2ª ed

MEDS

National Survey on Asthma Prevalence

Ana Isabel Alves de Sá e Sousa Santos

MESTRADO EM
EVIDÊNCIA E DECISÃO EM SAÚDE
2º CICLO DE ESTUDOS

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Sumário

Introdução: A asma é uma doença crónica frequente tanto em crianças como em adultos, afectando cerca de 300 milhões de pessoas em todo o mundo. Para avaliar as necessidades das populações relativamente à asma, têm sido realizados vários estudos em todo mundo. No entanto, em relação à prevalência de asma em Portugal existem poucos dados e, como a maior parte dos estudos realizados usam definições não estandardizadas, as estimativas de prevalência são difíceis de comparar.

Objectivos: Estimar a prevalência de asma na população portuguesa a partir de dados do *Inquérito Nacional sobre Asma* e, secundariamente, descrever a associação entre 'Asma atual' e as variáveis demográficas, hábitos tabágicos e comorbilidades.

Métodos: Foi realizado um estudo transversal, a nível nacional, baseado na população, por entrevista telefónica e incluindo todos os concelhos de Portugal. Os participantes foram selecionados aleatoriamente para responder a um questionário baseado na versão portuguesa do estudo GA²LEN. 'Asma atual' foi definida como 'asma durante a vida' auto-reportada *e* pelo menos um dos 3 sintomas nos 12 meses que antecederam a entrevista: pieira, acordar com falta de ar, ou ter tido um ataque de asma. Os resultados foram ponderados para os dados da população provenientes do Censo Nacional de 2001.

Resultados: Foram obtidos dados de 6003 participantes, com idade mediana 57 (min-max, 0-98) anos e 57.3% do sexo feminino. Na população portuguesa, a prevalência de 'Asma atual' foi 6.8% (95%CI 6.0-7.7), de 'Asma durante a vida' foi 10.5% (95%CI 9.5-11.6) e de 'Asma diagnosticada' 5.0% (95%CI 4.2-5.8). Usando a definição de asma do estudo GA²LEN [Jarvis, Newson et al.], a prevalência de asma estimada foi de 7.8% (95%CI 7.0-8.8). As estimativas de prevalência foram semelhantes para todos os subgrupos das variáveis demográficas. Do modelo de regressão logística proposto, observou-se que a exposição ao tabaco ambiental está associada à asma (Adjusted OR 1.45, 95%CI 1.02-2.09). Mais de metade dos sujeitos com 'Asma atual' tinham

também rinite alérgica (52.3%, 95%CI 45.8-58.6). Observou-se também uma forte associação entre sinusite e asma (OR 5.26, 95%CI 3.04-9.11) e a associação entre doenças alérgicas das vias aéreas superiores e asma foi mais forte em doentes com rinite alérgica e sinusite concomitantemente (OR 9.34, 95%CI 4.75-18.35).

Conclusões: A 'Asma atual' afecta 695 000 portugueses, o que corresponde à prevalência de 6.8%, e mais de um milhão (10.5%) tem ou teve asma durante a vida. A exposição ao tabaco ambiental parece estar relacionada com maior risco de asma. A asma está fortemente associada à sinusite e rinite alérgica.

Palavras-chave: Asma, Prevalência, Epidemiologia, *Computer-assisted-telephone–interviewing* (CATI)

Abstract

Introduction: Asthma is a frequent chronic respiratory disease in both children and adults, affecting around 300 million people worldwide. Surveys on asthma have been conducted throughout the world to address population needs. However, few data on asthma prevalence are available in Portugal and as most of the studies use non-standardized definitions, prevalence estimates are difficult to compare.

Aims: To estimate the prevalence of asthma in the Portuguese population using the data from *Inquérito Nacional sobre Asma* and, secondarily, to describe the association between 'Current asthma' and demographic variables, smoking habits and comorbidities.

Methods: A cross-sectional, population-based, nationwide telephone interview survey including all municipalities of Portugal was undertaken. Participants were randomly selected to answer a questionnaire based on the Portuguese version of the GA²LEN survey. 'Current asthma' was defined as self-reported lifetime asthma *and* at least one of 3 symptoms in the 12 months prior to the interview: wheezing, waking with breathlessness or having an asthma attack. Results were weighted for the population data from the National Census 2001.

Results: Data were obtained for 6 003 respondents, with median age of 57 (min-max, 0-98) years and 57.3% females. In the Portuguese population, the prevalence of 'Current asthma' was 6.8% (95%CI 6.0-7.7), of 'Lifetime asthma' was 10.5% (95%CI 9.5-11.6) and of 'Diagnosed asthma' was 5.0% (95%CI 4.2-5.8). Using GA²LEN definition for asthma [Jarvis, Newson et al.], our prevalence estimate was 7.8% (95%CI 7.0-8.8). Prevalence estimates were similar for the demographic subgroups. From the logistic regression model proposed, Environmental Tobacco Smoke is related to asthma (Adjusted OR 1.45, 95%CI 1.02-2.09). More than half of the subjects with 'Current asthma' also had allergic rhinitis (52.3%, 95%CI 45.8-58.6). Sinusitis had a strong association with asthma (OR 5.26, 95%CI 3.04-9.11) and the association between upper

airway diseases and asthma was stronger in patients with both allergic rhinitis and sinusitis (OR 9.34, 95%CI 4.75-18.35).

Conclusions: Current asthma affects 695 000 Portuguese, with a prevalence of 6.8%, and more than one million (10.5%) had lifetime asthma. Exposure to Environmental Tobacco Smoke seems to be related with higher risk for current asthma. Asthma is clearly associated with sinusitis and allergic rhinitis.

Keywords: Asthma, Prevalence, Epidemiology, Computer-assisted-telephone–interviewing (CATI)

Preamble

Since 2009, I work as research assistant for Prof. Doutor João Fonseca in several projects on asthma. Within these projects I've been gathering research information related to clinical aspects of asthma, asthma management, health education, patient empowerment and also cooperating in studies design, data analysis and in the field, collecting data directly from asthma patients. During this period, I became aware of the importance of health policies for the management of chronic diseases such as asthma and how these should be based on evidence. As so, the lack of consistent information related to asthma status for the Portuguese population, as been a growing concern.

During the first year of my graduate education in Health Evidence and Decision Master, I learnt how to address questions like the above, how to design studies, collect and analyse data so that the information provided may become the basis of decision making in health, either by doctors or other professionals, or even by managers or patients. When Prof. Doutor João Fonseca proposed a new project on asthma prevalence I saw an opportunity to learn more in the field about the theoretical aspects of evidence-based medicine learnt during classes.

Although focused on asthma prevalence, being involved in a wide array of research activities allowed me to learn as much as possible in clinical research.

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List of Acronyms

AR	Allergic Rhinitis
BMI	Body Mass Index
CATI	Computer Assisted Telephone Interviews
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
DALYs	Disability-Adjusted Life Years
ECRHS	European Community Respiratory Health Survey
ETS	Environmental Tobacco Smoke
GA²LEN	Global Allergy and Asthma European Network
GINA	Global Initiative for Asthma
INAsma	*Inquérito Nacional sobre Asma*
ISAAC	International Study of Asthma and Allergies in Childhood
NAS	National Asthma Survey
NHANES	National Health and Nutrition Examination Survey
NHS	National Health Survey
NPHS	National Population Health Survey
ONSA	*Observatório Nacional de Saúde*
OR	Odds Ration
ROC	Receiver Operating Curve
SES	Socioeconomic Status

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Thesis outline

This thesis describes the first phase of *Inquérito Nacional sobre Asma* (INAsma survey) in six sections.

The Introduction starts by a clinical definition of asthma, its factors, clinical manifestations and burden. Following, the presented epidemiological surveys give an idea of the prevalence of asthma worldwide and in Portugal and the difficulty to define asthma in epidemiological studies.

Rational and Aim section points out the need for the study presented in this thesis and clearly states the primary and secondary aims.

In Methods section a detailed description of the methodologies adopted is presented in subsections: study design, setting, sample size, sampling design, weighting procedures, variables, bias, statistical analysis, ethical approval.

Results are also organized in subsections. In Participants subsection the sampled participants are characterized; Prevalence of asthma subsection gives the major results of the estimates and of the regression models; Prevalence of symptoms subsection describes the prevalence of respiratory symptoms in the Portuguese population; Healthcare resources subsection presents the estimates for hospitalization, use of diagnostic tests and medication among people with asthma; finally, the association between asthma and comorbities is presented in Comorbidities subsection.

Discussion section gives a critical view of the results, comparing it with results from other studies and points out some limitations of the study.

Concluding remarks and future needs for improvement of the estimates accuracy are presented in Conclusion and Future work section.

Scientific Outcomes

Primeiro Inquérito Nacional sobre Asma (INAsma) – descrição da amostra. Poster presentation in SPAIC's XXI Annual Meeting held between 14 and 17 October 2010 in Madeira.

The Portuguese National Asthma Survey – What is the prevalence of asthma? Poster presentation of preliminary results in EAACI's 30th Congress held between 11 and 15 June 2011 in Istanbul.

Inquérito Nacional sobre Asma – Qual é a prevalência de asma em Portugal? Poster discussion and 2nd prize-winner in SPAIC's XXII Annual Meeting held between 1 and 3 October 2011 in Porto.

1. Introduction

Asthma

The first accurate written report of an asthma attack, describing signs and symptoms goes back to the second century A.D. [Unger and Harris 1974]. Nowadays, the clinical, physiological and pathological characteristics of asthma have been combined by the Global Initiative Program for Asthma (GINA) in the definition "Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment"[GINA].

Asthma is influenced by both host-specific factors and environmental factors. The first, that may cause the development of asthma include genetic disposition, maturation of the immune response and infection exposure during the first year of life [Bateman, Hurd et al.]. The latter factors include air pollution (cigarette smoke, fumes from heating, vehicle exhausts, cosmetics and aerosol sprays) [Jacquemin, Kauffmann et al.] and exposure to allergens (commonly dust mites and animal fur; less commonly pollens, moulds and allergens encountered in the workplace), and can interact with genetic factors to determine asthma susceptibility. They are also triggers of asthma symptoms, being associated with uncontrolled asthma [Bateman, et al.] . Other factors such as atopy and exposure to tobacco smoke influence the risk of allergic sensitization. Environmental tobacco smoke is associated with asthma in children and adults . Tobacco smoking increases the severity of symptoms, by accelerating lung function impairment and reducing the therapeutic response to corticosteroids [Thomson, Chaudhuri et al.] [Bousquet, Dahl et al.]. Rhinitis, particularly severe persistent rhinitis, is also

a risk factor for asthma development and both diseases frequently co-exist in the same patient [Bousquet, et al.].

Clinical manifestations of asthma can be controlled with appropriate therapy. Criteria for successfully managed asthma include no symptoms or very mild symptoms, no exacerbations, no emergency room visits, no limitation of activities, no airflow limitation (PEF ≥ 80% of predicted value), minimal bronchodilator use (< 2 times/week) and the least side effects possible [GINA] . Medications for asthma management are classified as controllers and relievers. Controllers are taken in a long-term basis and have anti-inflammatory effects that keep asthma under clinical control. Relievers are used on an as-needed basis and act quickly to reverse bronchoconstriction that occurs in asthma exacerbations. The most common way of administration for both controllers and relievers is the inhaled form [GINA]. Asthma guidelines also play an important role in asthma management, encouraging awareness and improving patient care, by focusing on the assessment of asthma symptoms and their severity, and recommendations for effective medicines in children and adults, as well as non-pharmacological measures .

Asthma affects around 300 million people worldwide corresponding to 15 million DALYs / year, similar to diabetes [Bousquet, et al.]. Asthma affects quality of life; school/work performance and family/social life; physical capabilities are further impaired by co-morbidities, mainly allergic rhinitis [Leynaert, Neukirch et al.]. Asthma has both individual and social impact and its costs are associated with emergency room use, hospitalizations and medication (direct costs) and time off work or school and early retirement (indirect costs) [Barnes, Jonsson et al.]. The costs of asthma are higher in severe or uncontrolled asthma [Godard, Chanez et al.] and are likely to rise as its prevalence increases [Barnes, et al.]. Hospitalization for asthma is one measure of asthma severity and burden. Hospitalization rates decreased in countries where asthma managements programs have been implemented [Bousquet, et al.] [Haahtela, Tuomisto et al.]. In mainland Portugal, between 2002 and 2007, 24 271 people were hospitalized because of asthma with a total cost of around €27 billion. Despite the implementation of a National Program for Asthma Management , only two main regions achieved its goals, reducing in at least 20% asthma hospitalizations in this period [Bugalho de Almeida, Covas et al.] [Bugalho De Almeida].

