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Costs of perennial allergic rhinitis and allergic asthma increase with severity and poor disease control

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Abstract (229 words)

Background: Perennial allergic rhinitis (PAR) represents a global and public health problem, due to its prevalence, morbidity, and impact on the quality of life. PAR is frequently associated to allergic asthma (AA). Costs of PAR with or without AA are poorly documented.

Objective: Our study aimed to detail medical resource utilization (MRU) and related direct cost for PAR, with or without concomitant AA, in France.

Methods: Using Electronic Health Records (EHRs), we identified in 2010 two cohorts of PAR patients, based on General Practitioners' diagnoses and prescribing data, with and without concomitant AA. For each patient, the EHRs were linked to corresponding claims data with MRU and costs during years 2011 to 2013. Predefined sub-group analyses were performed according to severity of PAR and level of AA control.

Results: The median annual cost reimbursed by social security system for a patient with PAR and no AA was 159€ in 2013. This varied from 111€ to 188€ depending on PAR severity. For patients with PAR and concomitant AA, the median annual cost varied between 266€ and 375€, and drug treatment accounted for 42%-55% of the costs, depending on asthma control.

Conclusion: This study linking diagnoses from EHRs to claims data collected valid information on PAR management, with or without concomitant AA, and on related costs. There was a clear increase of costs with severity of PAR and control of AA.

Key messages:

- Median annual costs reimbursed by social security system for patients with perennial allergic rhinitis in France varied from 125€ to 199€ according to PAR severity. For patients with

concomitant asthma, the median annual cost varied between 280€ and 394€.

- Costs related to medical resource utilization increased with the severity of PAR.
- Patients with very poorly controlled asthma had higher costs than other patients, particularly for therapy.

Key words: Perennial allergic rhinitis; allergic asthma; medical resource utilization; control; costs.

Abbreviations

AA: Allergic Asthma

AIT: Allergen ImmunoTherapy

ARIA: Allergic Rhinitis and its Impact on Asthma

ATC: Anatomical Therapeutic Chemical

CNIL: Commission Nationale Informatique et Libertés

COPD: Chronic Obstructive Pulmonary Disease

EHR: Electronic Health Records

ENT: Ears, Nose, Throat

FDC: Fixed-Dose Combination

GINA: Global Initiative for Asthma

GP: General Practitioner

ICD-10: International Classification of Disease, 10th version

ICS: Inhaled Corticosteroids

IDS: Institut des Données de Santé

LABAs: Long Acting Beta-Agonists

LTD: Long Term Disease

LTRA: LeukoTriene Receptor Antagonist

MRU: Medical Resource Utilization

OCS: Oral Corticosteroids

PAR: Perennial Allergic Rhinitis

PMSI: Programme de Médicalisation des Systèmes d'Information

SABAs: Short Acting Beta-Agonists

SNIIR-AM: Système National d'Information Inter-Régimes de l'Assurance Maladie

Introduction

Allergies, and in particular allergic rhinitis, have become the most frequent chronic disease in developed countries; in 2004 the estimated overall prevalence of airway allergies was 23% in Europe (1) and possibly up to 31% (2). Patients with perennial respiratory allergies can have symptoms from both the upper (perennial allergic rhinitis [PAR]) and lower (allergic asthma [AA]) respiratory tract.

Allergic rhinitis (AR) has been trivialized over past years, despite its prevalence, chronicity and the burden it imposes on individuals and society (3) (4). Fortunately, the burden of AR is now being recognised both by the European Academy of Allergy & Clinical Immunology (EAACI) (5), in order to highlight the profound impact this prevalent condition has on the quality of life (QoL) of AR sufferers and their families. Most AR patients attending their healthcare provider have persistent disease, with many using multiple therapies (6). AR imposes a high socioeconomic burden, particularly in terms of indirect costs, including absenteeism and presenteeism (i.e. productivity loss or under-performance at work and school) (7) (8). It has also been associated with poor asthma control; patients reporting severe rhinitis exhibit poorer asthma control than those with mild disease (9).

Asthma is a chronic disease with an estimated 300 million affected individuals throughout the world (10). In a large French 2006 survey, 10.2% of a general population sample declared having suffered from asthma symptoms at least once in their life time and 6.7% had asthma at the time of the survey (11). Asthma remains a pivotal public health issue mainly due to inappropriate use of controllers (poor adherence) (12), leading to poor asthma control (13,14), deteriorated quality of life (15), high costs for individuals and societies due to medical resource utilization (16), and loss of productivity (17). The recent publication from the Global Initiative for Asthma (GINA) updated international guidelines and highlighted the importance of achieving and maintaining control as a goal of treatment (10,11). The total cost of asthma was estimated at 1.5 billion euros in France (18). In 2006, a French survey estimated that the mean per-patient annual cost of ambulatory care was 1.6 times higher in partially controlled, and 2.9 times higher in uncontrolled asthma as compared to controlled asthma (19) but few European studies have provided data on costs related to asthma control (16).

French claims data (national primary and secondary care) offer a snapshot of disease management in real life conditions, e.g. from recorded drug dispensations and outcomes such as hospital admissions due to severe exacerbations (20,21). However, French claims data do not contain clinical diagnoses. Electronic Health Records (EHRs) with diagnoses from General Practitioners (GPs) linked to French claims data gave us the opportunity to perform this study, to detail exhaustive medical resource utilization (MRU) and related reimbursed cost in patients with PAR, with or without concomitant AA in France.

Methods

Using the panel of IMS Lifelink Disease Analyzer (DA), we identified two cohorts of patients in 2010, one with patients with PAR but no AA, and the other with patients having PAR and concomitant AA. DA is a database of longitudinal EHRs of about 5 million patients collected from a panel of about 1200 physicians since 2000. Its validity and representativeness have been analyzed and published previously (22). Diagnoses made by GPs are recorded using the International Classification of Diseases 10th version (ICD-10 codes), a standard diagnostic tool for epidemiology, health management and clinical purposes which has been cited in more than 20,000 scientific articles and used by more than 100 countries around the world.

The study population consisted of patients aged from 18 to 65 years in 2010, with a diagnosis of PAR (J30.2, J30.3, or J30.4 ICD-10 codes) between 2005 and 2010, or with any medical prescription of antihistamines (R06A ATC code) and nasal corticosteroids (R01AD ATC code) in 2 different semesters of 2010. Patients were excluded if a diagnosis of cystic fibrosis (E84 ICD-10 codes) or Chronic Obstructive Pulmonary Disease (COPD) (ICD-10 J41, J42, J44, J96.1, or J96.0 ICD-10 codes) was recorded in 2010. Patients were also excluded if a prescription of omalizumab (R03DX05 ATC code) was recorded from 2008 to 2010. For each patient included, the EHR was linked to corresponding French claims data with MRU and costs between 2011 and 2013. The probabilistic linkage between the two anonymized databases was based on year of birth, gender, dates of visits to GPs, and GP identifier.

