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A case scenario study on adherence to GINA recommendations by primary care physicians in an area of Southern Italy: the "Progetto Padre 2.0"

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Abstract

Background Accurate diagnosis and management of bronchial asthma are complex processes guided by national and international asthma guidelines, particularly the Global Initiative for Asthma (GINA). However, adherence to these guidelines is often suboptimal, varying across healthcare professionals and countries, which can lead to poor asthma control and increased healthcare costs.

Aim In this observational study, we assessed the alignment to GINA recommendations in the diagnosis and management of asthma among 15 primary care physicians in two metropolitan areas of the Campania region, Southern Italy.

Methods 120 patients were randomly selected from the electronic medical records of 15 primary care physicians. Afterwards, the alignment of diagnostic pathways and treatments with current GINA recommendations was assessed by an experienced chest physician. Three main outcomes were defined: diagnostic congruence, diagnostic workup congruence, and therapeutic congruence.

Results Overall, 26.7% of our sample presented with an incongruous asthma diagnosis, while only 46.7% patients had therapeutic prescriptions in line with the latest GINA document recommendations. Patients treated in accordance with GINA recommendations exhibited significantly higher ACT scores, averaging 20.5 ± 4.0, compared to those receiving non-guideline-directed therapy, who averaged 15.7 ± 6.1 ($p < 0.001$). Diagnostic congruence showed a direct correlation with atopy ($r = 0.277$, $p = 0.002$) and an inverse correlation with ACT score ($r = -0.335$, $p < 0.001$).

Conclusions The results of this study indicate that adherence to asthma guidelines in the metropolitan areas of Naples and Benevento remains insufficient. Further research focused on developing individualized interventions to manage non-adherence is warranted.

Keywords Asthma, Guidelines, Disability, Outcome, Chronicity, Therapy

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Introduction

Asthma is one of the most prevalent chronic inflammatory diseases affecting almost 300 million people worldwide causing around 455.000 deaths in 2019 [1]. The impact that asthma imposes on patients, their families, and society is high, especially when it becomes uncontrolled [2].

The diagnostic/therapeutic workup and the assessment of asthma control are complex processes. In this regard, national and international asthma guidelines (GLs) based on scientific evidence aim to standardise and optimise diagnosis, management, and the treatment of the disease [3].

Asthma diagnosis is obtained as the result of typical symptoms and signs and the presence of lung function alterations such as bronchial airway reversibility and/or airway hyperreactivity [4]. In particular, the latest GINA recommendations focus on the assessment of typical symptoms and a variability of lung function over time and suggest performing a spirometry of a peak expiratory flow (PEF) whenever feasible [5]. Accordingly, GLs emphasize the importance of both symptom patterns and objective lung function test assessment in order to make asthma diagnosis accurate [3]. Indeed, the relevance role of objective lung function tests in the diagnostic workup of asthma is invariably underlined by both national and international GLs. Asthma diagnosis not supported by lung function assessment may lead to the over-/misdiagnosis and, as consequence, to improper or unnecessary treatment [6].

However, although asthma guidelines are regularly updated the adherence to their recommendations is challenging and often far from optimal [7, 8]. and varying between different groups of healthcare professionals and different countries [3].

Non-adherence to asthma GLs is a significant issue that can lead to poor asthma control, increased healthcare cost, and difficulty in identifying true treatment-resistant asthma [9]. Primary care physicians (PCPs) are, in general, the first contacts for patient care and play a crucial healthcare role. In particular, PCPs are involved in the early identification and management of asthma patients [10]. In Italy, PCPs are central in providing the citizens with healthcare servces as drug prescriptions, referral to specialists and requests for elective hospitalizations.

In a previous study called "Progetto Padre" (Italian for: *Progetto Assistenziale Disabilità REspiratoria*; clinical project for respiratory disability) [11], Maniscalco et al. investigated the adherence of PCPs to the GOLD document indications for the diagnosis and management of COPD, highlighting an elevated prevalence of incongruous COPD diagnosis among PCPs records, and a limited agreement with GOLD 2018 indications for treatment.

