospital admissions due to asthma bouts in the previous year (17.4% versus 7%; p=0.027). A high proportion of asthmatics in both groups had had mild to moderate asthma exacerbations in the previous year, without significant differences between the groups, although more NEA seemed to have been affected. In fact, more NEA than EA had had to be put on a course of oral corticosteroids in the previous year (17% versus 6.5%; p=0.026).

Table 3. Further clinical characterization of asthma in elderly and non-elderly patients

		All (n=192)	**NEA (n=100)**	**EA (n=92)**	***p*-value**
Asthma severity	Mild intermittent Mild persistent Moderate persistent Severe	37 (19.3%) 62 (32.3%) 93 (48.4%) 0	23 (23%) 39 (39%) 38 (38%) 0	14 (15.2%) 23 (25%) 55 (59.8%) 0	0.058
Number of Admissions	0 ≥1	169 (88%) 23 (12%)	93 (93%) 7 (7%)	76 (82.6%) 16 (17.4%)	**0.027**[c]
Number of Exacerbations last year	0 ≥1	105 (54.6%) 87 (45.3%)	50 (50%) 50 (50%)	55 (59.8%) 37 (40.2%)	0.174[c]
Took oral steroids last year	No Yes	169 (88%) 23 (12%)	83 (83%) 17 (17%)	86 (93.5%) 6 (6.5%)	**0.026**[c]
Asthma control (ACT)	Well controlled Not well controlled Very poorly controlled	134 (69.8%) 58 (30.2%) 18 (9.4%)	67 (67%) 22 (22%) 11 (11%)	67 (72.8%) 18 (19.6%) 7 (7.6%)	0.573[c]
Lung function	FEV1 (L/min) Mean ± SD Median Range	 2.13 ± 0.73 2.08 1.74 - 4.31	 2.60 ± 0.64 2.55 1.74 - 4.31	 1.72 ± 0.53 1.68 0.87 - 3.19	***P*<0.0001**[a]

	FEV1 (%) Mean ± SD Median Range	102.9 ± 21.7 103.7 70.0 – 147.2	104.2 ± 16.2 103.1 70.0 – 147.2	101.9 ± 25.7 104.6 40.3 – 141.5	0.833
	FVC (L/min) Mean ± SD Median Range	2.86 ± 0.85 2.71 1.74 - 5.87	3.36 ± 0.80 3.25 1.74 - 5.87	2.42 ± 0.64 2.38 1.28 - 4.24	**<0.0001**[a]
	FVC (%) Mean ± SD Median Range	114.4 ± 19.3 113.6 77.5 – 147.2	113.9 ± 16.0 112.3 77.5 – 147.2	114.9 ± 21.9 117.6 74.0 – 150.2	0.772
	FEV1/FVC (Tiffeneau) Mean ± SD Median Range	74.1 ± 9.9 75.1 58.8 – 94.9	77.7 ± 8.1 78.1 58.8 – 94.9	70.9 ± 10.4 72.9 44.9 – 87.5	**<0.0001**[a]
	Patients with airway obstruction (n; %) Mild Moderate Severe	167 (86.9%) 17 (8.6%) 8 (4.2%)	100 (100%) 0 0	67 (72.8%) 17 (18.5%) 8 (8.7%)	**<0.0001**[b]
	Patients (n; %) with reversibility (positive response to bronchodilation)	93 (48.4%)	71 (71%)	22 (24.3%)	**<0.0001**[c]

In terms of asthma control, as assessed using the ACT, although most patients had their asthma well controlled in the past month (72.8% of EA and 67% of NEA) that, nevertheless, implies that around one third of the patients were either not well controlled or very poorly controlled, in spite of being on regular corticosteroids and or combination therapy (Table 3).

As far as lung function is concerned, as was expected, elderly asthmatics had lower FEV1 and FVC volumes than non-elderly asthmatics but no significant differences were observed between these groups, when values were reported as percentage of predicted values. However, elderly asthmatics had significantly lower FEV1/FVC (Tiffeneau) ratios than non-elderly asthmatics, suggesting generally more obstructed airways. Furthermore, when the degree of obstruction was analyzed, elderly asthmatics had clearly more moderate and severe cases of bronchial obstruction than non-elderly asthmatics. Finally, the percentage of patients with reversible airway obstruction, which responded to a test bronchodilator (SABA) was very significantly lower in elderly asthmatics than in non-elderly asthmatics (24.3% versus 71%, respectively; $p<0.0001$).

3.4. Asthma phenotypes

In order to study phenotypes taking into account the age of onset of manifestations data about atopy, personal/familiar background of diseases, triggers and other exposures, severity of asthma and clinical aspects about disease were analyzed.

3.4.1. Distribution according to age of first asthma episode and atopy

In the different age groups, the most predominant phenotype related to age of onset of asthma symptoms was LSA/EOA/COA (73% of NEA and 53.3% of EA). In terms of the presence of atopy, the most predominant phenotype was atopic, but only in the global sample (51%) and in NEA (80%), whereas most EA had non-atopic asthma (80.4%).

In terms of the global sample, and particularly for each age group, there was an association between phenotypes taking into account age of onset and atopy. For EA patients, the most predominant and associated phenotypes were LOA/AOA with non-atopic asthma. In contrast, for NEA patients the most predominant phenotype was the combination of LSA/EOA/COA with atopic asthma (Table 4).

Table 4. Phenotypes and presence of atopy

	NEA			**EA**			
	LSA/EOA/COA N (%)	LOA/AOA N (%)	*p*-value and OR(CI95%)	LSA N (%)	LOA N (%)	*p*-value and OR(CI95%)	Total NEA+EA *p*-value and OR (CI95%)
Non-Atopic	8 (11)	10 (38.5)	0.006[a]	27 (55.1)	34 (82.9)	0.006[a]	**<0.0001**[b]
Atopic	65 (89)	16 (61.5)		22 (44.9)	7 (17.1)		

3.4.2. Personal/Familiar background of diseases

Most patients had no history of illness in infancy (62.4% of population) (Table 5). In NEA and EA patients, the absence of childhood diseases was significantly different in terms of population proportion between the LSA/EOA/COA and LOA/AOA phenotypes with a preferential association between absence of childhood diseases and the LOA/AOA phenotype (p-value=0.018 for NEA and 0.046 for IA; Fisher's Exact test). In this context, the most frequently reported childhood disease in NEA patients was the combination of respiratory disease and allergies (16.2%) whereas respiratory disease was frequently reported in EA patients (22.4%), without significant differences between the phenotypes.

Rhinitis was the co-morbidity most frequently associated with asthma in both age groups. Curiously, in NEA patients, there was a significant difference in terms of proportion of

population with rhinitis or with a combination of rhinitis and dermatitis, between LOA/AOA and LSA/EOA/COA patients. Rhinitis and the combination of rhinitis with dermatitis were present in a major proportion of NEA with LSA/EOA/COA (41.7% and 29.2%, respectively).

A clear family history of allergies was reported in different age group (24.5% of NEA and 10.4% of EA) and there was an association between history of allergies and the LSA/EOA/COA phenotype (p-value=0.003), particularly in elderly asthmatic patients (p-value=0.036).

Table 5. Phenotypes and personal/family background of diseases

		NEA		**p-value and OR(CI95%)**	**EA**		**p-value and OR (CI95%)**	**Total NEA+EA p-value and OR (CI95%)**
		LSA N (%)	LOA N (%)		LSA N (%)	LOA N (%)		
Childhood diseases	None	33[c] (45.2)	20[c] (76.9)	0.011[a]	30[e] (61.2)	35[e] (85.4)	0.048[a]	<0.001[b]
	Respiratory disease	12 (16.4)	3 (11.5)		11 (22.4)	4 (9.8)		
	Allergies	12 (16.4	3 (11.5)		4 (8.2)	2 (4.9)		
	Respiratory disease+allergies	16[d] (21.9)	0[d] (0.0)		4 (8.2)	0 (0.0)		
Adulthood diseases	None beyond asthma	10(13.9)	2(7.7)	0.147[a]	19 (38.8)	14 (34.1)	0.185[a]	0.055[a]
	Rhinitis	30(41.7)	17(48)		18 (36.7)	21 (51.2)		
	Dermatitis	3 (4.2)	1 (3.8)		0 (0.0)	2 (4.9)		
	Rhinitis+dermatitis	21[d](29.2)	2[d](7.7)		10 (20.4)	4 (9.8)		
	Allergies	5 (6.9)	3 (11.5)		1 (2)	0 (0.0)		
	Others	3 (4.2)	1 (3.8)		1(2)	0 (0.0)		
Family history	Respiratory disease	36 (49.3)	11 (42.3)	0.539[b] 1.327 (0.537,3.278)	30 (61.2)	13 (31.7)	0.005[b] 3.401 (1.420,8.130)	0.016[b] 2.110 (1.143,3.906)
	Allergies	35 (47.9)	8 (30.8)	0.129[b] 2.070 (0.801,5.376)	15 (30.6)	5 (12.2)	0.036[b] 3.174 (1.042,9.709)	0.003[b] 2.882 (1.427,5.84)

[a] Fisher's exact test; [b] Chi-square test; [c d e] Significantly different proportions (proportions comparison test)

3.4.3. Triggers and other exposures

Factors such as strong smells, house dust (71.7% of NEA and 67.8% of EA), pollen (71.7% of NEA and 65.6% of EA), viral infections (53.5% of NEA and 61.1% of EA) and changes in temperature (54.5% of NEA and 56.7% of EA) were reported as triggers by more than half of both asthma phenotypes, and were the most common reported triggers, without significant differences between both groups. Physical activity (41.4% of NIA and 30% of EA), animals with fur (41.4% of NEA and 30% of EA) and emotions (34.4%of NIA and 24.4% of EA) were also frequently reported as triggers. Wool (22.2%), open fireplace (10.6%) and animals with feathers (19%) were reported by a minority. However, there were no significant differences between different phenotypes or among different age groups, in terms of triggers.