Asthma prevalence in epidemiological surveys

The World Health Organization recommends the assessment of population needs related to asthma and other chronic respiratory diseases, in order to define adequate health policies [Bousquet, et al.]. Epidemiological studies at a population level, contribute to that purpose. Prevalence studies are central in this regard. Several examples of nationwide prevalence studies are the *National Asthma Survey* (NAS) [O'Connor, Osborn et al.] and the *National Health and Nutrition Examination Survey* (NHANES) [McHugh, Symanski et al.] in USA; the *National Population Health Survey* (NPHS) in Canada [Ghosh, Pahwa et al.] and the *National Health Survey* (NHS) in Australia [McLennan]. From all the multinational studies on prevalence of asthma, the *European Community Respiratory Health Survey* (ECRHS) in adults [Burney, Luczynska et al.] and the *International Study of Asthma and Allergies in Childhood* (ISAAC) in children [Asher, Keil et al.] stand out. Recently, the EU-funded *Global Allergy and Asthma European Network* (GA²LEN) is conducting a large survey on the prevalence of airway and allergic diseases, based mainly on the questions and definitions used by the ECRHS [Bousquet, Burney et al.]. ISAAC aimed to describe the prevalence and severity of asthma, rhinitis and eczema in children with 6-7 years old and 13-14 years old living in different centres, and to make comparisons within and between countries [Asher, et al.]. ECHRS aimed to estimate the variation in the prevalence of asthma, asthma-like symptoms and bronchial responsiveness in Europe; to estimate variation in exposure to known or suspected risk factors for asthma and to estimate the variation in treatment practice for asthma in the European Community [Burney, et al.]. GA²LEN epidemiological survey is an extension of ECRHS to study a wider age range and a wider range of other conditions and aimed to assess the prevalence of allergic and airway diseases and to indicate the trends of prevalence and severity of allergic diseases and asthma in Europe [Bousquet, et al.].

Asthma affects people of all ages and all ethnic backgrounds [Bousquet, et al.]. Asthma prevalence tends to increase as communities adopt modern lifestyles and become urbanized: it is estimated that there may be an additional 100 million persons with asthma by 2025 [Masoli, Fabian et al.] . However, in some countries with high asthma prevalence, it seems that rising trends have reached a plateau or are even decreasing [Lotvall, Ekerljung et al.] [Asher, Montefort et al.] [Anderson, Ruggles et al.] [Zollner, Weiland et al.]. This may be due to an increased awareness of the disease, to the fact that asthma may have become milder or to the implementation of national and global asthma prevention and management guidelines and

consequent earlier detection and improved treatment of asthmatics [von Hertzen and Haahtela].

Portugal was one of the first countries to set up a national program on asthma . However, few population data on asthma prevalence is available in Portugal. The majority of the asthma studies in Portugal were done on school-attending children and teenagers from selected cities or regions. The prevalence of Current asthma in these populations ranged between 3% and 8% and of lifetime asthma between 4% and 15% (Appendix A). The ISAAC study in Portugal assessed the prevalence of asthma in four cities. For children aged 6-7 years old the global prevalence of asthma in last 12 months was 13% (in Lisboa, Portimão and Funchal); for teenagers with 13-14 years old the global prevalence of current asthma ranged between 9% in 1995 and 12% in 2002 (in Lisboa, Porto, Portimão, Funchal) [Rosado Pinto]. For adults, the asthma prevalence studies, published so far were done on military service conscripts [Chieira, Loureiro et al.], in primary care units [Nunes] [Correia-de-Sousa, Espirito-Santo et al.], using postal questionnaires [Loureiro, Chieira et al.] [Marques] or using postal questionnaire followed by a clinical visit [Alves, Hespanhol et al.]. The reported prevalence of asthma ranged between 3% and 10% (Appendix A). The ECRHS I included data collected in two Portuguese cities. A total of 3850 participants responded to the postal questionnaire, and the estimated prevalence of asthma diagnosis was 4% in Porto and 6 % in Coimbra [Burney, Chinn et al.]. The GA²LEN survey only included one Portuguese city, Coimbra, and the estimated asthma prevalence was 17% [Jarvis, et al.]. The telephone national survey about chronic illness that was conducted by the *Observatório Nacional de Saúde* (ONSA) included 2820 adults and estimated a prevalence of asthma of 9% [Branco, Nogueira et al.] however, it only included adults and asthma was addressed only in one question among other questions on chronic diseases, which arises problems with asthma definition [Pekkanen, Sunyer et al.]. The Portuguese National Health Survey of 2005/2006 [INE and INSA] included participants from all age groups and asthma questions were asked among other questions on chronic diseases. In this survey, 6% (581 725) of the Portuguese population reported having or have had asthma [INE and INSA].

Definition of asthma in epidemiological studies

There is no generally accepted definition of asthma for epidemiological surveys. The difficulty to correctly diagnose asthma in prevalence cross-sectional studies, lead to the use of validated questionnaires and operational definitions of asthma. Ideally, this definition cannot be a dichotomy but should be defined by a combination of symptoms, clinical diagnosis and bronchial responsiveness [Pekkanen, et al.] [Pekkanen and Pearce] [Toren, Brisman et al.] [Burney, Laitinen et al.] [de Marco, Cerveri et al.]. In fact, some studies use a symptoms questionnaire in a first phase and, in a second phase, perform a clinical assessment with lung function tests in subsamples of symptomatic and asymptomatic subjects in subsequent phases [Asher, et al.] [Burney, et al.]. However, in surveys, selecting the most valid combinations of questions for identifying asthma is not straightforward and may depend on the goal of the study. If the aim of applying a symptom questionnaire in a survey is to identify as many cases as possible, it is essential to select questions with high sensitivity; on the other hand, to estimate risk factors, questions with high specificity should be used. Studies on validation of asthma questionnaires used bronchial hyperresponsiveness tests and physician's diagnosis as gold standard and concluded that questions on wheeze are the most sensitive; questions as "Have you ever had asthma?" or questions on waking with attacks of shortness of breath and morning tightness have high specificity for predicting asthma [Burney, et al.] [de Marco, et al.] [Toren, et al.]. The definition of asthma varies considerably both in International and Portuguese studies (Appendix A) and can be grouped in 3 major definitions: 'Lifetime asthma' if the respondent reported ever having had asthma; 'Diagnosed asthma' if reported asthma diagnosis by a health professional or receiving medication in the 12 months previous to the interview and 'Current asthma' if having asthma symptoms during the 12 months previous to the study.

2. Rational and Aim

Evidence-based public health strategies for chronic diseases need to consider firstly their prevalence and then the proportion of patients not achieving the treatment objectives, as these correspond to most of the burden and costs [Canonica, Bousquet et al.]. Moreover, the involvement of participants from diverse countries and lifestyles in Europe-wide studies is fundamental to understand causes and development of allergic diseases [Bousquet, et al.].

Portugal was one of the first countries to set up a National Program for Asthma Control. Although one of the specific aims of the Programme was the improvement of the epidemiological asthma survey , few data on asthma prevalence are available in Portugal. In Portugal, both ECRHS and ISAAC were conducted in a limited number of cities [Marques] [Loureiro, et al.] [Nunes, Ladeira et al.]. In GA²LEN, only one Portuguese city was included [Bousquet, et al.]. Studies in Portuguese regions [Nunes and Ladeira] [Chieira, et al.] [Nunes] [Santos] [Alves, et al.] [Prata, Marto et al.] [Vicente, Rodrigues et al.] [Morais-Almeida, Câmara et al.] [Leiria Pinto] [Barros, Pereira et al.] [Falcão, Ramos et al.] [Correia-de-Sousa, et al.] [Pegas, Alves et al.] estimated the prevalence of asthma mostly on children. The only nationwide studies were ONSA in 2004 and Portuguese NHS in 2005/2006. However, the telephone national survey conducted by the ONSA [Branco, et al.] only included adults and asthma was addressed only in one question among other questions on chronic diseases, which arises problems with asthma definition [Pekkanen, et al.]; and the Portuguese National Health Survey of 2005/2006 [INE and INSA] included participants from all age groups but asthma questions were asked among other questions on chronic diseases. The first and only nation-wide survey regarding chronic diseases of the airways was on the prevalence of allergic rhinitis [Morais-Almeida, Loureiro et al.] but didn't address asthma prevalence. Thus, none of the published studies done exclusively on asthma in Portugal could be generalized to the Portuguese population and as most of the studies use non-standardized questionnaires and different operational definitions, prevalence estimates are difficult to compare.

The Portuguese national asthma survey – *Inquérito Nacional sobre Asma* (INAsma) was launched by the scientific societies, *Sociedade Portuguesa de Alergologia e Imunologia Clínica* and *Sociedade Portuguesa de Pneumologia* and was commissioned by the Portuguese Health Directorate (*Direcção Geral da Saúde)*. INAsma is the first population-based study that uses standardized methods. It comprises two phases. In the first phase, the aim is to estimate the prevalence of Current asthma and in the second phase, the aim is to determine the proportion of asthmatic patients with controlled disease.

Specifically, this thesis describes the first phase of INAsma and aims to:

1. Estimate the prevalence of asthma in the Portuguese population;
2. Describe the association between 'Current asthma' and demographic variables;
3. Describe the association between smoking habits and the risk of having 'Current asthma';
4. Describe the association between 'Current asthma' and comorbidities such as allergic rhinitis and sinusitis.

3. Methods

Study design

The general aim of the first phase of INAsma is to estimate the prevalence of asthma in the Portuguese population. The prevalence survey was a cross-sectional, population-based, nationwide telephone interview survey including all municipalities of Portugal.

Setting

The main instrument for data collection was the Portuguese version of the 21-item questionnaire used in the GA²LEN survey (Appendix B). This questionnaire includes the ECHRS questions on asthma symptoms [Bousquet, et al.] [Burney, et al.]. Questions adapted from previous studies [Fonseca, Vaz et al.] were used to collect information on airway symptoms, smoking, BMI, socio-educational variables and healthcare use.

A private company administered the questionnaire through Computer Assisted Telephone Interviews (CATI) performed by trained and experienced interviewers. Interviews were conducted between March and May of 2010, mostly between 17:00-22:00 at weekdays and 11:00-22:00h at weekend and holidays. Each telephone number was not abandoned before a minimum of ten attempts in different occasions. The interviews had a mean duration of 15 minutes.

Sample size

The sample size of this study was calculated considering the two phases of the project. In the first phase, we aimed to estimate Current asthma prevalence in the Portuguese population. In the second phase we aimed to estimate the

proportion of asthma patients that have their disease controlled. Thus, in the phase 2 of the project, in order to estimate the proportion of controlled asthma patients with a margin of error of 3% and a 95% confidence level, assuming a proportion of 20% of uncontrolled asthma patients in the population, we needed a sample of at least 554 asthma patients identified in the first phase of the project. Assuming a loss of patients to follow-up of 20%, we needed to recruit at least 665 asthma patients during the first phase. Within these premises, and assuming a prevalence of 6% in the Portuguese population and a margin of error of 0.65% we needed a sample of at least 6000 persons from the general Portuguese population willing to participate in the first phase of the project.

Sampling design

The defined target population was the Portuguese general population and the available population included all individuals living in Portugal in households with a landline telephone (sampling frame). To obtain a representative sample of the general population, a stratified cluster sampling design was used.

First, all municipalities were used as natural strata; in each municipality a sample of households with landline telephone numbers was selected with a probability proportional to municipality population as estimated in the 2001 National Census. The target number of households was set as 6 103. The sample of households was derived from the directory listed in residential *White Pages* from 2010. To draw a sample of telephone numbers in a municipality a list of all telephone numbers in that municipality was compiled. From the whole list of each municipality, a sample of household's telephone numbers was randomly selected. Because part of the selected telephone numbers are from companies or are not allocated, 4 lists were randomly selected for each municipality. A total of 24 412 telephone numbers were retrieved.

Next, one participant was randomly selected in each household. After questioning about all the residents in the household, the selected participant in each household was the last person having his/her birthday. When the selected individual was younger than 15 years old the respondent was the usual caregiver. Individuals were excluded if didn't understand spoken Portuguese or with cognitive or physical conditions that could hamper the interview. In the final 20% of the sample, an oversampling strategy of males and younger age

subjects was used to correct the common overrepresentation of participants from the female sex and older age groups.

Weighting procedures

To obtain a population-based estimate, a sampling weight was assigned to each sampled participant. This weight is composed of a sampling design weight (based sampling weight and subsampling adjustments). This final weight was post-stratified so that the sum of the weights at national level for each municipality equals the population totals from the National Census 2001.

The selected telephone numbers represent a random sample of all possible telephone numbers in each municipality. The first step in the weighting is to determine the 'base sampling weight' for each telephone number (or household, given that each telephone number corresponds to a single household). This must be reciprocal to the probability of selecting the household's telephone number. The probability of selecting a telephone number can be calculated; if in a given municipality exist 1 000 telephone numbers and 100 of those were selected for the study, the probability that any telephone number would be selected is 100/1000 (or 0.10). Then each selected telephone number represents 1/0.10 (or 10) telephone numbers in the given municipality. This number – the inverse of the 'probability of selection for any telephone' number (p) – is the 'base sampling weight' (w) for each interview in that municipality. The base sampling weight for a household in a particular municipality is given by

$$w = \frac{1}{p}$$

In the second step of sampling design, one household member was randomly selected from all the household members. As previously, in households with more than one member, the randomly selected person represents all the nonelected people in the household. Therefore, the sampling weight must reflect the probability of selection of one member among the total number of household members. The 'number of household members in a household' in an particular municipality is given by m_k. The sampling 'weight for the selected person' (w^p) is

$$w^p = w \cdot m_k$$

Even now, with the final sampling weighting, the estimated number of people is unlikely to match the number of people in the population sample. These discrepancies are due to possible random sampling error and response

bias. Therefore, post-stratification weight adjustments are needed to adjust the weight to match population counts from 2001 National Census for main demographic variables. INAsma weight was adjusted so that their sum corresponded the number of males and females in 21 age groups and in each NUTS II region given by the 2001 National Census.

