

Original article

The role of climate on the geographic variability of asthma, allergic rhinitis and respiratory symptoms: results from the Italian study of asthma in young adults

Background: Variations in the prevalence of respiratory symptoms according to geo-climatic factors could provide important clues to the knowledge of the aetiology of asthma.

Methods: Geo-climatic variations in the prevalence of current asthma, allergic rhinitis and chronic cough, and phlegm were assessed on a random sample of 18 873 subjects (response rate = 72.7%) from different climatic regions of Italy. An ecological analysis, supported by robust statistical methods, was employed to investigate potential trends.

Results: The prevalence of all symptoms was significantly heterogeneous throughout the peninsula. Only asthma-like symptoms showed a north–south trend: the prevalence increased at a decreasing latitude [odds ratio (OR) varies from 0.92 to 0.96, $P < 0.05$], at a decreasing distance from the sea (OR: 0.90–0.93 for 30 km distance, $P < 0.05$), at higher annual mean temperatures (OR: 1.11–1.14, $P < 0.05$) and at smaller annual temperature ranges (OR: 0.94–0.95, $P < 0.05$). Of the geo-climatic variables considered, temperature range had the greatest influence on most asthma-like symptoms. No association was found between geo-climatic variables and allergic rhinitis or chronic cough and phlegm.

Conclusions: Asthma prevalence seems to be significantly affected by climate as asthma-like symptoms were more common in central-southern Italy, with a Mediterranean climate, than in areas with a continental climate (northern Italy).

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The international multicentre studies European Community Respiratory Health Survey (ECRHS) and International Study of Asthma and Allergies in Childhood (ISAAC) have pointed out the great variability of asthma prevalence all over the world (1, 2). This variability is not explained by cultural, linguistic and diagnostic differences, as objective markers of asthma, such as bronchial hyperresponsiveness and specific IgE levels, present the same variability. However, genetics could explain only a

small part of this variation, because populations with a similar genetic background show a wide variation in the prevalence of asthma and allergy.

Other factors such as hygienic conditions, pollution and climate could explain the variability in asthma prevalence. In particular, the long-term effects of climate on asthma have been very rarely considered and deserve more attention. Some indications were given by some recent papers finding an association between warmer

average temperatures and the increase of asthma prevalence (3–5). An analysis of the international data collected by the ECRHS showed a positive association of asthma and asthma-like symptoms prevalence with the average nonsummer temperature (6).

Italy is not very wide, but it is quite long and therefore has different climatic areas: the northern mainland is characterized by sub-continental climatic conditions, while the central and southern parts of the peninsula and the islands have a more Mediterranean climate. The aims of this study were to evaluate any variation in the prevalence of asthma, allergic rhinitis and chronic respiratory symptoms in Italy and to find out which geographical variables and/or climatic conditions play a major role in determining prevalence. To achieve these aims, we analysed the data collected by the multicentre survey Italian Study of Asthma in Young Adults (ISAYA).

Materials and methods

Study design

Italian Study of Asthma in Young Adults is a multicentre survey carried out in 1998–2000 on a sample of 27 000 young Italian adults, aged 20–44 years, using the same design of the first stage of ECRHS (7). The aims of ISAYA are to measure the prevalence and geographical variability of asthma and asthma-like symptoms, of allergic rhinitis and chronic cough and phlegm, and to quantify the individual and social costs of asthma in Italy.

Nine centres participated in the study: six in northern Italy (Pavia, Torino, Verona, Udine, Ferrara and Sassuolo), one in central Italy (Pisa, also including two other neighbouring towns, Lucca and Livorno) and two in southern Italy (Sassari, on the Island of Sardinia, and Siracusa, on the Island of Sicily) (Fig. 1).

In each centre, the information on the presence of asthma and asthma-like symptoms, allergic rhinitis and chronic cough and phlegm, and also questions on the main life styles (professions and smoking habits), was collected through a screening questionnaire on a random sample of 3000 subjects (male : females = 1 : 1). The questionnaire has been published elsewhere (8).

To obtain a high response rate, nonresponders had been contacted up to three times by mail, depending on the centre, and finally by phone.

Geography and climate

Northern centres are characterized by a sub-continental climate, while the others (Pisa, Sassari and Siracusa), in central and southern Italy, belong to an area with a Mediterranean climate (Fig. 1). Mediterranean climate areas are characterized by a higher annual mean temperature and a lower temperature range, and also different levels of rain and air humidity (9).

The geographical and climatic variables included in the analysis were the latitude, the distance from the sea (in km), the annual mean temperature (in °C) obtained as the mean of the daily temperature mean values, the temperature range (°C) obtained as the difference between the average temperature of the hottest and the coldest month (Table 1).

The meteorological information was provided by Institute of Atmospheric and Oceanic Sciences (ISAO) and Regional Agencies