The *système national d'information inter-régimes de l'assurance maladie* [SNIIR-AM] (20,21,23), is a French nation-wide population-based record of individual and anonymized data on all reimbursements for healthcare use. No direct information on the medical indication is linked with each reimbursement, but the SNIIR-AM includes information on long-term disease (LTD) status coded using the ICD-10. LTD status allows patients to receive treatment for severe and costly conditions without out-of-pocket payment. SNIIR-AM also contains information on free-access-to-care status which enables patients of lower socioeconomic status to receive free medical care. Information from the SNIIR-AM database and medical information from the French hospital discharge database (*programme de médicalisation des systèmes d'information* [PMSI]) about all patients admitted to hospital in France, including discharge diagnoses coded using ICD-10, medical procedures and French diagnosis-related groups, are cross-referenced. Using the SNIIR-AM database, patients deceased between 2010 and 2013 were excluded, as were patients with any dispensation of omalizumab between 2010 and 2013 (this drug was excluded as it was used by more severe asthma managed by secondary care physicians), patients with hospitalization or LTD status for cystic fibrosis or COPD between 2010 and 2013, and patients without any medical resource use from 2011 to 2013.

From the overall cohort of PAR patients, two sub-cohorts were distinguished: one with patients with PAR but no AA ("PAR only"), and one with patients with PAR and concomitant AA ("PAR+AA"). Patients with AA were included using both databases (DA and SNIIR-AM). From DA, patients were included in the "PAR+AA" cohort if an asthma diagnosis (J45.0, J45.8, J45.9, or J46 ICD-10 codes) was recorded between 2005 and 2010 or if the GP prescribed at least one asthma controller therapy or one asthma reliever therapy in 2010. From the SNIIR-AM database, patients were included in the "PAR+AA" cohort if a hospitalization for asthma occurred in 2010, if the patient benefited from LTD status for asthma, or if any dispensation of controller or reliever therapy was recorded in 2010.

In the "PAR only" cohort, subgroups based on PAR severity according to treatment load were computed. Mild PAR was defined as 0 or 1 dispensation of antihistamine in 2010 or 0 or 1 dispensation of nasal corticosteroid in 2010. Severe PAR was defined as ≥ 1 dispensation of oral corticosteroid (OCS) in each semester of 2010 or ≥ 1 dispensation of antihistamine and ≥ 1 dispensation of nasal corticosteroid in each semester of 2010. Moderate PAR subgroup included patients with neither mild nor severe PAR.

In the "PAR+AA" cohort, 3 subgroups of patients were defined based on an asthma controller score. The controller-to-total-asthma-medication ratio threshold of $\geq 50\%$ has been found to be associated with fewer asthma exacerbations (24,25), and the Global Initiative for Asthma (GINA) guidelines define excess use of short acting beta agonists (SABAs) as a marker of poor asthma control (10). Patients with therapeutic ratio >0.5 in 2010 and 0, 1 or 2 dispensations of SABAs in 2010 were classified as having well controlled asthma; patients with therapeutic ratio ≤ 0.5 in 2010 and 3 or more dispensations of SABAs in 2010 very poorly controlled asthma; and patients with not well controlled asthma as patients not included in the two others subgroups. To compute therapeutic ratios, only patients with a dispensation of asthma treatment in 2010 were included in the analyses.

MRUs were described between 2011 and 2013 according to the above PAR and asthma controller scores. Patients were described according to baseline characteristics. MRU related to allergic rhinitis and/or asthma were defined as visits to healthcare professional, procedures (radiology and biology), hospitalizations for respiratory symptoms, emergency room visits, medications (respiratory drugs, ocular drugs, ENT disorders treatments, pain killers, anti-inflammatory drugs, antibiotics and treatments for insomnia or depression) and sick leave compensations (indirect costs). All costs were calculated from a National Health Service perspective, i.e. costs reimbursed by the Health Insurance, excluding the excess to be paid by the patient or by the health care mutual. For examples, treatments for allergic rhinitis are actually reimbursed at 30% and anti-asthmatic treatments at 65%. Quantitative variables were described using descriptive statistics: means and standard deviations or medians and interquartile ranges, and qualitative variables with counts and percentages. All analyses

were performed using SAS software, version 9.3 (SAS Institute Inc, Cary, NC, USA).

The study was conducted on anonymized data: the French data protection committee (*commission nationale de l'informatique et des libertés*, CNIL) delivered an authorization to use SNIIR-AM data for this project (approval n°1763241). This study was performed after approval by the French Institute for Health Data (*Institut des données de santé*, approval n° 87, September 9, 2014).

Results

Patient's characteristics

From the DA database, data for 60,359 patients aged from 18 to 65 years in 2010 and fulfilling the PAR criteria were extracted; this corresponded to 6.8% of patients in this age band recorded in the database in 2010. The great majority (90.3%) of the EHRs of these patients was linked to SNIIR-AM data. After exclusion criteria, a total of 52,621 patients were identified. 68.7% were included in the "PAR only" cohort, divided into 3 subgroups according to the rhinitis severity score: 32.1% mild, 51.1% moderate and 16.8% severe PAR. 26.2% were included in the "PAR+AA" cohort, after exclusion of 2,714 patients (5.2%) with no dispensation of asthma therapy in 2010. The "PAR+AA" cohort was divided into 3 subgroups according to asthma controller score: 54.2% well controlled, 34.1% not well controlled, and 11.7% very poorly controlled (Figure 1).

FIGURE 1

The "PAR only" cohort consisted of 59.0% to 61.5% of female, depending on severity. Few patients (less than 1%) benefited from LDT status (any comorbid condition), and between 6.3% and 8.3% had free-access-to-care status. Patients with mild PAR mostly had either no dispensation (43.6%) or between 1 and 5 units (56.1%) of anti-allergic drugs in 2010. Patients with moderate PAR had at least 1 unit of anti-allergic drugs: most had 1 to 5 units (62.4%) or 6 to 10 units (22.1%). One third of patients with severe PAR received between 1 and 5 units of anti-allergic drugs (31.6%), one third between 6 and 10 (32.9%), and the last third at least 11 units in 2010 (35.5%; Table 1).