Most asthmatic patients had lived in rural areas as a child, but there was no association between childhood residence and the different phenotypes (Table 6). Currently, most patients had an urban residence.

Approximately 40% of NEA and almost half of EA (48.9%) had had in the past or still had textile industry exposure. Around 16% of EA patients had worked more than 30 years in the textile industry.

Table 6. Phenotypes and place of residence and occupational exposure

		NIA			IA			
		LSA N (%)	LOA N (%)	p-value and OR(CI95%)	LSA N (%)	LOA N (%)	p-value and OR(CI95%)	Total NIA+IA p-value and OR(CI95%)
Childhood Residence	Rural	33(42.2)	17(65.4)	-- 0.437(0.172,1.107)	37(75.5)	31(75.6)	-- 0.945(0.379,2.612)	0.533(0.281,1.012)
	Urban	40(54.8)	9(34.6)		12(24.5)	10(24.4)		
Actual Residence	Rural	24(33.3)	12(46.2)	-- 0.583(0.234,1.454)	22(44.9)	21(51.2)	-- 0.776(0.338,1.783)	-- 0.632(0.346,1.155)
	Urban	48(66.7)	14(53.8)		27(55.1)	20(48.8)		
Time of textile industry exposure (years)	0-10	7(28)	3(20)	--	4(15.4)	1(5.3)		--
	11-20	3(12)	2(13.3)		11(42.3)	7(36.8)		
	21-30	8(32)	6(40)		3(11.5)	4(21.1)		
	>30	7(28)	4(26.7)		8(30.8)	7(36.8)		

[a] Fisher's exact test; [b] Chi-square test; [c d e] Significantly different proportions (proportions comparison test)

3.4.4. Severity of asthma

In order to evaluate whether the severity of asthma was different between phenotypes data regarding hospitalizations due to asthma, the number of acute exacerbations of asthma and the need for oral CES were analysed (Table 7). None of the criteria used to measure the severity of disease was significantly associated with any of the phenotypes. Only 9% of population reported one or two hospitalizations due to asthma in the previous year and 29.1% reported one or two acute exacerbations. Curiously, the frequency of these episodes was not higher in EA patients than in NEA patients for any of the age of onset phenotypes. However, the need for oral CES was relatively more frequent in NEA patients, both for LSA/EOA/COA and LOA/AOA.

Table 7. Phenotypes and asthma severity

		NIA			IA			
		LSA N (%)	LOA N (%)	p-value	LSA N (%)	LOA N (%)	p-value	NIA+IA p-value and OR (CI95%)
Hospitalization For asthma	None	68(93.2)	24(92.3)	0.224[a]	39(79.6)	35(85.4)	0.467[a]	0.994[a]
	1 or 2	5(6.8)	1(3.8)		6(12.2)	5(12.2)		
	3 or >3	0(0)	1(3.8)		4(8.2)	1(2.4)		
Acute exacerbation	None	35(47.9)	14(53.8)	0.168[a]	29(59.2)	25(61)	0.985[a]	0.496[a]
	1 or 2	24(32.9)	4(15.4)		15(30.6)	12(29.3)		
	3 or >3	14(19.2)	8(30.8)		5(10.2)	4(9.8)		
Need for oral CES	Yes	12(16.4)	5(19.2)	0.748[a]	3(6.1)	3(7.5)	0.797[a]	0.972[a]

[a] Fisher's exact test; [b] Chi-square test; [c d e] Significantly different proportions (proportions comparison test)

3.5. Clinical aspects of asthma according to phenotypes

Manifestations of asthma, treatment and control of disease were analyzed both in the total sample of patients as well in terms of each asthma phenotype (Table 8).

3.5.1. Asthma manifestations

Dyspnoea (92.1%) was the most frequently reported symptom, followed by wheezing (91.7%), and cough (90.9%). There was an association between dyspnoea and phenotype in each phenotypic group, independently of age (p-value = 0.038). In this context, both elderly and non-elderly asthmatic patients with LSA/EOA/COA were 4.237 more likely to have dyspnea than patients with the LOA/AOA phenotype. There was also an association between phenotypes and limitation of activities caused by dyspnoea. NEA patients with a LOA/AOA phenotype were 4.48 times more likely to have limitation of activities caused by dyspnoea (p-value =0.017, Odds ratio LOA/LSA).

The limitation of activities due to cough was present in 43.9% of EA with LSA/EOA/COA and in 68.4% of EA with LOA/AOA, suggesting that EA patients with the latter phenotype had more frequent limitation of activities caused by cough than EA patients with LSA/EOA/COA (p-value=0.028).

In terms of wheezing, there was an association, in terms of proportion, between the frequency of manifestation and phenotype, in NEA patients. In fact, more than half of NEA patients with LOA/AOA (59.1%) reported the occurrence of wheezing more than twice per week, whereas that only occurred in 28.6% of NEA patients with LSA/EOA/COA phenotype. Thus, with a level of significance of 3.7%, NEA with LOA/AOA had a manifestation of more persistent wheezing.
In terms of annual variation, for all symptoms, manifestations were more frequent in Spring and Summer.

Table 8. Phenotypes and asthma manifestations

		NEA			**EA**			
		LSA N (%)	LOA N (%)	p-value OR (CI95%)	LSA N (%)	LOA N (%)	p-value OR (CI95%)	NEA+EA p-value and OR (CI95%)
Dyspnoea								
Presence	Yes	70(95,9)	22(84,6)	0.072[a] 4.237 (0.881,20.4	46(93,9)	36(87,8)	0.314[a] 0.47(0.105, 2.097)	0.044[a] (3.003,8.85)
Frequency	<2 or =2x a week	36(53,7)	10(47,6)	0,875[a]	24(52,2)	17(47,2)	0.773[a]	0.457[a]
	>2x a week	16(23,9)	6(28,6)		17 (37)	16(44,4)		
Activity limitation	Presence	41[c](58,6)	19[c](86,4)	0.012[a] 0.22 (0.06,0.825)	72[a](62,1)	47[b](82,5)	0.202[a] 0.517(0.184 ,1.45)	0.005[a] 0.348(0.159 8,0.759)
Annual variation	Perennial	21(32,3)	7(33,3)	0.808[b]	19(41,3)	14(42,4)	0.332[a]	0.362[b]

	Spring and Summer	38(58,5)	13(61,9)		25(54,3)	19(57,6)		
	Autumn and Winter	6(9,2)	1(4,8)		2(4,3)	0(0,0)		
Cough								
Presence	Yes	66(93)	25(100)	0.078[a] 0.725(0.639 ,0.823)	40(81,6)	38(92,7)	0.115[a] 0.353(0.088 ,1.395)	0.09[a] 0.361(0.01, 1.304)
Frequency	<2 or =2x a week	24(36,9)	7(29,2)	0.508[b]	18(43,9)	14(36,8)	0.220[b]	0.105[a]
	>2x a week	29(44,6)	14(58,3)		17(41,5)	22(57,9)		
Activity limitation	Presence	22(33,3)	13(52,0)	0.105[a] 0.461(0.18 1,1.178)	18d(43,9)	26d(68,4)	0.027[a] 0.361(0.144 ,0.907)	0.002[a] 0.361(0.193 0.698)
Annual variation	Perennial	30(46,9)	9(37,5)	0.104[a]	16(39,0)	16(42,1)	0.620[a]	0.183[b]
	Spring and Summer	29(45,3)	15(62,5)		22(53,7)	21(55,3)		
	Autumn and Winter	5(7,8)	0(0)		3(7,3)	1(2,6)		
Wheezing								
Presence	Yes	64(88,9)	21(80,8)	0.311[a] 1.905(0.562 ,6.45)	46(95,8)	38(92,7)	0.520[a] 1.815(0.289 ,11.494)	0.429[a] 1.493(0.559 3.984)
Frequency	<2 or =2x a week	31(49,2)	6(27,3)	0.037[b]	19(41,3)	15(39,5)	0.703[a]	0.148[a]

	>2x a week	18[e](28,6)	13[e](59,1%)		18(39,1)	17(44,7)		
Activity limitation	Presence	20(31,3)	5(22,7%)	0.440[a] 1.546(0.5,4.785)	18(38,3)	19(50,0)	0.279[a] 0.621(0.261,1.493)	0.455[a] 0.781(0.408 1.493)
Annual variation	Perennial	24(40,7)	7(31,8%)		21(44,7)	22(59,5)		
	Spring and Summer	28(47,5)	14(63,6%)		24(51,1)	15(40,5)		
	Autumn and Winter	7(11,9)	1(4,5%)	0.367[b]	2(4,3)	0(0)	0.157[a]	0.195[b]
Chest tightness								
Presence	Yes	48(68,6)	20(80,0%)	0.265[a] 0.546(0.181,1.642)	34(69,4)	31(75,6)	0.510[a] 0.731(0.287,3.484)	0.220[a] 0.652(0.326 1.305)
Frequency	<2 or =2x a week	28(58,3)	8(42,1%)		21(58,3)	14(45,2)		
	>2x a week	9(18,8)	6(31,6%)	0.427[a]	10(27,8)	8(25,8)	0.299[a]	0.259[a]
Activity limitation	Presence	27(56,3)	12(60,0%)	0.775[a] 0.857(0.297,2.475))	21(58,3)	22(71,0)	0.280[a] 0.573(0.207,1.587)	0.270[a] 0.667(0.323 1.377)
Annual variation	Perennial	27(58,7)	13(68,4%)		18(50,0)	19(61,3)		
	Spring and Summer	15(32,6)	5(26,3%)	0.740[a]	17(47,2)	12(38,7)	0.386[a]	0.378[a]

	Autumn and Winter	4(8,7)	1(5,3%)		1(2,8)	0(0,0)		

[a] Fisher's exact test; [b] Chi-square test; [c d e] Significantly different proportions (proportions comparison test)

3.5.2. Treatment

Data were also collected on rescue medication, used in acute exacerbations, as well on daily medication used to control the manifestations and to stabilize the disease (Table 9). Finally, some data regarding additional medication was also obtained.