Variables

Prevalence studies are a subgroup of cross-sectional studies in which disease outcome is dichotomous. Given the difficulty to diagnose asthma in epidemiological surveys, most studies use a symptoms questionnaire in a first phase and a clinical assessment with lung function tests in subsamples of symptomatic and asymptomatic subjects in subsequent phases [Asher, et al.] [Burney, et al.].

The primary outcome, common co-morbidities and confounders were defined as follows; other operational definitions are listed in Appendix C.

Current asthma: positive answer to the question "Have you ever had asthma?" *and* at least one of 3 symptoms in the last 12 months: wheezing, waking with breathlessness or having an asthma attack.

Allergic Rhinitis: positive answer to the question "Do you have any nasal allergies, including hay fever?" Further classification of rhinitis in intermittent, persistent, mild and moderate/severe was done according to ARIA using GA²LEN survey questions [Bousquet, Khaltaev et al.]

Sinusitis: positive answer to questions "Have you been diagnosed as having chronic sinusitis by a doctor?" *and* "Have you felt sinus pressure, pain around the eyes or nose, for more than 12 weeks in last 12 months?"

Chronic bronchitis: positive answer to questions "Did you have phlegm when coughing for at least 3 months in the last year?" *and* smoked more than 10 Packs-year *and* have at least 40 years old.

Smokers reported smoking at least one cigarette every day for one year*; Ex-smokers* reported having quit smoking for more than one month; *Non-smokers*

reported neither smoking nor ex-smoking. *Packs-year* is the number of cigarettes smoked per day / 20 * number of years smoking.

Environmental Tobacco Smoke: Positive answer to "Does anyone smokes inside your home?"

Heart disease: Positive answer to "Have you a heart condition?"

Bias

The available population included all individuals living in Portugal in households with a landline telephone. Generalizability of the results may be compromised due the increasing preference for mobile phones over residential telephones. However, the use of mobile phone does not allow stratification by geographical region; reduces control over the sampling method and has a lower response rate [Brick, Brick et al.].

To minimize other potential biases in data collection, several quality assurance measures were followed: interviewers were selected based on their previous experience on health-related data collection; each question was discussed in training sessions held between researchers and all interviewers; a research assistant was present in the setup, training and daily work of the interviewers, motivating and checking the compliance with the standardized operational procedures; data validity was periodically verified soon after being collected and custom statistic algorithms were used to detect extreme, illogical and missing values; the clarity of the questionnaire and its telephonic administration was assessed in a pilot study with 25 individuals before starting the data collection.

Statistical analysis

The estimates from the sample were weighted so they could be generalized to the target population. The complex sampling analysis plan was built in two stages. A two-stage stratified sampling design was used, including two steps. First, a simple random sampling without replacement was used for selecting a random sample of households with landline telephone within each stratum (municipality). Second, within each selected household, one eligible household resident was randomly selected using simple random sampling without

replacement. Two types of weights were used has stated above (*Weighting procedures* section).

Categorical variables were described with absolute frequencies, proportions and 95% Confidence Interval (95% CI). Comparisons of proportions were tested with Pearson Chi-Square for complex samples. A p-value of <0.05 was considered as statistically significant. Univariate analysis was used to assess associations between Current asthma and rhinitis, sinusitis, chronic bronchitis and non-respiratory allergic disease. In order to have a more thorough understanding of the factors affecting its distribution and risk, analysis of factors associated with Current asthma were performed using univariate and multivariate weighted logistic regression modelling. In the multivariate logistic regression models, the dependent variable was presence of Current asthma and the independent variables were region, gender, age, body mass index (BMI), education level, socioeconomic status, smoking status, unit packs-years and Environmental Tobacco Smoke (ETS). Model goodness-of-fit was assessed by the Hosmer-Lemeshow test. Discriminative/predictive power of the model was evaluated by ROC curve analysis. Results are presented as odds ratios (OR) for each category as compared with a predefined reference category and their respective 95% Confidence Intervals (95%CI). For the initial model all the covariates with p-value of <0.25 were included. The final multiple logistic regression model included age, BMI, education level, Unit packs-year and ETS.

Statistical analyses were performed using IBM SPSS Statistics version 19 (2010 SPSS, Inc. an IBM Company).

Ethical approval

The study was approved by a Hospital Ethics Committee (*Comissão de Ética do Hospital de São João*, Porto). All participants gave oral informed consent and were informed that they could abandon the study whenever they pleased, without any implication for their healthcare. Data confidentiality was guaranteed by storing personal information separately from the study data.

4. Results

Participants

Of 17698 contacts, 6003 subjects completed the interview (Figure 4.1). The simple response rate[1] was 40%; the corrected response[2] rate was 50%.

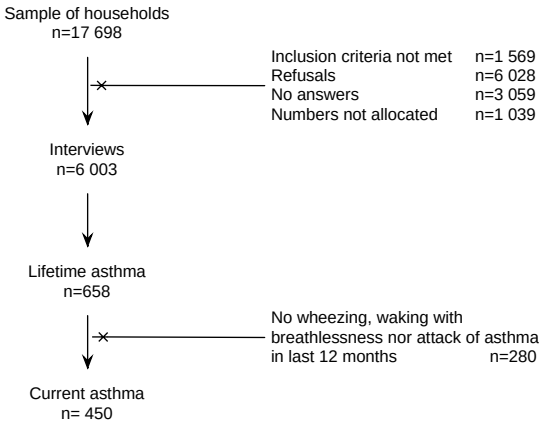

Figure 4.1: Participants flowchart. From the 17 698 households contacts, 6 003 participants were included in the study; 658 classified as having 'Lifetime asthma' and 450 as having 'Current asthma'

Participants' characteristics are summarized in Table 4.1. From the 6003 participants, 1993(33%) were from North region, 1391(23%) from Centre, 1651(28%) from Lisbon, 729(12%) from Alentejo and Algarve, 239(4%) from R. A. Madeira and R. A. Açores. The variable Alentejo was merged with Algarve, and R.A. Madeira with R.A. Açores because, although proportional with the population estimate for each region, the participations in these regions

[1]Interviews/(Contacts + Refusals + No answers).
[2] Interviews/(Contacts + Refusals)

were low (Alentejo 8%, n=483; Algarve 4%, n=246; R.A. Madeira 2%, n=122; R.A. Açores 2%, n=117). Most participants were adults (52%, n=3104); 57%(3438) belonged to female sex; 44% (2179) had normal weight and 66% (3907) had school education level inferior to 9th grade. 71% (4137) of the participants belonged to the medium social class. As for smoking status, 72% (4291) were non-smokers and 19% (1150) smoked more than 10 packs-year. From the 6 003 participants, 450 had 'Current asthma'. There were no missing data for each variable that comprised 'Current asthma' definition.

In Appendix D it is presented the comparison between the weighting procedures results and the values in the Portuguese population according to National Census of 2001 and the preliminary results of the National Census of 2011.

Table 4.1: Socio-demographic characteristics of the participants by Current asthma status. 'Current asthma was defined as positive answer to the question "Have you ever had asthma?" and at least one of 3 symptoms in the last 12 months: wheezing, waking with breathlessness or having an asthma attack.

		Current asthma	
	Total (n=6 003)	**Yes (n=450)**	**No (n=5 553)**
Female, n (%)	3438 (57.3)	282 (62.7)	3156 (56.8)
Age groups, n (%)			
<18 years old	716 (11.9)	56 (12.4)	660 (11.9)
18-65 years old	3104 (51.7)	211 (46.9)	2893 (52.1)
>65 years old	2178 (36.3)	183 (40.7)	1995 (36.0)
BMI†, n(%)			
Underweight (<18)	253 (5.1)	18 (4.9)	235 (5.1)
Normal weight (18-25)	2179 (43.9)	140 (38.4)	2039 (44.3)
Overweight (25-30)	1825 (36.7)	128 (35.1)	1697 (36.9)
Obese (>30)	710 (14.3)	79 (21.6)	631 (13.7)
Education level‡, n(%)			
<9 years	3907 (65.5)	312 (69.6)	3595 (65.1)
9-12 years	1175 (19.7)	85 (19.0)	1090 (19.7)
>12 years	732 (12.3)	40 (8.9)	692 (12.5)
SES††, n(%)			
Low	1289 (22.0)	111 (25.2)	1169 (21.7)
Medium	4137 (71.1)	1169 (21.7)	3831 (71.2)
High	405 (7.0)	23 (5.2)	382 (7.1)
Smoking status, n(%)			
Non-smoker	4291 (71.5)	333 (74.0)	3958 (71.3)
Ex-smoker	971 (16.2)	71 (15.8)	900 (16.2)
Current smoker	741 (12.3)	46 (10.2)	695 (12.5)
Unit Packs-year, n(%)			
≤10 Packs-year	4799 (79.9)	368 (82.3)	4431 (80.5)
>10 Packs-year	1150 (19.2)	79 (17.7)	1071 (19.5)
ETS‡‡, n(%)			
No	4843 (80.7)	347 (77.1)	4496 (81.0)
Yes	1160 (19.3)	103 (22.9)	1057 (19.0)

† Body Mass Index. ‡A total of 153 (2.5%) children were pre-schoolers (not shown). ††Socioeconomic Status was categorized in high (A social class), medium (B and C social classes) and low (D social class) based on occupation and school education of the person who contributes more for the household income. ‡‡Environmental Tobacco Smoke.

Prevalence of asthma

The prevalence of 'Current asthma' was 6.8% (95%CI 6.0-7.7), of 'Diagnosed asthma' was 5.0% (95%CI 4.2-5.8) and the 'Lifetime asthma' prevalence was 10.5% (95%CI 9.5-11.6). Using GA²LEN definition for asthma [Jarvis, et al.], our prevalence estimate was 7.8% (95%CI 7.0-8.8). In those with 'lifetime asthma', 72.8% had their first asthma attack before 18 years old, 25.5% between 18 and 64 years old and 1.7% after 65 years old.

'Current asthma' prevalence was similar in men and women and in all age groups (Table 4.2), however there is a tendency to be higher in male children and as children get older the prevalence differences between genders tend to narrow, being higher in female older adults (Figure 4.2). 'Current asthma' prevalence tended to be higher in obese and in older people (Table 4.2).

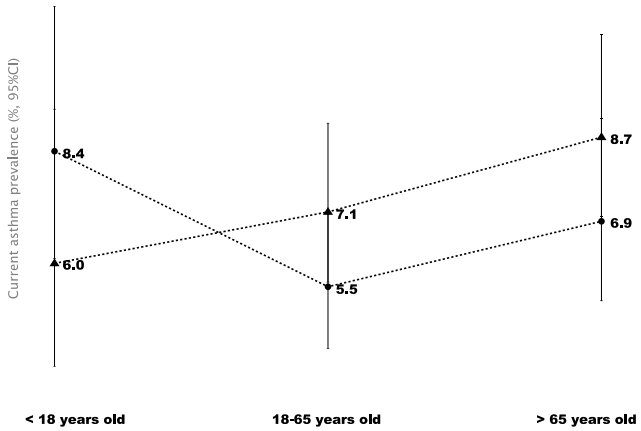

Figure 4.2: Asthma prevalence by age and gender. There is a tendency to be higher in male (circle) children and in female (triangle) older adults.

Exposure to Environmental Tobacco Smoke (ETS) at home was reported by 26.6% (95%CI 25.5-27.7) of the population. Prevalence of asthma was higher in people exposed to ETS (8.6%; p=0.020) and there is an association between ETS and 'Current asthma' (Crude OR 1.45, 95%CI 1.06-1.97) (Table 4.2).

Asthma was more frequent in people who did not smoke or smoked less than 10 packs-year (7.1%) than in those who smoked more than 10 packs-year (5.2%; p=0.042). Those who smoke more have lower risk of asthma (Crude OR 0.71, 95%CI 0.51-0.99) (Table 4.2). This tendency was significant after

adjustments of unit packs-years for gender, age, Body Mass Index (BMI), education level and for ETS (data not shown).

In the multiple logistic regression, the risk of 'Current asthma' was assessed for age, BMI, education level, unit packs-year and ETS (Adjusted OR, Table 4.2). After this adjustment, the risk of asthma was higher for people exposed to ETS (Adjusted OR 1.46, 95%CI 1.02-2.09, p=0.037). The Hosmer-Lemeshow statistic revealed poor calibration (p<0.001) and the predictive power was low (AUC=0.59, 95%CI 0.56-0.62).

Table 4.2: Prevalence of 'Current asthma' by socio-demographic characteristics groups and logistic regression models with crude and adjusted Odds Ratio (OR) for Current asthma.