The 3 sub-groups of patients with AA were mainly female; those with very poorly controlled asthma had the most men (42.8%). Just over 10% of patients with very poorly controlled asthma benefited from free-access-to-care status and 8.7% from LTD status. Two thirds of these patients (66.2%) received at least 6 units of anti-allergic drugs in 2010.

TABLE 1

Moreover, 12.9% of patients with well controlled asthma had mild PAR, 52.8% moderate and 34.3% severe PAR. For very poorly controlled asthma, only 8.6% of patients had a mild PAR, and 38.9% a severe PAR.

TABLE 2

Cost analysis

As there was no significant difference in MRU and costs between 2011 and 2013 for the 6 sub-groups, only 2013 results are included.

For the “PAR only” cohort, median annual costs per patient varied from 111€ to 188€ for 2013, according to PAR severity. Irrespective of PAR severity, at least 80% of patients visited a GP, whereas visits to ophthalmologists ranged from 15.8% of patients to 18.7%, depending on severity. A gradient appeared for all drug consumption: 30.9% of patients with mild PAR had at least one filled prescription of antihistamines, whereas 59.9% of patients with severe PAR received antihistamines. These results are similar for nasal corticosteroids (from 31.6% to 58.7%), for intramuscular injections of corticosteroids (from 4.5% to 7.2%), for allergen immunotherapy (0.8% to 7.0%), and for ocular drugs (from 10.2% to 18.7%; Table 3). Drug treatment accounted for a quarter of expenditure, with a median cost of 15.51€ for patients with mild PAR, 29.58€ for moderate PAR and 43.57€ for severe PAR (Figure 2). A gradient also appeared for non-drug-treatments, with a range from 85.52€ for mild PAR to 122.72€ for severe PAR.

TABLE 3

FIGURE 2

For the “PAR+AA cohort”, median annual costs per patient ranged from 266€ to 375€ for 2013 according to asthma control. Visits to lung specialists were rare, even among patients who had very poorly controlled asthma. Fixed-dose combinations of ICS + Long Acting Beta Agonists (LABAs) were dispensed to 33.7% of patients with well controlled asthma and to 46.2% of patients with very poorly controlled asthma. There was a gradient for increasing use of drugs in function of control for LABAs in a separate canister (from 2.0% to 10.5%), for ICS (from 16.9% to 22.8%), for leukotriene receptor antagonists (LTRA; from 11.4% to 22.8%), and for SABAs (from 19.4% to 77.9%; Table 4). Drug treatment accounted for 42%-55% of share expenditure, with a median cost of 77.71€ for patients with well controlled asthma, 67.6€ for not well controlled asthma and 175.5€ for very poorly controlled asthma (Figure 3). MRU for non-drug-treatments were stable between the three sub-groups (around 130€ per patient), as were hospitalizations.

TABLE 4

FIGURE 3

Discussion

In this observational study linking two health care databases, prescribing and claims, it was found that a quarter of those with PAR also had allergic asthma. In both patients with PAR only and PAR associated to AA, median costs per patient increased according to severity and control.

According to the GINA 2015 Guidelines (10), the goal of asthma treatment is to achieve and maintain asthma control and reduce risks. In this study, the level of control was based on the use of reliever treatments and on the controller-to-total-asthma-medication ratio. Previous studies estimated that approximately 40% of patients in France (26) have uncontrolled asthma. This estimate is in line with this study as 34.1% had not well controlled asthma and 11.7% very poorly controlled asthma. LTD status allows patients to receive treatment for severe and costly conditions without out-of-pocket payment. In the “PAR+AA” cohort, 8.7% of patients with very poorly controlled asthma benefited from LTD status for asthma, whereas only 1.6% and 3.1% of patients with well controlled and not well controlled asthma benefited from this status, respectively. Indeed, this status is restricted for patients with high MRU and costs, often associated with poor asthma control (27). In this study, the median total cost per patient over a 12-month period was higher when asthma was poorly controlled. The median annual cost varied between 266€ and 375€, and drug treatment accounted for 42%-55% of the costs, depending on asthma control. This result is in line with previous European results (19,28). Costs for asthma-related hospitalizations were stable between the three sub-groups. This result could be explained by the identification of patients from GP records. Indeed, in France, patients managed for their asthma by GPs tend to have less severe asthma, with few hospitalizations. In a global asthma population, costs for emergency room visits and for hospital admission should be higher (16). Likewise, excluding patients on omalizumab have probably decreased the costs of asthma treatment and hospitalizations (particularly for patients with very poorly controlled asthma). Free-access-to-care status enables patients of lower socioeconomic status to receive free medical care. This lower socioeconomic status was more frequent for patients with moderate or severe PAR (8.3%) than for patients with mild PAR; and for patients with not well controlled asthma (10.6%) or very poorly controlled asthma (10.9%) than for patients with well controlled asthma (8.0%), possibly linked with lower health literacy, that could contribute to the inappropriate management of asthma (29) (30)

ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines recommended oral antihistamines (31). Likewise, nasal glucocorticosteroids are currently the most effective class of medications available for the treatment of allergic rhinitis (32,33). In our study, only 59.9% and 58.7% of patients with severe rhinitis received antihistamines and nasal glucocorticosteroids, respectively. This is in agreement with a recent study conducted on 350 Belgian GPs that showed only 31% awareness of ARIA guidelines, while only 10% GPs stating implementation (34). Patients suffering from PAR seem to cope better with symptoms compared to patients with seasonal AR and probably get weary with taking lifelong pharmacotherapy. Indeed, patients with perennial allergies slowly get used to the symptoms whereas season allergies comes (and goes) more sudden and the patients better correlates the symptoms with the season. In our study, only 2.3% of patients with severe PAR received allergy immunotherapy, as well as 3.1% of patients with not well controlled asthma and 2.4% of patients with very poorly controlled asthma. These low frequencies could be explained by the fact that treatment with allergy immunotherapy is recommended for patients with evidence of clinically relevant IgE-mediated disease, in whom pharmacotherapy and avoidance measures provide inadequate control (35). Another reason might be the insufficient awareness of this therapy amongst GPs and the low access to allergists in France.

FDC of ICS+LABAs were dispensed to only 26.0% of patients with not well-controlled asthma and to 46.2% of patients with very poorly controlled asthma. Likewise, ICS in a separate canister were dispensed to only 22.8% of patients with very poorly controlled asthma. Underuse of controller therapy, especially ICS, has been highlighted by many studies (36) as a major issue in asthma management. A recent meta-analysis, focused on the risk of asthma exacerbation after stopping low-dose ICS, concluded that patients with well-controlled asthma who stop regular use of low-dose ICS have an increased risk of exacerbation compared with those who continue ICS (37). Patients with very poorly controlled asthma had indeed more unscheduled visits to GPs and more emergency room visits than patients with well controlled asthma.