Rescue medication was associated with phenotype in different age groups (p-value=0.016). As expected, short-Acting Beta2-Agonist (SABA) was the most frequent medication used by asthmatic patients when they had an acute exacerbation. Curiously, the use of SABA was preferentially associated with LSA/EOA/COA phenotypes (p-value=0.016), particularly in NEA patients p-value=0.015).

On the other hand, for the same age group (NEA), Long-Acting Beta2-Agonist (LABA) was preferentially associated with the LOA/AOA phenotype (p-value=0.015), which may suggest a more frequent presence of moderately severe persistent asthma in this age group and phenotype.

Inhaled Corticosteroids (IC) was the most frequent medication for NEA, followed by the combination of a Long-Acting Beta2-Agonist with an inhaled corticosteroid (LABA+IC). In NEA patients, its use was more frequent, in terms of proportion in patients with LOA/AOA phenotype than patients with LSA/EOA/COA phenotype, although this did not reach statistical significance.

The combination of IC with LABA was the most frequent daily medication for EA patients.

Antihistamines were the main additional drug in these asthmatics, used to help control rhinitis symptoms, and were more frequently used by NEA patients.

Finally, the use of anti-leukotriene drugs was associated with phenotypes, being more frequently used NEA patients with LOA/AOA (69.2%), with level of significance of 1.8%.

Table 9. Phenotypes and asthma treatment

		NEA			EA			
		LSA N(%)	LOA N(%)	p-value	LSA N(%)	LOA N(%)	p-value	Total NIA+IA p-value
Rescue medication	SABA	56[c](77.6)	11[c](42.3)	0.015[a]	22(44.9)	17(41.5)	0.402[a]	0.016[a]
	LABA	5[d](6.8)	6[d](23.1)		3(6.1)	7(17.1)		
	IC	0	0		1(2)	0(0)		
	IC+LABA	5(6.8)	3(11.5)		3(6.1)	3(7.3)		
ly m e di ca	SABA	1(1.4)	0(0)	0.116[a]	0(0)	0(0)	0.980[a]	0.252[a]
	LABA	0(0)	0(0)		2(4.1)	2(4.9)		

	IC	47(64.4)	15(57.7)		19(38.8)	17(41.5)		
	IC+LABA	14[c](19.2)	10[c](38.5)		26(53.1)	20(48.8)		
Support medication	Antileukotrienes	31[e](42.5)	18[e](69.2)	0.018[a]	16(32.7)	8(19.5)	0.157[a]	0.97[a]
	Antihistamine	58(79.5)	21(80.8)	0.886[b]	14(28.6)	11(26.8)	0.854[b]	0.132[b]

[a] Fisher's exact test; [b] Chi-square test; [c d e] Significantly different proportions (proportions comparison test)

3.6.3. Asthma control

Asthma control was also analysed in terms of all studied phenotypes, to determine whether there were differences between groups (Table 10). In this regard, patients with LSA/EOA/COA phenotype had a higher percentage of controlled asthma, when compared with the LOA/AOA phenotype. However, no statistically significant differences were found between phenotypes in NEA and EA patients.

Table 10. Phenotypes and asthma control

		NEA			**EA**			**Total NEA+EA**
		LSA N (%)	LOA N(%)	p-value OR(CI95%)	LSA N(%)	LOA N(%)	p-value OR(CI95%)	p-value OR(CI95%)
ACT	Uncontrolled	22(22.2)	9(9.1)	0.147[a]	12(13.3)	12(13.3)	0.639[a]	0.620[a]
	Controlled	51(51.5)	17(17.2)		37(41.1)	29(32.2)		

[a] Fisher's exact test; [b] Chi-square test; [c d e] Significantly different proportions (proportions comparison test)

4. Discussion

The present study is the first thorough phenotypic study of asthma in Portuguese patients, aiming to investigate features of asthma and their expression in different phenotypes in non-elderly and elderly patients with early onset and late onset asthma phenotypes. The most frequently observed phenotype in elderly asthmatic patients was late onset (LOA)/ adult-onset (AOA) asthma phenotype without atopy, whereas in non-elderly asthmatics the long-standing (LSA) / early-onset (EOA) / childhood-onset (COA) phenotype associated with atopy was more frequent. We also showed that elderly and non-elderly patients with LOA/AOA asthma phenotype and those with LSA/EOA/COA phenotype have significant differences in terms of manifestations of severity, family history of diseases and control medication. Nevertheless, these phenotypes may manifest to a similar extent, in different age groups.

Most patients in our sample were female, smokers, with low level of schooling and social class (Graffar III and IV), predominantly urban, although in childhood most had lived in rural areas. Although the predominance of women in our study may suggest that there was a bias in selection process, we believe that this is not the case since most of the patients who were contacted for recruitment, independently of refusing or accepting, were women. In fact, various studies have shown that there is an increased incidence of asthma in women (23) and in adults, namely in elderly patients, female patients tend to predominate, particularly in cases of LOA/AOA (39). Furthermore, women may have more severe and or persistent manifestations of asthma than men and this may account for them to be preferentially seen at outpatient speciality clinics (41).

Previous studies suggested the burden of asthma is more significant in the elderly than in their younger counterparts, particularly with regard to mortality, hospitalization, medical costs or health-related quality of life (20). There are data to suggest that asthma in older adults is phenotypically different from young patients, with potential impact on the diagnosis, assessment and management in this population (20). So, in this study we included approximately the same number of non-elderly and elderly patients and studied LSA/EOA/COA and LOA/AOA phenotypes, taking into account the presence of atopy, personal and family background of respiratory disease, triggers and occupational exposure, severity of disease, and clinical aspects about asthma, included asthma manifestations, treatment and its control. The most frequent phenotype both was LSA/EOA/COA, in terms of onset disease. In addition, atopy was also the most frequent phenotype in the general sample of asthmatics as well as in NEA but clearly not in EA, in whom a non-atopic phenotype predominated. It is known that Non atopic/allergic BA is generally less frequent than atopic/allergic BA (12). When we analysed a combination of phenotypes, the most frequently observed in NEA was LSA/EOA/COA with atopic asthma, but in EA patients the most phenotype observed was

LOA/AOA with non-atopic asthma. According to some studies this may imply that most patients with LOA had mild-to-moderate persistent asthma, particularly for EA patients because among patients with adult onset asthma, those with severe disease are less likely to be atopic (20).

We defined long standing asthma (LSA) as early- (EOA) or childhood-onset (COA) asthma, beginning before 18 years of age, and late-onset asthma (LOA) as adult-onset (AOA) asthma beginning after that age (8; 39). Although various researchers use the age of 40 as the threshold for discrimination between LSA and LOA (25), the threshold ages separating between these two subtypes in fact vary in different studies. However, generally speaking, asthma which begins in childhood or young adulthood is regarded as LSA (27,28) and we believe our definition is acceptable and capable of comparison with studies carried out elsewhere.

In terms of diseases associated with asthma, most asthmatic patients in our study had rhinitis, which is consistent with a predominant atopic phenotype, in the case of the non-elderly asthmatics. In fact, we observed that the presence of rhinitis or the combination of rhinitis and dermatitis was significantly higher in the LSA/EOA/COA phenotype in both age groups, although it did not reach no statistical significance. A review on European-wide epidemiological studies on the prevalence of chronic rhinosinusitis (CRS) confirmed the well-known association between allergic rhinitis and LSA (17). But, according some studies, rhinitis is a significant risk factor for adult-onset asthma in both atopic and non-atopic subjects (24).
Likewise, a family history of allergies was more frequently documented by patients with LSA, but in this case, with the particularity of being more common in EA patients. This fact corroborates other studies that showed that parental and/or sibling history of asthma and allergy were generally more strongly associated with LSA/EOA/COA when compared with early onset transient or late onset asthma (26,34).
Despite LSA being more frequently associated with a allergen sensitisation and more allergic symptoms (8), in this study no associations between triggers such as pollens, house dust, the presence of animals, or contact with wools and LSA were observed for any of the age groups.

In terms of clinical features, the LSA/EOA/COA phenotype was associated with the presence of dyspnoea, independently of age. In fact, NEA and EA patients with this phenotype seem to have a higher probability of having dyspnoea as a relevant asthma symptom. Although LOA/AOA is associated with a greater severity of disease this finding may be explained by the fact that LSA/EOA patients have an increased susceptibility to frequent exacerbations (28, 32) due to being exposed to environmental triggers. It is also consistent with the more frequent use of SABA for NEA patients with LSA/EOA. Nevertheless, this phenotype was also associated with a higher percentage of patients with controlled asthma, when compared with

the LOA/AOA phenotype, although without statistical significance. This apparent discrepancy may be justified by the fact that the test measuring asthma control (ACT) only focuses upon the previous four weeks whereas the other parameters regarding SABA use and exacerbations involve the previous 12 months.