	Current asthma % (95%CI)	**Crude OR (95%CI)**	**Adjusted OR (95% CI)§**
All Portuguese Population	6.8 (6.0- 7.7)		
North	6.7 (5.5- 8.2)	1.00 (Ref)	
Centre	6.2 (4.6- 8.3)	0.92 (0.63-1.35)	
Lisbon	6.8 (5.4- 8.6)	1.01 (0.72-1.42)	
Alentejo/Algarve	7.9 (5.4-11.3)	1.18 (0.75-1.87)	
Madeira/Azores	6.6 (3.9-10.9)	0.98 (0.55-1.77)	
Gender			
Female	7.2 (6.0- 8.5)	1.00 (Ref)	
Male	6.3 (5.2- 7.6)	0.87 (0.66-1.14)	
Age groups			
<18 years old	7.2 (5.4- 9.5)	1.00 (Ref)	1.00 (Ref)
18-65 years old	6.3 (5.3- 7.5)	0.86 (0.61-1.23)	0.83 (0.52-1.34)
>65 years old	8.0 (6.7- 9.5)	1.11 (0.78-1.59)	1.08 (0.64-1.81)
BMI†			
Underweight (<18)	6.6 (4.0-10.5)		
Normal weight (18-25)	6.1 (4.9- 7.7)	1.00 (Ref)	1.00 (Ref)
Overweight (25-30)	6.4 (5.1- 8.0)	1.04 (0.75-1.44)	1.12 (0.79-1.59)
Obese (>30)	8.7 (6.5-11.7)	1.44 (0.98-2.14)	1.54 (1.02-2.32)
Education level‡			
<9 years	7.1 (6.1- 8.2)	1.00 (Ref)	1.00 (Ref)
9-12 years	7.4 (5.6- 9.7)	1.05 (0.75-1.47)	1.24 (0.87-1.77)
>12 years	4.5 (3.0- 6.6)	0.62 (0.40-0.96)	0.67 (0.41-1.10)
SES††			
Low	6.9 (5.3- 8.9)	1.00 (Ref)	
Medium	6.9 (5.9- 8.0)	1.00 (0.73-1.37)	
High	6.3 (3.8-10.3)	0.91 (0.50-1.66)	
Smoking status			
Non-smoker	6.9 (6.0- 8.0)	1.00 (Ref)	
Ex-smoker	6.3 (4.7- 8.5)	0.91 (0.63-1.30)	
Current smoker	6.3 (4.3- 9.1)	0.90 (0.59-1.34)	

	Current asthma % (95%CI)	Crude OR (95%CI)	Adjusted OR (95% CI)§
Unit Packs-year			
≤ 10 Packs-year	7.1 (6.2- 8.2)	1.00 (Ref)	1.00 (Ref)
>10 Packs-year	**5.2 (3.9- 6.8)**	**0.71 (0.51-0.99)***	0.72 (0.51-1.02)
ETS‡‡			
No	6.1 (5.3- 7.0)	1.00 (Ref)	1.00 (Ref)
Yes	**8.6 (6.7-11.0)**	**1.45 (1.06-1.97)****	**1.45 (1.02-2.07)*****

† Body Mass Index - for logistic regression 'underweight' and 'normal weight' were merged. ‡Pre-schoolers' and <9 years were merged. *p=0.042. ††Socioeconomic status was categorized in high (A social class), medium (B and C social classes) and low (D social class) based on occupation and school education of the person who contributes more for the household income. ‡‡Environmental Tobacco Smoke. **p=0.020. § Final multiple logistic regression model included age, BMI, education level, unit packs-year and ETS as independent risk factors for Current asthma. ***p=0.037. Significant results in bold. OR – odds ratio.

To exclude possible confounding of asthma related symptoms with symptoms from self-reported heart disease, heavy smoking habits (smoking more than 10 packs-year) and chronic bronchitis a subgroups analysis was performed. The prevalence of 'Current asthma' did not change significantly after adjustment for these conditions (Figure 4.3). However, in the older adults subgroup the participants with self-reported heart disease had a significantly lower prevalence of Current asthma (older adults without heart disease 4.9%, 95%CI 3.9-6.2; all older adults 8.0%, 95%CI 6.7-9.5).

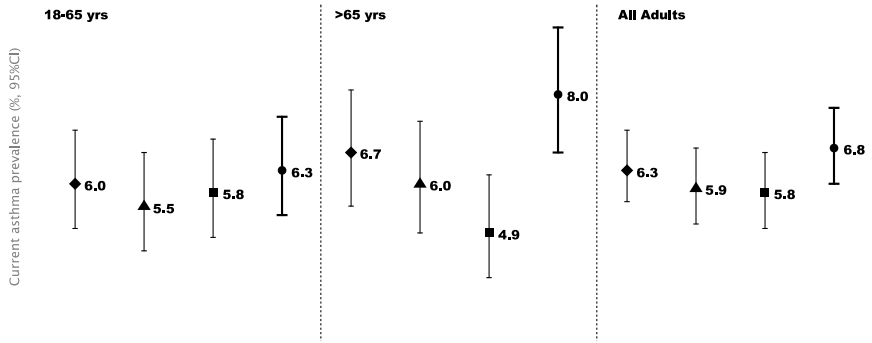

Figure 4.3: Current asthma prevalence in subgroups of adults by symptoms possible to affect the estimates. Symbols represents the prevalence of 'Current asthma' in people: ◆ without chronic bronchitis; ▲ who smoked ≤10 packs-year; ■ without self reported heart disease and ● all participants of the age group.

Prevalence of symptoms

The most common respiratory symptom in the group with 'Current asthma' was wheeze (89%, 95%CI 85.8-91.6), followed by nocturnal symptoms (75.8%, 95%CI 70.8-80.2) (Table 4.3). Of those who reported wheeze and wheeze with breathlessness and wheeze without a cold 42.2% (95%CI 36.7-47.8) denied having 'Current asthma'.

Table 4.3: Prevalence of self-reported symptoms in the last 12 months for 'Current asthma' subjects (n= 450) and for the total sample (n=6003).

	Current asthma subjects, % (95%CI)	**Total sample, % (95%CI)**
Asthma Symptoms		
Wheeze	89.0 (85.8-91.6)	18.1 (16.8-19.4)
Nocturnal symptoms	75.8 (70.8-80.2)	35.6 (33.9-37.3)
Waking with breathlessness	36.4 (30.7-42.6)	6.8 (5.9- 7.7)
Waking with tightness in the chest	39.2 (33.3-45.4)	11.9 (10.9-13.1)
Waking with cough	55.7 (49.1-62.0)	28.0 (26.4-29.7)
Attack of asthma	46.9 (41.4-52.4)	3.2 (2.6- 3.9)
Sputum for at least 3 months	45.4 (39.0-51.9)	18.5 (17.1-19.9)
Blocked nose	27.5 (22.4-33.3)	12.5 (11.4-13.7)
Sinus pressure	25.0 (20.4-30.3)	11.2 (10.2-12.4)

Healthcare resources

About 243 000 subjects from the Portuguese general population were hospitalized because of asthma at least once in their lifetime (2.4%, 95%CI 1.9-2.9). As for clinical evaluation, 23.6% (95%CI 22.2-25.2) of the subjects performed lung function tests and 25.2% (95%CI 23.7-26.8) did allergy tests.

In Portuguese subjects with 'Current asthma', 25.6% (95%CI 20.4-31.5) were hospitalized because of their asthma; more than half performed lung function tests (57.4%, 95%CI 50.9-63.7) and allergy tests (65.7%, 95%CI 59.5-71.5) (Table 4.4). Current use of asthma medication (inhaled, nebulized and/or oral medication) was reported by 60.1% of Portuguese subjects with 'Current asthma', 35.2% used inhaled controller medications and 21.6% takes reliever medications only (Table 4.4).

Table 4.4: Healthcare resources (Medication, diagnosis and hospitalization) for 'Current asthma' subjects (n= 450) and for the total sample (n=6003).

	Current asthma subjects, % (95%CI)	Total sample, % (95%CI)
Hospitalization because of asthma	25.6 (20.4-31.5)	2.4 (1.9- 2.9)
Lung function tests	57.4 (50.9-63.7)	23.6 (22.2-25.2)
Allergy tests		
Any allergic test	65.7 (59.5-71.5)	25.2 (23.7-26.8)
Skin-prick test	55.2 (48.7-61.4)	17.9 (16.6-19.3)
Blood test	46.7 (40.3-53.1)	16.0 (14.7-17.4)
Asthma medication		
Any asthma medication	60.1 (53.5-66.2)	5.0 (4.2- 5.8)
Inhaled Controller	35.2 (29.2-41.6)	2.9 (2.4- 3.6)
Only inhaled Reliever	21.6 (16.7-27.5)	1.5 (1.1- 1.9)
Nebulized aerosols	36.3 (30.2-42.9)	2.5 (2.0- 3.1)
Nebulized aerosols without controller†	17.6 (13.2-23.0)	1.2 (0.9- 1.6)
Anti-allergic medication		
Nasal spray	24.9 (19.8-30.7)	1.7 (1.3- 2.1)
Oral medication	45.3 (39.1-51.8)	3.1 (2.6- 3.7)

†Includes the participants using nebulized aerosols but not inhaled controller medication.

Comorbidities

More than half of the subjects with 'Current asthma' also had allergic rhinitis (AR) (52.3%, 95%CI 45.8-58.6), of which most were classified as intermittent moderate/severe AR (29.9%, 95%CI 24.4-36.0). Sinusitis had a strong association with asthma (OR 5.26, 95%CI 3.04-9.11) (Table 4.5). Association between upper airway diseases and asthma was stronger in patients with both AR and sinusitis (OR 9.34, 95%CI 4.75-18.35) (Table 4.5).

Table 4.5: Asthma comorbities for 'Current asthma' subjects (n= 450) and for the total sample (n=6003).

	Current asthma subjects, % (95%CI)	**Total sample, % (95%CI)**	**OR (95%CI)**
Upper airways disease			
None (AR-/Sinusitis-)	46.9 (40.5-53.4)*	77.2 (75.7-78.7)	0.23 (0.17-0.30)
Allergic Rhinitis (AR)	52.3 (45.8-58.6)*	22.1 (20.7-23.6)	4.40 (3.34-5.79)
Mild	14.0 (10.4-18.8)*	8.3 (7.4- 9.3)	1.90 (1.31-2.77)
Intermittent	12.1 (8.6-16.7)	7.4 (6.6- 8.4)	
Persistent	1.9 (1.0- 3.8)	0.9 (0.6- 1.2)	
Moderate/Severe	38.2 (32.3-44.5)*	13.8 (12.6-15.1)	4.52 (3.40-6.01)
Intermittent	29.9 (24.4-36.0)	11.1 (10.1-12.3)	
Persistent	8.3 (5.7-12.0)	2.7 (2.2- 3.3)	
AR+ /Sinusitis-	46.7 (40.4-53.2)*	3.2 (2.6- 3.8)	3.67 (2.79-4.82)
Sinusitis	6.4 (4.3- 9.4)*	1.6 (1.2- 2.1)	5.26 (3.04-9.11)
AR - /Sinusitis+	0.9 (0.3- 2.2)	0.1 (0.0- 0.1)	1.33 (0.47-3.76)
Both (AR+/Sinusitis+)	5.5 (3.5- 8.5)*	0.4 (0.2- 0.6)	9.34 (4.75-18.35)
Chronic bronchitis	5.7 (3.8- 8.5)*	2.7 (2.2- 3.2)	2.45 (1.52-3.93)
Non-respiratory allergic disease	55.4 (48.9-61.7)*	33.0 (31.4-34.7)	2.71 (2.07-3.57)
Eczema/atopic dermatitis	11.5 (9.6-13.7)*	26.1 (24.6-27.7)	0.41 (0.32-0.54)
Drug allergy	13.3 (9.8-17.9)*	7.5 (6.7- 8.5)	0.50 (0.34-0.73)
Food allergy	12.2 (8.3-17.6)*	5.3 (4.5- 6.1)	0.36 (0.23-0.57)

AR- Allergic Rhinitis; (-) indicates absence; (+) indicates presence; OR – odds ratio; *p<0.001.

5. Discussion

The prevalence of 'Current asthma' in the Portuguese population was 6.8% (95%CI 6.0-7.7). Prevalence estimates were similar for the demographic subgroups. This study also showed a strong association of asthma with AR and sinusitis, which is in agreement with the known risk of the chronic disease of upper airways for asthma [Bousquet, et al.]. Furthermore, exposure to ETS seems to increase the risk of asthma.

This study has the intrinsic limitations of a telephone survey on asthma; such as the impossibility to determine causality factors without risking biased inferences. Other limitation is the fact that the only data available by the time of the data collection was the National Census of 2001; demographic changes in the years in between could influence the sampling size. Moreover, the response rate was relatively low, still was among the highest obtained in Portuguese nationwide telephone surveys [Correia, Dinis et al.] [Correia, Dinis et al.]. Nevertheless, this is the only Portuguese study using a study-proved questionnaire on asthma that includes a large sample size from all municipalities and all age groups and which estimates represent the true prevalence in Portuguese population.

Our definition of 'Current asthma' uses a conservative combination of questions from the GA²LEN survey. The selection of the questions aimed to improve the specificity, namely by including 'asthma attack' and 'waking with breathlessness' [Burney, et al.] [de Marco, et al.] [Toren, et al.] (the less frequent nocturnal asthma-related symptom) and not including 'waking with a feeling of tightness in the chest' or 'waking with cough'. Our prevalence estimate using this definition is comparable to those found in GA²LEN survey for Sweden (Gothenburg, 7.1%), Poland (Krakow 7.1% and Lodz 6.0%), Netherlands (6.4%), Belgium (7.6%) and Germany (Brandenburg 6.3%) but is inferior to Coimbra estimates (16.8%) [Jarvis, et al.].