In this "twin" observational study, named "Padre 2.0" we aimed to assess the electronic medical records of asthmatic patients from 15 PCPs to determine the alignment of diagnostic pathways, diagnoses, and ongoing treatments with the latest GINA recommendations.

Patients and methods

Study population

PCPs belonging to the referral network of the ICS Maugeri Institute of Telese Terme were invited to join the study and 15 out of 21 agreed to participate. Patients were randomly selected to be included in the study using PCPs' databases, consisting of a total of 21,536 individuals. All the 15 PCPs were operating in the metropolitan areas of Naples and Benevento, two cities in the Campania region, Southern Italy.

The inclusion criteria were the following: presence of a diagnosis of bronchial asthma in the PCP's clinical record; current or past use of at least one drug licensed for bronchial asthma; age range 18–70 years. Exclusions were applied to those patients who did not wish or were not able to sign the informed consent file.

Whenever feasible, the study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [12] to limit possible sources of bias. The study was conducted according to the Declaration of Helsinki and its protocol was reviewed and approved by the Institutional Review Board Campania 1 (approval number: 1/24). Each participant provided written informed consent prior to the enrolment.

Study procedures

After inclusion, each patient underwent a specialist visit by an experienced respiratory physician not actively practicing primary care medicine. During the visit, anamnesis was collected, the health-related quality of life by the Asthma Control Test (ACT) was assessed, and a spirometry was performed using a portable spirometer. When, as a result of this visit, there was a discrepancy between the specialist diagnosis and the one made by the PCP or further investigations were considered necessary, the patient was directed towards a second-level examination. The second-level assessment was carried out at the Pulmonary Rehabilitation Unit of the Istituti Clinici Scientifici Maugeri IRCCS in Telese Terme, Italy. Here, the patients underwent, whenever necessary, broncho-reversibility test, methacholine test, skin prick test using common aeroallergens and exhaled nitric oxide sampling. Particularly, skin prick tests and exhaled nitric oxide were used to investigate aspects such as atopy or airway type 2 (T2) inflammation, but were not considered as diagnostic exams, in line with GINA recommendations [5] and evidence from the Literature [13–15]. Circulating eosinophils were not retrievable from the PCPs records

and were not included in the final evaluation, in line with GINA recommendations [5] which do not identify any diagnostic role for this biomarker in the general setting of asthma.

Three endpoints were established: diagnostic congruence, diagnostic workup congruence, and therapeutic congruence. Diagnosis was deemed congruent whenever the respiratory physician visit or the second-level exams were confident with a diagnosis of asthma. Particularly, in case of confirmed history of variable respiratory symptoms and confirmed variable expiratory airflow limitation, the diagnosis was deemed to be congruent (Table 1). In case of missing evidence of at least one of these features, the diagnosis was deemed to be possibly incongruent. In case of missing evidence of both points, the diagnosis was deemed to be incongruent. The examinations were performed with appropriate wash-out from any inhalatory therapy, if already ongoing. Diagnostic workflow congruence was assessed through the evaluation of five consecutive steps, according to the latest GINA report [5] and the Campania regional guidelines ("*piano diagnostico-terapeutico-assistenziale dell'asma bronchiale*") [16] (Table 1). If steps from 1 to 4 were followed, diagnostic workup was deemed to be congruent. If steps 1–3 were followed but there was no evidence for steps 4–5 or 6, diagnostic workflow was deemed to be possibly incongruent. If steps were not followed in the right order, diagnostic workflow was deemed to be incongruent. Finally, therapeutic congruence was evaluated on the accordance to the latest GINA report [5] indications. In brief, treatment was considered congruent if patients were treated with inhaled corticosteroids and/or an additional controller, such as a long-acting bronchodilator or an anti-leukotriene agent, at the minimum efficient dose and frequency, following the GINA-approved treatment tracks. Patients in treatment with single or double inhaled bronchodilators, patients with no treatment despite symptoms, and patients treated only with oral corticosteroids in absence of inhalatory treatment were deemed to have an incongruent treatment. If the treatment included ICS, but was not optimized according to the GINA recommendations, it was deemed to be possibly incongruent.