We also analyzed the personal and family background of patients to determine factors that might be associated with the development of each phenotype. An association was found between absence of respiratory diseases or allergies in childhood and the LOA/AOA phenotype in both elderly and non-elderly asthmatics. Thus, the presence of respiratory diseases may indicate the earlier development of asthma. Various studies have indeed shown that the LOA/AOA phenotype is less often associated with allergy and atopic diseases (34) and suggested that many patients with this phenotype describe the onset of asthma symptoms following a viral illness, occupational exposure, or the ingestion of aspirin, while such histories are less frequent among those with LSA/EOA/COA asthma (7).

An association between limitation of activities caused by dyspnoea and LOA was found in non-elderly asthmatic patients. In fact, a young patient with LOA/AOA was 4.48 times more likely to have limitation of activities caused by dyspnoea. In the same way, LOA/AOA was associated with a greater frequency of wheezing manifestations (more than twice per week) in non-elderly asthmatics. Curiously, limitation of activities caused by cough was associated with LSA/EOA/COA in the general sample of patients, and particularly in EA patients. This tendency towards more frequent manifestations and limitation of activities may be explained by the clinical characteristics of LOA/AOA since patients with this phenotype have been shown to have marked airflow restriction, probably related to airway inflammation and remodeling, and with a faster decline in forced expiratory volume in 1 second (FEV1) (28). The fact that limitation caused by dyspnea and a higher frequency of wheezing manifestations were more frequently reported by younger patients could be due to decreased perception or under-reporting of symptoms by elderly patients (20) and also to the fact that elderly patients tend to be less mobile than younger patients and, therefore, less likely to have physical exercise induced dyspnoea. In contrast, a limitation of activities caused by cough was more frequently reported by EA patients with the LSA/AOA phenotype. Studies about cough in the elderly showed that EA tend to have an increased incidence of illnesses, including those affecting the lungs and though the cough is a common symptom, and this may suggest a more serious underlying disease, in view of its frequent association with chronic bronchitis, ACE inhibitor-treated high blood pressure, and heart failure (17, 21, 22). In the same way, persistent coughing in elderly may more easily lead to exhaustion, insomnia, dizziness and musculoskeletal pain (22). Thus, the fact those patients with LSA/EOA had chronic cough earlier than patients with LOA/AOA, could be a more limiting factor to physical activities in the former phenotype.

In terms of the global sample of asthmatic patients, when we analyzed asthma medication separately, inhaled corticosteroids (ICS) were the most frequent drug used. However, when we investigated the combination of medication taken daily to control the disease, there were differences between EA and NEA patients. In fact, whereas in the EA group most patients required a combination of a LABA and ICS, most NEA patients required isolated therapy with an ICS for partial or full control of their asthma symptoms. According to the *16ª Norma da Direção Geral de Saúde 2011* on approach to asthma and its control, as well as GINA 2016 (1), most NEA were therefore in step 2 of treatment, which suggests mild-persistent asthma. On the other hand, EA were in step 3 or 4, suggesting that a high percentage of EA patients had more frequently persistent moderately severe asthma. In fact, other studies have shown that elderly asthmatic patients usually require higher doses of corticosteroids to achieve the same level of symptom control as that obtained in younger patients of similar baseline asthma severity (29). The greater severity of asthma in the elderly may be explained by a lower level of intentional (cost-related) or non-intentional adhesion to therapy as well as to errors in the inhalational technique (30, 31). However, we did not find differences between two age groups in terms of inhalational technique or in asthma control, probably because these were patients regularly followed up at a clinic. In fact, inhaled glucocorticosteroids are currently the most effective anti-inflammatory medications for the treatment of persistent asthma (1,2,34). Also the use of short-acting beta agonists (SABA) as rescue medication was preferentially associated with LSA/EOA/COA phenotypes, particularly in NEA patients, while LABA was associated with LOA/AOA phenotype. The preferential use of medication in NEA patients may be explained by greater therapeutic adherence in this age group. In addition, studies have shown that in patients with mild asthma exacerbation, the application of SABA is usually sufficient in resolving symptoms (42). Long-acting beta-agonists (LABA), as well as anti-leukotriene drugs were more frequently associated with the LOA/AOA phenotype in NEA patients, which, again, may further suggest a more frequent presence of moderately severe persistent asthma in these asthmatics. In fact, patients with LOA/AOA tend to have a poor prognosis, with a faster decline in lung function and more severe persistent airflow limitation (34,38), frequently needing high-dose ICS and long-acting b2-agonists (LABAs) as well as anti-leukotrienes, oral corticosteroids and/or anti-IgE therapy (31,33). In line with these reports, our study showed that a lower percentage of patients with the LOA/AOA phenotype had controlled asthma, in comparison with patients with the LSA/EOA/COA phenotype.

We also studied the severity of disease between phenotypes and in both age groups, collecting data about number of hospitalizations, acute exacerbations and the need for oral CS. Systemic corticosteroids are more potent than ICS, but also have higher risks of side effects, being recommended only as step 5 management in the GINA guidelines, although they can be used as short-term therapy to control exacerbations (1,16), as mostly happened with the patients in our study. Most NEA and EA had no history of hospitalization or acute

exacerbation in the previous year and few of them had needed to take oral CS, which suggested a good control of disease in the general population. The number of co-morbidities associated with asthma increases with age and some of those conditions, or the medications required to treat these last, can sometimes affect asthma control (17). In spite of some studies having showed that elderly patients tend to have higher morbidity and rate of hospital admissions for asthma than younger patients, which may be due to a frequent under- or mis-diagnosis, poor assessment and under-treatment of asthma (34), we did not find this. This can be explained by the fact that our patients were regularly followed up in Pulmonology or Imunoallergology outpatient clinics which allows a better monitoring of multiple factors that may affect disease control as well a more regular tailoring of medication. Furthermore, this regular follow up may also be associated with a higher probability of self-management asthma plans being followed (31). It is known that the improvement of self-caring and self-efficacy behaviors is vital in the successful management of asthma (5).

This study had some limitations. Firstly, the number of volunteers may not have been sufficient to detect some clinical aspects related to phenotypes or to find differences between asthma manifestations in different age groups. Although the number of our volunteers was higher than that seen in several other similar studies, it would be desirable to increase the number of recruited volunteers, preferably in the context of a multi-centre study.

Another limitation of the study was that questionnaires such as ACT and AQLQ have not been specifically validated for an elderly population. This may be a factor of misunderstanding, which may have influenced some results. In addition, these questionnaires, as well as the clinical questionnaire are based upon self-report, which is known to be potentially influenced by memory or humour-related biases. Nevertheless, we resorted to hospital records in order to confirm patient information and patient self-reports are well accepted epidemiological tools.

Since we analyzed various aspects in our study, some aspects were asked more than once and taking account the extended duration of questionnaire, patients may have become tired during its completion, particularly elderly patients, which could be contribute towards inattention of patients and inaccuracy of their responses towards the end of the questionnaires, thereby being associated with further biases. Nevertheless, we attempted to take the questionnaires at each patient's own pace.

In conclusion, we showed that patients with elderly and non-elderly patients with lato-onset asthma had more limitation caused by dyspneoa and more frequently wheezing manifestations, resorting a combination of LABA with IC to obtain asthma control, suggesting a more persistent disease. A background of family history of allergies and the presence of rhinitis is associated with LSA/EOA, as well, more frequently the existence of limitation in

activities by cough, particularly in elderly patients. There were no significant differences between two phenotypes for different age groups. Thus, in general, in our study, the age did not change the characteristics of onset-related phenotypes.

5. Future prospects

This study was successful in achieving the desired number of sample volunteers, thereby allowing us to clarify aspects about clinical phenotypes in two age groups. However, we had difficulties in selection and recruitment of asthmatic patients, particularly elderly patients and some aspects must be improved.

Firstly, it is important create a computer platform working in a network at various participating healthcare units. Thus, professionals could participate in the study to directly and easily fill in study protocols without the patients having to attend a single unit for collection of data. Patients, particularly elderly have difficulties of accessibility to hospital. This would make it easier for patients just to come to their local health care Centre, thereby avoiding unnecessary travel and costs. The easier work at recruitment patients would result in increasing of sample size in order to increase the relevance of the various possible complex phenotypes of LOA/AOA.

Secondly, it is important to perform some adjustments in terms of applied questionnaires. The overall questionnaire was too long and caused some lack of attention by patients. It will be possible eliminate some data collected about subjective aspects of disease because they were not objectified. Also, statistically, some variables had many categories thereby causing the dispersion of the sample and with low level of significance.

In order to classify phenotypes it would be extremely to develop a cluster analysis to identify specific and clinically adult-onset asthma phenotypes, given that recognition of specific subphenotypes may further improve our understanding of underlying genetic basis, pathophysiologic mechanisms, treatment response and prognosis. Again, having a multi-centre study with a higher number of patients will be crucial to reach this goal.

Finally, it will be important to act directly in education of patients, teaching them the importance of therapy adhesion, what could be an acute exacerbation and the indicators of bad control of disease.

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7. Appendix

Appendix I: STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page Nº
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	v
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	v
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1
Objectives	3	State specific objectives, including any prespecified hypotheses	2-3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	NA
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6-10
		(b) Indicate number of participants with missing data for each variable of interest	6-10
Outcome data	15*	Report numbers of outcome events or summary measures	11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-19
		(*b*) Report category boundaries when continuous variables were categorized	11-19
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-19
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	20-25
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20-25
Generalisability	21	Discuss the generalisability (external validity) of the study results	20-25
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	NA

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Appendix II: Informed Consent

Centro Hospitalar Cova da Beira
Covilhã/Fundão

IMPRESSO

Consentimento Livre e Informado

Código: CHCB.IMP.CINVEST.18 | *Edição:* 1 | *Revisão:* 0

Bruna Filipa Vilaça Rodrigues, da Faculdade Ciências da Saúde- Universidade da Beira Interior, a realizar um trabalho de investigação subordinado ao tema "Caracterização Clínica da Asma Brônquica em Não Idosos e Idosos ", vem solicitar a sua colaboração neste estudo.