A direct comparison of our results with other studies previously done in Portugal is not straightforward, given the differences in the methods used. As stated before, most of the asthma studies in Portugal were done on school-

attending children and teenagers from selected cities or regions (Appendix A). ISAAC study in Portugal assessed the prevalence of asthma in four cities [ISAAC]. For adults, the asthma prevalence studies, published so far were done on military service conscripts [Chieira, et al.], in primary care units [Nunes] [Correia-de-Sousa, et al.], using postal questionnaires [Loureiro, et al.] [Marques] or using postal questionnaire followed by a clinical visit [Alves, et al.] (Appendix A). The ECRHS I included Portugal and data were collected in two cities (Porto and Coimbra) [Burney, et al.]. None of the previously published studies exclusively on asthma conducted in Portugal can be confidently generalized to the Portuguese population because of methodological reasons (sampling methods, data collection or asthma definition used). Prevalence ranged between 5% for 'Diagnosed asthma' and 23% for 'Current symptoms of asthma', depending on the definition of asthma considered (Appendix A). For comparison purposes, using the data from the INAsma, asthma prevalence was calculated for each definition and sample age used in the other studies (Appendix A). Table 5.1 summarizes prevalence of asthma results in International and Portuguese studies. This illustrates the effect of the operational definition of asthma on prevalence estimates.

Table 5.1: Summary of prevalence of asthma results according to several definitions from international and Portuguese studies.

	International Studies (n=9)	**Portuguese Studies (n=15)**	**INAsma**
Life-time asthma	9.7% (1 study, 1 definition)	4.4 to 13.2% (8 studies, at least 3 definitions)	10.5%
Diagnosed asthma	2.0 to 20.3% (4 studies, 2 definitions)	3.4 to 10.2% (5 studies, 3 definitions)	-*
Current asthma	5.2 to 29.9% (8 studies, 7 definitions)	3.2 to 7.7% (5 studies, at least 4 definitions)	6.8%

*Questions related to 'Physician-diagnosed asthma' variable were not asked in INAsma survey.

The only study done in the entire population addressing both children and adults, was the Portuguese National Health Survey of 2005/2006. In this survey 5.5% (581 725) of the Portuguese population reported having or having had asthma and 3.5% (368 184) reported having had asthma in last 12 months [INE and INSA], these are numerically inferior to the number of Portuguese with 'Lifetime asthma' and 'Current asthma' estimated in the present study (1 079 991 and 695 000, respectively). This could suggest an increase of asthma prevalence commonly to other westernized countries [Anderson, et al.] [Toelle, Ng et al.]

[Pallasaho, Lundback et al.] [Soriano, Kiri et al.]. However, the comparison of the two studies may be compromised due to the methodological differences stated above.

There are a variety of demographic factors associated with asthma, including region, age and gender. No differences between regions were found in the present study, comparably to ONSA survey findings [Branco, et al.]. The higher prevalence of asthma observed in older adult population, is in agreement with the results of the Portuguese National Health Survey [INE and INSA] and ONSA [Branco, et al.]. Additionally, the higher prevalence tendency observed in male children and female adults is in accordance to Global Initiative for Asthma (GINA) Report which states that in childhood male sex is a risk factor for asthma, however as children get older the prevalence differences between gender narrows, being higher in female adults [GINA]. In ONSA survey, asthma prevalence between genders was similar [Branco, et al.] comparably to the findings of the present study.

Bias and confounding are limitations of all epidemiological studies. To address this, we took into account possible information and selection bias and adjusted for conditions with similar symptoms. Chronic Obstructive Pulmonary Disease (COPD) can be difficult to differentiate from asthma in surveys [Bateman, et al.], especially when the proportion of elders with respiratory symptoms is high, as we have observed. Nevertheless, we believe misclassification of COPD patients had a limited effect on our estimates. The analysis of the participants without 'chronic bronchitis' (phlegm when coughing for at least 3 months in the last year and smoked more than 10 packs-year and is at least 40 years old) didn't change asthma prevalence estimates. In fact, the asthma prevalence was superior in non-smokers or in those who smoked up to 10 packs-year. After these adjustments, the prevalence of asthma was lower in elders without self-reported 'heart disease'. This overestimation of asthma symptoms in people with heart disease may indicate a possible bias or confounding of the two conditions, since heart disease is an alternative cause of recurrent respiratory symptoms [GINA].

Obesity is also related to asthma [GINA]. Obese patients have decreased lung volumes, more severe symptoms and increased difficulty in asthma control. Whether this association is causal or denotes co-morbidity remains unclear [van Huisstede and Braunstahl] [Beuther, Weiss et al.]. Although results of the present study suggest higher asthma prevalence for obese people, we cannot relate the two diseases. Similarly, in the Portuguese National Health Survey increased BMI could not be associated with significant odds ratio for asthma [Moreira, Moreira et al.].

Additionally, SES have been linked to an increased risk of asthma. Prevalence of asthma seems to be higher in developed nations and in poor populations within developed nations when compared to developing nations. This reflects lifestyle differences such as exposure to allergens and access to health care [GINA]. However, this association is not free from controversy since it is based on cross-sectional studies, with different SES and asthma definitions and that reached contradictory results. Hancox developed a longitudinal cohort study to clarify this association and concluded that there was no consistent association between SES or educational attainment and asthma prevalence, lung function, or airway responsiveness at any age, suggesting that previously reported associations may be due to confounding [Hancox, Milne et al.]. This is in agreement with the results of the present work, despite the methodological differences between the studies.

'Current asthma' prevalence tended to be higher in non-smokers or in those who smoked up to 10 packs-year, suggesting either underreporting of asthma symptoms by participants with tobacco-related diseases or that individuals with respiratory symptoms are less likely to become smokers or tend to quit smoking. The association between smoking habits and asthma are still unclear. Bjornsson et al. found significant association between current smoking and asthma symptoms (OR 1.5; 95% CI 1.3–1.7) [Bjornsson, Plaschke et al.]. In contrast, a cohort study in adult women showed that current and ex-smokers were at significantly lower risk for asthma than women who never smoked [Troisi, Speizer et al.]. And in a case-control study based on ECHRS survey data, smokers showed a 42% lower risk of asthma than did non-smokers (OR: 0.58; 95% CI: 0.36 to 0.92) [de Marco, Locatelli et al.], similarly to the present study association results.

ETS has several effects on patients in risk of asthma. It increases allergic sensitisation, asthma severity, affects therapeutic response to corticosteroids and mechanisms of the disease [GINA]. Among children, exposure to ETS is considered to be a co-factor provoking wheezing attacks and, in children with asthma, is associated with more severe disease [Strachan and Cook]. According to a FinEsS epidemiological study in Orebro on prevalence risk factor of asthma, childhood exposure to ETS is associated with an increased prevalence of diagnosed asthma among adult non-smokers without a family history of asthma (OR 1.82, 95%CI 1.28–2.58), representing a major lower airway irritant [Larsson, Frisk et al.]. In the present study, exposure to ETS at home is a significant risk factor for 'Current asthma'.

Almost half of the people with 'Current asthma' aren't receiving any asthma treatment, and a fifth is using only rescue medication. Furthermore, about 40%

of people with wheeze denied having asthma. These facts seem to suggest the need for improvement of diagnosis and treatment of asthma stated by the Global Alliance against Chronic Respiratory Diseases [Bousquet, et al.].

The association between asthma and AR found in the present study (OR 4.40, 95%CI 3.34-5.79) is similar to other European studies [Cruz, Popov et al.] supporting the concept of a frequent co-existence of asthma and AR in the same patient [Bousquet, et al.]. In fact, rhinitis has been considered an important risk factor for asthma development and severity [Cruz, et al.]. A even stronger association was found with sinusitis (OR 5.26, 95%CI 3.04-9.11). However, this association is significant only when both AR and sinusitis are present (OR 9.34, 95%CI 4.75-18.35) and not in the few participants reporting sinusitis without AR (OR 1.33, 95%CI 0.47-3.76), comparably to results from previous studies [Jarvis, et al.] [Guerra, Sherrill et al.].

6. Conclusion and Future work

In conclusion, 695 000 Portuguese have Current asthma, with a prevalence of 6.8%, and more than one million (10.5%) had life-time asthma. There is no association between demographic variables and asthma. However, exposure to ETS seems to be related to higher risk of having asthma and people who reported rhinitis and sinusitis had the strongest risk of having asthma.

An additional clinical evaluation including lung function tests would improve the accuracy of asthma classification [Burney, et al.] [Asher, et al.]. We designed and intend to proceed with a clinical evaluation in a subsample of the participants that will evaluate the effect of the survey misclassification on asthma prevalence estimates. Adjustments in asthma estimates according to data from the National Census 2011 will be done upon publication of census data.

7. References

1. Jarvis D, Newson R, Lotvall J, Hastan D, Tomassen P, Keil T, et al. Asthma in adults and its association with chronic rhinosinusitis: The GA2LEN survey in Europe. *Allergy* 2011.
2. Unger L, Harris MC. Stepping stones in allergy. Chapter VI. The many faces of allergy. *Ann Allergy* 1974;33(6):353-63.
3. Global strategy for asthma management and prevention (update 2009), Global Initiative for Asthma (GINA).2009 http://www.ginasthma.org/
4. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald M, et al. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J* 2008;31(1):143-78.
5. The Global Asthma Report 2011.Paris, France-The International Union Against Tuberculosis and Lung Disease,2011
6. Jacquemin B, Kauffmann F, Pin I, Le Moual N, Bousquet J, Gormand F, et al. Air pollution and asthma control in the Epidemiological study on the Genetics and Environment of Asthma. *J Epidemiol Community Health* 2011.
7. Thomson NC, Chaudhuri R, Livingston E. Asthma and cigarette smoking. *Eur Respir J* 2004;24(5):822-33.
8. Bousquet J, Dahl R, Khaltaev N. Global alliance against chronic respiratory diseases. *Allergy* 2007;62(3):216-23.
9. Leynaert B, Neukirch C, Liard R, Bousquet J, Neukirch F. Quality of life in allergic rhinitis and asthma. A population-based study of young adults. *Am J Respir Crit Care Med* 2000;162(4 Pt 1):1391-6.
10. Barnes PJ, Jonsson B, Klim JB. The costs of asthma. *Eur Respir J* 1996;9(4):636-42.
11. Godard P, Chanez P, Siraudin L, Nicoloyannis N, Duru G. Costs of asthma are correlated with severity: a 1-yr prospective study. *Eur Respir J* 2002;19(1):61-7.
12. Haahtela T, Tuomisto LE, Pietinalho A, Klaukka T, Erhola M, Kaila M, et al. A 10 year asthma programme in Finland: major change for the better. *Thorax* 2006;61(8):663-70.
13. *National Programme for Asthma Control*. Lisboa: Directorate-General of Health, 2005.

14. Bugalho de Almeida A, Covas A, Prates L, Fragoso E. Asthma hospital admission and mortality in mainland Portugal 2000-2007. *Rev Port Pneumol* 2009;15(3):367-83.
15. Bugalho De Almeida A. Plano Nacional de Controlo da Asma - Plano de actividades, 2008.
16. O'Connor KS, Osborn L, Olson L, Blumberg SJ, Frankel MR, Srinath KP, et al. Design and operation of the National Asthma Survey. National Center for Health Statistics. *Vital Health Stat 1* (46):1-122. 2008.
17. McHugh MK, Symanski E, Pompeii LA, Delclos GL. Prevalence of asthma among adult females and males in the United States: results from the National Health and Nutrition Examination Survey (NHANES), 2001-2004. *J Asthma* 2009;46(8):759-66.
18. Ghosh S, Pahwa P, Rennie D, McDuffie HH. Opposing trends in the prevalence of health professional-diagnosed asthma by sex: a Canadian National Population Health Survey study. *Can Respir J* 2008;15(3):146-52.
19. 4373.0 - National Health Survey: Asthma and Other Respiratory Conditions.Australia-Australian Bureau of Statistics,1998
20. Burney PG, Luczynska C, Chinn S, Jarvis D. The European Community Respiratory Health Survey. *Eur Respir J* 1994;7(5):954-60.
21. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8(3):483-91.
22. Bousquet J, Burney PG, Zuberbier T, Cauwenberge PV, Akdis CA, Bindslev-Jensen C, et al. GA2LEN (Global Allergy and Asthma European Network) addresses the allergy and asthma 'epidemic'. *Allergy* 2009;64(7):969-77.
23. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004;59(5):469-78.
24. Lotvall J, Ekerljung L, Ronmark EP, Wennergren G, Linden A, Ronmark E, et al. West Sweden Asthma Study: prevalence trends over the last 18 years argues no recent increase in asthma. *Respir Res* 2009;10:94.
25. Asher MI, Montefort S, Bjorksten B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006;368(9537):733-43.
26. Anderson HR, Ruggles R, Strachan DP, Austin JB, Burr M, Jeffs D, et al. Trends in prevalence of symptoms of asthma, hay fever, and eczema in 12-14 year olds in the British Isles, 1995-2002: questionnaire survey. *BMJ* 2004;328(7447):1052-3.
27. Zollner IK, Weiland SK, Piechotowski I, Gabrio T, von Mutius E, Link B, et al. No increase in the prevalence of asthma, allergies, and atopic sensitisation among children in Germany: 1992-2001. *Thorax* 2005;60(7):545-8.

