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Asthma, habits and lifestyle

"A retrospective analysis in asthmatic patients at pneumology clinic of a tertiary level outpatient hospital"

Asma, abitudini e stile di vita

"Analisi retrospettiva di un campione di pazienti asmatici seguito in ambulatorio di terzo livello"

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ABSTRACT

Growing evidence suggest the importance of different environments in promoting the pathogenesis and/or exacerbation of asthma. Indoor air pollution is a major contributor to human exposure, since people spend up to 90% of their day indoors. Apart from active smoking, indoor pollution is considered one of the major preventable risk factors of chronic respiratory diseases.

The professional activity can also be dangerous because it exposes the subject to environments that can promote the onset of asthma or worsening of the latter in those already affected. Even bad habits such as incorrect diet, lead to more difficulty in controlling their disease.

However asthma is a multifactorial disease in nature so it is not easy to distinguish the role of occupational exposure, pollution and normal habits such as smoking, nutrition, sports, etc.

This retrospective study was conducted on a sample of asthma patients residing in the metropolitan area of Parma. 116 patients were selected among those who are followed up at least two years at the Asthma outpatient Clinic of Parma University Hospital. The sample in question is therefore closely controlled and monitored; it comes to patients who are well educated on the control of their disease, are able to take appropriate measures to minimize the symptomatology. With this tight approach is proposed to minimize the effect of confounding and then traced with greater certainty the possible cause of the failure to control the disease.

For this purpose, each patient was subjected to regular checkups; we took as a reference the period of time between April and October 2015. During each visit, in addition to general data for each patient, we were collected personal information about their habits and way of life through a validated questionnaire delivered and completed by the patient during the visit in the presence of the permanent staff. The questionnaire covers mainly the qualification of the patient, its possible occupational exposure, his home, with information about nearby traffic, time spent outside, physical activity (place and time), exposure to chemicals, exposure to various fumes (fireplace or stove) and cigarette smoke, comorbidities and any drugs taken during the visits considered. Regarding the respiratory conditions of patients during every examination we were considered: Asthma Control Test (a test performed by patients to assess the state of the disease during the month preceding the test), the measurement of exhaled nitric oxide (FeNO) as an index of airways inflammation, measuring the

resistance level of small airways (R_5-R_{20}) and some spirometric values observed in experiment; in particular the forced vital capacity (FVC), forced expiratory volume in the first second (FEV $_1$), FEV_1/FVC ratio, forced expiratory flow rate over the middle 50% of the FVC ($FEF_{25–75}$) and FEF_{25-75}/FVC were recorded. The sample has been studied considering both the changes of the respiratory parameters for every patient in their examinations, and the respiratory parameters of all the examinations took as a whole in relation with the variables considered.

From the results obtained, the patients are clinically stable; their adopted lifestyle and the exposure to possible sources of outdoor pollution, seems not affect the overall control of their disease.

Some findings of our study are of interest. First, the subjects who carry a steroid therapy show a clinical worst, as revealed by the decrease of most spirometric indices, particularly FEF_{25}, FEF_{75}, FEF_{25-75} and R_5-R_{20}; also, the presence of comorbidities and the subsequent intake of other drugs, in addition to normal therapy for asthma, seem to be conditions associated with poorer performance in the functional respiratory parameters in particular FEV_1/FVC, FEF_{75} and FEF_{25-75}. Spirometric indexes that are down are mainly those related to obstruction imposed on small airways; this suggests a neglect to the latter on the contrary should be further explored and treated accordingly.

It is also observed that both patients are overweight than those living on the lower floors and/or who have the most windows exposed to traffic, showed a decrease of pulmonary function, especially those relate to an obstruction at the small airways level.

In conclusion, our results provided the evidence that a most appropriate therapy, specific to reach the small airways, associated with a healthy lifestyle, can help improve the management of asthma.

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INTRODUCTION

THE ENVIRONMENT ABOUT US

Major everyday habits

Epidemiological studies suggest an important role of the environments, in which we spend our days, in the pathogenesis/exacerbation of chronic respiratory diseases[10]. Factors such as allergens (pollens/mushrooms outside, dust mites/mold/allergens pet/cockroaches inside) have been considered for years one of the most important causes of asthma[1,10]. It is still unclear whether the exposure is actually the primary cause of the onset of asthma, or a trigger flare-ups in people who are already suffering. Different environments can favor the development or exacerbation of asthma, not only in childhood[1] but in adulthood too. In Italy, as in other industrialized countries, the measures taken to improve energy efficiency (windows sealed/use of insulating materials), the use of carpets/upholstery and air conditioners/humidifiers have helped provide an ideal habitat for growth of indoor allergens[2]. More than 10% of Italian children are exposed to mold in the bedroom and children exposed in childhood have almost doubles the risk of developing asthma later.

Indoor air pollution is a major contributor to human exposure, since people spend up to 90 % of their day indoors. Very young children spend most of their time at home and at school and indoor air pollution is a major risk factor for allergic/respiratory childhood[54]. Apart from active smoking, indoor pollution is considered one of the main risk factors for preventable chronic respiratory diseases. One of the risk factors most studied is the passive smoke (ETS: Environmental Tobacco Smoke) the main source of indoor PM. The risk of death from respiratory diseases has doubled in non-smokers exposed to ETS. There is evidence that, in patients who have never smoked and are heavily exposed to ETS, there is an increased risk of chronic cough than in non-exposed, regardless of gender[3].

As regards the outdoor air pollution, several large retrospective studies have established that this is associated with an increased risk of adverse pulmonary[14,15] and cardiovascular events[4-8].

There is growing evidence that atmospheric pollution increases the incidence of asthma in both children[17-20] and adults[16,18,19]. The elderly and the people with health problems such as asthma[42] and chronic bronchitis[43] or with cardiopulmonary disease, are the most vulnerable to air pollution exposure[23-27].The children are at greater risk because their lungs are still growing and they play outside and are active so they breathe more outdoor air pollution than most adults. The extent to which an individual is harmed by air pollution usually depends on the total exposure to the damaging chemicals[27-29]: the duration of exposure, the concentration and the type of the chemicals must be taken into account. They are now known the acute effects of air pollution on mortality[9] and on the use of the health services (hospitalization, appeal to the emergency room, medical visits)[25,30,31], especially for the great health impact of the three serious pollution incidents occurred in the years '30 to Meuese Valley in Belgium, in 1948 in Denora, Pennsylvania, USA and in the years '50 in London.

In the early '90 epidemiological studies have revealed new damage (worsening respiratory symptoms and cardiac in predisposed individuals, acute respiratory infections, asthma crisis, decline in lung capacity, etc) for health in relation to concentrations of the pollutants commonly found in urban areas[10-12]. The relationship between outdoor pollution and respiratory disease has been described in terms of development of pathology due to long-term exposures to different pollutants, including particulate matter (PM), nitrogen oxides, ozone[36,40].

The pollution of the city, caused mainly by fine particles, known as PM_{10} and $PM_{2.5}$, it is a major cause of the increase in allergies and respiratory diseases[35-39,44], including asthma, in children living in urban areas in contact with smog[1,2]. The fine particles are not filtered by the nose and thus more easily reach the airways and lungs. The pollution tends to increase the awareness process of allergies especially among the younger generations. The prevalence of asthma varies considerably in different geographical areas and increases with the rate of urbanization; italian children most exposed to road traffic show a higher prevalence of asthma symptoms[2]. High exposures to PM and NO_2 can increase

even more than double the risk of emergency department for asthma attacks[40,41], especially with regard to children and the elderly[9,12,16].

An epidemiological study in Italy shows that the whole area of the Po valley is definitely high risk, because high density of cars, excessive domestic heating, especially in the winter months, and is poorly ventilated and slightly rainy; this condition involves a worsening of asthma symptoms. In general, it should greatly improve the old Italian fleet , pollute less with wood heating and find cleaner fuels for domestic heating [13,14,17,19,21,22].
The report on the State of Health of the country , recently published by the Ministry of Health, raised the alarm: “The indoor pollution, both in the home and in work environments, it is the cause of allergic diseases, asthma and respiratory disorders especially in childhood”.

Occupational exposure can indeed cause many of the respiratory diseases; acute respiratory diseases such as bronchitis and pneumonia can achieve to inhalation of high concentrations of irritants such as chlorine, ammonia, fires smoke[32]. More often, occupational risk factors can cause chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD) and asthma[28]. However, the origin of these diseases can not be distinguished according to their clinical characteristics, functional and pathological; in addition, they are often multi-factorial in nature, so it is not easy to distinguish the role of occupational exposure than common factors, such as smoking, air pollution or atopy[32-34]. A person with pre-existing non professional asthma may experience exacerbation of the disease in the workplace due to exposure to cold air, exercise or respiratory irritants. The analysis of the geographic distribution of occupational asthma in Europe has shown greater risk in southern countries (Italy, Spain) than the countries of central (Belgium, Germany, France, Switzerland) and northern ones (Norway, Sweden). A review of 43 studies conducted in 19 countries showed that the risk of asthma attributable to exposure working is 9% (interquartile range 25° 75° equal to 5 % - 19 %)[33].

Eating habits are also a risk factor for asthmatic subjects. An improper diet can lead the person to become overweight going against a greater difficulty in controlling their disease[87].

Although actually the data of clinical research can not accurately explain the real relations that exist between obesity and asthma, it is certain that the obese have a greater chance of developing asthma in life. Epidemiological studies suggest that important consequence of obesity could be the more easily that obese individuals have to present a gastro-oesophageal reflux, with all the risks associated with the onset of asthma attacks favored with this mechanism[85-87].

Physical activity can be a double edged sword for an asthmatic, as it could in the long term increase breathing capacity but direct worsen asthma symptoms. The so-called "exercise-induced asthma" (EIA) is a clinical condition characterized by transient constriction of the airways, triggered by intense exercise in people with bronchial hyperreactivity. Advances in medicine, sports and pharmacological have allowed the coexistence of asthma and a quiet sport; fitness to practice sports in asthmatics is still subject to the effectiveness of treatment and the type of sport practiced[90,91].

Ultimate determination of how much asthma may be related to occupational or environmental exposures will require better surveillance of asthma, along with a better understanding of this disease and its natural history (Fig.1).

ASTHMA

Asthma is defined by the Global Initiative for Asthma as "a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper-responsiveness 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"[45].

The inflammation of the airways makes them swollen, very sensitive and highly reactive to certain inhaled substances. When the airways react, the muscles around them tighten (Fig.2A, 2B). This narrows the airways, causing less air to flow into the lungs and the classic symptoms of wheezing. Cells in the airways might make more mucus than usual (Fig.2C). Mucus is a sticky, thick liquid that can further narrow the airways (Fig.3). Also another typical changes in the airway include an increase in eosinophils and thickening of the lamina reticularis.

Symptoms and exacerbation

Asthma is characterized by recurrent episodes of wheezing, shortness of breath, chest tightness, and coughing[45]. Symptoms are often worse at night and in the early morning or in response to exercise or cold air[46]. Some people with asthma only rarely experience symptoms, usually in response to triggers, whereas others may have marked and persistent symptoms[45]. Some individuals will have stable asthma for weeks or months and then suddenly develop an episode of acute asthma with asthma attacks that can last for minutes to days, and can become dangerous if the airflow is severely restricted. Different individuals react differently to various factors[47]. Most individuals can develop severe exacerbation from a number of triggering agents[47]. Psychological stress may worsen symptoms, it's thought that stress alters the immune system and thus increases the airway inflammatory response to allergens and irritants[48].

Causes

Asthma is caused by a combination of environmental and genetic factors[49]. These factors influence both its severity and how responsive it is to treatment. Many environmental factors have been associated with asthma's development and

exacerbation including: allergens, air pollution, and other environmental chemicals. There is a relationship between exposure to air pollutants and the development of asthma[50]. Smoking during pregnancy and after delivery is associated with a greater risk of asthma-like symptoms[45]. Low air quality, from traffic pollution or high ozone levels has been associated with both asthma development and increase asthma severity[17-21,23,24,26]. Exposure to indoor volatile organic compounds may be a trigger for asthma; formaldehyde exposure, for example, has a positive association[51]. Also, phthalates in PVC are associated with asthma in children and adults[52,53] as are high levels of endotoxin exposure. Asthma is also associated with exposure to indoor[54] and outdoor allergens. Common indoor allergens include: dust mites, cockroaches, animal dander, and mold[55,56]. The most common outdoor allergens are pollen. Family history is a risk factor for asthma with many different genes being implicated[57]. By the end of 2005, 25 genes had been associated with asthma in six or more separate populations including: GSTM1, IL10, CTLA-4, SPINK5, LTC4S, IL4R and ADAM33 among others[58]. Many of these genes are related to the immune system or to modulating inflammation. Even among this list of genes supported by highly replicated studies, results have not been consistent among all populations tested[58], in fact these studies are still in developing. The strongest risk factor for developing asthma is a history of atopic disease; with asthma occurring at a much greater rate in those who have either eczema or hay fever[45]. There is a correlation between obesity and the risk of asthma with both having increased in recent years[59,60]. Several factors may be at play including decreased respiratory function due to a buildup of fat and the fact that adipose tissue leads to a pro-inflammatory state[61].