Informo que a sua participação é voluntária, podendo desistir a qualquer momento sem que por isso venha a ser prejudicado nos cuidados de saúde prestados pelo CHCB, EPE; informo ainda que a sua privacidade será respeitada, todos os dados recolhidos serão confidenciais e não serão fornecidas quaisquer compensações.

Objetivo do trabalho de investigação: Comparar as características clínicas da asma em idosos e não idosos, tendo em conta a necessidade de medicação, o tipo de asma e a sua severidade, sinais e sintomas mais frequentes, antecedentes familiares, história de exposição, grau de controlo da doença, número de episódios de agravamento, entre outros, de modo a determinar se existe um padrão tendencial da doença nas diferentes faixas etárias.

Critérios de inclusão: Idosos (idade igual ou superior a 65A) e Não Idosos (idade entre 18-65A)

Critérios de exclusão: patologia cardíaca e outras patologias respiratórias e doentes com défice cognitivo.

Procedimentos necessários: Estudo de 100 idosos asmáticos e 100 jovens asmáticos, aplicando um questionário sobre história da doença atual/caracterização do quadro clínico, antecedentes patológicos, antecedentes familiares, hábitos medicamentosos, história de exposição, ACT, CARAT, entre outos. A população de controlo será constituída por 100 idosos e 100 jovens não asmáticos.

Risco/ Benefício da sua participação: Este estudo permitirá aumentar o conhecimento sobre a Asma Brônquica nos idosos, podendo influenciar um diagnóstico mais precoce, uma orientação terapêutica mais eficaz, um melhor controlo dos sintomas mais frequentes, e uma pesquisa mais acentuada das co morbilidades que poderão estar associadas. Todos procedimentos supracitados serão efetuados pelos investigadores, com experiência na aplicação das mesmas.

Duração da participação no estudo: Outubro 2015 – Março 2016

Nº aproximado de participantes: 400

Clinical Characterization of Bronchial Asthma in Elderly and Non-Elderly Patients: the relevance of clinical phenotypes

Contactos para esclarecimento de dúvidas: a26824@fcsaude.ubi.pt

Consentimento Informado – Participante

Ao assinar esta página está a confirmar o seguinte:

* O Sr. (a) leu e compreendeu todas as informações desta informação, e teve tempo para as ponderar;

* Todas as suas questões foram respondidas satisfatoriamente;

* Se não percebeu qualquer das palavras, solicitou ao aluno/investigador uma explicação, tendo este esclarecido todas as dúvidas;

* O Sr. (a) recebeu uma cópia desta informação, para a manter consigo.

_____ _____

Nome do Participante (Legível) Representante Legal

_____ ____ / ____ / ____

(Assinatura do Participante ou Representante Legal) Data

Consentimento Informado – Aluno / Investigador

Ao assinar esta página está a confirmar o seguinte:

* Entregou esta informação;

* Explicou o propósito deste trabalho;

* Explicou e respondeu a todas as questões e dúvidas apresentadas pelo participante ou representante legal.

_____

Nome do Aluno / Investigador (Legível)

_____ ____ / ____ / ____

Assinatura do Aluno / Investigador Data

Consentimento Informado

(conforme "Declaração de Helsínquia, da Associação Médica Mundial, de 1964")

NOME DO ESTUDO: CARACTERIZAÇÃO DE DOENTES IDOSOS COM ASMA BRÔNQUICA: PERSPECTIVAS CLÍNICAS E FUNCIONAL, DE QUALIDADE DE VIDA E RELATIVA AOS AUTO-CONHECIMENTO DA DOENÇA E USO DE INALADORES

A Asma Brônquica em Idosos é na atualidade pouco diagnosticada, frequentemente por coexistir com outras doenças do foro cardíaco e pulmonar, que podem mascarar o quadro clínico de Asma. Para além disso, no idoso há uma menor perceção dos sintomas, bem como dificuldade em aceitar a falta de ar como sendo um problema de saúde e não devido ao avançar da idade. Assim com vista a definir melhor o diagnóstico, o controlo, o autoconhecimento e a qualidade de vida associados à Asma Brônquica nos idosos levamos a cabo o presente estudo, desenvolvido pela Universidade da Beira Interior, para o qual agradecemos a sua participação.

Para o estudo necessitamos da sua colaboração, através do preenchimento de alguns questionários, da realização de testes cutâneos de alergia, de uma pequena amostra de sangue (20 ml), de provas respiratórias (espirometria e FENO) e da demonstração da técnica de uso do inalador que utiliza habitualmente.

Os testes cutâneos de alergia são uma técnica muito segura e frequentemente usada. Consistem na colocação de uma pequena gota de substâncias do ambiente que frequentemente causam alergia, que com a ajuda de uma lanceta com uma ponta de 1mm será introduzida na pele (sentirá uma leve "picada"). Caso haja alergia formar-se-á uma pequena pápula associada a comichão que desaparece passado pouco tempo.

A colheita de sangue é uma técnica de rotina, sem riscos, que acarreta um desconforto mínimo, semelhante à utilizada para a realização de análises clínicas de rotina.

A espirometria é um exame também conhecido pelo "exame do sopro", que permite determinar o volume de ar inspirado e expirado, assim como os fluxos respiratórios. Como o próprio nome indica terá que soprar para uma máquina que determinará todos esses parâmetros. Exceto alguns problemas de saúde que o possam contraindicar, trata-se de um exame extremamente útil no diagnóstico da asma e normalmente sem complicações para a saúde daqueles que o realizam.

O FENO, fração exalada de Óxido Nítrico, é um marcador da inflamação da via aérea. É não invasivo, simples e bem tolerado. Para realizá-lo terá que também soprar para um aparelho eletrónico que determinará os parâmetros necessários para avaliação da asma.

Todos os procedimentos supracitados serão efetuados pelos investigadores, com experiência na aplicação das mesmas.

Este estudo poderá ajudar a caracterizar melhor a forma de apresentação clínica e funcional, o grau de controlo, o autoconhecimento e a qualidade de vida da Asma Brônquica em idosos. Contribuirá para uma melhoria da qualidade de vida dos mesmos, traduzida por um diagnóstico atempado, correto e com a respetiva adequação do tratamento aos mais vários níveis da prevenção.

Caso assim o deseje, poderá recusar participar neste estudo em qualquer altura, sem que isso prejudique os seus direitos em termos de assistência de saúde.

Os resultados deste estudo poderão ser consultados pelos responsáveis científicos do projeto de investigação e ser publicadas em revistas científicas. No entanto, os dados de carácter pessoal serão mantidos confidenciais.

Estudo para caracterização da população idosa asmática inscrita no Centro de Saúde da Covilhã e no Centro Hospitalar da Cova da Beira (CHCB).

Eu, abaixo assinado (nome completo do voluntário)

_____

compreendi a explicação que me foi fornecida acerca do meu caso clínico e do método ou tratamento que se tenciona instituir, tendo-me sido dada a oportunidade de discutir e fazer as perguntas que julguei necessárias.
Por isso, consinto que me seja aplicado os métodos propostos para o estudo atual.

Data: ____/___/_____
Assinatura: _____

Testemunha (caso haja)
Data: ____/___/_____
Assinatura: _____

Eu, abaixo assinado, _____, investigador responsável, certifico que foram postas à disposição, informações respeitantes ao estudo supracitado, "de modo simples, inteligível e leal", conforme o disposto no Decreto-Lei nº 97/94, de 09 de Abril.

Data: ____/___/_____
Assinatura: _____

Appendix III: Demographic and Clinical Characterization

HISTÓRIA CLÍNICA

IDENTIFICAÇÃO/CARACTERIZAÇÃO DEMOGRÁFICA

Nome:_____

Código de identificação:_____ Telefone:_____

Sexo: F ___ M____ Peso:_____Kg Altura: _____cm

Idade: _____ Data de nascimento:_____/_____/_____

Naturalidade:_____

Residência na **infância**: (rural (aldeia/vila/quinta) (urbano) Localidade:_____

Residência na **idade adulta/atual** : (rural (aldeia/vila/quinta) (urbano) Localidade:_____

Características habitacionais:

Tem casa **alcatifada**?	Sim	Não
A sua casa tem **fungos/bolores** nas paredes/teto?	Sim	Não
Tem **animais**?	Sim: Onde? No quintal Dentro de casa Quais? Cão Gato Pássaros Outros, quais?_____	Não

Atividade laboral:

Reformado: Sim ____ Não: ____Qual atividade _____Tempo de exposição: _____anos

Profissões ao longo da vida:	Duração:	Mais recente
Indústria têxtil		
Minas		
Agricultura		
Outra, qual?		

Atividades extralaborais:	Duração
Caça	
Pesca	
Caminhadas	
Jardinagem	
Trabalho com lãs	
Arraiolos	
Outra, qual?	

Habilitações literárias/acadêmicas:

Não estudou
De 4 anos
De 4 a 9 anos
De 9 a 12 anos
+ de 12 anos

CLASSIFICAÇÃO SOCIAL INTERNACIONAL DE GRAFFAR

1. PROFISSÃO:
   1° Grau - Diretores de bancos, diretores técnicos de empresas, licenciados, engenheiros, profissionais com títulos universitários ou de escolas especiais e militares de alta patente.
   2° Grau - Chefes de secções administrativas ou de negócios de grandes empresas, subdirectores de bancos, peritos e técnicos.
   3° Grau - Adjuntos técnicos, desenhadores, caixeiros, contramestres, oficiais de primeira, encarregados, capatazes e mestres de obras.
   4° Grau - Motoristas, policias, cozinheiros, dactilógrafas, etc
   5° Grau - Jornaleiros, porteiros, contínuos, ajudantes de cozinha, mulheres de limpeza, etc ....