Statistical analysis

Statistical analysis was performed with SPSS v. 29.0 (IBM, Chicago, USA). Categorical variables have been reported as absolute numbers and relative frequencies, and the Pearson's chi-square test or the Fisher's exact test were used to make comparisons. Continuous variables have been reported as mean ± standard deviation and were compared through Student's t-test for independent

Table 1 Detailed criteria adopted for assessing diagnostic, diagnostic workup and therapeutic congruence. Abbreviations: FEV_1, forced expiratory volume in the first second; FVC, forced vital capacity; PEF, peak of expiratory flow; PCP, primary care physician; GINA, global initiative for asthma

DIAGNOSTIC CONGRUENCE
1. History of typical variable respiratory symptoms
- more than one kind of respiratory symptom (wheeze, shortness of breath, chest tightness, and cough)
- symptoms worse at night or early morning
- symptom variations over time in intensity
- symptoms triggered by colds, exercise, allergen exposure, laughter, or smoke
2. Confirmed variable expiratory airflow limitation
A. Documented excessive variability of lung function (one or more items)
- Bronchodilator reversibility (FEV_1 increase of 200 ml and 12% after inhaling a bronchodilator)
- Excessive variability (≥ 20%) in twice-daily PEF over 2 weeks
- FEV_1 increases of at least 12% after 4 weeks anti-inflammatory treatment
- Positive bronchial challenge test
- Positive exercise challenge test
B. Documented expiratory airflow limitation
When FEV_1 is reduced, confirm that the ratio FEV_1/FVC is also reduced below the lower limit of normal
WORKFLOW CONGRUENCE
Step 1. Collection of relevant anamnestic data, symptoms, comorbidities and ongoing treatments
Step 2. Physical examination is performed.
Step 3a. A spirometry with bronchodilator reversibility test is prescribed/performed by the PCP or a specialist.
Step 3b. In case of patients already under inhalatory treatment, lung function tests are repeated after an appropriate wash-out/decalage time.
Step 4. Allergology tests are performed by the PCP or a specialist.
Step 5 (optional). Referral to specialist for additional tests (FeNO measurement, bronchial challenge test).
Step 6. Monitoring and reassessment of asthma each 3–6 months.
THERAPEUTIC CONGRUENCE
Stabile treatment with inhaled corticosteroids and, whenever appropriate, an additional controller, according to the latest GINA recommendations.

samples. Pearson's and Spearman's correlation coefficients were employed to explore relationships between variables. Finally, a logistic regression model was applied to investigate eventual determinants of diagnostic congruence. A post-hoc power analysis (1-β) was performed to confirm whether the sample size was sufficient to detect the observed effect sizes. A P-value of less than 0.05 was considered to be statistically significant.

Results

To reach the pre-specified target sample size of 120 patients, 265 random patients were extracted from the database and consecutively contacted. Of these 265, 12 did not meet the inclusion or exclusion criteria, and 98 declined to participate. The remaining 34 could not be reached after three attempts on three different days and were subsequently discarded.

The demographics of the study sample are shown in Table 2. Out of 120 patients, 88 (73.3%) were atopic. Pollen sensitization was found in 57 patients (47.5%), followed by house dust mite sensitization in 41 (34.2%), and drug allergy in 7 patients (5.8%). Spirometry was available for 64 out of 120 patients (53.3%), with altered results found in 40 of them (62.5%). Overall, lung function was preserved (Table 2). Asthma diagnosis was supported by a bronchoprovocation test with methacholine in only four patients (3.3%), despite normal spirometry results in 24 patients. Patients were moderately symptomatic, with a mean ACT score of 17.6 ± 6.0. Finally, 69 out of 120 patients (57.5%) had at least one comorbidity. The most common comorbidity was rhinitis, reported in 51 patients (42.5%), followed by chronic rhinosinusitis with nasal polyps (CRSwNP), reported in 12 patients (10%).