Diagnosis

A diagnosis of asthma should be suspected if there is a history of: recurrent wheezing, coughing or difficulty breathing and these symptoms occur or worsen due to exercise, viral infections, allergens or air pollution. There are two tests that can confirm the diagnosis: spirometry and methacoline challenge testing. Spirometry assesses lung function through different parameters, one of these is

FEV_1 (forced expiratory volume in one second) that is the volume of air you can breathe out in one second; if the FEV_1 measured by this technique improves more than 12% following administration of a bronchodilator such as salbutamol this is supportive of the diagnosis. The methacoline challenge involves the inhalation of increasing concentrations of a substance that causes airway narrowing in those predisposed. If positive it's possible establish the diagnosis of asthma. Other supportive evidence includes: a ≥20% difference in peak expiratory flow rate on at least three days in a week for at least two weeks, a ≥20% improvement of peak flow following treatment with either salbutamol, inhaled corticosteroids or prednisone, or a ≥20% decrease in peak flow following exposure to a trigger[62]. Testing peak expiratory flow is more variable than spirometry, however, and thus not recommended for routine diagnosis. It may be useful for daily self-monitoring in those with moderate to severe disease and for checking the effectiveness of new medications. It may also be helpful in guiding treatment in those with acute exacerbations.

Management

While there is no cure for asthma, symptoms can be improved. A specific, customized plan for proactively monitoring and managing symptoms should be created. This plan should include the reduction of exposure to allergens, testing to assess the severity of symptoms, and the usage of medications. The treatment plan should be written down and advise adjustments to treatment according to changes in symptoms.

The most effective treatment for asthma is identifying triggers, such as cigarette smoke, air pollution or pets and eliminating exposure to them. If trigger avoidance is insufficient, the use of medication is recommended. Pharmaceutical drugs are selected based on, among other things, the severity of illness and the frequency of symptoms.

Two types of asthma medications include short-acting, quick relief, medications and long-acting, controller, medications. Quick relief medications are used to treat asthma symptoms when they occur. They relieve symptoms rapidly and are

usually taken only when needed. Long-acting medications are preventative and are taken daily to help a patient achieve and maintain control of asthma symptoms.

Bronchodilators are recommended for short-term relief of symptoms. In those with occasional attacks, no other medication is needed. If mild persistent disease is present (more than two attacks a week), low-dose inhaled glucocorticoids or alternatively, an oral leukotriene antagonist or a mast cell stabilizer is recommended. For those who have daily attacks, a higher dose of inhaled glucocorticoid is used. In a moderate or severe exacerbation, oral glucocorticoids are added to these treatments[63].

Epidemiology

As of 2011, ~235 million people worldwide are affected by asthma, and approximately 250,000 people die per year from the disease [45]. Rates vary between countries with prevalence between 1% and 18%[45]. It is more common in developed than developing countries[45]. One thus sees lower rates in Asia, Eastern Europe and Africa[64]. Within developed countries it is more common in those who are economically disadvantage while in contrast in developing countries it is more common in the affluent[45]. The reason for these differences is not well know[45].Low and middle income countries make up more than 80% of the mortality[64]. While asthma is twice as common in boys than girls[45], severe asthma occurs at equal rates[59]. In contrast adult women have a higher rate of asthma than men[45] and it is more common in the young than the old[65].

Global rates of asthma have increased significantly between the 1960s and 2008[66] with it being recognized as a major public health problem since the 1970s[65]. Rates of asthma have stabilized in the developed world since the mid 1990s with recent increases primarily in the developing world. Asthma affects approximately 7% of the population of the United States[67] and 5% of people in the United Kingdom[68]. In Italy 11% of the population suffers from Bronchial Asthma. The figure emerged in the 110th Congress of the Italian Society of Internal Medicine.

ASTHMA AND SMALL AIRWAYS

The small airways (distal airways with diameter < 2mm) in asthma have a clinical relevance: it is important site of inflammation and structural alterations contributing in large part to the increase of the total resistance and the airflow limitation in asthma patients (Fig.4). The small airways are difficult to study: the values are influenced by the obstruction of the large airways and do not always correlate with inflammation of those small. FEF_{25-75} is an important parameter, more sensitive than FEV_1, in highlighting the obstructive disease due to small airways[88]; it is highly variable even in normal subjects and the lower limit of normality increases with increasing age.

Anyway, studies suggest that an early closure of the small airways seems be a defining aspect of asthmatics suffering from poor control and moderate-severe forms. The "variability" of asthma, in patients with similar values of FEV_1, may be due to the different involvement of small airways that affects the clinical course[88,89].

ASTHMA AND COMORBIDITIES

In recent years, research has dealt with studying diseases that are often associated with asthma; some interesting results have revealed that asthma is actually accompanied by many diseases, so-called comorbidity[76]. Among these we note cardiovascular diseases, autoimmune, endocrine, gastro-oesophageal, cancer and psychiatric. These comorbidities may change the asthma phenotype, be part of the same pathophysiological process, act as confounding factors in the diagnosis or assessment of control of asthma, and/or result from specific environmental exposures. The influences of these conditions on asthma are variable and for many of them still uncertain; nevertheless, they may alter asthma responses to current therapy[79, 80].

Several studies have shown a strong link between depression and asthma in adulthood is that in old age: to be precise it is much more common in people with asthma than the general population. The nature of this link is not yet entirely clear, as it should be established whether the asthma is due to depression or conversely if the depression in some way is a predisposing factor for asthma. In the absence of definitive evidence, one certainty is that depression has a role in worsening asthma. For those who suffer from depression it tend not to care as it should and then undergoes asthma exacerbations more frequently. Depression may also alter the perception and description of the respiratory symptoms, and then, once again, lead to inadequate treatment is not sufficient for a good control of asthmatic disease[76-78].

A systematic evaluation and an appropriate treatment of asthma-associated comorbid conditions should be part of asthma management, particularly for severe disease. With regard to clinical research, associated conditions may influence the results of trials and should be taken into account in the subjects' inclusion criteria and analysis of data[79].

ASTHMA CONTROL

THE IMPORTANCE TO CONSIDER A CLOSELY MONITORED SAMPLE

Although the guidelines GINA (Global Initiative on Asthma) recommend an appropriate management and adequate treatment of bronchial asthma, with the aim to achieve and maintain control of the disease, observational studies show that a significant number of patients is still poorly checked[81]. The reasons for the difficulties in the stabilization of the disease may be different, including drug treatment inappropriate and/or poor patient adherence to recommended therapy. The latter may be partly due to the tendency for many patients, to underestimate the intensity and frequency of their symptoms and with difficulty to accept the continuation of “maintenance therapy". It should also be considered that, unlike

other chronic diseases in which the evaluation parameters are quantified by a numeric value (blood glucose for diabetes, blood pressure for hypertension), bronchial asthma does not have a simple control indicator, reproducible and quantifiable in a precise score[81-82].

These considerations have led to the development of a simple educational program that is based on close collaboration between patient and physician, with frequent revision and reinforcement of the care plan; an educational process aimed at the self management through which the patient the treatment changes depending on the severity of asthma, according to the directions predetermined by the attending physician[83].

Patients are so well educated on interpretation of their symptoms, the type of drugs to be used regularly and on the need to use those instead. Education is a continuous process that begins at the time of first diagnosis of asthma and is being carried out during all subsequent meetings, during treatment and follow-up, with particular regard to the possibility of hospitalization for acute exacerbation of asthmatic disease[84].

A population of asthma patients well educated and monitored closely is a good sample for the purpose of a clinical trial to evaluate the possible influence of the factors taken into consideration on controlling the disease. Patients well controlled have a better quality of life, thanks to their awareness of the risks which may go against and the subsequent limitation of the latter; this allows to minimize confounding such as smoking, obesity, eating habits, etc., allowing you to go back with more certainty the cause of any worsening of symptoms[83-84].

AIM OF THE STUDY

The aim of the present study was to evaluate the impact of habits and lifestyle on lung function parameters in a cohort of asthmatic patients monitored closely.

MATERIALS AND METHODS

Subjects

The retrospective study was conducted on a sample of patients resident in the metropolitan area of Parma; 116 patients, with asthma diagnosis according to the international guidelines[69], were selected from those who have been followed up at least two years at the Asthma outpatient Clinic of Parma University Hospital. For this reason the sample under examination is to be well controlled and monitored; it's about patients who are well educated on the control of their disease, are therefore able to take appropriate measures to minimize the symptomatology.
Each of them has been subjected to regular checkups; we took as a reference those implemented in the period of time between April and October 2015. During the following visits have been several clinical tests to measure lung function parameters and information was gathered about the habits and lifestyle of the patient; these were obtained by administering to each patient, during the visit, a questionnaire to fill out in the presence of structured personnel.

In addition, information was gathered regarding family history of asthma, atopy, smoking habit, BMI, any therapy for asthma. Atopy was assessed by skin prick tests with a battery of 10 common inhalant allergens. BMI was defined as the weight in kilograms divided by the square of the height in meters; in each subject it was calculated from patients'self-reported height and weight. Therapies normally taken by patients are bronchodilators and steroids.
The sample has been studied considering both the changes of the respiratory parameters for every patient in their examinations, and the respiratory parameters of all the examinations took as a whole in relation with the variables considered.

Questionnaire of habits and lifestyles

The questionnaire is structured in three parts. The first relates to the qualification of the patient, his home with information about nearby traffic and his profession with the possible occupational exposure; the second is related to the time spent outside, any physical activity (time and place), any exposure to chemicals in the

last three days (hours and areas of exposure), any exposure over the last two days in smoke General (stoves or fireplaces), and cigarette smoking; the last part concerning comorbidities and any drugs taken (Fig.5).

Clinical test functional

Regarding the respiratory conditions of patients during every examination, these tests were taken into consideration: Asthma Control test (a test performed by patients to evaluate the pathology grade during the month prior to the test), the fraction of exhaled nitric oxide (FeNO) measurement as an inflammatory index of the airways, oscillometry pulse and simple spirometry.

Asthma Control Assessment

Asthma control was assessed using the Italian version of the ACT[70] . Patients subjectively evaluated the degree of impairment caused by their disease during the preceding 4 weeks by responding to five questions using a five-point scale. The ACT is reliable, valid, and responsive to changes in asthma control over time[70,71]. The sum of the scores of the five questions gave the total ACT score (range 0–25). A cut-off score of 19 or less identifies patients with poorly controlled asthma.

FeNO measurement

We ensured that the patients were not affected by any acute respiratory infection and had followed the pretest instructions, i.e. no nitrate-rich foods or beverages, including alcoholic ones, no tobacco smoking, and no exercise within 1 h preceding the test, as these factors can affect the test results. Moreover, all patients underwent FeNO measurement before the lung function test. Only

patients able to perform at least two acceptable FeNO measurements were included in the analysis. FeNO was measured according to American Thoracic Society/European Respiration Society (ATS/ERS) guidelines[72] using an FeNO stationary chemiluminescence analyzer (NIOX; Aerocrine AB, Solna, Sweden). All FeNO measurements were performed at the same time of day (±2 h) to allow a possible circadian rhythm effect. Patients were seated in the upright position without a nose clip and were asked to inhale nitric oxide-free air through a filter connected to the device deeply to total lung capacity and then to exhale for 10s at a constant pressure guided by a visual cue to stabilize the flow rate. All tests were performed at an exhalation pressure of 10–20 cm H_2O to maintain a fixed flow rate of 50 ml/s. Measurements were repeated after a brief rest period until two acceptable values (±2.5 ppb for measurements <50 ppb and ±5% for measurements ≥50 ppb) were obtained (maximum six attempts). The mean of two adequate values for each subject was recorded for analysis. The system calibration was performed every 14 days.

Oscillometry pulse

Technique that allows the measurement of airway resistance to breathing tidal volume against a source of vibrations in different frequency[75]. Obstruction of small airways is associated with increased resistance mainly at low frequencies.

In particular the measurements at 5 and 20 Hz are indices of total resistance and proximal respectively, while the difference between the resistances measured at 5 and 20 Hz (R_5-R_{20}) is considered an index of resistance of peripheral airways; a value of R_5-R_{20} less than 0,075 KPas/l is considered normal.

Simple spirometry

Lung function was measured by a flow-sensing spirometer connected to a computer for data analysis (CPFS/D Spirometer; MedGraphics, St. Paul, Minn., USA) which met the ATS standards. The forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), FEV_1/FVC ratio, forced expiratory flow rate over the middle 50% of the FVC ($FEF_{25–75}$) and FEF_{25-75}/FVC[73] were recorded. FVC, FEV_1 and $FEF_{25–75}$ are expressed as percents of predicted values[74], FEV_1/FVC is expressed as a percent and FEF_{25-75}/FVC is expressed as absolute values.