2. INSTRUÇÃO:
   1 ° Grau -Ensino Universitário ou equivalente;
   2° Grau -Ensino médio ou técnico superior; 3°
   Grau -Ensino médio ou técnico inferior;
   4° Grau -Ensino Primário completo;
   5° Grau -Ensino primário incompleto.

3. PRINCIPAL FONTE DE R ENDIMENTOS FAMILIARES

Qual é a principal fonte de rendimentos?
Fortuna herdada ou adquirida (Ex: Propriedades)
Altos vencimentos ou honorários (Ex: Lucros de empresas)
Vencimento mensal fixo (Ex: Funcionários)
Remuneração incerta (Ex: Remuneração semanal ou de horas de serviço)
Assistencial (Ex: Beneficência pública ou privada)
Outra. Qual ? _____

4. TIPO DE HABITAÇÃO

De que tipo é a sua habitação?
Casa ou andar luxuoso e muito grande, oferecendo o máximo de conforto Casa ou andar que, sem ser luxuoso, é espaçoso e confortável
Casa ou andar modesto, bem construído, bem conservado, bem iluminado e arejado, com cozinha e casa de banho Casa ou andar degradado, sem electrodomésticos mas com cozinha e casa de Banho
Alojamento impróprio, andar ou barraca desprovido de conforto, ventilação e iluminação, ou onde moram demasiadas pessoas
Outro. Qual ? _____

5. LOCAL DA RESIDÊNCIA

Qual é o aspecto da zona onde habita ?
Bairro residencial elegante, onde o valor do terreno ou os alugueres são elevados (Ex: Bairro elegante)
Bairro residencial bom, de ruas largas com casas confortáveis e bem conservadas (Ex: Bom local)
Ruas comerciais ou estreitas e antigas com casas de aspecto geral menos confortável (Ex: Zonas antigas)
Bairro operário, populoso, mal arejado ou bairro em que o valor do terreno está diminuído como consequência da proximidade de fábricas (Ex: Bairro operário/social)
Bairro "de lata"
Outro. Qual ? _____

CLASSIFICAÇÃO SOCIAL

Aplicando coeficientes de ponderação de 1 a 5 em cada um dos grupos encontrados, obteremos a seguinte classificação:

- Classe 1 – Famílias cuja soma de pontos vai de 5 a 9
- Classe II – Famílias cuja soma de pontos vai de 10 a 13
- Classe III – Famílias cuja soma de pontos vai de 14 a 17
- Classe IV – Famílias cuja soma de pontos vai de 18 a21
- Classe V – Famílias cuja soma de pontos vai de 22 a 25

Antecedentes patológicos

		Não	Sim	Idade	Qual	Caraterização
Infância	Doença respiratória					
	História de alergias					
Idade adulta	Doença respiratória					
	História de alergias					
	Rinite alérgica:					No último ano/nºvezes
	Dermatite atópica:					No último ano/nºvezes
	Outras: Depressão Demência Doenças gástricas:____ DMtipo_____ HTA EAM ICC Antecedentes de Cirurgia Cardiotorácica					

Antecedentes familiares

		Não	Sim	Idade	Qual	Caraterísticas
Doença respiratória	Pai					
	Mãe					
	Irmãos					
História de alergias	Pai					
	Mãe					
	Irmãos					

Hábitos medicamentosos

	Não	Sim, qual?	Dose	Posologia
BAAC (beta agonista acção curta):				
BAAL (beta agonista acção longa):				
IC (inalador corticoide):				
Modificador de Leucotrienos:				
Teofilina:				
CTO (Corticoterapia oral):				
Anti-IgE:				
Vacina anti gripe				
Vacina anti pneumocócica				
Anti-histamínicos				
Antidepressivos tricíclicos				

Beta bloqueadores				
AAS				
Outros: 1. Antidepressivos 2. Anti-hipertensores 3. Anti-deslipidemicos 4. Antidiabéticos orais 5. Insulina 6. IBP				

História de exposição

EXPOSIÇÃO				PRECIPITANTE	
	Não	Sim	Duração	não	sim
Tabagismo ativo	Nunca fumou? Deixou de fumar? Há quanto tempo deixou de fumar?	UMA (anos de fumador*nºcigarros dia/20)=			
Tabagismo passivo					
Lareiras abertas					
Fogão a lenha					
Outros Fumos (qual)					
Aerossóis químicos (inseticidas, sprays desodorizantes, ambientadores…)					
Cheiros intensos (perfumes, lixivia, amoníaco, tintas, vernizes, diluentes)					
Tóxicos agrícolas					
Lãs					
Animais com pêlo					
Animais com penas					
Pó de casa					
Ácaros domésticos					
Pólens					
Fungos					
Infeções virais					
Exercício físico					
Frio/ Variações de temperatura/nevoeiro					
Emoções fortes					
Fármacos, como: AAS B-bloqueadores Ibuprofeno					

Appendix IV: GDS-15, CES-D and MMES

IDOSOS - Escala de depressão geriátrica- GDS

	0	**1**
1 – Satisfeito com a sua vida?	S	N
2 – Teve de abandonar muitas das suas actividades?	N	S
3 – Acha que a sua vida é vazia?	N	S
4 – Aborrece-se muitas vezes?	N	S
5 – Está alegre a maior parte das vezes?	S	N
6 – Tem medo de que lhe aconteça algo de mau?	N	S
7 – Sente-se feliz a maior parte do tempo?	S	N
8 – Sente-se frequentemente sem auxílio?	N	S
9 – Prefere ficar em casa a sair para a rua e fazer coisas novas?	N	S
10 – Acha que tem mais problemas de memória que os outros?	N	S
11 – Acha que é bom estar vivo?	S	N
12 – Acha que a sua vida, como está agora, já não tem valor?	S	N
13 – Acha-se cheio de energia?	S	N
14 – Acha que a sua situação não tem remédio?	S	N
15 – Acha que a maior parte das pessoas está melhor que você?	N	S
	TOTAL	

Chave:

Normal	0-5	
Ligeiramente deprimido, em progressão	6-10	
Gravemente deprimido	11-15	

NÃO IDOSOS – ESCALA DE DEPRESSÃO (CES-D)

Nº.....

CES-D

Encontra nesta página uma lista das maneiras como se pode ter sentido ou reagido. Indique com que frequência se sentiu dessa maneira **durante a semana passada** fazendo uma cruz no quadrado correspondente.

Use a seguinte chave:
- ☐ Nunca ou muito raramente (menos de 1 dia)
- ☐ Ocasionalmente (1 ou 2 dias)
- ☐ Com alguma frequência (3 ou 4 dias)
- ☐ Com muita frequência ou sempre (5 ou 7 dias)

Durante a semana passada:	Nunca ou muito raramente	Ocasional-mente	Com alguma frequência	Com muita frequência ou sempre
1. **Fiquei aborrecido com coisas que habitualmente não me aborrecem**	☐	☐	☐	☐
2. **Não me apeteceu comer; estava sem apetite**	☐	☐	☐	☐
3. **Senti que não conseguia livrar-me da neura ou da tristeza, mesmo com a ajuda da família ou dos amigos**	☐	☐	☐	☐
4. **Senti que valia tanto como os outros**	☐	☐	☐	☐
5. **Tive dificuldade em manter-me concentrado no que estava a fazer**	☐	☐	☐	☐
6. **Senti-me deprimido**	☐	☐	☐	☐
7. **Senti que tudo o que fazia era um esforço**	☐	☐	☐	☐
8. **Senti-me confiante no futuro**	☐	☐	☐	☐
9. **Pensei que a minha vida tinha sido um fracasso**	☐	☐	☐	☐
10. **Senti-me com medo**	☐	☐	☐	☐
11. **Dormi mal**	☐	☐	☐	☐
12. **Senti-me feliz**	☐	☐	☐	☐
13. **Falei menos do que o costume**	☐	☐	☐	☐
14. **Senti-me sozinho**	☐	☐	☐	☐
15. **As pessoas foram desagradáveis ou pouco amigáveis comigo**	☐	☐	☐	☐
16. **Senti prazer ou gosto na vida**	☐	☐	☐	☐
17. **Tive ataques de choro**	☐	☐	☐	☐
18. **Senti-me triste**	☐	☐	☐	☐
19. **Senti que as pessoas não gostavam de mim**	☐	☐	☐	☐
20. **Senti falta de energia**	☐	☐	☐	☐

T.Faculha & B.Goncalves. FPCE-UL. Versão para estudo. Circulacão restrita.