Table 2 Baseline characteristics of the study sample

Males, *n* (%)	50 (41.7)
Age, years	47.7 ± 16.6
Disease length, years	14.5 ± 12.6
BMI, kg/m^2	27.4 ± 5.1
Smoking history, n (%)	34 (28.3)
Atopy, n (%)	88 (73.3)
Dust mite sensitization, n (%)	41 (34.2)
Pollen sensitization, n (%)	57 (47.5)
Drug sensitization, n (%)	7 (5.8)
Historical normal spirometry, n (%)	24 (20.0)
Historical abnormal spirometry, n (%)	40 (33.3)
Historical methacholine test, n (%)	4 (3.3)
Rhinitis, n (%)	51 (42.5)
CRSwNP, n (%)	12 (10.0)
FEV_1, L	2.72 ± 0.88
FEV_1, %	86.6 ± 20.3
FEV_1/FVC, %	77.6 ± 10.6
ACT score	17.6 ± 6.0

Abbreviations: BMI, body mass index. CRSwNP, chronic rhinosinusitis with nasal polyps. FEV_1, forced exhaled volume in the first second. L, liters. ACT, asthma control test

Diagnosis, workup, and therapy congruence

Out of 120 patients, 32 (26.7%) had completely incongruous asthma diagnoses, while for another 3 (2.5%), asthma was a possible diagnosis. Specialists from the national healthcare system made the diagnoses in 5 cases, while PCPs diagnosed 29 cases. The origin of the diagnosis was unclear in one case. No difference was observed in the distribution of non-congruent diagnoses among the PCPs involved in the study ($P = 0.879$).

Additionally, the diagnosis of asthma was not supported by any lung function testing in 20 patients. Regarding the diagnostic workup, it was deemed inconsistent in 53 patients (44.2%) and possibly inconsistent in 2 (1.6%). A specialist respiratory physician from the national health system conducted the diagnostic workup in 15 patients, a general practitioner in 32, and the workup occurred at hospital discharge for 6 patients.

Regarding pharmacological treatment, inhaled therapy was prescribed to 67 (55.8%) of the patients, while 29 (24.2%) underwent cycles of oral corticosteroids. Notably, eight (6.7%) patients received cycles of oral steroid treatment without any inhaled therapy. In the studied sample, 56 (46.7%) patients had therapeutic prescriptions in line with the latest GINA document recommendations. Patients treated in accordance with GINA recommendations exhibited significantly higher ACT scores, averaging 20.5 ± 4.0, compared to those receiving non-guideline-directed therapy, who averaged 15.7 ± 6.1 ($p < 0.001$, 1-β = 0.995). However, spirometry results showed no statistically significant difference between patients treated according to GINA recommendations and those who were not (shown in Fig. 1).

Determinants of diagnostic congruence

Diagnosis and therapeutic congruences correlated significantly with one another ($p < 0.001$). Diagnostic congruence showed a direct correlation with atopy ($r = 0.277$, $p = 0.002$, 1-β = 0.871) and an inverse correlation with ACT score (r = -0.335, $p < 0.001$, 1-β = 0.966). Workup congruence inversely correlated with PCP-diagnosed asthma (r = -0.295, $p = 0.004$, 1-β = 0.910). Among various factors, including age, sex at birth, BMI, smoking status and atopy, the only significant predictor of diagnostic congruence was atopy, independently of the PCP who oversaw the patient. Specifically, atopic patients were 2.9 times more likely to receive an appropriate diagnosis (Table 3).