Statistical Analysis

For descriptive analysis, data were summarized in terms of frequencies, of means, standard deviations (sd), minimum and maximum values. We coded the FVC, FEV_1, FEV_1/FVC, $FEF_{25,}$ $FEF_{75,}$ $FEF_{25/75,}$ as well as the FeNO *measurement* and the measurement of airway resistance to breathing in dichotomous values that represent the values above and below the cut-off respectively (scheme 1, scheme 2). At first we investigated the risk association by personal characteristics (gender, atopy, overweight, smoking habit and ongoing therapy) and respiratory functions throughout crude Odds ratio at 95% confidence intervals. Then we assessed the possible association between the outcome variables (spirometry tests etc.) and the questionnaire items by a logistic regression model where the personal characteristics were imputed as confounding variables. Results were expressed as adjusted ORs.

RESULTS

The study population consists in 116 patients: 42 males and 74 females. The mean age was higher in women (52 years vs 43.5 years) statistically significantly, while there were no statistically significant differences between men and women, with respect to the distribution of the presence of pollen allergies, atopic condition, smoking habit and taking specific medications for asthma. (Table1).
As for respiratory conditions of individual patients, the sample, divided by type, has been described in terms of mean values of ACT, FeNO, R_5-R_{20}, FVC, FEV_1, FEV_1/FVC (Tiffenau index), FEF_{25}, FEF_{75}, $FEF_{25\,/\,75}$. Also in this case there were no statistically significant differences (Table 2).

The test sample, shows an overall good level of clinical control of asthma symptoms (only 6.9% of the subjects examined, reports an ACT score below 20), however, both in spirometric values (FVC, FEV_1, FEV_1/FVC), and is mainly in the respiratory indices related to the study of small airways (Oscillometry and FEF25, FEF_{75}, $FEF_{25\,/\,75}$), the proportion of subjects with suboptimal is considered high, reaching, in the case of FEF_{25} and $FEF_{25/75}$, 80% and 53% respectively (Graphic 1).

To study our sample were made two types of analysis:

1. Relation between the personal characteristics of patients (sex, atopy, BMI, smoking habit, ongoing therapy) of the whole sample and respiratory parameters in terms of risk (Tables 3.1-3.5)

2. Association between respiratory parameters and the items of the questionnaire through a logistic regression model, where the personal characteristics were considered as confounding variables (Tables 4.1-4.18)

Women and people who are overweight appear to have greater resistance to airflow [OR 2.77 (CI95% 1.27- 6.06) and OR 4.26 (CI95% 1.86-9.73), respectively], (Table 3.1, Table 3.4); non-atopic subjects have spirometric indices worst against FEV_1, FEF_{75} and $FEF_{25/75}$ (Table 3.2); subjects following treatment with at least a steroid have the worst values of both forced expiratory flow (FEF_{25},

FEF_{75}, $FEF_{25/75}$) and peripheral resistance (R_5-R_{20}) (Table 3.5). Smoking status was not associated with an increased risk of spirometric indices worst.

The results relating to the possible association of the factors investigated through the questionnaire and spirometric indexes are shown in Tables 4.1 to 4.18. The analysis made it possible to calculate, for each item, the adjusted ORs for sex, atopy, smoking habit, BMI and steroid therapy.

Risk factors such as a low level of education, occupational exposure or exposure to various chemicals or fumes do not seem to be associated with worsening of respiratory indices; exposure to passive smoke, however, although not reaching statistical significance, seems associated with worse spirometric indices (Table 4.3).

Considering the information related to the patient's home, showed that those living on the lower floors, especially from the second floor down, have a decrease of the following parameters: FEV_1/ FVC, FEF_{25} and $FEF_{25/75}$ (Table 4.6); FVC and FEV_1 instead seem to be affected in a statistically significant presence of windows exposed to traffic (Table 4.7).

The practice of sport, especially so in areas of high traffic, is associated with an increased risk (Table 4.12, Table 4.13).

Patients taking cortisone have a clinical worst as demonstrated by spirometric values of forced expiratory flow (FEF_{25}, FEF_{75}, $FEF_{25/75}$) (Table 4.14); comorbidity patients and taking other drugs, in addition to the specific therapy for asthma, have a decrease of both the FEV_1/FVC parameter both those concerning the forced expiratory flow, particularly FEF_{75} and $FEF_{25/75}$ (Table 4.15, table 4.16).

Taking vitamin supplements instead, although not statistically significant, it would seem to decrease the risk of spirometric indices poor (Table 4.17).

From the results we note that, despite the various factors considered, the respiratory parameters involved are almost always those related to forced expiratory flow (FEF_{25}, FEF_{75}, $FEF_{25/75}$) and the peripheral resistance (R_5- R_{20}). These results suggest an involvement of the small airways.

DISCUSSION

The study population consists in closely monitored and followed up periodically patients; they were selected from those who are in care at least two years at the Asthma outpatient Clinic of Parma University Hospital. Their adopted lifestyle and the exposure to possible sources of outdoor pollution, investigated by administering a validated questionnaire, seems not affect the overall control of their disease.

Some findings of our study are of interest. First, despite the presence of an excellent clinical control, as evidenced by higher average scores of Asthma Control Test, some individual characteristics are associated with a higher risk of poor results of spirometric indices in particular those that assess the function of small airways. Female gender, non-atopic performing a steroid therapy, have a worse functional framework, as evidenced by the decrease of most spirometric indices, particularly FEF_{25}, FEF_{75}, FEF_{25-75} and R_5-R_{20}. In addition, the presence of comorbidities and the subsequent intake of other drugs, in addition to normal therapy for asthma, seem to be conditions associated with poorer performance in the functional respiratory parameters in particular FEV_1/FVC, FEF_{75} and FEF_{25-75}. Spirometric indexes that are down are mainly those related to obstruction imposed on small airways, designed as a forced expiratory flow (FEF), both during normal respiration in terms of airflow resistance (R_5-R_{20}); this suggests that greater attention to the most distal breathing districts, both in terms of functional-diagnostic study and in terms of therapy. As was said in the introduction, the small airways are difficult to study: the values are influenced by proximal airways obstruction and are not always related to inflammation of the distal ones. This difficulty often implies that, these districts are not evaluated enough, so in patients whose compromised, the control of the disease is generally less effective and the quality of life at more risk because of asthma attacks not prevented. It is therefore essential deepening of small airways in terms of clinical and functional so that you can confirm in advance the presence of this inflammation and intervene with more specific drugs can get more depth. Unfortunately, a limitation of the study was not assessed the therapeutic adherence, so-called "compliance" that is the conform of the patient to the doctor's recommendations about how to use the medicine.

Anyway to reduce the chances that may affect control of the disease, it is intended to help the individual patient with medicine, ensuring that it is taken properly. From our sample analyzed, data have further emerged which, although of minor

and already observed in other studies, give us more confirmations. It is seen that air pollution has a negative impact on the progress of developing asthma as patients living on the lower floors and/or who have the most windows exposed to traffic, showed a decrease of pulmonary function and specifically of those that indicate obstruction of small airways; also patients who are overweight have a worsening of the clinical picture and, also in this case, with particular involvement of small airways.

In conclusion, our results provided the evidence that a most appropriate therapy, specific to reach the small airways, associated with a healthy lifestyle, such as reducing the body weight, can help improve the management of asthma.

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FIGURES AND SCHEMES

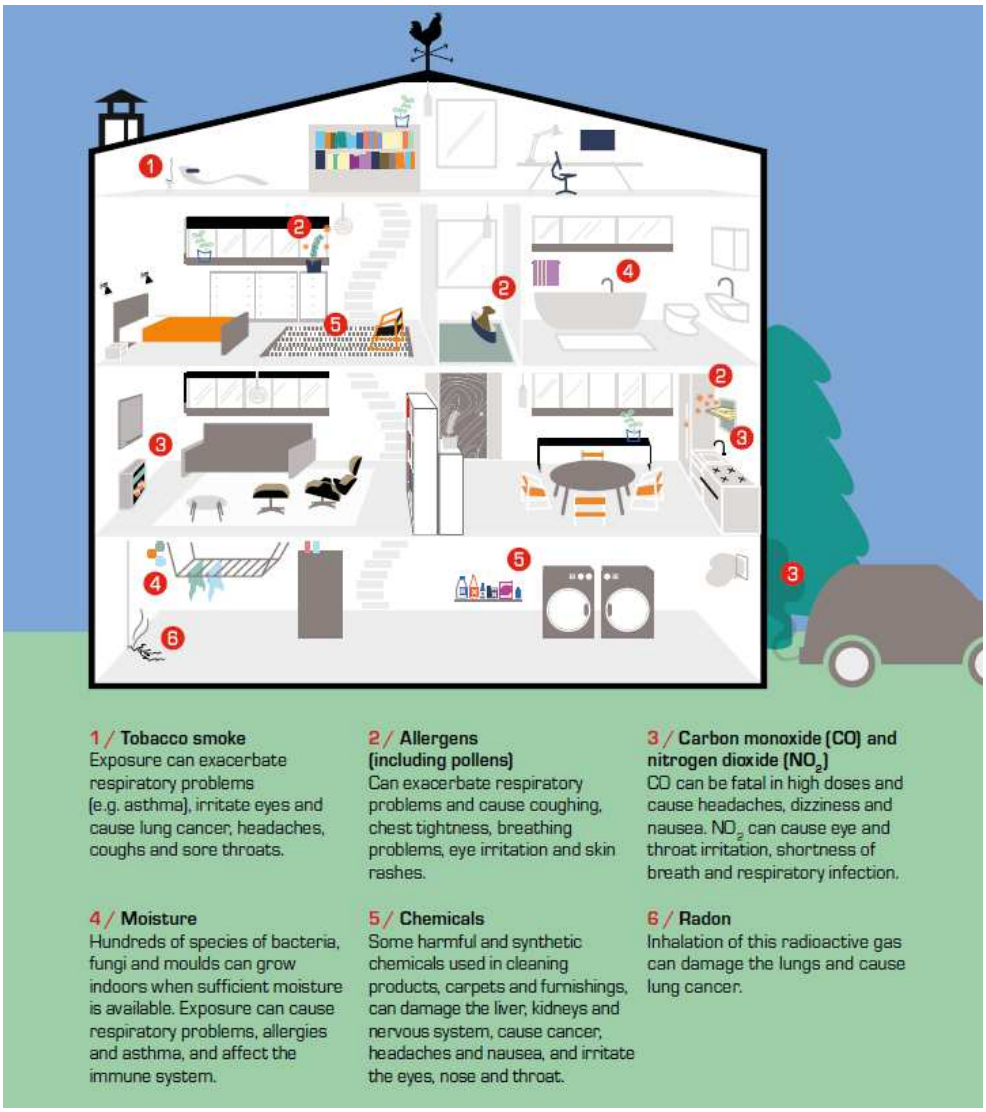

Figure 1: Main factors we are exposed every day that may contribute to asthma.

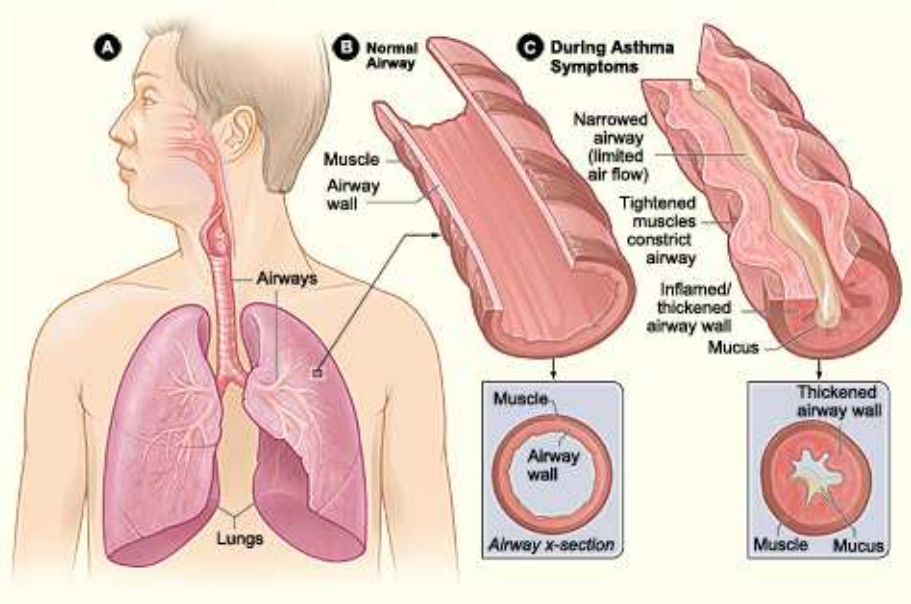

Figure 2

A) The location of the lungs and airways in the body; **B**) A cross section of a normal airway; **C**) A cross-section of an airway during asthma symptoms.