Mini Mental State Examination (MMSE)

1. Orientação (1 ponto por cada resposta correcta)
Em que ano estamos? _____
Em que mês estamos? _____
Em que dia do mês estamos? _____
Em que dia da semana estamos? _____
Em que estação do ano estamos? _____

Nota:____

Em que país estamos? _____
Em que distrito vive? _____
Em que terra vive? _____
Em que casa estamos? _____
Em que andar estamos? _____

Nota:____

2. Retenção (contar 1 ponto por cada palavra correctamente repetida)

"Vou dizer três palavras; queria que as repetisse, mas só depois de eu as dizer todas; procure ficar a sabê-las de cor".
Pêra _____
Gato _____
Bola _____

Nota:____

3. Atenção e Cálculo (1 ponto por cada resposta correcta. Se der uma errada mas depois continuar a subtrair bem, consideram-se as seguintes como correctas. Parar ao fim de 5 respostas)

"Agora peco-lhe que me diga quantos são 30 menos 3 e depois ao número encontrado volta a tirar 3 e repete assim até eu lhe dizer para parar".
27_ 24_ 21 _ 18_ 15_

Nota:____

4. Evocação (1 ponto por cada resposta correcta.)

"Veja se consegue dizer as três palavras que pedi há pouco para decorar". Pêra _____
Gato _____
Bola _____

Nota:____

5. Linguagem (1 ponto por cada resposta correcta)

a. "Como se chama isto? Mostrar os objectos: Relógio ____
Lápis_____

Nota:____

b. "Repita a frase que eu vou dizer: O RATO ROEU A ROLHA"

Nota:____

c. "Quando eu lhe der esta folha de papel, pegue nela com a mão direita, dobre-a ao meio e ponha sobre a mesa"; dar a folha segurando com as duas mãos.
Pega com a mão direita____
Dobra ao meio ____
Coloca onde deve____

Nota:____

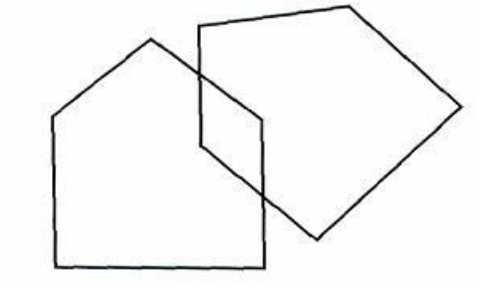
d. "Leia o que está neste cartão e faça o que lá diz". Mostrar um cartão com a frase bem legível, "FECHE OS OLHOS"; sendo analfabeto lê-se a frase.
Fechou os olhos____

Nota:____

e. "Escreva uma frase inteira aqui". Deve ter sujeito e verbo e fazer sentido; os erros gramaticais não prejudicam a pontuação.
Frase:

Nota:____

. Habilidade Construtiva (1 ponto pela cópia correcta.)
Deve copiar um desenho. Dois pentágonos parcialmente sobrepostos; cada um deve ficar com 5 lados, dois dos quais intersectados. Não valorizar tremor ou rotação.



Cópia:

Nota:____

TOTAL(Máximo 30 pontos):____

Considera-se com defeito cognitivo: • analfabetos ≤ 15 pontos
• 1 a 11 anos de escolaridade ≤ 22
• com escolaridade superior a 11 anos ≤ 27

Appendix V: SF36 and AQLQ

QUESTIONÁRIO DE ESTADO DE SAÚDE (SF-36v2)

INSTRUÇÕES: As questões que se seguem pedem-lhe opinião sobre a sua saúde, a forma como se sente e sobre a sua capacidade de desempenhar as actividades habituais.

Pedimos que leia com atenção cada pergunta e que responda o mais honestamente possível. Se não tiver a certeza sobre a resposta a dar, dê-nos a que achar mais apropriada e, se quiser, escreva um comentário a seguir à pergunta.

Para as perguntas 1 e 2, por favor coloque um círculo no número que melhor descreve a sua saúde.

1. Em geral, diria que a sua saúde é:

Óptima	Muito boa	Boa	Razoável	Fraca
1	2	3	4	5

2. Comparando com o que acontecia há um ano, como descreve o seu estado geral actual:

Muito melhor	Com algumas melhoras	Aproximadamente igual	Um pouco pior	Muito pior
1	2	3	4	5

3. As perguntas que se seguem são sobre actividades que executa no seu dia-a-dia. Será que a sua saúde o/a limita nestas actividades? Se sim, quanto?

(Por favor assinale com um círculo um número em cada linha)

	Sim, muito limitado/a	Sim, um pouco limitado/a	Não, nada limitado/a
a. **Actividades violentas**, tais como correr, levantar pesos, participar em desportos extenuantes ...	1	2	3
b. **Actividades moderadas**, tais como deslocar uma mesa ou aspirar a casa.....	1	2	3
c. Levantar ou pegar nas compras de mercearia....	1	2	3
d. Subir **vários** lanços de escada	1	2	3
e. Subir **um** lanço de escadas	1	2	3
f. Inclinar-se, ajoelhar-se ou baixar-se	1	2	3
g. Andar **mais de 1 km**.....	1	2	3
h. Andar **várias** centenas de metros	1	2	3
i. Andar **uma** centena de metros	1	2	3
j. Tomar banho ou vestir-se sozinho/a.....	1	2	3

4. Durante as últimas 4 semanas teve, no seu trabalho ou actividades diárias, algum dos problemas apresentados a seguir como consequência do seu estado de saúde físico?

Quanto tempo. nas **últimas quatro semanas**…	**Sempre**	**A maior parte do tempo**	**Algum tempo**	**Pouco tempo**	**Nunca**
a. Diminuiu o **tempo gasto** a trabalhar ou noutras actividades……	1	2	3	4	5
b. Fez **menos** do que queria? ……	1	2	3	4	5
c. Sentiu-se limitado/a no **tipo** de trabalho ou outras actividades……	1	2	3	4	5
d. Teve **dificuldade** em executar o seu trabalho ou outras actividades (por exemplo, foi preciso mais esforço)……	1	2	3	4	5

5. Durante as últimas 4 semanas, teve com o seu trabalho ou com as suas actividades diárias, algum dos problemas apresentados a seguir devido a quaisquer problemas emocionais (tal como sentir-se deprimido/a ou ansioso/a)?

Quanto tempo, nas **últimas quatro semanas**…	**Sempre**	**A maior parte do tempo**	**Algum tempo**	**Pouco tempo**	**Nunca**
a. Diminuiu o **tempo gasto** a trabalhar ou noutras actividades……	1	2	3	4	5
b. Fez **menos** do que queria? ……	1	2	3	4	5
c. Executou o seu trabalho ou outras actividades **menos cuidadosamente** do que era costume. …..	1	2	3	4	5

Para cada uma das perguntas 6,7 e 8, por favor ponha um círculo no número que melhor descreve a sua saúde.

6. Durante as últimas 4 semanas, em que medida é que a sua saúde física ou problemas emocionais interferiram no seu relacionamento social normal com a família, amigos, vizinhos ou outras pessoas?

Absolutamente nada	**Pouco**	**Moderadamente**	**Bastante**	**Imenso**
1	2	3	4	5

7. Durante as últimas 4 semanas teve dores?

Nenhumas	Muito fracas	Ligeiras	Moderadas	Fortes	Muito fortes
1	2	3	4	5	6

8. Durante as últimas 4 semanas, de que forma é que a dor interferiu com o seu trabalho normal (tanto o trabalho fora de casa como o trabalho doméstico)?

Absolutamente nada	Pouco	Moderadamente	Bastante	Imenso
1	2	3	4	5

9. As perguntas que se seguem pretendem avaliar a forma como se sentiu e como lhe correram as coisas nas últimas quatro semanas.

Para cada pergunta, coloque por favor um círculo à volta do número que melhor descreve a forma como se sentiu.

Certifique-se que coloca um círculo em cada linha.

Quanto tempo, nas **últimas quatro semanas**...		**Sempre**	**A maior parte do tempo**	**Algum tempo**	**Pouco tempo**	**Nunca**
a.	Se sentiu cheio/a de vitalidade?	1	2	3	4	5
b.	Se sentiu muito nervoso/a?	1	2	3	4	5
c.	Se sentiu tão deprimido/a que nada o/a animava?	1	2	3	4	5
d.	Se sentiu calmo/a e tranquilo/a?	1	2	3	4	5
e.	Se sentiu com muita energia?	1	2	3	4	5
f.	Se sentiu deprimido/a?	1	2	3	4	5
g.	Se sentiu estafado/a?	1	2	3	4	5
h.	Se sentiu feliz?	1	2	3	4	5
L	Se sentiu cansado/a?	1	2	3	4	5

10. Durante as últimas quatro semanas, até que ponto é que a sua saúde física ou problemas emocionais limitaram a sua actividade social (tal como visitar amigos ou familiares próximos)?

Sempre	A maior parte do tempo	Algum tempo	Pouco tempo	Nunca
1	2	3	4	5

11. Por favor, diga em que medida são verdadeiras ou falsas as seguintes afirmações. Ponha um círculo para cada linha.

	Absolutamente verdade	Verdade	Não sei	Falso	Absolutamente falso
a. Parece que adoeço mais facilmente do que os outros	1	2	3	4	5
b. Sou tão saudável como qualquer outra pessoa	1	2	3	4	5
c. Estou convencido/a que a minha saúde vai piorar	1	2	3	4	5
d. A minha saúde é óptima	1	2	3	4	5

MUITO OBRIGADO!

Data: _____

Código: _____

AQLQ

Dom.	Cartão	Questão	1	2	3	4	5	6	7
	Ver anexo4	Gostaria que me dissesse até que ponto é que as suas 5 actividades mais importantes foram limitadas pela asma durante as últimas semanas (ver lista de sugestões em anexo3)	1) _____ 2)_____ 3)_____ 4)_____ 5)_____						
A	Verde	1. Por favor diga até que ponto se sentiu limitado pela actividade 1:_____ durante as 2 últimas semanas escolhendo uma destas opções:							
A	Verde	2. Actividade 2:_____							
A	Verde	3. Actividade 3:_____							
A	Verde	4. Actividade 4:_____							
A	Verde	5. Actividade 5:_____							
S	Vermelho	6. Que grau de mal-estar ou aflição sentiu durante as 2 últimas semanas por causa de APERTO/SENSAÇÂO DE PESO NO PEITO?							
EM	Azul	7. Em geral, quanto tempo durante as 2 últimas semanas sentiu PREOCUPADO/A POR TER ASMA?							
S	Azul	8. Quanto tempo durante as 2 últimas semanas sentiu FALTA DE AR por causa da asma?							
EN	Azul	9. Quanto tempo durante as 2 últimas semanas teve sintomas de asma POR ESTAR EXPOSTO/A AO FUMO DE TABACO?							
S	Azul	10. Quanto tempo durante as 2 últimas semanas sentiu PIEIRA (“GATINHOS”/CHIAR) no peito?							
A	Azul	11. Quanto tempo durante as 2 últimas semanas sentiu que TINHA DE EVITAR UMA SITUAÇÃO OU UM AMBIENTE POR CAUSA DO FUMO DE TABACO?							
S	Vermelho	12. Que grau de mal-estar ou aflição sentiu durante as 2 últimas semanas por causa da TOSSE?							
EM	Azul	13. Em geral, quanto tempo durante as 2 últimas semanas teve um sentimento de FRUSTRAÇÃO, TRISTEZA OU REVOLTA por causa da asma?							
S	Azul	14. Quanto tempo durante as 2 últimas semanas teve uma sensação de PESO/APERTO NO PEITO?							
EM	Azul	15. Quanto tempo durante as 2 últimas semanas se sentiu preocupado/a por TER DE TOMAR MEDICAMENTOS OU “BOMBAS” para a asma?							