28. von Hertzen L, Haahtela T. Signs of reversing trends in prevalence of asthma. *Allergy* 2005;60(3):283-92.
29. Rosado Pinto J. ISAAC - 20 anos em Portugal. *Acta Pediatr Port* 2011;42(5):S35-S40.
30. Chieira C, Loureiro AC, Rodrigues VL. Estudos epidemiológiocs alergológiocs numa população de mancebos (20 anos). . *Via Pneumológica* 1990;1:67.
31. Nunes C. Epidemiologic study of asthma at health primary care in Algarve – Portugal. . *Arq Med* 1992;9:187-96.
32. Correia-de-Sousa J, Espirito-Santo M, Colaco T, Almada-Lobo F, Yaphe J. Asthma in an Urban Population in Portugal: A prevalence study. *BMC Public Health* 2011;11(1):347.
33. Loureiro AC, Chieira C, Pereira AC, Todo Bom A, Faria E, Alendouro P, et al. Estudos Epidemiológicos da Asma Brônquica numa População Adulta. *Rev Port Imunoalergologia* 1996;4(1):35-54.
34. Marques JA. Epidemiologia da asma em Portugal [Epidemiology of asthma in Portugal]. *Arq Med* 1993;7(2):116-20.
35. Alves J, Hespanhol V, Magalhaes A, Almeida J, Marques JA. [Prevalence of asthma in the city of Porto]. *Acta Med Port* 1994;7(1):21-4.
36. Burney P, Chinn C, Luczynska C, Jarvis D, Vermeire P, Bousquet J, et al. Variations in the prevalence of respiratory symptoms, selfreported asthma attacks, and use of asthma medication in the European Community Respiratory Health Survey (ECRHS). *Eur Respir J* 1996;9:687-95.
37. Branco MJ, Nogueira P, Contreiras T. *Report on prevalence estimates of some chronic diseases in mainland Portugal*. Lisboa: Observatório Nacional de Saúde, 2005.
38. Pekkanen J, Sunyer J, Anto JM, Burney P. Operational definitions of asthma in studies on its aetiology. *Eur Respir J* 2005;26(1):28-35.
39. Inquérito Nacional de Saúde 2005/2006.Lisboa-Instituto Nacional de Estatística/Inquérito Nacional de Saúde,2009
40. Pekkanen J, Pearce N. Defining asthma in epidemiological studies. *Eur Respir J* 1999;14(4):951-7.
41. Toren K, Brisman J, Jarvholm B. Asthma and asthma-like symptoms in adults assessed by questionnaires. A literature review. *Chest* 1993;104(2):600-8.
42. Burney PG, Laitinen LA, Perdrizet S, Huckauf H, Tattersfield AE, Chinn S, et al. Validity and repeatability of the IUATLD (1984) Bronchial Symptoms Questionnaire: an international comparison. *Eur Respir J* 1989;2(10):940-5.
43. de Marco R, Cerveri I, Bugiani M, Ferrari M, Verlato G. An undetected burden of asthma in Italy: the relationship between clinical and epidemiological diagnosis of asthma. *Eur Respir J* 1998;11(3):599-605.
44. Canonica GW, Bousquet J, Mullol J, Scadding GK, Virchow JC. A survey of the burden of allergic rhinitis in Europe. *Allergy* 2007;62 Suppl 85:17-25.

45. Nunes C, Ladeira S, Rosado Pinto J. Definição, Epidemiologia e Classificação da Asma na Criança. In: Euromédice EM, Lda., editor. *A Criança Asmática no Mundo da Alergia*. Lisboa, 2003:35-55.
46. Nunes C, Ladeira S. Epidemiologic study of asthma in schoolchildren. The lung and environment. *SEP* 1987;99.
47. Santos JM. Aspectos epidemiológicos da asma pediátrica numa comunidade portuguesa. *A criança asmática*. Lisboa, 1993.
48. Prata C, Marto J, Mouzinho I, Menezes M, Susano R. [Epidemiologic study of bronchial asthma in schoolchildren from the Azores (Faial)]. *Acta Med Port* 1994;7(10):541-4.
49. Vicente O, Rodrigues T, Silva AM, Tzer TS, Barros H. Prevalência de asma em estudantes das escolas secundárias portuguesas. *Arq Med* 1995;9(2):90-2.
50. Morais-Almeida M, Câmara R, Ornelas P. Prevalência de asma brônquica e de atopia em crianças da Ilha da Madeira. . *Rev Epidemiol* 1996;2(39-40).
51. Leiria Pinto P. Asma brônquica e o adolescente. Conhecimentos e atitudes. [Master Thesis]. Faculdade Ciências Médicas Universidade Nova de Lisboa, 1998.
52. Barros H, Pereira C, Mateus P. Asma em crianças dos 6 aos 9 anos. Um estudo populacional em duas cidades
portuguesas (Porto e Viseu)*. *Rev Port Imunoalergologia* 1999;7(1):9-18.
53. Falcão H, Ramos E, Marques JA, Barros H. Prevalence of asthma and rhinitis in 13 year old adolescents in Porto, Portugal. *Rev Port Pneumol* 2008;14(6):747-68.
54. Pegas PN, Alves CA, Scotto MG, Evtyugina MG, Pio CA, Freitas MC. [Risk factors and prevalence of asthma and rhinitis among primary school children in Lisbon]. *Rev Port Pneumol* 2011;17(3):109-16.
55. Morais-Almeida M, Loureiro C, Todo-Bom A, Nunes C, Pereira C, Delgado L, et al. Rhinitis prevalence and characterization survey in primary care centres of mainland Portugal – ARPA study. *Rev Port Imunoalergologia* 2005;13(1):69-80.
56. Fonseca J, Vaz M, Tavares C, Cernadas JR, Moreira A, Costa-Pereira A, et al. Perspectiva do doente do controlo da asma, utilização de serviços de saúde e qualidade de vida. *Rev Port Pneumol* 2001;9(1):35-42.
57. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 2008;63 Suppl 86:8-160.
58. Brick JM, Brick PD, Dipko S, Presser S, Tucker C, Yuan Y. Cell phone survey feasibility in the us: Sampling and calling cell numbers versus landline numbers. *Public Opinion Quarterly* 2007;71(1):23.
59. Correia S, Dinis P, Rolo F, Lunet N. Sampling procedures and sample representativeness in a national telephone survey: a Portuguese example. *Int J Public Health* 2010;55(4):261-9.

60. Correia S, Dinis P, Rolo F, Lunet N. Prevalence, treatment and known risk factors of urinary incontinence and overactive bladder in the non-institutionalized Portuguese population. *Int Urogynecol J Pelvic Floor Dysfunct* 2009;20(12):1481-9.
61. ISAAC SC. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998;12(2):315-35.
62. Toelle BG, Ng K, Belousova E, Salome CM, Peat JK, Marks GB. Prevalence of asthma and allergy in schoolchildren in Belmont, Australia: three cross sectional surveys over 20 years. *BMJ* 2004;328(7436):386-7.
63. Pallasaho P, Lundback B, Laspa SL, Jonsson E, Kotaniemi J, Sovijarvi AR, et al. Increasing prevalence of asthma but not of chronic bronchitis in Finland? Report from the FinEsS-Helsinki Study. *Respir Med* 1999;93(11):798-809.
64. Soriano JB, Kiri VA, Maier WC, Strachan D. Increasing prevalence of asthma in UK primary care during the 1990s. *Int J Tuberc Lung Dis* 2003;7(5):415-21.
65. Global strategy for asthma management and prevention (update 2008), Global Initiative for Asthma (GINA).2008 http://www.ginasthma.org/
66. van Huisstede A, Braunstahl GJ. Obesity and asthma: co-morbidity or causal relationship? *Monaldi Arch Chest Dis* 2010;73(3):116-23.
67. Beuther DA, Weiss ST, Sutherland ER. Obesity and asthma. *Am J Respir Crit Care Med* 2006;174(2):112-9.
68. Moreira P, Moreira A, Padrao P, Delgado L. Obesity and asthma in the Portuguese National Health Survey. *Allergy* 2006;61(12):1488-9.
69. Hancox RJ, Milne BJ, Taylor DR, Greene JM, Cowan JO, Flannery EM, et al. Relationship between socioeconomic status and asthma: a longitudinal cohort study. *Thorax* 2004;59(5):376-80.
70. Bjornsson E, Plaschke P, Norrman E, Janson C, Lundback B, Rosenhall A, et al. Symptoms related to asthma and chronic bronchitis in three areas of Sweden. *Eur Respir J* 1994;7(12):2146-53.
71. Troisi RJ, Speizer FE, Rosner B, Trichopoulos D, Willett WC. Cigarette smoking and incidence of chronic bronchitis and asthma in women. *Chest* 1995;108(6):1557-61.
72. de Marco R, Locatelli F, Sunyer J, Burney P. Differences in incidence of reported asthma related to age in men and women. A retrospective analysis of the data of the European Respiratory Health Survey. *Am J Respir Crit Care Med* 2000;162(1):68-74.
73. Strachan DP, Cook DG. Health effects of passive smoking. 6. Parental smoking and childhood asthma: longitudinal and case-control studies. *Thorax* 1998;53(3):204-12.
74. Larsson ML, Frisk M, Hallstrom J, Kiviloog J, Lundback B. Environmental tobacco smoke exposure during childhood is associated with increased prevalence of asthma in adults. *Chest* 2001;120(3):711-7.

75. Cruz AA, Popov T, Pawankar R, Annesi-Maesano I, Fokkens W, Kemp J, et al. Common characteristics of upper and lower airways in rhinitis and asthma: ARIA update, in collaboration with GA(2)LEN. *Allergy* 2007;62 Suppl 84:1-41.
76. Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. *J Allergy Clin Immunol* 2002;109(3):419-25.
77. Janson C, Chinn S, Jarvis D, Burney P. Physician-diagnosed asthma and drug utilization in the European Community Respiratory Health Survey. *Eur Respir J* 1997;10(8):1795-802.
78. Lethbridge-Cejku M, Schiller JS, Bernadel L. Summary health statistics for U.S. adults: National Health Interview Survey, 2002. National Center for Health Statistics. *Vital Health Stat 10* (222):1-151. 2004.
79. Dey AN, Schiller JS, Tai DA. Summary health statistics for U.S. children: National Health Interview Survey, 2002. National Center for Health Statistics. *Vital Health Stat 10* (221):1-78. 2004.
80. Asthma in Australia: findings from the 2004–05 National Health Survey.Canberra-Australian Institute of Health and Welfare.,2007
81. Couto M, Almeida MM. Allergic disease diagnosis in Portugal: An exploratory study [Diagnóstico da doença alérgica em Portugal: Um estudo exploratório]. *Rev Port Imunoalergologia* 2011;1:23-32.
82. Censos 2001: resultados definitivos Lisboa-Instituto Nacional de Estatística.,2001
83. Censos 2011: resultados preliminares.Lisboa-Instituto Nacional de Estatística,2011

Appendixes

A. Prevalence of asthma according to several definitions in epidemiological surveys

Table A.1: Prevalence of asthma according to several definitions from International asthma prevalence studies.

Survey	Sample	Definition	Asthma Prevalence	
			Study, %	INAsma, % (95%CI)
ECHRS I 1994 **[Burney, et al.]**	Adults between the ages 20-44 from 48 centres	*Diagnosed current asthma*: positive if reported an attack of asthma in the previous 12 months *or* currently receiving medication for asthma	Ranged from 2.0(Tartu) to 8.4 (Cambridge)	5.6 (4.9-6.5)
ECHRS 1996 **[Janson, Chinn et al.]**	17029 adults between the ages 20-48 from 34 centres in 14 countries	*Asthma-related symptoms:* was defined as reporting at least one of the following: wheezing or whistling in the chest; waking with a feeling of tightness in the chest; having had an attack of shortness of breath during the day at rest; having had an attack of shortness of breath	§	23.0 (20.5-25.8) ‡

Survey		Sample	Definition	Asthma Prevalence	
				Study, %	INAsma, % (95%CI)
			following strenuous activity *or* waking by an attack of shortness of breath in the last 12 months.		
ISAAC [ISAAC]	**1995**	Subjects from two age groups: the 13–14 years old (n=463,801) from 155 centres (56 countries) and the 6–7 years old (n=257,800) from 91 centres (38 countries)	*Asthma*: positive "Have you had wheezing or whistling in the chest in the last 12 months?"	Ranged from 6.0 (South-East Asia) to 29.9 (Oceania)	12.4 (9.3-16.4)
GA²LEN (in press) [Jarvis, et al.]	**2009**	Adults aged 15–74 years	*Asthma*: positive to " Have you ever had asthma?" *and* at least one of the three symptoms in the last 12 months wheezing or whistling in the chest; waking with a feeling of tightness in the chest; waking with an attack of shortness of breath *or* waking with cough	Range from 5.2 (Poland) to 16.8 (Coimbra)	7.6 (6.6-8.7)