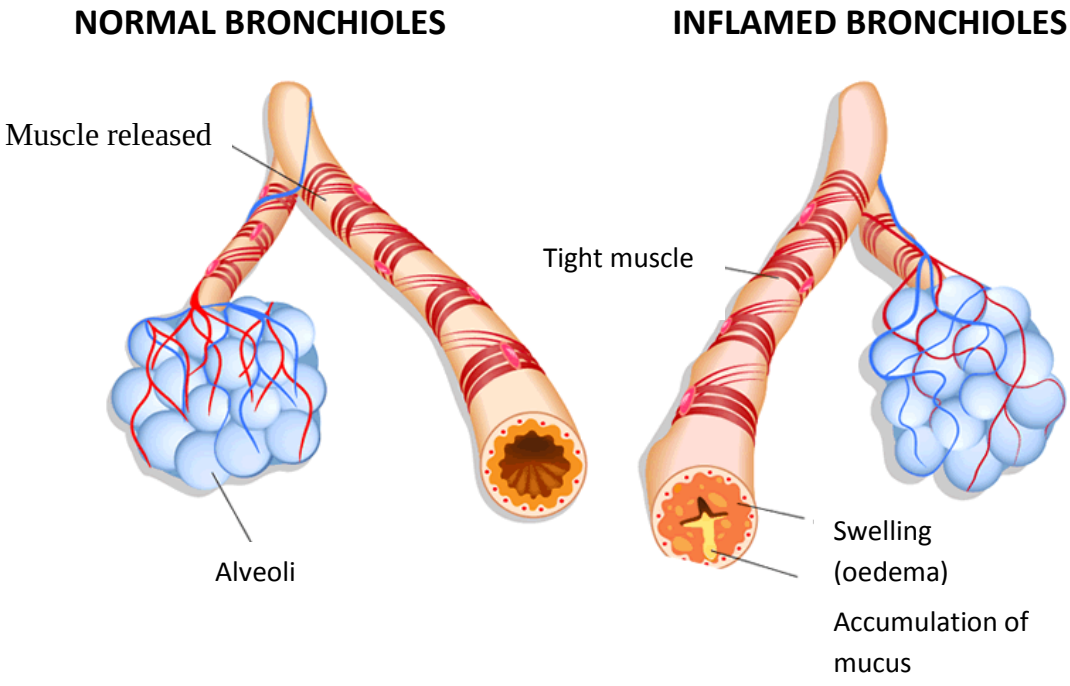

Figure 3: Normal bronchioles and inflamed bronchioles.

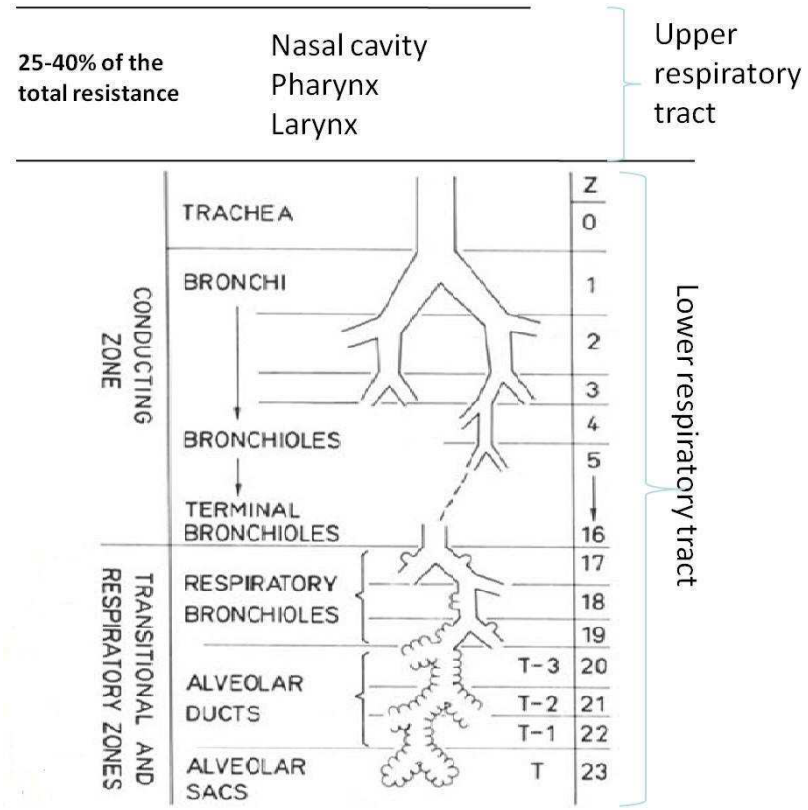

Figure 4:

Bronchial tree

OUTCOMEs	**Cut-Off**
ACT	≥ 20
FeNO	≤ 30 ppb
R_5-R_{20}	≤ 0,03 KPas/l
FVC	≥ 80 %
FEV_1	≥ 80 %
FEV_1/FVC	≥ 70 %
FEF_{25}	≥ 60 %
FEF_{75}	≥ 60 %
$FEF_{25/75}$	≥ 60 %

Scheme 1: Cut-off parameters

CONDITION	**BMI** (Body Max Index)
Overweight subjects	≥ 25 Kg/m^2
Not overweight subjects	< 25 Kg/m^2

Scheme 2: Reference values BMI

PIANO OPERATIVO BIO-MARCATORI

QUESTIONARIO

1. Sezione anagrafica

N. Identificativo_____ Data: _____ Ora_____

Cognome_____ Nome_____

Età_____ Sesso: M □ F □

Titolo di studio:

- □ licenza elementare
- □ licenza media
- □ diploma
- □ laurea

2. Storia professionale

Professione attuale**:** Azienda_____

Indirizzo_____

Reparto di Lavoro_____

Mansione svolta_____

Da quando? ___ /___ /___

Lavora spesso fuori sede? □ SI □ NO

Se si, quante ore passa mediamente fuori sede? _____

Se deve eseguire lavori manuali, usa i guanti? □ SI □ No

Le è capitato di imbrattarsi la pelle con sostanze chimiche negli ultimi tre giorni?
□ SI □ NO

Se SI, specificare:

mani:	□ TANTO	□ MEDIO	□ POCO
altre zone:	□ TANTO	□ MEDIO	□ POCO

Ha svolto qualche altra professione prima di questa? ☐ SI ☐ NO

Se SI, indichi la professione precedente:

Azienda_____

Indirizzo_____

Reparto di Lavoro_____

Mansione svolta_____

Da ___ /___ /___ a ___ /___ /__

3. Storia residenziale

Indirizzo attuale:

via _____

n° civico _____

Città _____

Comune_____

Da quando? ___ /___

Indirizzo precedente e da quando a quando ci ha vissuto:

_____

_____

Di che tipo è la Sua abitazione?

- ☐ appartamento (specificare il piano_____)
- ☐ villetta a schiera
- ☐ casa indipendente
- ☐ altro_____

La maggior parte delle finestre si affacciano su strade trafficate? ☐ SI ☐ NO

I davanzali delle finestre sono spesso sporchi di fuliggine? ☐ SI ☐ NO

Ci sono incroci o semafori entro 100 m dalla casa che provocano il formarsi di code di traffico? ☐ SI ☐ NO

Intorno alla casa ci sono linee di autobus o passaggi di camion? ☐ SI ☐ NO

Che tipo di riscaldamento utilizza nella Sua abitazione?

- Riscaldamento centralizzato
- Riscaldamento autonomo
- Camino a legna
- Stufa a legna, a carbone, a cherosene

Se ha un camino, quantifichi l'uso

- Meno di 20 giorni all'anno
- Fra 20 e 40 giorni all'anno
- Uno o due giorni a settimana nei mesi freddi
- Tutti i giorni o quasi, nei mesi freddi

4. Abitudini e stile di vita

Quanto tempo trascorre mediamente all'aperto ogni giorno:

meno di 1 ora tra 1 e 3 ore più di 3 ore

Esercita attività fisica all'esterno (compresi spostamenti a piedi o in bici)? SI NO

Se SI, quanto tempo dedica settimanalmente all'attività fisica all'aperto?

- Meno di un'ora
- Tra 1 e 3 ore
- Più di 3 ore

Dove svolge prevalentemente l'attività fisica?

- In prossimità di strade ad alto traffico
- In prossimità di aree verdi urbane o extraurbane

Negli ultimi 12 mesi, ha fatto uso **almeno una volta a settimana** dei seguenti prodotti?

	In ambiente chiuso?	
Smacchiatori	☐ SI	☐ NO
Sverniciatori	☐ SI	☐ NO
Colle per carte da parati o pavimenti	☐ SI	☐ NO
Mastici	☐ SI	☐ NO
Solventi	☐ SI	☐ NO
Benzina	☐ SI	☐ NO
Catrame	☐ SI	☐ NO
Olii esausti	☐ SI	☐ NO
Altro _____	☐ SI	☐ NO

5.ESPOSIZIONE A FUMI

- ☐ Non fumatore
- ☐ Ex-fumatore (almeno 4 mesi senza fumo)
- ☐ Fumatore sigaretta elettronica (con o senza nicotina)
- ☐ Fumatore (sigarette, sigari, pipa)

Esposizione a fumi nelle 48 ore precedenti alla raccolta delle urine

Nelle 48 ore precedenti alla raccolta del campione, è stato in ambienti in cui vi era una forte presenza di fumo di tabacco?

☐ SI, n° di ore di esposizione_____ ____

☐ NO

Nelle 48 ore precedenti alla raccolta del campione, è stato in ambienti in cui vi erano stufe o camini a legna accesi?

☐ SI, n° di ore di esposizione_____ ____

☐ NO

6. Anamnesi

Ha qualche patologia di rilievo? ☐ SI ☐ NO

Se SI, specifici quale _____

Assume abitualmente questi farmaci?

		Nome farmaco	N° di volte al giorno	Per quanti giorni?
Antibiotici	☐ SI ☐ NO			
Antidepressivi	☐ SI ☐ NO			
Cortisonici	☐ SI ☐ NO			
Tranquillanti	☐ SI ☐ NO			
Sedativi	☐ SI ☐ NO			
Insulina	☐ SI ☐ NO			
Vitamina A	☐ SI ☐ NO			
Vitamina B	☐ SI ☐ NO			
Vitamina C	☐ SI ☐ NO			
Vitamina D	☐ SI ☐ NO			
Complesso polivitaminico	☐ SI ☐ NO			
Antiossidanti	☐ SI ☐ NO			
Integratori	☐ SI ☐ NO			
Altro	☐ SI ☐ NO			

Utilizza medicine alternative?

- ☐ No
- ☐ Si, quotidianamente
- ☐ Si, settimanalmente
- ☐ Si, mensilmente
- ☐ Si, saltuariamente

Figure 5: Questionnaire of habits and lifestyle

TABLES AND GRAPHICS

Table 1: Descriptive of information about the sample of patients

Age (year)	**N. (116) Mean (sd)**	**min**	**max**			***p****
Male (42)	43.50 (16.27)	19	84			
Female (74)	51.95 (12.38)	24	75			
All (116)	48.89 (14.43)	19	84			0.002
BMI						
Male	24.33 (2.78)	17.00	30.90			n.s.
Female	25.19 (4.38)	16.50	38.60			n.s.
All	24.880 (3.89)	16.50	38.60			n.s.
Pollen	**Not influenced by pollens**	**Low concentration of pollen**	**Average concentration of pollen**	**High concentration of pollen**		***p***§
	N. (%)	N. (%)	N. (%)	N. (%)		
Male	16 (40.00)	4 (10.00)	5 (12.50)	15 (37.50)		
Female	39 (52.70)	6 (8.10)	4 (5.40)	25 (33.80)		
All	55 (48.20)	10 (8.80)	9 (7.90)	40 (35.10)		n.s.
Atopy	**No atopy** N. (% di riga)	**Seasonal atopy** N. (% di riga)	**Perennial atopy** N. (% di riga)	**Seasonal and perennial atopy** N. (% di riga)	**Only drugs and metal atopy** N. (% di riga)	
Male	5 (11.90)	6 (14.30)	8 (19.00)	23 (54.80)	0 (0.00)	
Female	14 (18.90)	7 (9.50)	8 (10.80)	39 (52.70)	6 (8.10)	
All	19 (16.40)	13 (11.20)	16 (13.80)	62 (53.40)	6 (5.20)	n.s.
Smoking habit	**Never smoked** N. (% di riga)	**Former smoker** N. (% di riga)	**Occasional smoker or electronic cigarette** N. (% di riga)	**Active smoker** N. (% di riga)		
Male	28 (66.70)	9 (21.40)	1 (2.40)	4 (9.50)		
Female	56 (75.70)	9 (12.20)	1 (1.40)	8 (10.80)		
All	84 (72.40)	18 (15.50)	2 (1.70)	12 (10.30)		n.s.
Therapy	**No therapy** N. (% di riga)	**Therapy with at least a steroid** N. (% di riga)				
Male	17 (40.50)	25 (59.50)				
Female	28 (37.80)	46 (62.20)				
All	45 (38.80)	71 (61.20)				n.s.