			1	2	3	4	5	6	7
S	Azul	16. Quanto tempo durante as 2 últimas semanas sentiu necessidade de PIGARREAR (LIMPAR A GARGANTA)?							
EN	Azul	17. Quanto tempo durante as 2 últimas semanas teve sintomas de asma por ESTAR EXPOSTO/A A PÓ?							
S	Azul	18. Quanto tempo durante as 2 últimas semanas teve DIFICULDADE EM EXPIRAR OU INSPIRAR AR?							
A	Azul	19. Quanto tempo durante as 2 últimas semanas sentiu que TINHA DE EVITAR UMA SITUAÇÃO OU UM AMBIENTE POR CAUSA DO PÓ?							
S	Azul	20. Quanto tempo durante as 2 últimas semanas ACORDOU DE MANHÃ COM SINTOMAS DE ASMA?							
EM	Azul	21. Quanto tempo durante as 2 últimas semanas TEVE MEDO OU RECEIO DE NÃO TER À MÃO A MEDICAÇÃO PARA A ASMA?							
S	Azul	22. Quanto tempo durante as 2 últimas semanas se sentiu incomodado/a POR TER DIFICULDADE EM RESPIRAR?							
EN	Azul	23. Quanto tempo durante as 2 últimas semanas teve sintomas de asma por causa do TEMPO, DO CLIMA OU DA POLUIÇÃO DO AR?							
S	Azul	24. Quanto tempo durante as 2 últimas semanas ACORDOU DURANTE A NOITE por causa da asma?							
A	Azul	25. Quanto tempo durante as 2 últimas semanas EVITOU SAIR, OU SAIU MENOS VEZES, POR CAUSA DO TEMPO, DO CLIMA OU DA POLUIÇÃO DO AR?							
EN	Azul	26. Quanto tempo durante as 2 últimas semanas teve sintomas de asma POR ESTAR EXPOSTO/A A CHEIROS FORTES OU PERFUMES?							
EM	Azul	27. Quanto tempo durante as 2 últimas semanas teve MEDO OU RECEIO DE FICAR COM FALTA DE AR?							
A	Azul	28. Quanto tempo durante as 2 últimas semanas sentiu que tinha de EVITAR UMA SITUAÇÃO OU UM AMBIENTE POR CAUSA DE CHEIROS FORTES OU PERFUMES?							
S	Azul	29. Quanto tempo durante as 2 últimas semanas é que a sua asma O/A IMPEDIU DE DORMIR BEM DE NOITE?							
S	Azul	30. Quanto tempo durante as 2 últimas semanas teve de FAZER UM GRANDE ESFORÇO PARA CONSEGUIR RESPIRAR?							
A	Amarelo	31. Pense em TODAS AS COISAS que gostaria de ter feito durante as 2 últimas semanas. Até que ponto é que O NÚMERO DAS SUAS ACTIVIDADES foi limitado pela asma?							
A	Verde	32. De um modo geral, em relação a TODAS AS COISAS que fez durante as 2 últimas semanas, até que ponto é que se sentiu limitado/a por ter asma?							

Cartões de resposta (AQLQ)

Questionário da qualidade de vida na Ama ***Cartão verde***

1. COMPLETAMENTE LIMITADO/A, INCAPAZ DE QUALQUER ACTIVIDADE
2. EXTTREMAMENTE LIMITADO/A
3. MUITO LIMITADO/A
4. MODERADAMENTE LIMITADO/A
5. POUCO LIMITADO/A
6. MUITO POUCO LIMITADO/A
7. NADA LIMITADO/A

Questionário da qualidade de vida na Ama ***Cartão vermelho***

1. MUITÍSSIMO
2. MUITO
3. BASTANTE
4. MODERADO
5. ALGUM
6. MUITO POUCO
7. NENHUM

Questionário da qualidade de vida na Ama ***Cartão azul***

1. SEMPRE
2. QUASE SEMPRE
3. BASTANTE TEMPO
4. ALGUM TEMPO
5. POUCO TEMPO
6. QUASE NUNCA
7. NUNCA

Questionário da qualidade de vida na Ama ***Cartão amarelo***

1. ABSOLUTAMENTE LIMITADO/A – A MAIORIA DAS ATIVIDADES NÃO FOI DESEMPENHADA
2. MUITO LIMITADO/A
3. MODERADAMENTE LIMITADO/A – VÁRIAS ATIVIDADES DESEMPENHADAS
4. POUCO LIMITADO
5. MUITO POUCO LIMITADO/A – MUITAS POUCAS ATIVIDADES NÃO DESEMPENHADAS
6. QUASE NÃO LIMITADO/A
7. ABSOLUTAMENTE NADA LIMITADO/A – DESEMPENHEI TODAS AS ATIVIDADES QUE QUIS

Appendix VI – ACT, CARAT e GINA

1. Durante as últimas 4 semanas, quanto tempo é que a asma o/a impediu de fazer as suas tarefas habituais no trabalho, na escola/universidade ou em casa?				
1 Sempre	**2** A maior parte do tempo	**3** Algum tempo	**4** Pouco tempo	**5** Nunca
❑	❑	❑	❑	❑
2. Durante as últimas 4 semanas, quantas vezes teve falta de ar?				
1 Mais que uma vez por dia	**2** Uma vez por dia	**3** 3 a 6 vezes por semana	**4** Uma ou duas vezes por semana	**5** Nunca
❑	❑	❑	❑	❑
3. Durante as últimas 4 semanas, quantas vezes os sintomas da asma (pieira, tosse, falta de ar, aperto ou dor no peito) o/a fizeram acordar de noite ou mais cedo do que é costume de manhã?				
1 4 ou mais noites por semana	**2** 2 ou 3 noites por semana	**3** Uma vez por semana	**4** Uma ou duas vezes	**5** Nunca
4. Durante as últimas 4 semanas, quantas vezes usou os seus medicamentos para alívio rápido, em inalador ou nebulizador, como por exemplo salbutamol?				
1 3 ou mais vezes por dia	**2** 1 ou 2 vezes por dia	**3** 2 ou 3 vezes por semana	**4** Uma vez por semana ou menos	**5** Nunca
❑	❑	❑	❑	❑
5. Como avaliaria o seu controlo da asma nas últimas 4 semanas?				
1 Não controlada	**2** Mal controlada	**3** Mais ou menos controlada	**4** Bem controlada	**5** Completamente controlada
❑	❑	❑	❑	❑

Interpretação:

5-19 – Asma Não Controlada

> 19 - Asma Controlada

Por favor assinale com uma cruz (☒).

Nas últimas 4 semanas, por causa da sua asma/rinite/alergia, em média, quantas vezes teve:				
	Nunca	**Até 1 ou 2 dias por semana**	**Mais de 2 dias por semana**	**Quase todos ou todos os dias**
1. Nariz entupido?	❑	❑	❑	❑
2. Espirros?	❑	❑	❑	❑
3. Comichão no nariz?	❑	❑	❑	❑
4. Corrimento/pingo do nariz?	❑	❑	❑	❑
5. Falta de ar/dispneia?	❑	❑	❑	❑
6. Chiadeira no peito/pieira?	❑	❑	❑	❑
7. Aperto no peito com esforço físico?	❑	❑	❑	❑
8. Cansaço/dificuldade em fazer as suas atividades ou tarefas do dia-a-dia?	❑	❑	❑	❑
9. Acordou durante a noite?	❑	❑	❑	❑

Nas últimas 4 semanas, por causa da sua asma/rinite/alergia, quantas vezes teve que:				
	Não estou a tomar medicamentos	**Nunca**	**Menos de 7 dias**	**7 ou mais dias**
10. Aumentar a utilização dos seus medicamentos?	❑	❑	❑	❑

SCORE RINITE:_____	**SCORE ASMA:_____**	**SCORE TOTAL:_____**
Controlada	**Controlada**	**Controlada**
Não Controlada	**Não Controlada**	**Não Controlada**
Interpretação:	**Interpretação:**	**Interpretação:**
Até 8 – Mau Controlo	Até 15 – Mau Controlo	Até 24 – Mau Controlo
> 8 - Bom Controlo	≥ 16 – Bom Controlo	> 24 – Bom Controlo

QUESTIONÁRIO GINA 2014

Nas últimas 4 semanas, o doente teve:	
Sintomas diurnos mais que 2 vezes por semana?	Sim Não
Algum despertar noturno devido à asma?	Sim Não
Necessidade de medicação para alívio mais do que 2 vezes por semana?	Sim Não
Alguma limitação da atividade devido à asma?	Sim Não

Bem controlados	**Parcialmente controlados**	**Não Controlados**
Nenhuma destas situações	1-2 destas situações	3-4 destas situações