The results of this study revealed a clear increase of costs with severity of perennial allergic rhinitis, and with asthma control. There are many ways to improve the identified care gap in asthma and in allergic rhinitis. Clinicians could improve the quality of prescribing (38) and patients should be informed on appropriate use of therapy (39) and technical use of inhalers (40). Clinicians should be informed on the actual drugs use of their patients, e.g. via feedback from claims data or from consulting practice prescribing records. The ratio of inhaled corticosteroids to bronchodilators is reported to serve as a potential indicator of the quality of prescribing for asthma. A higher ratio reflects greater prescribing of inhaled corticosteroids relative to bronchodilators and this feature is regarded as good practice (41). Other clinical healthcare providers (e.g. nurses) could also review the

use of therapy, and provide training and support to patients (42). Policymakers should develop actions targeting both clinicians (e.g., via asthma audits) and patients (e.g., by providing ways for patients to have direct contacts with advisors, e.g. using IT, or through pharmacies). Patients should also be aware of diagnosis procedures and the promises of the available treatments, including allergen immunotherapy.

Some limitations must be acknowledged. Patients were included based on GPs diagnoses and prescribing data. Each assumption (diagnosis, disease severity/control) is made by proxies, and ICD-10 codes used for approaching PAR and AA do not possibly identified all patients. Thereby, asthma patients included are not representative of the overall asthma patients. The most severe patients may be only seen in secondary and tertiary settings. Indeed, patients exclusively managed by lung specialist may not be captured. However, the vast majority of asthma patients visit their GP at least once a year (43), and they should have been included, if the GPs had mentioned a diagnosis of asthma. As allergy is not a medical specialty in France, there was no possibility to distinguish “standard” GPs and GPs with the national allergology diploma. However, it would have been interesting to assess the burden of PAR for patients managed by allergists, compared to others.

Also, indirect costs were described using costs associated with sick leave. However, reasons for sick leaves are not recorded, which does not ensure specificity for asthma or rhinitis. Nevertheless, number of days per year found in this study (11 or 12 days) are in line with a study recently conducted in the UK on the burden of adult allergic rhinitis (44). Several treatments of allergic rhinitis can be accessed ‘over the counter’ without a prescription from a pharmacy and some may be obtained from any retail outlet. As claims data recorded only reimbursed medications (with a prescription), medical resource utilization and associated costs could have been underestimated. A study conducted on nonsteroidal anti-inflammatory drug and paracetamol revealed that at least 80% of over-the-counter medications are prescribed and reimbursed in France (45). Furthermore, only costs reimbursed by National Health Service were calculated, which excluding the excess to be paid by the patient or by the health care mutual.

This study linking diagnoses from Electronic Health Records to claims data was one of the first of its kind to be conducted in France, where the MRU of the overwhelming majority of the population is recorded and available for research projects. The study collected valid data on perennial allergic rhinitis management, with or without concomitant asthma, and on related costs. There was a clear increase of medical resource utilization and associated costs with severity of perennial allergic rhinitis and asthma control. Improved disease control for patients with perennial allergic rhinitis and asthma would decrease the burden of disease.

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Tables & Figures

Table 1: Characteristics of patients in 2010 from cohorts “PAR only” and “PAR+AA”, according to PAR severity and asthma control

Variables	“PAR only” cohort (n=36,136) N (%)			“PAR+AA” cohort (n=13,771) N (%)		
	Mild PAR (n=11,600)	Moderate PAR (n=18,460)	Severe PAR (n=6,076)	Well controlled asthma (n=7,458)	Not well controlled asthma (n=4,700)	Very poorly controlled asthma (n=1,613)
Gender						
Male	4,754 (41.0%)	7,253 (39.3%)	2,337 (38.5%)	2,710 (36.3%)	1,669 (35.5%)	691 (42.8%)
Female	6,846 (59.0%)	11,207 (60.7%)	3,739 (61.5%)	4,748 (63.7%)	3,031 (64.5%)	922 (57.2%)
Mean age in 2010 (SD)	40.7 (13.9)	43.5 (13.2)	43.1 (12.7)	44.6 (12.8)	40.9 (13.1)	42.3 (12.9)
LTD status for severe chronic respiratory failure	3 (0.03%)	7 (0.04%)	6 (0.1%)	118 (1.6%)	145 (3.1%)	141 (8.7%)
Free-access-to-care status	732 (6.3%)	1,537 (8.3%)	506 (8.3%)	597 (8.0%)	499 (10.6%)	176 (10.9%)
Number of units of anti-allergic drugs dispensed in 2010						
0	5,061 (43.6%)	0 (0.0%)	0 (0.0%)	221 (3.0%)	209 (4.5%)	209 (2.7%)
1-5	6,512 (56.1%)	11,527 (62.4%)	1,917 (31.6%)	3,183 (42.7%)	2,148 (45.7%)	2,148 (31.1%)
6-10	24 (0.2%)	4,084 (22.1%)	1,996 (32.9%)	1,934 (25.9%)	1,122 (23.9%)	1,122 (25.5%)
11-15	2 (0.0%)	1,738 (9.4%)	983 (16.2%)	1,043 (14.0%)	572 (12.2%)	572 (18.1%)
>15	1 (0.0%)	1,111 (6.0%)	1,180 (19.3%)	1,077 (14.4%)	649 (13.8%)	649 (22.6%)

PAR: perennial allergic rhinitis; AA: allergic asthma; LTD: long term disease

Table 2: Severity of PAR according to asthma control

	Well controlled asthma (n=7,458)		Not well controlled asthma (n=4,700)		Very poorly controlled asthma (n=1,613)	
	n	%	n	%	n	%
Mild PAR	962	12.4	757	16.1	138	8.6
Moderate PAR	3,939	52.8	2,353	50.1	847	52.5
Severe PAR	2,557	34.3	1,590	33.8	628	38.9
Total	7,458	100.0	4,700	100.0	1,613	100.0

Table 3: Medical resource utilization of patients and costs in 2013 for “PAR only” cohort, according to PAR severity (N=36,136)