* T Student test; § Chi Square Test

Table 2: Stratification of respiratory parameters by sex

	N.	mean	sd	min	max	p*
ACT						
Male	42	24.10	2.33	15	25	
Female	74	23.69	2.39	13	25	n.s.
All	116	23.84	2.37	13	25	
FeNO						
Male	36	43.44	31.14	8	160	
Female	66	29.98	26.78	2	159	n.s.
All	102	34.74	28.97	2	160	
R5R20						
Male	42	0.03	0.04	-0.03	0.17	
Female	74	0.09	0.12	-0.05	0.56	n.s.
All	116	0.07	0.10	-0.05	0.56	

	N.	mean	sd	min	max	p*
FVC						
Male	42	95.62	16.34	41.00	122.00	
Female	74	100.66	15.69	59.20	128.00	n.s.
All	116	98.84	16.04	41.00	128.00	
FEV1						
Male	42	84.54	14.66	30.40	106.00	
Female	74	89.13	15.35	48.60	116.00	n.s.
All	116	87.47	15.20	30.40	116.00	
TIFFENAU						
Male	42	71.82	6.79	54.79	91.00	
Female	74	72.30	8.43	48.00	93.99	n.s.
All	116	72.12	7.85	48.00	93.99	
FEF25						
Male	40	47.97	17.55	13.40	101.00	
Female	72	44.40	18.14	9.50	107.00	n.s.
All	112	45.67	17.94	9.50	107.00	
FEF75						
Male	41	74.21	20.04	18.00	121.00	
Female	74	83.43	25.93	21.00	137.00	n.s.
All	115	80.14	24.31	18.00	137.00	
FEF2575						
Male	41	58.88	17.24	13.50	102.00	
Female	74	61.00	22.73	14.00	123.00	n.s.
All	115	60.26	20.89	23.50	123.00	

Continuous variables are expressed as mean, standard deviations and minimum and maximum values

Graphic 1

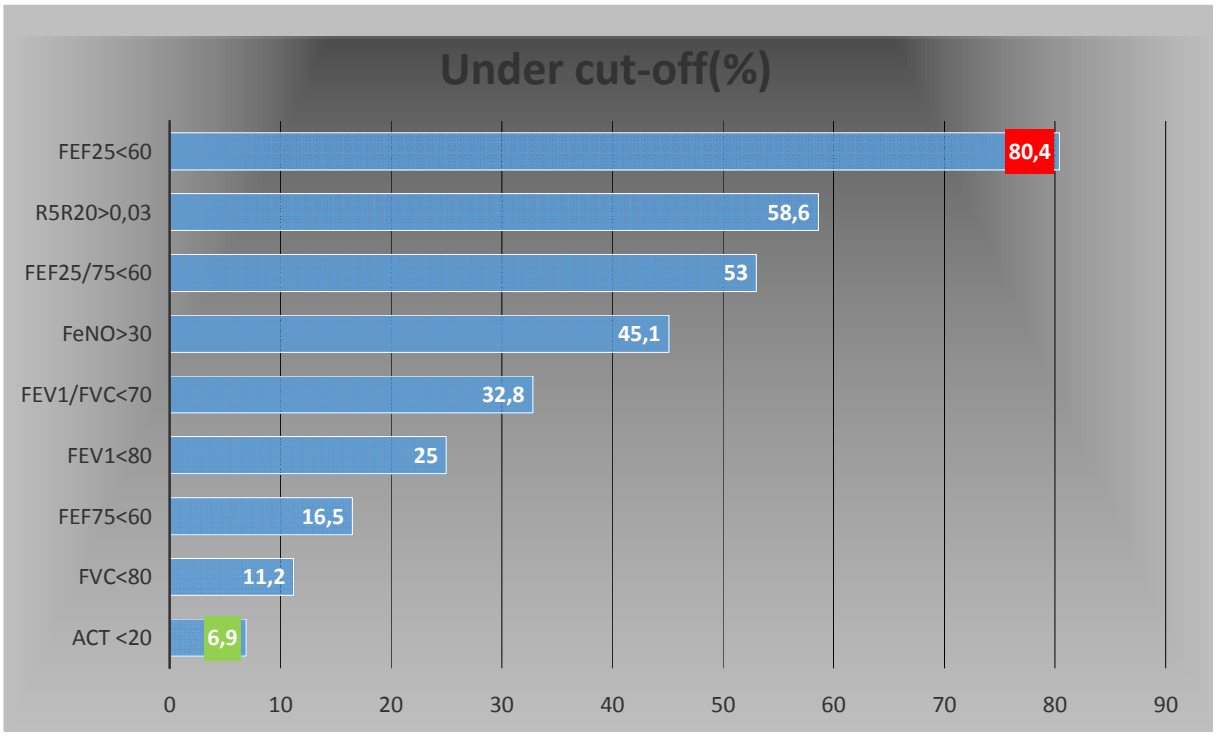
Under cut-off(%)
FEF25<60
R5R20>0,03
FEF25/75<60
FeNO>30
FEV1/FVC<70
FEV1<80
FEF75<60
FVC<80
ACT <20
80,4
58,6
53
45,1
32,8
25
16,5
11,2
6,9
0
10
20
30
40
50
60
70
80
90

Table 3.1: The risk association between gender and respiratory functions

	OUTCOMEs				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Male	39 (92.90)	3 (7.10)	1		
Female	69 (93.20)	5 (6.80)	0.94	0.21-4.16	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Male	15 (41.70)	21 (58.30)	1		
Female	41 (62.10)	25 (37.90)	0.44	0.19-0.99	0.07
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Male	24 (57.10)	18 (42.90)	1		
Female	24 (32.40)	50 (67.60)	2.77	1.27-6.06	0.016
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Male	38 (90.50)	4 (9.50)	1		
Female	65 (87.80)	9 (12.20)	1.31	0.38-4.56	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Male	33 (78.60)	9 (21.40)	1		
Female	54 (73.00)	20 (27.00)	1.36	0.55-3.33	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Male	28 (66.70)	14 (33.30)	1		
Female	50 (67.60)	24 (32.40)	0.96	0.43-2.15	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Male	9 (22.50)	31 (77.50)	1		
Female	13 (18.10)	59 (81.90)	1.32	0.51-3.42	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Male	35 (85.40)	6 (14.60)	1		
Female	61 (82.40)	13 (17.60)	1.24	0.43-3.56	n.s.
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Male	19 (46.30)	22 (53.70)	1		
Female	35 (47.30)	39 (52.70)	0.96	0.45-2.07	n.s.
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 3.2: The risk association between atopy and respiratory functions

	OUTCOMEs				
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Atopic subjects	91 (93.80)	6 (6.20)	1		
Not atopic subjects	17 (89.50)	2 (10.50)	1.78	0.33-9.59	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Atopic subjects	46 (54.10)	39 (45.90)	1		
Not atopic subjects	10 (58.80)	7 (41.20)	1.21	0.42-3.48	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Atopic subjects	43 (44.30)	54 (55.70)	1		
Not atopic subjects	5 (26.30)	14 (73.70)	0.44	0.15-1.34	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Atopic subjects	88 (90.70)	9 (9.30)	1		
Not atopic subjects	15 (78.90)	4 (21.10)	2.61	0.71-9.56	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Atopic subjects	77 (79.40)	20 (20.60)	1		
Not atopic subjects	10 (52.60)	9 (47.40)	3.47	1.24-9.67	0.03
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Atopic subjects	68 (70.10)	29 (29.90)	1		
Not atopic subjects	10 (52.60)	9 (47.40)	2.11	0.78-5.74	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Atopic subjects	20 (21.50)	73 (78.50)	1		
Not atopic subjects	2 (10.50)	17 (89.50)	2.33	0.50-10.93	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Atopic subjects	84 (87.50)	12 (12.50)	1		
Not atopic subjects	12 (63.20)	7 (36.80)	4.08	1.34-12.40	0.02
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Atopic subjects	50 (52.10)	46 (47.90)	1		
Not atopic subjects	4 (21.10)	15 (78.90)	4.08	1.26-13.18	0.026
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 3.3: The risk association between smoking habit and respiratory functions

	OUTCOME				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not smoking subjects	79 (94.00)	5 (6.00)	1		
Smoking subjects	29 (90.60)	3 (9.40)	1.63	0.37-7.27	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not smoking subjects	37 (48.70)	39 (51.30)	1		
Smoking subjects	19 (73.10)	7 (26.90)	0.35	0.13-0.93	0.05
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not smoking subjects	32 (38.10)	52 (61.90)	1		
Smoking subjects	16 (50.00)	16 (50.00)	0.61	0.27-1.39	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not smoking subjects	75 (89.30)	9 (10.70)	1		
Smoking subjects	28 (87.50)	4 (12.50)	1.19	0.34-4.18	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not smoking subjects	64 (76.20)	20 (23.80)	1		
Smoking subjects	23 (71.90)	9 (28.10)	1.25	0.50-3.14	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Smoking subjects	24 (75.00)	8 (25.00)	0.6	0.24-1.50	n.s.
Not smoking subjects	54 (64.30)	30 (35.70)	1		
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not smoking subjects	16 (19.80)	65 (80.20)	1		
Smoking subjects	6 (19.40)	25 (80.60)	1.03	0.36-2.92	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not smoking subjects	69 (82.10)	15 (17.90)	1		
Smoking subjects	27 (87.10)	4 (12.90)	0.68	0.21-2.24	n.s.
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not smoking subjects	40 (47.60)	44 (52.40)	1		
Smoking subjects	14 (45.20)	17 (54.80)	1.10	0.48-2.52	n.s.
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 3.4: The risk association between BMI and respiratory functions

	OUTCOMEs				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not overweight subjects	63 (94.00)	4 (6.00)	1		
Overweight subjects	45 (91.80)	4 (8.20)	1.40	0.33-5.90	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not overweight subjects	26 (48.10)	28 (51.90)	1		
Overweight subjects	30 (62.50)	18 (37.50)	0.56	0.25-1.23	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not overweight subjects	37 (55.20)	30 (44.80)	1		
Overweight subjects	11 (22.40)	38 (77.60)	4.26	1.86-9.73	0.001
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not overweight subjects	63 (94.00)	4 (6.00)	1		
Overweight subjects	40 (81.60)	9 (18.40)	3.54	1.02-12.28	0.07
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not overweight subjects	54 (80.60)	13 (19.40)	1		
Overweight subjects	33 (67.30)	16 (32.70)	2.01	0.86-4.71	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not overweight subjects	46 (68.70)	21 (31.30)	1		
Overweight subjects	32 (65.30)	17 (34.70)	1.16	0.53-2.54	n.s.
All	78 (67.20)	36 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not overweight subjects	13 (20.00)	52 (80.00)	1		
Overweight subjects	9 (19.10)	38 (80.90)	1.06	0.41-2.72	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not overweight subjects	59 (89.40)	7 (10.60)	1		
Overweight subjects	37 (75.50)	12 (24.50)	2.73	1,0-7.57	0.08
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not overweight subjects	34 (51.50)	32 (48.50)	1		
Overweight subjects	20 (40.80)	29 (59.20)	1.54	0.73-3.25	n.s.
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 3.5: The risk association between therapy and respiratory functions

	OUTCOMEs				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
No therapy	43 (95.60)	2 (4.40)	1		
Therapy with at least a steroid	65 (91.50)	6 (8.50)	1.98	0.38-10.29	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
No therapy	20 (51.30)	19 (48.70)	1		
Therapy with at least a steroid	36 (57.10)	27 (42.90)	0.78	0.35-1.76	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
No therapy	24 (53.30)	21 (46.70)	1		
Therapy with at least a steroid	24 (33.80)	47 (66.20)	2.23	1.04-4.80	0.05
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
No therapy	44 (97.80)	1 (2.20)	1		
Therapy with at least a steroid	59 (83.10)	12 (16.90)	8.95	1.12-71.42	0.03
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
No therapy	38 (84.40)	7 (15.60)	1		
Therapy with at least a steroid	49 (69.00)	22 (31.00)	2.44	0.94-6.30	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
No therapy	35 (77.80)	10 (22.20)	1		
Therapy with at least a steroid	43 (60.60)	28 (39.40)	2.28	0.97-5.33	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
No therapy	14 (31.80)	30 (68.20)	1		
Therapy with at least a steroid	8 (11.80)	60 (88.20)	3.5	1.32-9.26	0.018
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
No therapy	42 (93.30)	3 (6.70)	1		
Therapy with at least a steroid	54 (77.10)	16 (22.90)	4.15	1.13-15.18	0.043
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
No therapy	31 (68.90)	14 (31.10)	1		
Therapy with at least a steroid	23 (32.90)	47 (67.10)	4.52	2.02-10.11	0.001
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 4.1: Adjusted ORs