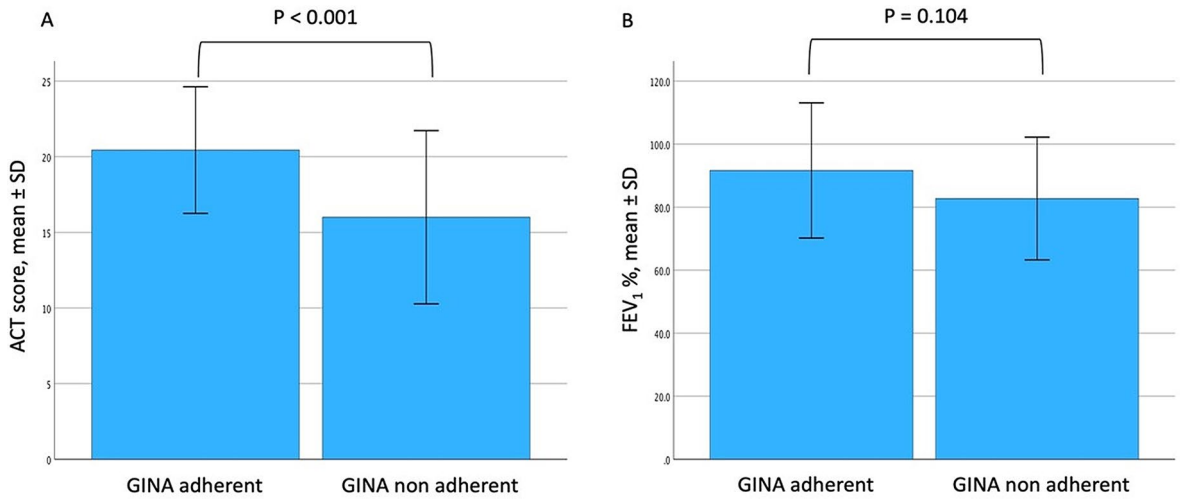

Fig. 1 Comparison between patients with a GINA adherent asthma treatment and GINA non adherent one. Panel **A**: Asthma Control Test score (ACT). Panel **B**: Percent predicted forced exhaled volume in the first second (FEV_1%). Data are expressed as mean ± standard deviation (SD)

Table 3 Logistic regression model predicting chance of diagnostic congruence.

Variable	Code	B	Adj. OR	95% CI	Significance
Age	Years	0.005	.005	0.975–1.035	*P* = 0.766
BMI	Unit (kg/m^2)	−0.028	1.028	0.934–1.132	*P* = 0.567
Smoking History	0: no / 1: yes	0.528	1.695	0.736–3.905	*P* = 0.215
Atopy	0: no / 1: yes	1.057	2.878	1.089–7.603	***P* = 0.033**
Sex	0: female / 1: male	−0.821	0.440	0.178–1.089	*P* = 0.076
PCP	-	−0.19	0.981	0.888–1.084	*P* = 0.707

Significant p-values are in bold. Abbreviations: CI, confidence interval; Adj. OR, adjusted odds ratio; BMI, body mass index; PCP, primary care physician

Discussion

The results of the present study indicate the existence, at least in this area of Southern Italy, of relevant gaps in the correct application of GINA recommendations in both the diagnostic and therapeutic processes, with a 26.7% rate of completely incongruous asthma diagnoses, and only a 46.7% rate of adherence to GINA recommendations for treatment. Specifically, a non-negligible proportion of patients (45 patients, accounting for the 37.5% of the study population) were diagnosed with asthma but did not follow any inhalatory treatment, which is considered the cornerstone of asthma management, while eight patients (6.6%) were undergoing treatment with oral steroids only.

Asthma is a complex and heterogeneous disease which necessitates comprehensive guidelines for accurate diagnosis and effective evidence-based treatment. International asthma guidelines and recommendations such as GINA provide detailed and evidence-based protocols for assessing and managing asthma based on its severity ensuring that patients receive an accurate diagnosis and tailored treatments. In particular, GINA recommendations are updated annually to reflect the latest scientific research and clinical practices [17].