MRU	Mild PAR (n=11,600)			Moderate PAR (n=18,460)			Severe PAR (n=6,076)		
	n (%)	median units (Q1 - Q3)	median cost per patient in € (Q1-Q3)	n (%)	median units (Q1 - Q3)	median cost per patient in € (Q1-Q3)	n (%)	median units (Q1 - Q3)	median cost per patient in € (Q1-Q3)
Visits to health care professional									
GP (visits scheduled)	9,496 (81.9)	4 (3 - 7)	75.5 (41.4 - 128.8)	15,773 (85.4)	5 (3 - 9)	92 (48.3 - 156.4)	5,230 (86.1)	6 (4 - 9)	96.6 (57.5 - 165.6)
GP (visits unscheduled)	442 (3.8)	1 (1 - 1)	29.44 (16.1 - 45.6)	746 (4.0)	1 (1 - 1)	31.92 (20.7 - 46.4)	295 (4.9)	1 (1 - 1)	31.92 (17.7 - 46.4)
Lung specialist	103 (0.9)	1 (1 - 1)	25 (17.5 - 46)	253 (1.4)	1 (1 - 1)	25 (17.5 - 35)	110 (1.8)	1 (1 - 2)	25 (17.5 - 35)
Ophthalmologist	1,835 (15.8)	1 (1 - 1)	32.2 (17.5 - 35)	3,163 (17.1)	1 (1 - 1)	17.5 (16.1 - 23)	1,134 (18.7)	1 (1 - 1)	17.5 (16.1 - 23)
≥1outpatient hospital visit	2,820 (24.3)	2 (1 - 3)	32.2 (16.1 - 64.4)	5,008 (27.1)	1.5 (1 - 3)	32.2 (16.1 - 64.4)	1,700 (28.0)	2 (1 - 3)	32,2 (16,1 - 64,4)
Procedures									
Investigations of nasal cavity	383 (3.3)	1 (1 - 1)	21.55 (21.32 - 30.78)	852 (4.6)	1 (1 - 1)	21.55 (21.32 - 30.78)	396 (6.5)	1 (1 - 1)	24,61 (21,32 - 30,78)
X-rays of lungs	767 (6.6)	1 (1 - 1)	18,14 (18,1 - 25,9)	1,362 (7.4)	1 (1 - 1)	18.14 (18.1 - 25.9)	500 (8.2)	1 (1 - 1)	21.28 (18.1 - 25.9)
Blood cell counts	5,248 (45.2)	1 (1 - 2)	5,02 (5 - 10)	9,490 (51.4)	1 (1 - 2)	7.53 (5 - 10)	3,180 (52.3)	1 (1 - 2)	7.53 (5 - 13.4)
Emergency room visit	1,466 (12.6)	1 (1 - 1)	25.32 (25.3 - 27.1)	2,361 (12.8)	1 (1 - 1)	25.32 (25.3 - 25.3)	819 (13.5)	1 (1 - 1)	25.32 (25.3 - 25.3)
Hospitalization for respiratory symptoms	44 (0.4)	1 (1 - 1)	1133.63 (861.42 - 1422.45)	75 (0.4)	1 (1 - 1)	1239.71 (935 - 1770.28)	43 (0.7)	1 (1 - 1)	1126,93 (763,41 - 1503,88)
Allergy and asthma drugs									
Antihistamines	3,587 (30.9)	2 (1 - 3)	2.6 (1.6 - 5.51)	9,119 (49.4)	3 (1 - 8)	5.51 (2.2 - 15.75)	3,637 (59.9)	4 (2 - 10)	7.26 (2.7 - 18.56)
Nasal corticosteroids	3,660 (31.6%)	1 (1 - 2)	2.86 (1.12 - 5.35)	8,103 (43.9)	2 (1 - 3)	2.89 (1.12 - 7.56)	3,566 (58.7)	2 (1 - 5)	5,72 (2,46 - 14,22)
Intramuscular injections of corticosteroids	526 (4.5)	1 (1 - 2)	3.62 (3.5 - 7.11)	1,009 (5.5)	2 (1 - 3)	5.47 (3.5 - 10.34)	437 (7.2)	2 (1 - 3)	6.23 (3.5 - 10.84)
OCS	2,547(22.2)	1 (1 - 2)	2.81 (2.8 - 5.55)	4,941 (26.8)	1 (1 - 2)	3.15 (2.8 - 5.63)	2,409 (39.6)	1 (1 - 3)	4.33 (2.8 - 8.22)
AIT	98 (0.8)	2 (2 - 4)	325.35 (122.85 - 577.48)	279 (1.5%)	2 (1 - 4)	332.45 (144.67 - 567.15)	139 (2.3)	2 (1 - 4)	314,9 (130,31 - 577,15)
ICS	427 (3.7)	1 (1 - 1)	22.98 (17.2 - 31.22)	995 (5.4)	1 (1 - 1)	22.98 (17.2 - 30.93)	425 (7.0)	1 (1 - 2)	24.22 (17.5 - 37.57)
LABAs	33 (0.3)	1 (1 - 2)	17.34 (15.4 - 24.7)	65 (0.4)	1 (1 - 3)	17.47 (16.7 - 50.1)	31 (0.5)	1 (1 - 2)	17.34 (15 - 32.76)
FDC ICS + LABAs	296 (2.6)	1 (1 - 2)	37.86 (28.9 - 62.83)	641 (3.5)	1 (1 - 2)	40.84 (31.2 - 69.65)	289 (4.8)	1 (1 - 2)	44.01 (31.8 - 85.22)
LTRAs	110 (0.9)	1 (1 - 4)	22.31 (16.9 - 77.92)	324 (1.8)	2 (1 - 6)	27.87 (15.2 - 88.9)	189 (3.1)	3 (1 - 8)	44.27 (22 - 110.14)
SABAs	390 (3.4)	1 (1 - 1)	5.06 (3.3 - 6.74)	800 (4.3)	1 (1 - 2)	5.06 (3.3 - 6.74)	355 (5.8)	1 (1 - 2)	5.06 (3.3 - 6.74)
Ocular drugs	1,180 (10.2)	1 (1 - 3)	2.34 (1.62 - 5.14)	2,764 (15.0)	2 (1 - 3)	2.86 (1.95 - 6.44)	1,139 (18.7)	2 (1 - 4)	3.67 (2.04 - 7.35)
ENT disorders treatments	641 (5.5)	1 (1 - 1)	1.42 (0.78 - 2.6)	1,381 (7.5)	1 (1 - 2)	1.42 (0.78 - 2.52)	572 (9.4)	1 (1 - 2)	1.58 (0.78 - 2.65)
Pain killers and anti-inflammatory drugs	8,118 (70.0)	5 (3 - 11)	7.8 (3.81 - 16.53)	14,132 (76.6)	7 (3 - 15)	10.35 (5.02 - 22.68)	4,937 (81.3)	7 (3 - 15)	11.4 (5.07 - 23.63)
Antibiotics	5,021 (43.3)	3 (2 - 4)	11.71 (6.51 - 23.06)	9,161 (49.6)	3 (2 - 5)	13.03 (7.22 - 25.73)	3,555 (58.5)	3 (2 - 6)	15.22 (7.62 - 32.04)
Treatments for insomnia or depression	1,571 (13.5)	7 (2 - 15)	29.28 (7.65 - 86.03)	3,360 (18.2)	9 (3 - 18)	36.47 (9.95 - 93.76)	1,129 (18.6)	8 (2 - 17)	33.15 (9.34 - 93.96)
Sick leave compensations	1,382 (11.9)	7 (3 - 17)	211.55 (84.36 - 503.2)	2,375 (12.9)	8 (3 - 17)	243.1 (90.96 - 548.31)	811 (13.3)	8 (3 - 17)	237.42 (84.62 - 506.16)
Total costs			124.79 (57.38 - 255.11)			167.05 (83.31 - 333.82)			198.88 (102.28 - 377.91)