	OUTCOME				
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
Qualification	N. (%)	N. (%)			
High school/degree	68 (90.70)	7 (9.30)	1		
Elementary/middle school	40 (97.60)	1 (2.40)	0.15	0.01-1.50	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
Qualification	N. (%)	N. (%)			
High school/degree	31 (45.60)	37 (54.40)	1		
Elementary/middle school	25 (73.50)	9 (26.50)	0.34	0.12-0.90	0.030
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
Qualification	N. (%)	N. (%)			
High school/degree	34 (45.30)	41 (54.70)	1		
Elementary/middle school	14 (34.10)	27 (65.90)	1.29	0.50-3.28	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
Qualification	N. (%)	N. (%)			
High school/degree	69 (92.00)	6 (8.00)	1		
Elementary/middle school	34 (82.90)	7 (17.10)	1.66	0.44-6.34	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
Qualification	N. (%)	N. (%)			
High school/degree	59 (78.70)	16 (21.30)	1		
Elementary/middle school	28 (68.30)	13 (31.70)	1.26	0.48-3.26	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
Qualification	N. (%)	N. (%)			
High school/degree	52 (69.30)	23 (30.70)	1		
Elementary/middle school	26 (63.40)	15 (36.60)	1.33	0.55-3.24	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
Qualification	N. (%)	N. (%)			
High school/degree	13 (17.60)	61 (82.40)	1		
Elementary/middle school	9 (23.70)	29 (76.30)	0.52	0.17-1.51	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
Qualification	N. (%)	N. (%)			
High school/degree	67 (89.30)	8 (10.70)	1		
Elementary/middle school	29 (72.50)	11 (27.50)	2.85	0.87-9.27	n.s.
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
Qualification	N. (%)	N. (%)			
High school/degree	39 (52.00)	36 (48.00)	1		
Elementary/middle school	15 (37.50)	25 (62.50)	1.61	0.65-3.98	n.s.
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 4.2: Adjusted ORs

	OUTCOMEs				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not occupational exposure	88 (92.60)	7 (7.40)	1		
Possible occupational exposure	20 (95.20)	1 (4.80)	0.51	0.05-4.72	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not occupational exposure	46 (55.40)	37 (44.60)	1		
Possible occupational exposure	10 (52.60)	9 (47.40)	1.41	0.47-4.26	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not occupational exposure	42 (44.20)	53 (55.80)	1		
Possible occupational exposure	6 (28.60)	15 (71.40)	2.17	0.65-7.23	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not occupational exposure	87 (91.60)	8 (8.40)	1		
Possible occupational exposure	16 (76.20)	5 (23.80)	2.98	0.73-12.11	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not occupational exposure	73 (76.80)	22 (23.20)	1		
Possible occupational exposure	14 (66.70)	7 (33.30)	1.46	0.46-4.57	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not occupational exposure	63 (66.30)	32 (33.70)	1		
Possible occupational exposure	15 (71.40)	6 (28.60)	0.82	0.26-2.54	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not occupational exposure	19 (20.90)	72 (79.10)	1		
Possible occupational exposure	3 (14.30)	18 (85.70)	1.78	0.43-7.30	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not occupational exposure	79 (84.00)	15 (16.00)	1		
Possible occupational exposure	17 (81.00)	4 (19.00)	1.00	0.23-4.24	n.s.
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not occupational exposure	44 (46.80)	50 (53.20)	1		
Possible occupational exposure	10 (47.60)	11 (52.40)	0.89	0.29-2.72	n.s.
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 4.3: Adjusted ORs

	OUTCOME				
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to passive smoke	102 (92.70)	8 (7.30)			
Exposure to passive smoke	6 (100.00)	0 (0.00)			
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to passive smoke	54 (55.70)	43 (44.30)	1		
Exposure to passive smoke	2 (40.00)	3 (60.00)	2.18	0.29-16.31	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to passive smoke	45 (40.90)	65 (59.10)	1		
Exposure to passive smoke	3 (50.50)	3 (50.50)	1.73	0.27-11.14	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to passive smoke	97 (88.20)	13 (11.80)			
Exposure to passive smoke	6 (100.00)	0 (0.00)			
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to passive smoke	83 (75.50)	27 (24.50)	1		
Exposure to passive smoke	4 (66.70)	2 (33.30)	0.28	0.42-18.90	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to passive smoke	75 (68.20)	35 (31.80)	1		
Exposure to passive smoke	3 (50.00)	3 (50.00)	4.60	0.76-27.91	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to passive smoke	20 (18.90)	86 (81.10)	1		
Exposure to passive smoke	2 (33.30)	4 (66.70)	0.64	0.09-4.42	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to passive smoke	90 (82.60)	19 (17.40)			
Exposure to passive smoke	6 (100.00)	0 (0.00)			
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to passive smoke	51 (46.80)	58 (53.20)	1		
Exposure to passive smoke	3 (50.00)	3 (50.00)	1.49	0.24-9.12	n.s.
All	54 (47.00)	61 (53.00)			

* Chi Square test or Fisher's Exsact Test

Table 4.4: Adjusted ORs

	OUTCOME				
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to various fumes	106 (93.00)	8 (7.00)			
Exposure to various fumes	2 (100.00)	0 (0.00)			
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to various fumes	54 (54.00)	46 (46.00)			
Exposure to various fumes	2 (100.00)	0 (0.00)			
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to various fumes	46 (40.40)	68 (59.60)			
Exposure to various fumes	2 (100.00)	0 (0.00)			
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to various fumes	101 (88.60)	13 (11.40)			
Exposure to various fumes	2 (100.00)	0 (0.00)			
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to various fumes	85 (74.60)	29 (25.40)			
Exposure to various fumes	2 (100.00)	0 (0.00)			
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to various fumes	76 (66.70)	38 (33.30)			
Exposure to various fumes	2 (100.00)	0 (0.00)			
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to various fumes	21 (19.10)	89 (80.90)	1		
Exposure to various fumes	1 (50.00)	1 (50.00)	0.27	0.01-6.04	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to various fumes	94 (83.20)	19 (16.80)			
Exposure to various fumes	2 (100.00)	0 (0.00)			
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to various fumes	53 (46.90)	60 (53.10)	1		
Exposure to various fumes	1 (50.00)	1 (50.00)	1.02	0.05-21.12	n.s.
All	54 (47.00)	61 (53.00)			

* Chi Square test or Fisher's Exact Test

Table 4.5: Adjusted ORs

	OUTCOME				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to chemicals in the last three days	101 (93.50<9	7 (6.50)	1		
Exposure to chemicals in the last three days	5 (83.30)	1 (16.70)	3.37	0.26-43.13	n.s.
All	106 (93.00)	8 (7.00)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to chemicals in the last three days	52 (54.20)	44 (45.80)	1		
Exposure to chemicals in the last three days	2 (50.00)	2 (50.00)	0.79	0.08-7.37	n.s.
All	54 (54.00)	46 (46.00)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to chemicals in the last three days	44 (40.70)	64 (59.30)	1		
Exposure to chemicals in the last three days	3 (50.00)	3 (50.00)	1.45	0.24-8.77	n.s.
All	47 (41.20)	67 (58.80)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to chemicals in the last three days	96 (88.90)	12 (11.10)	1		
Exposure to chemicals in the last three days	5 (83.30)	1 (16.70)	3.26	0.25-41.83	n.s.
All	101 (88.60)	13 (11.40)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to chemicals in the last three days	81 (75.00)	27 (25.00)	1		
Exposure to chemicals in the last three days	4 (66.70)	2 (33.30)	2.31	0.34-15.43	n.s.
All	85 (74.60)	29 (25.40)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to chemicals in the last three days	72 (66.70)	36 (33.30)	1		
Exposure to chemicals in the last three days	4 (66.70)	2 (33.30)	1.14	0.17-7.35	n.s.
All	76 (66.70)	38 (33.30)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to chemicals in the last three days	21 (20.00)	84 (80.00)	1		
Exposure to chemicals in the last three days	1 (20.00)	4 (80.00)	0.56	0.05-6.47	n.s.
All	22 (20.00)	88 (80.00)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to chemicals in the last three days	88 (82.20)	19 (17.80)			
Exposure to chemicals in the last three days	6 (100.00)	0 (0.00)			
All	94 (83.20)	19 (16.80)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not exposure to chemicals in the last three days	49 (45.80)	58 (54.20)	1		
Exposure to chemicals in the last three days	4 (66.70)	2 (33.30)	0.35	0.05-2.33	n.s.
All	53 (46.90)	60 (53.10)			

*Chi Square Test with Yates's Continuity Correction or Fisher's Exact Test

Table 4.6: Adjusted ORs

	OUTCOME				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
House plan	N. (%)	N. (%)			
Flat from the third floor up	24 (96.00)	1 (4.00)	1		
Flat from the second floor down	49 (90.70)	5 (9.30)	2.47	0.25-24.11	n.s.
Indipendent house	35 (94.60)	2 (5.40)	1.68	0.13-21.45	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
House plan	N. (%)	N. (%)			
Flat from the third floor up	14 (66.70)	7 (33.30)	1		
Flat from the second floor down	21 (46.70)	24 (53.30)	3.33	1.10-11.03	0.04
Indipendent house	21 (58.30)	15 (41.70)	1.07	0.32-3.53	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
House plan	N. (%)	N. (%)			
Flat from the third floor up	13 (52.00)	12 (48.00)	1		
Flat from the second floor down	22 (40.70)	32 (59.30)	1.81	0.59-5.50	n.s.
Indipendent house	13 (35.10)	34 (64.90)	2.08	0.64-6.78	n.s.
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
House plan	N. (%)	N. (%)			
Flat from the third floor up	23 (92.00)	2 (8.00)	1		
Flat from the second floor down	47 (87.00)	7 (13.00)	1.52	0.25-9.10	n.s.
Indipendent house	33 (89.20)	4 (10.80)	1.72	0.25-11.56	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
House plan	N. (%)	N. (%)			
Flat from the third floor up	20 (80.00)	5 (20.00)	1		
Flat from the second floor down	41 (75.90)	13 (24.10)	1.00	0.28-3.53	n.s.
Indipendent house	26 (70.30)	11 (29.70)	2.03	0.28-3.53	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
House plan	N. (%)	N. (%)			
Flat from the third floor up	23 (92.00)	2 (8.00)	1		
Flat from the second floor down	35 (64.80)	19 (35.20)	7.42	1.49-36.84	0.014
Indipendent house	20 (54.10)	17 (45.90)	12.27	2.34-64.31	0.003
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
House plan	N. (%)	N. (%)			
Flat from the third floor up	7 (29.20)	17 (70.80)	1		
Flat from the second floor down	10 (19.60)	41 (80.40)	1.82	0.53-6.25	n.s.
Indipendent house	5 (13.50)	32 (86.50)	3.65	0.90-14.79	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
House plan	N. (%)	N. (%)			
Flat from the third floor up	23 (92.00)	2 (8.00)	1		
Flat from the second floor down	43 (81.10)	10 (18.90)	2.48	0.45-13.66	n.s.
Indipendent house	30 (81.10)	7 (18.90)	2.96	0.51-17.09	n.s.
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
House plan	N. (%)	N. (%)			
Flat from the third floor up	16 (64.00)	9 (36.00)	1		
Flat from the second floor down	23 (43.40)	30 (56.60)	2.98	0.97-9.11	0.05
Indipendent house	15 (40.50)	22 (59.50)	4.59	1.35-15.62	0.014
All	54 (47.00)	61 (53.00)			

*Chi Square Test or Fisher's Exact Test

Table 4.7: Adjusted ORs

	OUTCOMEs				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The windows of the house aren't exposed to traffic	87 (93.50)	6 (6.50)	1		
The windows of the house are exposed to traffic	21 (91.30)	2 (8.70)	1.32	0.22-7.78	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The windows of the house aren't exposed to traffic	42 (51.20)	40 (48.80)	1		
The windows of the house are exposed to traffic	14 (70.00)	6 (30.00)	0.53	0.17-1.63	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,003	**R5R20>0,003**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The windows of the house aren't exposed to traffic	43 (46.20)	50 (53.80)	1		
The windows of the house are exposed to traffic	5 (21.70)	18 (78.30)	2.15	0.65-7.07	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The windows of the house aren't exposed to traffic	86 (92.50)	7 (7.50)	1		
The windows of the house are exposed to traffic	17 (73.90)	6 (26.10)	4.50	1.10-18.34	0.036
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The windows of the house aren't exposed to traffic	74 (79.60)	19 (20.40)	1		
The windows of the house are exposed to traffic	13 (56.50)	10 (43.50)	2.88	1,00-8.31	0.05
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The windows of the house aren't exposed to traffic	65 (69.90)	28 (30.10)	1		
The windows of the house are exposed to traffic	13 (56.50)	10 (43.50)	1.78	0.64-4.91	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The windows of the house aren't exposed to traffic	19 (20.90)	72 (79.10)	1		
The windows of the house are exposed to traffic	3 (14.30)	18 (85.70)	1.14	0.27-4.84	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The windows of the house aren't exposed to traffic	79 (85.90)	13 (14.10)	1		
The windows of the house are exposed to traffic	17 (73.90)	6 (26.10)	2.06	0.58-7.24	n.s.
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The windows of the house aren't exposed to traffic	47 (51.10)	45 (48.90)	1		
The windows of the house are exposed to traffic	7 (30.40)	16 (69.60)	2.29	0.77-6.83	n.s.
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 4.8: Adjusted ORs