The distribution of diagnostic congruence among specialist physicians, PCPs and hospitals highlighted significant discrepancies in diagnostic accuracy between different healthcare providers in our sample. In line with previous findings [18], we were able to observe that the presence of atopy was associated with a higher probability of a congruous diagnosis of asthma. While this might be helpful and easily applicable in a paediatric setting, adult-onset asthma is often non-allergic, with a different pathogenesis and different outcomes [19]; therefore, clinicians should be made aware that asthma and atopy, albeit often intertwined, are not necessarily coexistent within the same patient.

Out of 120 patients, spirometry results were available in only 64 (53.3%) patients. This observation is consistent with another study in which approximately 60% of patients with by a PCP-based asthma diagnosis never performed spirometry suggesting that the majority of such patients did not follow a diagnostic algorithm according to guidelines [20]. Moreover, a study by Sokol KC et al. less than half of adult asthmatic performed a spirometry within one year of diagnosis [21]. Interestingly, 20 of the 32 patients who were misdiagnosed with asthma had never undergone spirometry, highlighting a detrimental gap in the diagnostic workup where spirometry is a crucial test.

Reversible airflow limitation is the key element in the diagnosis of asthma, however 40 patients of our

study sample, despite having altered spirometry results, the reversibility of bronchial obstruction after the use of a beta$_2$-agonists was not evaluated. Finally, out of 24 patients with normal spirometry results, only in 4 patients was there assessment of bronchial reactivity using methacholine stimulation to confirm the diagnosis of asthma.

Based on GINA recommendations asthma treatment is approached in a stepwise fashion with inhaled corticosteroids being the mainstay of asthma treatment. GLs suggest of regularly review asthma control, adjusting treatment accordingly, stepping up inhaled corticosteroids when asthma is not well controlled and stepping down once good asthma control has been achieved and maintained for 3 months [22] with the aim to minimize, on the one hand the costs of treatment and, on the other hand, the potential for adverse effects. In this regard, in our sample inhaled therapy was prescribed in 67 (55.8%) patients and 29 (24.2%) took cycles of oral corticosteroids. Surprisingly, eight patients were only prescribed oral steroid treatment whenever necessary, with no background inhaled therapy. Our findings might be explained with both PCP- and patient-related factors. On one hand, in fact, low rates of adherence to inhaled medications have been reported, due to the misperception of it not being necessary or useful at all [23], thus leading to an increased risk of exacerbation, requiring oral steroids. On the other hand, oral steroids are overused in asthma, so that in 2021 the Thoracic Society of Australia and New Zealand has advocated for an appropriated stewardship in order to limit potential harms deriving from steroid misuse [24].

Overall, however, therapeutic prescription was in line with the recommendations of the latest available GINA document in only 46.7% of study patients. This result is in accord to a 2021 study examining asthma therapy in Australia, Canada, China, and Philippines where 47% of patients were on guideline-directed therapy [25].

In accord with previous reports [7, 26] the results of our observational study clearly indicate that despite GINA recommendations are regularly updated there is still no real acceptance of them by the PCPs. This seems to apply also to different recommendations and guidelines, as observed in this recent study by Piñel Jimenez and collaborators [27] PCPs' failure to adhere to GINA guidelines is multifaceted and includes lack of training, limited resources, poor physician-patient communication, and availability of medications and diagnostic tools [27–30]. Finally, personal experiences and clinical inertia (the tendency to not change treatments despite new evidence) of PCPs may cause them to deviate from guidelines [27–30]. This is a particularly important issue because, on the one hand, they manage the majority of asthma visits and, on the other hand, because adherence to guideline improves asthma outcomes [8]. The impact of guideline adherence in real life is deemed to be significant: as observed in our study, significantly higher ACT score values were found among those patients treated according to GINA recommendations in comparison to those treated differently. Consequently, non-adherence to asthma guidelines should be contrasted as it leads to poorer asthma control [7] and subsequent increased healthcare costs. Possible solutions to this issue could include development of simpler and more integrated systems enabling a direct communication between specialists, PCPs and hospitals, as well as the promotion of joint educational events between specialists and PCPs. Such events could be employed to spread knowledge about the existing guidelines and protocols as well as promote direct confrontation between different healthcare providers and, finally, opportunities to create referral networks and cooperation systems.