AIT: allergy immunotherapy; GP: general practitioner; OCS: oral corticosteroids; ICS: inhaled corticosteroids; LABAs: Long Acting Beta-Agonists; FDC: fixed-dose combination; LTRAs: Leukotriene Receptor Antagonist; SABAs:

Short Acting Beta-Agonists; ENT: Ears, Nose, Throat

Table 4: Medical resource utilization of patients and costs in 2013 for “PAR+AA” cohort, according to asthma control (N=13,771)

MRU	Well controlled asthma (n=7,458)			Not well controlled asthma (n=4,700)			Very poorly controlled asthma (n=1,613)		
	n (%)	median units (Q1 - Q3)	median cost per patient in € (Q1-Q3)	n (%)	median units (Q1 - Q3)	median cost per patient in € (Q1-Q3)	n (%)	median units (Q1 - Q3)	median cost per patient in € (Q1-Q3)
Visits to health care professional									
GP (visits scheduled)	6,441 (86.4)	6 (4 - 10)	112.7 (64.4 - 184)	4,038 (85.9)	6 (3 - 10)	96.6 (48.3 - 177.1)	1,414 (87.7)	6 (4 - 10)	103.6 (62.1 - 204.7)
GP (visits unscheduled)	375 (5.0)	1 (1 - 1)	31.92 (18.4 - 46.4)	280 (6.0)	1 (1 - 1)	32.2 (21.7 - 50.4)	96 (6.0)	1 (1 - 2)	42.06 (23 - 60)
Lung specialist	164 (2.2)	1 (1 - 1)	25 (17.5 - 33.6)	117 (2.5)	1 (1 - 2)	25 (17.5 - 33.6)	38 (2.4)	1 (1 - 1)	23 (17.5 - 35)
Ophthalmologist	1,329 (17.8)	1 (1 - 1)	32.2 (23 - 41.4)	799 (17.0)	1 (1 - 1)	32.2 (18.2 - 43.9)	226 (14.0)	1 (1 - 1)	32.2 (20.7 - 41.4)
≥1outpatient hospital visit	2,218 (29.7)	2 (1 - 3)	32.2 (16.1 - 69)	1,481 (31.5)	2 (1 - 3)	32.2 (16.1 - 69)	535 (33.2%)	2 (1 - 3)	32.2 (16.1 - 69)
Procedures									
Investigations of nasal cavity	454 (6.1)	1 (1 - 1)	29.16 (21.32 - 40.67)	256 (5.4)	1 (1 - 1)	27.5 (21.32 - 30.78)	74 (4.6%)	1 (1 - 2)	30.46 (21.32 - 40.82)
X-rays of lungs	898 (12.0)	1 (1 - 1)	21.28 (18.1 - 25.9)	559 (11.9)	1 (1 - 1)	23.33 (18.1 - 25.9)	211 (13.1)	1 (1 - 1)	25.92 (18.1 - 25.9)
Blood cell counts	4,124 (55.3)	1 (1 - 2)	8.37 (5 - 13.4)	2,405 (51.2)	1 (1 - 2)	8.37 (5 - 13.4)	798 (49.5)	1 (1 - 2)	8.37 (5 - 15.1)
Emergency room visit	1104 (14.8)	1 (1 - 1)	25.32 (25.3 - 25.3)	781 (16.6)	1 (1 - 2)	25.32 (25.3 - 43.1)	296 (18.4)	1 (1 - 2)	25.32 (25.3 - 41.7)
Hospitalization for respiratory symptoms	64 (0.9)	1 (1 - 1)	1169.88 (591.66 - 1592.98)	42 (0.9)	1 (1 - 1)	1285.14 (693.27 - 1770.44)	20 (1.2%)	1 (1 - 1)	975.35 (471.44 - 1878.65)
Allergy and asthma drugs									
Antihistamines	4,431 (59.4)	4 (2 - 10)	7.5 (2.5 - 19.61)	2,861 (60.9)	4 (2 - 10)	7.49 (2.8 - 20.01)	1,140 (70.7)	6 (2 - 12)	12.66 (4.6 - 25.01)
Nasal corticosteroids	3,972 (53.3)	2 (1 - 4)	4.91 (2.46 - 11.57)	2,373 (50.5)	2 (1 - 4)	4.44 (2.46 - 10.62)	845 (52.4%)	2 (1 - 5)	5.78 (2.62 - 15.15)
Intramuscular injections of corticosteroids	545 (7.3)	2 (1 - 3)	7.05 (3.6 - 10.94)	304 (6.5)	2 (1 - 3)	7.05 (3.5 - 10.92)	109 (6.8)	2 (1 - 3)	6.23 (3.6 - 10.84)
OCS	3,015 (40.4)	1 (1 - 2)	4.33 (2.8 - 8.21)	1,886 (40.1)	1 (1 - 2)	4.33 (2.8 - 8.21)	709 (44.0)	2 (1 - 3)	5.33 (2.8 - 8.66)
AIT	175 (2.3)	2 (2 - 4)	350 (125.03 - 630.3)	144 (3.1)	2 (2 - 4)	308.51 (151.31 - 648.14)	35 (2.2%)	2 (1 - 3)	351 (150.36 - 478.62)
ICS	1,258 (16.9)	1 (1 - 3)	27.21 (20.3 - 53.57)	841 (17.9)	2 (1 - 4)	35.07 (20.3 - 73.36)	367 (22.8)	3 (1 - 7)	56.48 (24.7 - 123.71)
LABAs	149 (2.0)	2 (1 - 5)	32.76 (17.3 - 98.28)	357 (7.6)	5 (2 - 10)	96.36 (30.7 - 183.07)	169 (10.5)	7 (4 - 12)	133.4 (77.1 - 212.75)
FDC ICS + LABAs	2,517 (33.7)	4 (2 - 8)	137.09 (55.4 - 278.47)	1,223 (26.0)	3 (1 - 8)	122.51 (40.8 - 305.32)	745 (46.2)	5 (2 - 9)	170.43 (63.6 - 343.13)
LTRAs	848 (11.4)	6 (2 - 11)	88.18 (22.3 - 161.56)	588 (12.5)	7 (2 - 11.5)	108.41 (33.3 - 169.14)	367 (22.8)	7 (2 - 12)	119.33 (35 - 186.89)
SABAs	1,444 (19.4)	1 (1 - 3)	6.58 (3.3 - 12.73)	1,848 (39.3)	2 (1 - 4)	6.74 (3.3 - 16.45)	1,257 (77.9)	5 (2 - 9)	19.73 (9.9 - 39.47)