	OUTCOMEs				
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not dirty window sills	71 (94.70)	4 (5.30)	1		
Dirty window sills	36 (90.00)	4 (10.00)	2.04	0.42-9.90	n.s.
All	107 (93.00)	8 (7.00)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not dirty window sills	36 (54.50)	30 (45.50)	1		
Dirty window sills	19 (54.30)	16 (45.70)	1.41	0.55-3.58	n.s.
All	55 (54.50)	46 (45.50)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not dirty window sills	37 (49.30)	38 (50.70)	1		
Dirty window sills	11 (27.50)	29 (72.50)	1.93	0.72-5.15	n.s.
All	48 (41.70)	67 (58.30)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not dirty window sills	69 (92.00)	6 (8.00)	1		
Dirty window sills	33 (82.50)	7 (17.50)	2.00	0.56-7.25	n.s.
All	102 (88.70)	13 (11.30)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not dirty window sills	57 (76.00)	18 (24.00)	1		
Dirty window sills	30 (75.00)	10 (25.00)	0.83	0.30-2.24	n.s.
All	87 (75.70)	28 (24.30)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not dirty window sills	51 (68.00)	24 (32.00)	1		
Dirty window sills	26 (65.00)	14 (35.00)	0.99	0.39-2.49	n.s.
All	77 (67.00)	38 (33.00)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not dirty window sills	15 (20.50)	58 (79.50)	1		
Dirty window sills	7 (18.40)	31 (81.60)	0.79	0.24-2.54	n.s.
All	22 (19.80)	89 (80.20)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not dirty window sills	64 (86.50)	10 (13.50)	1		
Dirty window sills	31 (77.50)	9 (22.50)	1.54	0.48-4.88	n.s.
All	95 (83.30)	19 (16.70)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not dirty window sills	35 (47.30)	39 (52.70)	1		
Dirty window sills	19 (47.50)	21 (52.50)	0.79	0.30-2.03	n.s.
All	54 (47.40)	60 (52.60)			

*Chi Square Test with Yates's Continuity Correction

Table 4.9: Adjusted ORs

	OUTCOMEs				
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject doesn't live near bus lines	48 (92.30)	4 (7.70)	1		
The subject lives **near** bus lines	59 (93.70)	4 (6.30)	0.73	0.16-3.30	n.s.
All	107 (93.00)	8 (7.00)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject doesn't live near bus lines	24 (50.00)	24 (50.00)	1		
The subject lives **near** bus lines	31 (58.50)	22 (41.50)	0.93	0.39-2.19	n.s.
All	55 (54.50)	46 (45.50)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject doesn't live near bus lines	23 (44.20)	29 (55.80)	1		
The subject lives **near** bus lines	25 (39.70)	38 (60.30)	1.24	0.52-2.96	n.s.
All	48 (41.70)	67 (58.30)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject doesn't live near bus lines	47 (90.40)	5 (9.60)	1		
The subject lives **near** bus lines	55 (87.30)	8 (12.70)	1.33	0.36-4.89	n.s.
All	102 (88.70)	13 (11.30)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject doesn't live near bus lines	38 (73.10)	14 (26.90)	1		
The subject lives **near** bus lines	49 (77.80)	14 (22.20)	0.68	0.27-1.75	n.s.
All	87 (75.70)	28 (24.30)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject doesn't live near bus lines	31 (59.60)	21 (40.40)	1		
The subject lives **near** bus lines	46 (73.00)	17 (27.00)	0.50	0.21-1.19	n.s.
All	77 (67.00)	38 (33.00)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject doesn't live near bus lines	11 (21.60)	40 (78.40)	1		
The subject lives **near** bus lines	11 (18.30)	49 (81.70)	1.07	0.38-2.99	n.s.
All	22 (19.80)	89 (80.20)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject doesn't live near bus lines	40 (76.90)	12 (23.10)	1		
The subject lives **near** bus lines	55 (87.90)	7 (11.30)	0.32	0.09-1.03	n.s.
All	95 (83.30)	19 (16.70)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject doesn't live near bus lines	22 (42.30)	36 (57.70)	1		
The subject lives **near** bus lines	32 (51.60)	30 (48.40)	0.57	0.24-1.38	n.s.
All	54 (47.40)	60 (52.60)			

*Chi Square Test with Yates's Continuity Correction

Table 4.10: Adjusted ORs

	OUTCOMEs				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject lives **more** than 100 meters from a traffic light	77 (91.70)	7 (8.30)	1		
The subject lives **less** than 100 meters from a traffic light	30 (96.80)	1 (3.20)	0.34	0.03-2.96	n.s.
All	107 (93.00)	8 (7.00)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject lives **more** than 100 meters from a traffic light	41 (54.70)	34 (45.30)	1		
The subject lives **less** than 100 meters from a traffic light	14 (53.80)	12 (46.20)	1.17	0.44-3.06	n.s.
All	55 (54.50)	46 (45.50)			
	R5R20<=0,3	**R5R20>0,3**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject lives **more** than 100 meters from a traffic light	38 (45.20)	46 (54.80)	1		
The subject lives **less** than 100 meters from a traffic light	10 (32.30)	21 (67.70)	1.36	0.52-3.59	n.s.
All	48 (41.70)	67 (58.30)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject lives **more** than 100 meters from a traffic light	74 (88.10)	10 (11.90)	1		
The subject lives **less** than 100 meters from a traffic light	28 (90.30)	3 (9.70)	0.69	0.16-2.95	n.s.
All	102 (88.70)	13 (11.30)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject lives **more** than 100 meters from a traffic light	63 (75.00)	21 (25.00)	1		
The subject lives **less** than 100 meters from a traffic light	24 (77.40)	7 (22.60)	0.75	0.27-2.10	n.s.
All	87 (75.70)	28 (24.30)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
The subject lives **more** than 100 meters from a traffic light	57 (67.90)	27 (32.10)	1		
The subject lives **less** than 100 meters from a traffic light	20 (64.50)	11 (35.50)	1.05	0.42-2.62	n.s.
All	77 (67.00)	38 (33.00)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject lives **more** than 100 meters from a traffic light	19 (23.50)	62 (76.50)	1		
The subject lives **less** than 100 meters from a traffic light	3 (10.00)	27 (90.00)	2.36	0.62-9.03	n.s.
All	22 (19.80)	89 (80.20)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject lives **more** than 100 meters from a traffic light	68 (81.90)	15 (18.10)	1		
The subject lives **less** than 100 meters from a traffic light	27 (87.10)	4 (12.90)	0.57	0.16-2.05	n.s.
All	95 (83.30)	19 (16.70)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject lives **more** than 100 meters from a traffic light	39 (47.00)	44 (53.00)	1		
The subject lives **less** than 100 meters from a traffic light	15 (48.40)	16 (51.60)	0.72	0.28-1.79	n.s.
All	54 (47.40)	60 (52.60)			

*Chi Square Test with Yates's Continuity Correction

Table 4.11: Adjusted ORs

	OUTCOME				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
Time spent outside	N. (%)	N. (%)			
Less than one hour	23 (100.00)	0 (0.00)			
Between one and three hours	58 (95.10)	3 (4.90)			n.s.
More than three hours	19 (82.60)	4 (17.40)			
All	100 (93.50)	7 (6.50)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
Time spent outside	N. (%)	N. (%)			
Less than one hour	14 (66.70)	7 (33.30)	1		
Between one and three hours	26 (47.30)	29 (52.70)	2.82	0.91-8.66	n.s.
More than three hours	9 (50.00)	9 (50.00)	3.23	0.74-14.00	n.s.
All	49 (52.10)	45 (47.90)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
Time spent outside	N. (%)	N. (%)			
Less than one hour	8 (34.80)	15 (65.20)	1		
Between one and three hours	29 (47.50)	32 (52.50)	0.88	0.26-2.46	n.s.
More than three hours	8 (34.80)	15 (65.20)	1.67	0.41-6.81	n.s.
All	45 (42.10)	62 (57.90)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
Time spent outside	**N. (%)**	**N. (%)**			
Less than one hour	19 (82.60)	4 (17.40)	1		
Between one and three hours	57 (93.40)	4 (6.60)	0.36	0.07-1.88	n.s.
More than three hours	19 (82.60)	4 (17.40)	1.16	0.19-6.84	n.s.
All	95 (88.80)	12 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
Time spent outside	N. (%)	N. (%)			
Less than one hour	15 (65.20)	8 (34.80)	1		
Between one and three hours	47 (77.00)	14 (23.00)	0.56	0.17-1.75	n.s.
	17 (73.90)	6 (26.10)	0.69	0.15-2.56	n.s.
All	79 (73.80)	28 (26.20)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
Time spent outside	N. (%)	N. (%)			
Less than one hour	15 (65.20)	8 (34.80)	1		
Between one and three hours	39 (63.90)	22 (36.10)	1.15	0.40-3.35	n.s.
More than three hours	17 (73.90)	6 (26.10)	0.71	0.18-2.80	n.s.
All	71 (66.40)	36 (33.60)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
Time spent outside	N. (%)	N. (%)			
Less than one hour	3 (13.00)	20 (87.00)	1		
Between one and three hours	13 (22.00)	46 (78.00)	0.59	0.14-2.46	n.s.
More than three hours	4 (18.20)	18 (81.80)			
All	20 (19.20)	84 (80.80)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
Time spent outside	N. (%)	N. (%)			
Less than one hour	18 (78.30)	5 (21.70)	1		
Between one and three hours	52 (85.20)	9 (14.80)	0.71	0.18-2.76	n.s.
More than three hours	18(81.80)	4 (18.20)	0.92	0.17-4.87	n.s.
All	88 (83.00)	18 (17.00)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
Time spent outside	N. (%)	N. (%)			
Less than one hour	11 (47.80)	12 (52.20)	1		

Between one and three hours	30 (49.20)	31 (50.80)	1.20	0.40-3.60	n.s.
More than three hours	7 (31.80)	15 (68.20)	2.92	0.70-12.12	n.s.
All	48 (45.30)	58 (54.70)			

* Chi Square test or Fisher's Exact Test

Table 4.12: Adjusted ORs

	ACT => 20	**ACT <20**	**OR**	**CI95%**	* **p**
	N. (%)	N. (%)			
Not practicing sport	71 (94.70)	4 (5.30)	1		
Practicing sport	37 (90.20)	4 (9.80)	2.19	0.49-9.72	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not practicing sport	42 (62.70)	25 (37.30)	1		
Practicing sport	14 (40.00)	21 (60.00)	2.81	1.11-7.13	0.029
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not practicing sport	32 (42.70)	43 (57.30)	1		
Practicing sport	16 (39.00)	25 (61.00)	2.03	0.80-5.15	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not practicing sport	66 (88.00)	9 (12.00)	1		
Practicing sport	37 (90.20)	4 (9.80)	1.07	0.28-4.11	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not practicing sport	57 (76.00)	18 (24.00)	1		
Practicing sport	30 (73.20)	11 (26.80)	1.54	0.59-4.00	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not practicing sport	48 (64.00)	27 (36.00)	1		
Practicing sport	30 (73.20)	11 (26.80)	0.73	0.30-1.77	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not practicing sport	16 (22.20)	56 (77.80)	1		
Practicing sport	6 (15.00)	34 (85.00)	2.28	0.75-6.92	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not practicing sport	60 (80.00)	15 (20.00)	1		
Practicing sport	36 (90.00)	4 (10.00)	0.53	0.15-1.90	n.s.
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**

	N. (%)	N. (%)			
Not practicing sport	36 (48.00)	39 (52.00)	1		
Practicing sport	18 (45.00)	22 (55.00)	1.63	0.67-3.99	n.s.
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 4.13: Adjusted ORs