Survey	Sample	Definition	Asthma Prevalence	
			Study, %	INAsma, % (95%CI)
NAS 2002 [O'Connor, et al.] [Lethbridge-Cejku, Schiller et al.] [Dey, Schiller et al.]	31044 adults (18 years old or over) and 12524 children (under 18 years old)	*Ever diagnosed asthma*: Positive to "Have you (or your child) ever been told by a doctor or other health professional that you have (he/she has) asthma?"	11 (adults) and 12 (children)	*
		Current asthma: Positive to 'Ever diagnosed asthma' *and* "Do you still have asthma?"	7 (adults)	*
		Asthma attack: "During the past 12 months, has your child had an episode of asthma or an asthma attack?"	6 (children)	*
NPHS 1994-2001 [Ghosh, et al.]	17276 participants of all ages in four cycles (1994-1995; 1996-1997; 1998-1999 and 2000-2001)	*Ever diagnosed asthma:* Positive to "Do you have asthma diagnosed by a health professional?"	Ranged from 7.3 in cycle1 to 7.5 in cycle4	*
NHANES 2001-2004) [McHugh, et al.]	9243 adults in two cycles (2001-2002 and 2003-2004)	*Ever diagnosed asthma*: Positive to "Has a doctor or other health professional ever told you that you have asthma?"	13.7 (women) and 10.4(men)	*
		Current asthma: Positive to "Do you still have asthma?"	8.8 (women) and 5.8 (men)	*

Survey	Sample	Definition	Asthma Prevalence	
			Study, %	INAsma, % (95%CI)
NHS in Australia 2005 [ACAM].	25900 respondents of all ages	*Ever diagnosed asthma*: Positive to "Have you ever been told by a doctor or a nurse that you have asthma?"	20.3	*
		Current asthma: Positive to 'Ever asthma' *and* "Do you still get asthma?"	10.3	*
West Sweden Asthma Study 2008 [Lotvall, et al.]	29218 adults between the ages 16-75 in West Sweden	*Ever asthma:* positive to "Have you ever had asthma?"	9.7	10.3 (9.2-11.6)
		Active asthma: positive if reported 'Ever asthma' *or* 'Physician diagnosed' asthma *and* at least one out of: use of asthma medicine, attacks of shortness of breath, any wheeze, or recurrent wheeze	6.9	7.2 (6.2-8.4) †

ECHRS European Community Respiratory Health Survey; ISAAC International Study of Asthma and Allergies in Childhood; GA²LEN Global Allergy and Asthma European Network; NAS National Asthma Survey; NHANES National Health and Nutrition Examination Survey; NPHS National Population Health Survey; NHS National Health Survey

*Questions related to 'Physician-diagnosed asthma' variable were not asked in INAsma survey. † In the absence of the variable 'Physician-diagnosed asthma', prevalence result is based on 'Ever asthma' and at least one of the 4 symptoms listed. ‡ Instead of the variables 'attack of shortness of breath during the day at rest' and 'attack of shortness of breath following strenuous activity', prevalence result is based on 'asthma attack'. § The prevalence of 'asthma-related symptoms' are not available in the mentioned paper since it wasn't the primary aim of the study.

Table A.2: Prevalence of asthma according to several definitions from Portuguese asthma prevalence studies.

Survey	Sample	Definition	Asthma Prevalence	
			Study, %	INAsma, % (95%CI)
1990[Chieira, et al.]	557 twenty years old males conscripts into military service	*Asthma* based on diagnosis (further detail not available)	5.2	*
1992[Nunes]	55254 adult patients from primary care healthcare unit in Algarve	(Not available)	5.5	-----
1993[Santos]	Children from one school of Porto urban area	*Lifetime asthma* (further detail not available)	7.1	-----
		Current (further detail not available)	3.0	-----
1994[Prata, et al.]	927 children between the ages 6-12 in one Azores island	*Diagnosed asthma:* if diagnosed by a doctor *or* had visited their physicians for dyspnoea accompanied by wheezing *and* had received asthma medication in the last 12 months.	8	*
1994[Alves, et al.]	2075 inhabitants of Porto between the ages 20-44.	*Current asthma symptoms:* symptoms that usually define the attack of asthma (further detail not available)	6.5	-----

Survey	Sample	Definition	Asthma Prevalence	
			Study, %	INAsma, % (95%CI)
		Diagnosed asthma: positive if reported receiving medication for asthma in last 12 months	3.4	5.0 (4.2-5.8)
1995[Vicente, et al.]	17164 participants between the ages 12-19 from 18 district capital cities	*Lifetime asthma*: positive to wheeze *and* wheeze with breathlessness *and* negative to wheeze with a cold in lifetime.	4.4	†
		Current asthma: positive to wheeze *and* wheeze with breathlessness *and* negative to wheeze with a cold in last 12 months.	3.2	4.2 (2.8-6.3)
1996[Morais-Almeida, et al.]	1061 children between the ages 6-10 in the Madeira Island	*Lifetime asthma* (further detail not available)	15	-----
1998[Leiria Pinto]	1334 participants between the ages 12-16 in Lisbon	*Lifetime asthma* (further detail not available)	11.4	-----
1999[Barros, et al.]	Children between the ages 6-9 from Porto (n=2505) and Viseu (n=897).	*Lifetime asthma*: positive to dyspnoea *and* wheeze *and* negative to respiratory infection in lifetime.	9.8 (Viseu) and 13.2 (Porto)	§
		Current asthma: positive to dyspnoea *and* wheeze *and* negative to respiratory infection in last 12 months.	5.4 (Viseu) and 7.7 (Porto)	§

Survey	Sample	Definition	Asthma Prevalence	
			Study, %	INAsma, % (95%CI)
ONSA 2004 [Branco, et al.]	2820 adults aged 18 or older of mainland Portugal.	*Ever diagnosed asthma*: Positive to "Have you ever been told by a doctor or a nurse that you have asthma?"	8.6	*
NHS in Portugal 2005/2006 [INE and INSA]	41193 participants of all ages and from Portugal mainland and islands	*Lifetime asthma:* positive to 'Have you ever had asthma?'	5.5	10.5
		Diagnosed asthma: positive to 'Have you ever been diagnosed asthma by a medical doctor?'	5.3	*
		Current asthma: positive to 'Have you had asthma in last 12 months?'	3.5	††
2008[Falcão, et al.]	2161 teenagers with 13 years old from Porto	*Lifetime asthma:* positive to "Has your child ever had asthma?"	12.9	10.2 (5.9-16.9)
2008[Pegas, et al.]	342 children between the ages 5-12 from Lisbon	*Lifetime asthma:* positive to "Has your child ever had asthma?"	5.6	12.5 (9.5-16.4)
2009[Correia-de-Sousa, et al.]	590 adult patients from one primary care healthcare unit in Porto urban area	*Physician diagnosed asthma*: Assessed by a physician, based on the GINA criteria	10.2	*

Survey	Sample	Definition	Asthma Prevalence	
			Study, %	INAsma, % (95%CI)
2011[Couto and Almeida]	1253 adult participants from all country	*Diagnosed asthma*: reported asthma diagnosis by a physician	6.0	*

*Questions related to 'Physician-diagnosed asthma' variable were not asked in INAsma survey. † Questions on 'Wheeze' were asked only for the last 12 months. § Questions related to respiratory infection were not asked in INAsma survey. †† This questions wasn't asked in INAsma survey.

B. Questionnaire used for the 1st phase of INAsma

I. Selecção do Entrevistado

F1 Estou a falar para que concelho? _____

F2. (Entrevistador: registe Região NUTS II):

Norte	1
Centro	2
Lisboa	3
Alentejo	4
Algarve	5

F3.1. Podia dizer-me quantas pessoas existem no seu agregado familiar do **sexo masculino e com que idades**?

N.º de elementos	Idade
	Anos
	Anos
	Anos
	Anos
	Anos
	Anos

F3.2. Podia dizer-me quantas pessoas existem no seu agregado familiar do **sexo feminino e com que idades**?

N.º de elementos	Idade
	Anos
	Anos
	Anos
	Anos
	Anos
	Anos

F2. Qual desses elementos é o último aniversariante no seu agregado familiar?

Sexo		Idade
Masculino	1	____ anos
Feminino	2	____ anos

NOTA AO ENTREVISTADOR: Se o indivíduo selecionado for < de 15 anos pedir para entrevistar a pessoa que cuida habitualmente da criança (desde que autorizada para tal pelo encarregado de educação).

II. Questões

1. Alguma vez teve chiadeira ou pieira ou "gatinhos" no peito nos **últimos 12 meses**?

Sim	1
Não	2 **- Passar para P2**

1.1 Teve falta de ar quando a chiadeira estava presente?

Sim	1
Não	2

1.2 Teve a chiadeira ou a pieira sem estar constipado?

Sim	1
Não	2

2. Acordou com a sensação de aperto no peito **nos últimos 12 meses?**

Sim	1
Não	2

3.Alguma vez foi acordado devido a um ataque de falta de ar **nos últimos 12 meses?**

Sim	1
Não	2

4. Alguma vez foi acordado devido a um ataque de tosse **nos últimos 12 meses?**

Sim	1
Não	2

5. Num ano produziu pelo menos durante **3 meses** muco do seu peito na maioria dos dias?

Sim	1
Não	2

6. Já alguma vez teve asma? (ou "Bronquite asmática")

Sim	1
Não	2 **- Passar para P7**

6.1 Que idade tinha quando teve o seu primeiro ataque de asma? (Se estiver indeciso, assinale a sua melhor estimativa!)

	anos

6.2 Alguma vez esteve hospitalizado (internado) por asma?

Sim	1
Não	2

6.3 Teve um ataque de asma nos **últimos 12 meses**?

Sim	1
Não	2

6.4 **Presentemente**, está a tomar remédios (inaladores/"bomba", aerossóis/nebulizador ou comprimidos/xarope) para a **asma ou falta de ar**?

Sim	1
Não	2

6.5 E **nos últimos 12 meses**, usou algum inalador ("bomba") para a asma ou falta de ar?

Sim	1
Não	2 **- Passar para P6.7**

6.6. De que cor?

Azul (p.ex. Bricanyl, Ventilan, Foradil, Oxis, Formoterol)	1
Cinza (p.ex. Spiriva)	2
Verde (p.ex. Serevent, Dilamax, UltraBeta)	3
Lilás/roxo (p.ex. Seretaide, Brisomax, Maizair)	4
Vermelho (p.ex. Symbicort, Assieme)	5
Castanho (p.ex. Pulmicort)	6
Laranja (p.ex. Flixotaide, Brisovent, Veraspir)	7
Não sei	8

6.7 **Nos últimos 12 meses**, fez uma ou mais vezes aerossóis/nebulizações (fuminhos/respirar um vapor/fumo feito por uma máquina ou num serviço de saúde) para a asma ou falta de ar?

Sim	1
Não	2

7. Alguma vez fez um exame para avaliar a sua função respiratória (a capacidade de respirar, p.ex. espirometria, soprar com muita força para uma máquina ou respirar dentro de uma caixa de vidro. **Não "conta"** ter só soprado rapidamente para um tubo de plástico)

Sim	1
Não	2

8. Teve rinite incluindo febre dos fenos ou alergias do nariz?

Sim	1
Não	2 **- Passar para P9**

8.1 Foi perturbado pela rinite **nos últimos 12 meses?**

Sim	1
Não	2

8.2 Alguma vez teve problemas de rinite que durassem mais do que **4 dias numa semana?**

Sim	1
Não	2

- Passar para P9

8.3 **Se sim,** isso aconteceu **mais do que 4 semanas (1 mês) continuamente?**

Sim	1
Não	2

9. O seu nariz esteve entupido **mais de 12 semanas (3 meses) nos últimos 12 meses?**

Sim	1
Não	2

10. Teve dor ou pressão na zona da testa, nariz ou olhos **durante mais de 12 semanas (3 meses) nos últimos 12 meses?**

Sim	1
Não	2

11. O seu médico **alguma vez** lhe disse que tem rinite alérgica?

Sim	1
Não	2

12. O seu médico **alguma vez** lhe disse que tem sinusite **crónica**?

Sim	1
Não	2

13. Nos últimos 12 meses usou alguma vez sprays (gotas) nasais durante mais de 2 semanas seguidas? (p.ex. Pulmicort nasal, Flutaide, Nasomet, Eustidil, Rontilona, Aeromax, Avamys)

Sim	1
Não	2

14. Nos últimos 12 meses usou alguma vez comprimidos/xarope para as alergias (anti-histaminicos – p.ex. Zyrtec, Aerius, Rinialer, Xyzal, Claritine, Telfast, Atarax, Levrix, Ceterizina, Loratadina, ...)

Sim	1
Não	2

15. Alguma vez teve eczema ou qualquer tipo de alergia de pele?

Sim	1
Não	2

16. Alguma vez algum **médico** lhe disse que tinha alergias a medicamentos?

Sim	1
Não	2 **- Passar para P17**

16.1 Já fez algum teste ou prova para diagnóstico da alergia a medicamentos?

Sim	1
Não	2

17. Alguma vez algum **médico** lhe disse que tinha alergias alimentares?

Sim	1
Não	2 **- Passar para P18**

17.1 Já fez algum teste ou exame para alergias alimentares?

Sim	1
Não	2

18. Alguma vez fez testes cutâneos (na pele do braço) para despiste de alergia?

Sim	1
Não	2

19. Alguma vez fez análises ao sangue para despiste de alergia?

Sim	1
Não	2

20.Já alguma vez fumou, pelo menos 1 cigarro por dia (ou um charuto por semana) durante 1 ano? **[SIM significa pelo menos 1 cigarro por dia ou um charuto por semana durante 1 ano]**

Sim	1
Não	2 **- Passar para P21**

20.1 Que idade tinha quando começou a fumar?

[ ] anos

20.2 Fumou durante o último mês?

Sim	1 **- Passar para P20.3**
Não	2

20.2.1 Que idade tinha quando deixou de fumar?

[ ] anos

20.2.2 **Em média, por dia** quantos cigarros fumou?