Ocular drugs	1,280 (17.2)	2 (1 - 4)	3.3 (2.03 - 7.03)	888 (18.9)	2 (1 - 3)	3.39 (2.03 - 7.14)	320 (19.8)	2 (1 - 4)	4.21 (2.15 - 9.11)
ENT disorders treatments	636 (8.5)	1 (1 - 2)	1.42 (0.76 - 2.52)	408 (8.7)	1 (1 - 2)	1.56 (0.78 - 2.6)	143 (8.9)	1 (1 - 2)	1.67 (0.78 - 2.6)
Pain killers and anti-inflammatory drugs	6,026 (80.8)	8 (4 - 17)	11.52 (5.3 - 25.35)	3,703 (78.8)	7 (3 - 16)	11.23 (5.07 - 25.09)	1,286 (79.7)	10 (4 - 23)	14.82 (6.44 - 37.17)
Antibiotics	4,559 (61.1)	3 (2 - 6)	16.4 (8.56 - 36.01)	2,755 (58.6)	4 (2 - 6)	16.24 (8.06 - 36.63)	971 (60.2)	4 (2 - 6)	17.45 (8.81 - 39.81)
Treatments for insomnia or depression	1,522 (20.4)	9 (2 - 18)	33.55 (8.89 - 94.18)	935 (19.9)	7 (2 - 18)	32.77 (9.04 - 95.99)	329 (20.4)	11 (4 - 22)	41.18 (13.27 - 109.68)
Sick leave compensations	978 (13.1)	9 (3 - 18)	253.05 (94.5 - 570.46)	630 (13.4)	9 (3 - 19)	266.15 (95.13 - 544.14)	204 (12.6)	8 (3,5 - 18)	243.81 (97.98 - 557.16)
Total costs			280.31 (132.66 - 552.12)			270.97 (117.1 - 556.65)			394.14 (197.68 - 779.19)

AIT: allergen immunotherapy; GP: general practitioner; OCS: oral corticosteroids; ICS: inhaled corticosteroids; LABAs: Long Acting Beta-Agonists; FDC: fixed-dose combination; LTRAs: Leukotriene Receptor Antagonist; SABAs: Short Acting Beta-Agonists; ENT: Ears, Nose, Throat

Figure 1: Flowchart of patients

From DA database, 60,359 patients aged from 18 to 65 in 2010 and responding to PAR criteria were extracted. 90.3% of the EHRs of these patients were linked to SNIIR-AM data. Cohort “PAR only” was divided in 3 subgroups according to PAR severity: 32.1%, 51.1% and 16.8% of patients with mild, moderate and severe PAR, respectively. Cohort “PAR+AA” was made of 54.2%, 34.1% and 11.7% of patients with asthma respectively well controlled, not well controlled, and very poorly controlled asthma.

Figure 2: Median costs per patient in “PAR only” cohort, according to PAR severity

A gradient of median costs per patient appeared between the three sub-groups of PAR severity for drug treatment (from 15.51€ to 4.57€), and non-drug treatment (from 85.52€ to 122.72€). Percentages describe share expenditure of each expenditure items.

Figure 3: Median costs per patient in “PAR+AA” cohort, according to asthma control

Patients with very poorly controlled asthma had a high median costs per patient (175.5€) compared to patients with well controlled asthma (77.71€) and to patients with not well controlled asthma (67.6€) for drug treatment. Medical resource utilization for non-drug-treatments were stable between the three sub-groups (around 130€ per patient), as well as hospitalizations. Percentages describe share expenditure of each expenditure items.