	OUTCOMEs				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
Practicing sport place	N. (%)	N. (%)			
Green areas in urban or suburban	21 (87.50)	3 (12.50)	1		
High traffic areas	16 (94.10)	1 (5.90)	0.42	0.03-5.90	n.s.
All	37 (90.20)	4 (9.80)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
Practicing sport place	N. (%)	N. (%)			
Green areas in urban or suburban	8 (42.10)	11 (57.90)	1		
High traffic areas	6 (37.50)	10 (62.50)	1.79	0.30-10.46	n.s.
All	14 (40.00)	21 (60.00)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
Practicing sport place	N. (%)	N. (%)			
Green areas in urban or suburban	9 (37.50)	15 (62.50)	1		
High traffic areas	7 (41.20)	10 (58.80)	1.01	0.24-4.16	n.s.
All	16 (39.00)	25 (61.00)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
Practicing sport place	N. (%)	N. (%)			
Green areas in urban or suburban	21 (87.50)	3 (12.50)	1		
High traffic areas	16 (94.10)	1 (5.90)	0.18	0.01-5.48	n.s.
All	37 (90.20)	4 (9.80)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
Practicing sport place	N. (%)	N. (%)			
Green areas in urban or suburban	17 (70.80)	7 (29.20)	1		
High traffic areas	13 (76.50)	4 (23.50)	0.69	0.12-3.69	n.s.
All	30 (73.20)	11 (26.80)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
Practicing sport place	N. (%)	N. (%)			
Green areas in urban or suburban	20 (83.30)	4 (16.70)	1		
High traffic areas	10 (58.80)	7 (41.20)	5.33	0.91-31.11	n.s.
All	30 (73.20)	11 (26.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
Practicing sport place	N. (%)	N. (%)			
Green areas in urban or suburban	4 (17.40)	19 (82.60)	1		
High traffic areas	2 (11.80)	15 (88.20)	1.08	0.13-8.85	n.s.
All	6 (15.00)	34 (85.00)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
Practicing sport place	N. (%)	N. (%)			
Green areas in urban or suburban	21 (91.30)	2 (8.70)	1		
High traffic areas	15 (88.20)	2 (11.80)	1.52	0.03-75.75	n.s.
All	36 (90.00)	4 (10.00)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
Practicing sport place	N. (%)	N. (%)			

Green areas in urban or suburban	11 (47.80)	12 (52.20)	1		
High traffic areas	7 (41.20)	10 (58.80)	1.26	0.29-5.46	n.s.
All	18 (45.00)	22 (55.00)			

*Chi Square Test with Yates's Continuity Correction

Table 4.14: Adjusted ORs

	OUTCOMEs				*
	ACT => 20 N. (%)	**ACT <20** N. (%)	**OR**	**CI95%**	**p**
Not use of cortisone	40 (95.20)	2 (40.80)	1		
Use of cortisone	68 (91.90)	6 (8.10)	1.65	0.31-8.83	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30 N. (%)	**FeNO >30** N. (%)	**OR**	**CI95%**	**p**
Not use of cortisone	18 (50.00)	18 (50.00)	1		
Use of cortisone	38 (57.60)	28 (42.40)	0.92	0.38-2.20	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of cortisone	22 (52.40)	20 (47.60)	1		
Use of cortisone	26 (35.10)	48 (64.90)	2.01	0.86-4.71	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of cortisone	41 (97.60)	1 (2.40)	1		
Use of cortisone	62 (83.80)	12 (16.20)	7.46	0.90-61.73	0.062
All	103 (88.80)	13 (11.20)			
	FEV1=>80 N. (%)	**FEV1<80** N. (%)	**OR**	**CI95%**	**p**
Not use of cortisone	36 (85.70)	6 (14.30)	1		
Use of cortisone	51 (68.90)	23 (31.10)	2.70	0.95-7.66	0.06
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70 N. (%)	**FEV1/FVC<70** N. (%)	**OR**	**CI95%**	**p**
Not use of cortisone	32 (76.20)	10 (23.80)	1		
Use of cortisone	46 (62.20)	28 (37.80)	2.19	0.89-5.35	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of cortisone	14 (34.10)	27 (65.90)	1		
Use of cortisone	8 (11.30)	63 (88.70)	4.38	1.60-11.99	0.004
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of cortisone	39 (92.90)	3 (7.10)	1		
Use of cortisone	57 (78.10)	16 (21.90)	4.11	1.01-16.69	0.04
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**

	N. (%)	N. (%)			
Not use of cortisone	29 (69.00)	13 (31.00)	1		
Use of cortisone	25 (34.20)	48 (65.80)	4.86	2.02-11.70	<0.001
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 4.15: Adjusted ORs

	OUTCOMEs				*
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Comorbidity (not)	51 (96.20)	2 (3.80)	1		
Comorbidity (yes)	57 (90.50)	6 (9.50)	2.41	0.43-13.29	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Comorbidity (not)	25 (55.60)	20 (44.40)	1		
Comorbidity (yes)	31 (54.40)	26 (45.60)	1.33	0.56-3.17	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Comorbidity (not)	28 (52.80)	25 (47.20)	1		
Comorbidity (yes)	20 (31.70)	43 (68.30)	1.74	0.74-4.07	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Comorbidity (not)	51 (96.20)	2 (3.80)	1		
Comorbidity (yes)	52 (82.50)	11 (17.50)	4.15	0.81-21.22	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Comorbidity (not)	43 (81.10)	10 (18.90)	1		
Comorbidity (yes)	44 (69.80)	19 (30.20)	1.36	0.53-3.46	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Comorbidity (not)	41 (77.40)	12 (22.60)	1		
Comorbidity (yes)	37 (58.70)	26 (41.30)	2.34	1.0-5.63	0.05
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Comorbidity (not)	11 (21.60)	40 (78.40)	1		
Comorbidity (yes)	11 (18.00)	50 (82.00)	1.05	0.38-2.90	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Comorbidity (not)	47 (90.40)	5 (9.60)	1		
Comorbidity (yes)	49 (77.80)	14 (22.20)	1.86	0.56-6.12	n.s.
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**

	N. (%)	N. (%)			
Comorbidity (not)	30 (57.70)	22 (42.30)	1		
Comorbidity (yes)	24 (38.10)	39 (61.90)	1.95	0.84-4.52	n.s.
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 4.16: Adjusted ORs

	OUTCOMEs				
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject doesn't assume therapies other than those for asthma	56 (96.60)	2 (3.40)	1		
The subject **assumes therapies** other than those for asthma	52 (89.70)	6 (10.30)	3.05	0.52-17.71	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject doesn't assume therapies other than those for asthma	29 (56.90)	22 (43.10)	1		
The subject **assumes therapies** other than those for asthma	27 (52.90)	24 (47.10)	1.49	0.60-3.70	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,3	**R5R20>0,3**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject doesn't assume therapies other than those for asthma	30 (51.70)	28 (48.30)	1		
The subject **assumes therapies** other than those for asthma	18 (31.00)	40 (69.00)	1.38	0.58-3.28	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject doesn't assume therapies other than those for asthma	56 (96.60)	2 (3.40)	1		
The subject **assumes therapies** other than those for asthma	47 (81.00)	11 (19.00)	4.10	0.78-21.46	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject doesn't assume therapies other than those for asthma	49 (84.50)	9 (15.50)	1		
The subject **assumes therapies** other than those for asthma	38 (65.50)	20 (34.50)	1.99	0.75-5.28	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject doesn't assume therapies other than those for asthma	48 (82.80)	10 (17.20)	1		
The subject **assumes therapies** other than those for asthma	30 (51.70)	28 (48.30)	4.33	1.68-11.14	0.002
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject doesn't assume therapies other than those for asthma	15 (26.80)	41 (73.20)	1		
The subject **assumes therapies** other than those for asthma	7 (12.50)	49 (87.50)	1.99	0.69-5.73	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			

The subject doesn't assume therapies other than those for asthma	54 (94.70)	3 (5.30)	1		
The subject **assumes therapies** other than those for asthma	42 (72.40)	16 (27.60)	4.32	1.07-17.32	0.039
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**P**
	N. (%)	N. (%)			
The subject doesn't assume therapies other than those for asthma	36 (63.20)	21 (36.80)	1		
The subject **assumes therapies** other than those for asthma	18 (31.00)	40 (69.00)	3.10	1.29-7.41	0.011
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

Table 4.17: Adjusted ORs

	OUTCOMEs				
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Use of supplements_vitamine	21 (100.00)	0 (0.00)			
Not use of supplements_vitamine	86 (92.50)	7 (7.50)			
All	107 (93.90)	7 (6.10)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Use of supplements_vitamine	13 (68.40)	6 (31.60)	1		
Not use of supplements_vitamine	42 (51.20)	40 (48.80)	0.69	0.22-2.14	n.s.
All	55 (54.50)	46 (45.50)			
	R5R20<=0,3	**R5R20>0,3**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Use of supplements_vitamine	6 (28.60)	15 (71.40)	1		
Not use of supplements_vitamine	40 (43.00)	53 (57.00)	1.78	0.55-5.75	n.s.
All	46 (40.40)	68 (59.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Use of supplements_vitamine	19 (90.50)	2 (9.50)	1		
Not use of supplements_vitamine	82 (88.20)	11 (11.80)	0.56	0.09-3.23	n.s.
All	101 (88.60)	13 (11.40)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Use of supplements_vitamine	16 (76.20)	5 (23.80)	1		
Not use of supplements_vitamine	69 (74.20)	24 (25.80)	0.79	0.23-2.63	n.s.
All	85 (74.60)	29 (25.40)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Use of supplements_vitamine	19 (90.50)	2 (9.50)	1		
Not use of supplements_vitamine	57 (61.30)	36 (38.70)	0.16	0.034-0.79	0.025
All	76 (66.70)	38 (33.30)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Use of supplements_vitamine	5 (26.30)	14 (73.70)	1		
Not use of supplements_vitamine	17 (18.70)	74 (81.30)	0.64	0.18-2.14	n.s.
All	22 (20.00)	88 (80.00)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			

Use of supplements_vitamine	18 (90.00)	2 (10.00)	1		
Not use of supplements_vitamine	76 (81.70)	17 (18.30)	0.38	0.06-2.15	n.s.
All	94 (83.20)	19 (16.80)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Use of supplements_vitamine	14 (70.00)	6 (30.00)	1		
Not use of supplements_vitamine	39 (41.90)	54 (58.10)	0.22	0.66-0.77	0.018
All	53 (46.90)	60 (53.10)			

* Chi Square test or Fisher's Exsact Test

Table 4.18: Adjusted ORs

	OUTCOME				
	ACT => 20	**ACT <20**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of generic tranquilizers	93 (93.90)	6 (6.10)	1		
Use of generic tranquilizers	15 (88.20)	2 (11.80)	2.07	0.36-11.92	n.s.
All	108 (93.10)	8 (6.90)			
	FeNO <= 30	**FeNO >30**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of generic tranquilizers	47 (54.70)	39 (45.30)	1		
Use of generic tranquilizers	9 (56.30)	7 (43.80)	1.11	0.35-3.50	n.s.
All	56 (54.90)	46 (45.10)			
	R5R20<=0,03	**R5R20>0,03**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of generic tranquilizers	42 (42.40)	57 (57.60)	1		
Use of generic tranquilizers	6 (35.30)	11 (64.70)	1.45	0.44-4.77	n.s.
All	48 (41.40)	68 (58.60)			
	FVC => 80	**FVC < 80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of generic tranquilizers	89 (89.90)	10 (10.10)	1		
Use of generic tranquilizers	14 (82.40)	3 (17.60)	2.32	0.47-11.40	n.s.
All	103 (88.80)	13 (11.20)			
	FEV1=>80	**FEV1<80**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of generic tranquilizers	76 (76.80)	23 (23.20)	1		
Use of generic tranquilizers	11 (64.70)	6 (35.30)	2.06	0.64-6.66	n.s.
All	87 (75.00)	29 (25.00)			
	FEV1/FVC=>70	**FEV1/FVC<70**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of generic tranquilizers	65 (65.70)	34 (34.30)	1		
Use of generic tranquilizers	13 (76.50)	4 (23.50)	0.65	0.19-2.25	n.s.
All	78 (67.20)	38 (32.80)			
	FEF25=>60	**FEF25<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of generic tranquilizers	20 (21.10)	75 (78.90)	1		
Use of generic tranquilizers	2 (11.80)	15 (88.20)	1.95	0.39-9.65	n.s.
All	22 (19.60)	90 (80.40)			
	FEF75=>60	**FEF75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of generic tranquilizers	81 (82.70)	17 (17.30)	1		

Use of generic tranquilizers	15 (88.20)	2 (11.80)	0.80	0.15-4.32	n.s.
All	96 (83.50)	19 (16.50)			
	FEF25/75=>60	**FEF25/75<60**	**OR**	**CI95%**	**p**
	N. (%)	N. (%)			
Not use of generic tranquilizers	45 (45.90)	53 (54.10)	1		
Use of generic tranquilizers	9 (52.90)	8 (47.10)	0.75	0.24-2.31	n.s.
All	54 (47.00)	61 (53.00)			

*Chi Square Test with Yates's Continuity Correction

…Thanks

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