Our study has strengths and limitations. The main strengths are the following: (1) data collection was conducted in real-life by direct acquisition from PCPs electronic records; (2) selection bias was overcome by the random selection of consecutive patients; (3) the records were reviewed by a trained and experienced chest physician, and additional testing was performed in a specialised setting, thus securing the reliability of the results; (4) to our knowledge, this is the first study that specifically investigated the adherence to GINA recommendations in the local areas of Naples and Benevento.

The main limitation of the current study is linked to its local dimension, since it was carried out using data collected from a spatially limited primary care setting, and therefore cannot be fully generalized to PCPs practicing in the whole Campania region and Italy. The relatively low number of patients evaluated for each PCP constituted a limitation for the execution of sub-analyses, especially when considering that only half of them could perform a spirometry. Moreover, the overall number of PCPs participating in the study (15 out of 21 invited PCPs), as well as potential differences in their background and experience affecting their expertise and sensibility towards asthma, may constitute a further limitation, especially when considering that over 1,900 PCPs were active between the provinces of Naples and Benevento in 2019 [31]. Nonetheless, each PCP included in our study was in charge of at least 1,300 adult patients and a variable asthmatic population. Also, it must be noted that the PCP diagnosis of asthma might have been formulated by another PCP in the past, thus reducing the potential nesting effect. Finally, we cannot exclude that some patients labelled with a diagnosis other than asthma, such as, for instance, chronic obstructive pulmonary disease, were instead asthmatic. Taken together, these limitations might have affected the overall prevalence of the

diagnostic congruence in our sample and should be carefully taken into account when overviewing our results.

Conclusions

Effective asthma management includes accurate diagnosis, personalized asthma action plans, and regular re-evaluation of patients, as asthma symptoms can change over time. This ensures that treatment remains appropriate. Although it is well-established that asthmatics who are treated according to GINA recommendations have better outcomes than those without adequate treatment, the results of this study, albeit with some relevant limitations, suggest that adherence to asthma guidelines in the metropolitan areas of Naples and Benevento might be still insufficient. Our results, however, should be further corroborated by wider, possibly multicentre and more comprehensive studies, ideally involving a more significant proportion of PCPs operating in the Campania region.

Also, addressing the causes of non-adherence requires a multidisciplinary approach and is essential for improving asthma outcomes and ensuring that treatments are appropriately targeted.

Further research focused on developing individualized interventions to manage non-adherence is also warranted. Identifying and eliminating the barriers to adherence to asthma guidelines are key goals for achieving the correct diagnosis and treatment of patients, ultimately reducing the burden of asthma.

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Author contributions
M.M. and S.F. conceived and designed the study. C.C. and S.F. performed statistical analysis, interpreted results and drafted the first version of the manuscript. S.E.D.A., M.C., C.L., C.M, A.I. and P.A. collected clinical data. C.C., A.M. and M.M. made critical revisions and drafted the manuscript in its final form. S.F. supervised the project. All Authors read and approved the final version of the manuscript.

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Data availability
The research data will be available upon request to Corresponding Author.

Declarations

Ethics approval
The study was approved by the Institutional Review Board Campania 1 (Approval number: 1/24).

Human ethics and consent to participate
The study was conducted according to the Declaration of Helsinki and each participant provided written informed consent prior to the enrolment.

Competing interests
The authors declare no competing interests.

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