[ ] Cigarros por dia **– Passar para P21**

20.3 **Em média, por dia** quantos cigarros fuma?

	Cigarros por dia

21. Na sua residência alguém fuma?

Sim	1
Não	2

21A. Sofre de alguma doença do coração?

Sim	1
Não	2

III. Dados pessoais

22. Qual a sua data de nascimento?

Dia	
Mês	
Ano	

23. Registe o Sexo do entrevistado:

Masculino	1
Feminino	2

24. Qual o Código Postal da sua residência:

|_____|_____|_____|_____| - |_____|_____|_____|

25. Qual a sua Profissão? _____

	Para codificação interna:
Pensionistas, estudantes e domésticas	1
Trabalhadores não especializados/qualificados	2
Trabalhadores agrícolas	3
Trabalhadores especializados/qualificados	4
Empregados do comércio	5
Empregados dos serviços/administrativos	6
Pequenos proprietários	7
Técnicos especializados	8
Profissionais liberais	9
Quadros médios	10
Quadros superiores	11
Grandes empresários	12

26. Qual a sua Escolaridade?

1.º ciclo incompleto / Analfabeto	1
1.º ciclo (até 4.ª classe)	2
2.º ciclo (5.º e 6.º ano)	3
3.º ciclo (7.º, 8.º e 9.º ano)	4
10.º / 11.º / 12.º ano	5
Curso profissional / artístico	6
Curso médio / Frequência universitária	7
Novas Licenciaturas	8
Licenciatura	9
Pós-Graduação/Mestrado/Doutoramento	10

27. Qual a Profissão da pessoa que mais contribui para o agregado familiar?

	Para codificação interna:
Pensionistas, estudantes e domésticas	1
Trabalhadores não especializados/qualificados	2
Trabalhadores agrícolas	3
Trabalhadores especializados/qualificados	4
Empregados do comércio	5
Empregados dos serviços/administrativos	6
Pequenos proprietários	7
Técnicos especializados	8
Profissionais liberais	9
Quadros médios	10
Quadros superiores	11
Grandes empresários	12

28. Qual a Escolaridade da pessoa que mais contribui para o agregado familiar?

1.º ciclo incompleto / Analfabeto	1
1.º ciclo (até 4.ª classe)	2
2.º ciclo (5.º e 6.º ano)	3
3.º ciclo (7.º, 8.º e 9.º ano)	4
10.º / 11.º / 12.º ano	5
Curso profissional / artístico	6
Curso médio / Frequência universitária	7
Novas Licenciaturas	8
Licenciatura	9
Pós-Graduação/Mestrado/Doutoramento	10

29. Qual é o seu peso? |_____| kg

30. Qual é a sua altura? |_____|,|_____|_____|

31. Utiliza email/correio electrónico?

Sim	1
Não	2 **- Passar para P32**

31.1 Podemos tornar a contactá-lo(a) por email no por causa deste estudo?

Sim	1
Não	2 **- Passar para P32**

31.2 Então diga-nos qual é o email/correio electrónico que utiliza.

IV. Convite para futura participação

32. Podemos tornar a contactá-lo para nos ajudar no próximo estudo sobre asma e doenças respiratórias? (esta pergunta **é para todos** os entrevistados independentemente das respostas anteriores)

Sim	1
Não	2

V. Questão para entrevistas adicionais

33. Na sua família alguém tem problemas de asma?

Sim	1
Não	2 **- Agradeça e termine**

33.1 Quem?

33.2 Vive(m) consigo?

Sim	1
Não	2 **- Agradeça e termine**

34. Gostaríamos de o(s) entrevistar para realizar um conjunto de questões sobre esta temática. É possível?

Sim	1
Não	2 **- Agradeça e termine**

Nota ao entrevistador: se existir mais algum elemento do agregado familiar com problemas de asma e que aceite ser entrevistado, realize a entrevista a esse elemento

Agradeça e termine a entrevista!

C. Operational definitions

Table C.1: List of the operational definitions used in 1st phase of INAsma.

Variable	Operational definition	Type	Variable groups
	Outcome variables		
Lifetime asthma	Positive answer to "Have you ever had asthma?"	Dichotomous nominal	Yes No
Current asthma	Positive answer to "Have you ever had asthma?" *and* at least one of 3 symptoms in the last 12 months: wheezing, waking with breathlessness or having an asthma attack.	Dichotomous nominal	Yes No
Diagnosed asthma	Positive answer to "Have you ever had asthma?" *and* "Are you taking any medication for asthma?"	Dichotomous nominal	Yes No

Variable	Operational definition	Type	Variable groups
	Predictive variables		
Wheeze	Positive answer to "Did you have wheezing or whistling in your chest in the last 12 months?"	Dichotomous nominal	Yes No
Waking with breathlessness	Positive answer to "Did you wake up with an attack of shortness of breath in the last 12 months?"	Dichotomous nominal	Yes No
Asthma attack	Positive answer to "Did you have an asthma attack in the last 12 months?"	Dichotomous nominal	Yes No
Wheeze with breathlessness	Positive answer to wheeze *and* "Did you have breathlessness when the wheezing sound present?"	Dichotomous nominal	Yes No
Wheeze without a cold	Positive answer to wheeze *and* "Did you have wheezing without a could?"	Dichotomous nominal	Yes No
Nocturnal symptoms	At least on of 3 symptoms in the last 12 months: waking with tightness in the chest, with breathlessness or with cough.	Dichotomous nominal	Yes No

Variable	Operational definition	Type	Variable groups
Waking with tightness in the chest	Positive answer to "Did you wake up with a feeling of chest tightness in in the last 12 months?"	Dichotomous nominal	Yes No
Waking with cough	Positive answer to "Did you wake up with a attack of cough in in the last 12 months?"	Dichotomous nominal	Yes No
Chronic bronchitis	Positive for: sputum for at least 3 months *and* smoked more than 10 Packs-year *and* have at least 40 years old.	Dichotomous nominal	Yes No
Sputum for at least 3 months	Positive answer to "Did you have phlegm when coughing for at least 3 months in the last year?"	Dichotomous nominal	Yes No
Allergic rhinitis	Positive answer to "Do you have any nasal allergies, including hay fever?"	Dichotomous nominal	Yes No
Rhinitis frequency	Classification according to ARIA using GA²LEN survey questions [Bousquet, et al.]	Dichotomous nominal	Intermittent Persistent

Variable	Operational definition	Type	Variable groups
Rhinitis severity	Classification according to ARIA using GA²LEN survey questions [Bousquet, et al.]	Dichotomous nominal	Mild Moderate/severe
Rhinitis diagnosis	Positive answer to "Have you been diagnosed as having allergic rhinitis by a doctor?"	Dichotomous nominal	Yes No
Sinusitis	Positive answer to "Have you been diagnosed as having chronic sinusitis by a doctor?" *and* sinus pressure in last 12 months	Dichotomous nominal	Yes No
Sinus pressure	Positive answer to "Have you felt sinus pressure, pain around the eyes or nose, for more than 12 weeks in last 12 months?"	Dichotomous nominal	Yes No
Blocked nose	Positive answer to "Have you felt nose blockage for more than 12 weeks in last 12 months?"	Dichotomous nominal	Yes No
Eczema/atopic dermatitis	Positive answer to "Have you ever had eczema or skin allergy?"	Dichotomous nominal	Yes No

Variable	Operational definition	Type	Variable groups
Drug allergy	Positive answer to "Have you been diagnosed as having drug allergy by a doctor?"	Dichotomous nominal	Yes No
Food allergy	Positive answer to "Have you been diagnosed as having food allergy by a doctor?"	Dichotomous nominal	Yes No
Allergic test	Positive to having done skin-prick test and/or blood analysis for allergy screening	Dichotomous nominal	Yes No
Skin-prick test	Positive answer to "Have you ever done skin-prick test for allergy screening?"	Dichotomous nominal	Yes No
Blood analysis	Positive answer to "Have you ever done blood analysis for allergy screening?"	Dichotomous nominal	Yes No
Hospitalization because of asthma	Positive answer to "Have you ever been hospitalized because of asthma?"	Dichotomous nominal	Yes No

Variable	Operational definition	Type	Variable groups
Lung function examination	Positive answer to "Have you ever done any examination to assess your lung function?"	Dichotomous nominal	Yes No
Asthma medication	Positive answer to "Are you taking any medication for asthma?"	Dichotomous nominal	Yes No
Asthma inhaled medication	Positive answer to "Have you used any inhaler for asthma in the last 12 months?"	Dichotomous nominal	Yes No
Inhaled therapy	Classification based on inhaler colour/brand name	Dichotomous nominal	Controller Reliever Both
Nebulized aerosols	Positive answer to "Have you used nebulized aerosols because of asthma in the last 12 months?"	Dichotomous nominal	Yes No
Nasal anti-allergic medication	Positive answer to "Have you used nasal sprays for more than 2 weeks in the last 12 months?"	Dichotomous nominal	Yes No

Variable	Operational definition	Type	Variable groups
Oral anti-allergic medication	Positive answer to "Have you used oral medications for allergies in the last 12 months?"	Dichotomous nominal	Yes No
Heart disease	Positive answer to "Have you a heart condition?"	Dichotomous nominal	Yes No
Smoking status	*Smokers* reported smoking at least one cigarette every day (or one cigar every week) for one year*; Ex-smokers* reported having quit smoking for more than one month; *Non-smokers* reported neither smoking nor ex-smoking.	Categorical nominal	Smoker Ex-smoker Non-smoker
Packs-year	Number of cigarettes smoked per day /20 × × Number of years smoking	Dichotomous nominal	> 10 Packs-year ≤ 10 Packs-year
Environmental tobacco smoke (ETS)	Positive answer to "Does anyone smoke in your home?"	Dichotomous nominal	Yes No

Variable	Operational definition	Type	Variable groups
Region	NUTS II region based on the municipality	Categorical nominal	North Centre 1. Lisboa Alentejo Algarve
Age groups	Classified according to the self-reported age	Categorical ordinal	< 18 years old 18 - 65 years old > 65 years old
Asthma onset	Age when had the first asthma attack	Continuous	
Gender	Classified according to the answer to "What is your gender?"	Dichotomous nominal	Male Female
Body Mass Index (BMI)	$\frac{\text{Weight (in kG)}}{\text{Height (in m)}^2}$	Categorical ordinal	< 18 (Underweight) 18-25 (Normal) 25-30 (Overweight) >30 (Obese)

Variable	Operational definition	Type	Variable groups
Weight	Weight in kG	Continuous	
Height	Height in cm	Continuous	
Education level	Years of school education	Categorical ordinal	<9 years 9-12 years >12years
Socioeconomic status (SES)	Based on occupation and school education of the person who contributes more for the household income	Categorical ordinal	High (A social class) Medium (B and C social classes) Low (D social class)

D. INAsma sample and estimates

Table D.1: Characterization of INAsma sample, comparing INAsma estimates and Portuguese population data from National Census 2001.

	INAsma sample (n=6 003)	**INAsma estimate (10 284 536)**	**Portuguese Population 2001 [INE 2001] (10 356 117)**	**Portuguese Population 2011* [INE 2011] (10 555 853)**
Regions, n(%)				
North	1993 (33.2)	3685316 (35.8)	3687293 (35.6)	3689713 (35.0)
Centre	1391(23.2)	2343790 (22.8)	2348397 (22.7)	2327026 (22.0)
Lisbon	1651 (27.5)	2654119 (25.8)	2661850 (25.7)	2815851 (26.7)
Alentejo/Algarve	729 (12.1)	1165122 (11.3)	1171803 (11.3)	1209223 (11.5)
Madeira/Azores	239 (4.9)	436188 (4.2)	486774 (4.7)	514040 (4.9)
Female, n(%)	3438 (57.3)	5335839 (51.9)	5355976 (51.7)	55036127 (52.1)
Age groups†, n(%)				‡
<18 years old	716 (11.9)	2066953 (20.1)	1656602 (16.0)	
18-65 years old	3104 (51.7)	6549606 (63.7)	7006022 (67.7)	
>65 years old	2178 (36.3)	1667976 (16.2)	1693493 (16.4)	

	INAsma sample (n=6 003)	INAsma estimate (10 284 536)	Portuguese Population 2001 [INE 2001] (10 356 117)	Portuguese Population 2011* [INE 2011] (10 555 853)
Education level, n(%)				
Pre-schooler	153 (2.5)	625392 (6.1)	1475812 (14.3)	‡
<9 years	3907 (65.5)	5537758 (54.1)	6065864 (58.6)	
9-12 years	1175 (19.7)	2613679 (25.5)	1620816 (15.6)	
>12 years	732 (12.3)	1464781 (14.3)	1193625 (11.5)	

*Preliminary results from the National Census of 2011. †For the Portuguese population data age groups were <15 years old; 15-65 years old and >65 years old. ‡ Preliminary results from the National Census of 2011 related to age and education level will be released starting from January 2012.