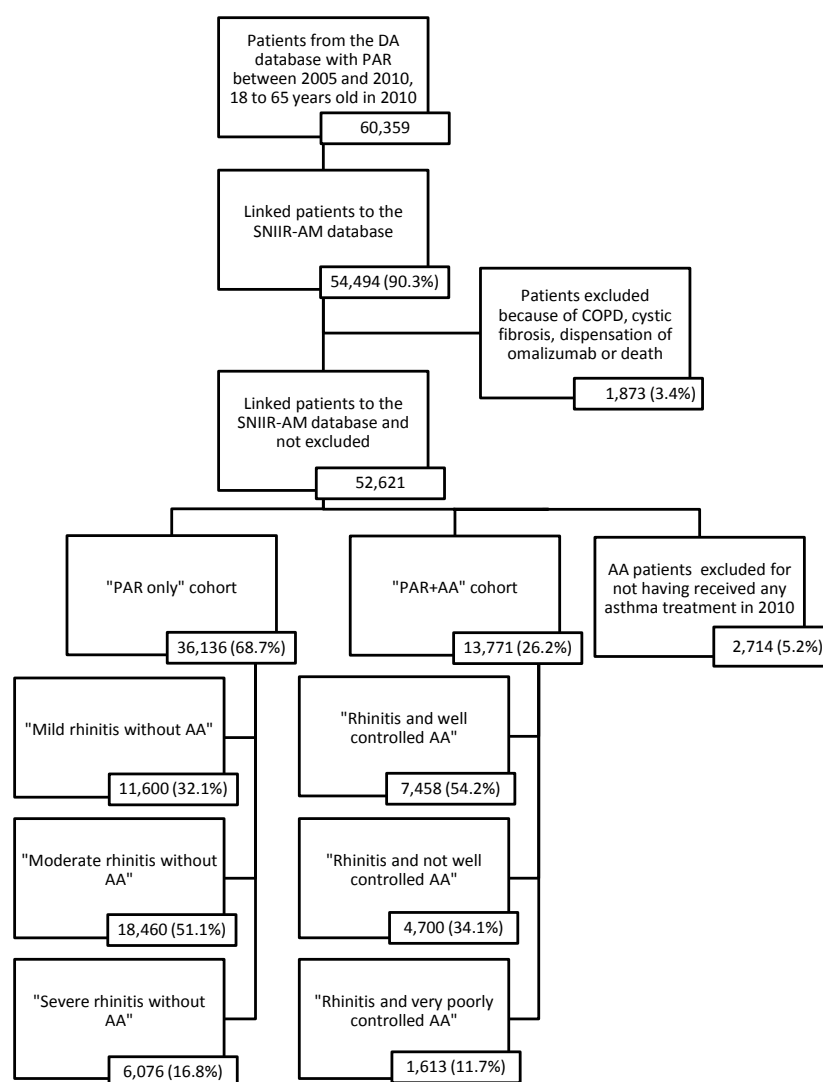


Figure 1: Flowchart of patients

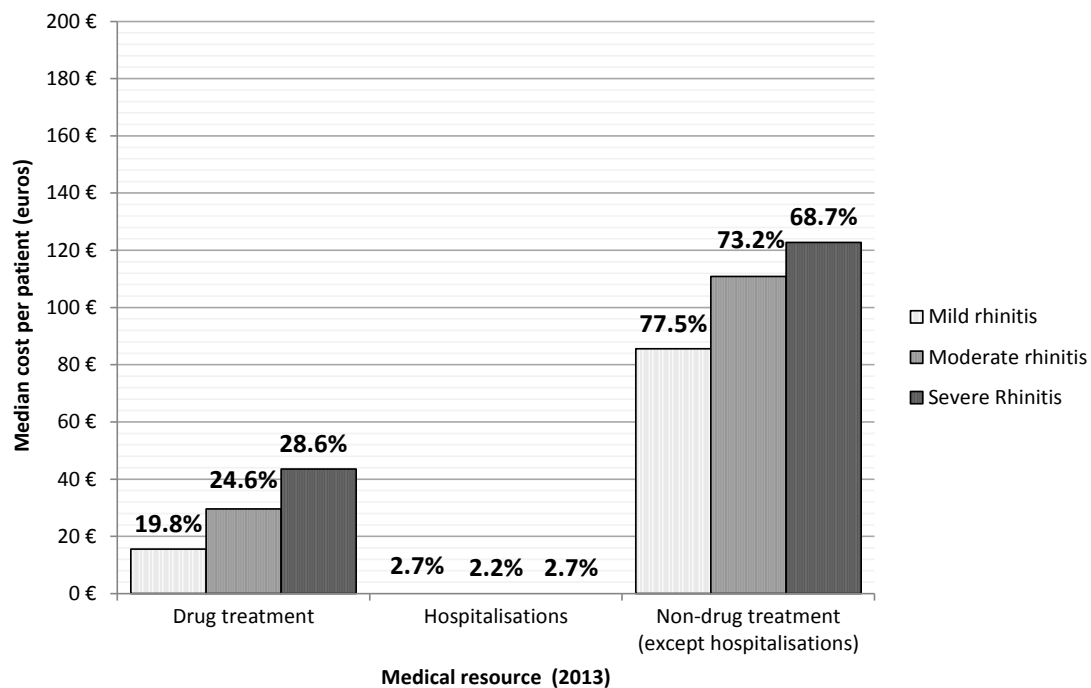


Figure 2: Median costs per patient in "PAR only" cohort, according to PAR severity

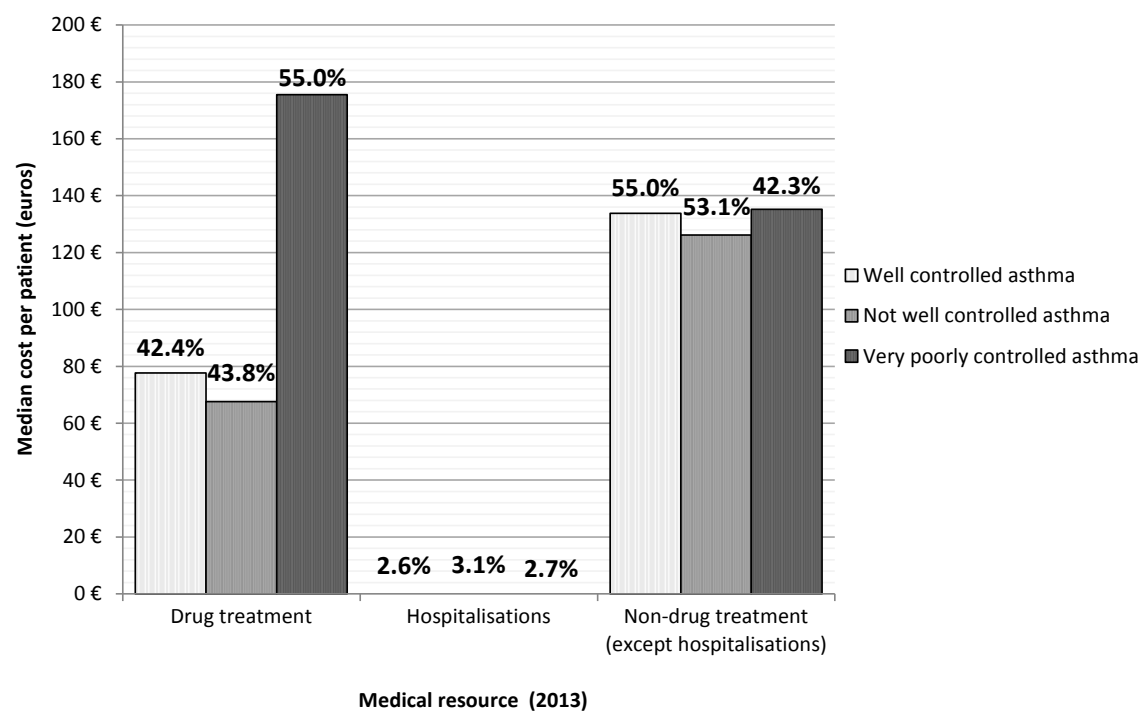


Figure 3: Median costs per patient in "PAR+AA" cohort, according to asthma control