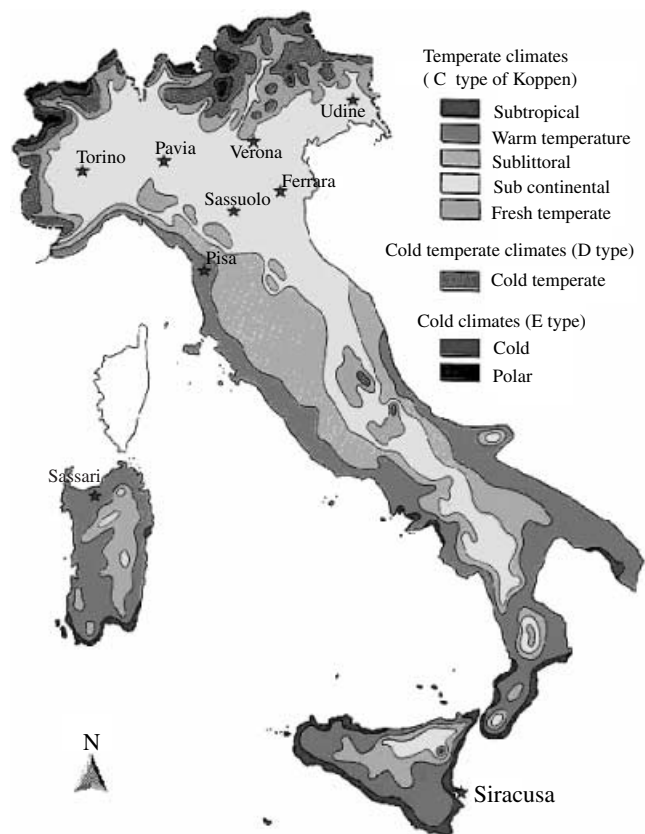


Figure 1. Centres participating in Italian Study of Asthma in Young Adults and climatic areas (9).

for the Protection of the Environment (ARPA) and are consistent with the values published by the World Meteorological Organization (WMO).

Data management and statistical analysis

Subjects were classified as having: *wheeze*, *tightness in the chest* and *shortness of breath* if they answered affirmatively to the following questions respectively: 'Have you had wheezing or whistling in your chest at any time in the last 12 months?', 'Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?',

Table 1. Geographical and climatic characteristics of centres

Centers	Latitude	Distance from the sea (km)	Mean temperature (°C)	Temperature range (°C)
Udine (UD)	46.06	39	12.7	19.8
Verona (VR)	45.44	103	13.7	21.4
Pavia (PV)	45.18	89	12.6	23.0
Torino (TO)	45.08	106	12.4	22.9
Ferrara (FE)	44.84	50	13.0	22.5
Sassuolo (SL)	44.54	118	13.3	22.9
Pisa (PI)	43.72	9	15.2	17.1
Sassari (SS)	40.76	12	15.3	15.4
Siracusa (SR)	37.17	1	17.5	15.1

'Have you been woken by an attack of shortness of breath at any time in the last 12 months?'; *asthma attacks*, in the case of a positive response to the question: 'Have you had an attack of asthma in the last 12 months?'; *medicines for asthma*, in the case of a positive response to the question: 'Are you currently taking any medicines (including inhalers, aerosols or tablets) for asthma?'; *allergic rhinitis*, in the case of a positive response to the question: 'Do you have any nasal allergies including hay fever?'; *chronic cough and phlegm*, in the case of a positive response to the question: 'Have you had cough and phlegm on most days for a minimum of 3 months a year and for at least two successive years?'

Subjects were classified according to their smoking habits (*smoke*) as: *smokers*, if they stated in the questionnaire that they were current smokers and had smoked at least one cigarette per day or one cigar a week for 1 year; *ex-smokers*, if they had smoked for at least 1 year (as defined above) but not during the last month; all the other subjects were considered to be *nonsmokers*.

Moreover, subjects were classified into six groups according to their socio-economic status (*social*): managers, entrepreneurs and businessmen; clerks; workers; retired and unemployed persons; housewives and students; other conditions.

To allow for the different final cumulative response rate, each subject was attributed the median of the cumulative response rate of the contact to which he/she had answered (*cumres*). Each subject was also attributed a dummy indicator of the type of interview (*int*, telephone *vs* postal) to adjust for the possible bias because of a different way of administering the questionnaire.

Heterogeneity of the prevalence rates among the different areas was assessed by the chi-square test for comparing proportions from independent populations (10).

A two-step analysis was used to estimate the relationship between the respiratory symptoms and the geo-climatic variables.

In the first step, the following logistic regression model was fitted:

$$\text{logit}(\pi) = \beta_0 + \beta_{1-8}\text{centre} + \beta_9\text{sex} + \beta_{10}\text{age} + \beta_{11}\text{cumres} + \beta_{12}\text{int} + \beta_{13-14}\text{smoke} + \beta_{15-20}\text{social} + \epsilon$$

where π is the prevalence of a specific symptom.

Then the adjusted prevalence rates were estimated through the equation:

$$\text{prevalence} = \exp[\text{logit}(p)] / \{1 + \exp[\text{logit}(p)]\}$$

where p is the estimation of π and *sex*, *age*, *cumres*, *int* were set equal to the overall mean or distribution, respectively. Adjusted prevalence rates and their 95% confidence intervals were obtained using STATA 7.0 (11).

In the second step, the relationship between the adjusted prevalence rates and geo-climatic variables was assessed using the following simple regression model: $\mathbf{L} = \alpha\mathbf{X} + \epsilon$, where $\mathbf{L}$ is the vector of the estimated centre logits ($b_1 \dots b_8$) obtained from the logistic model in the first step and $\mathbf{X}$ is the geo-climatic variable (latitude, distance from the sea, temperature and temperature range). Each logit $\mathbf{L}_i$ was weighted by the inverse of its sample variance (12).

The relationship between the symptom prevalence and the geo-climatic variable was expressed by odds ratio [OR = $\exp(\alpha)$]. As the joint distribution of symptoms and climatic variables was unknown, confidence intervals for α and OR were obtained using bootstrap methods (13). Least trimmed squared regression, a robust estimation technique, was finally performed to confirm the estimated trend obtained through ordinary least squared estimates (14). Efroymson's stepwise method (15) was used to choose the best subset of geo-climatic predictors for each symptom. These last steps were performed using S-PLUS software (16).

Results

Of the 25 969 eligible subjects 18 873 filled in the questionnaire. The overall response rate was 72.7% (Table 2) ranging from 48.7% (Siracusa) to 82.0% (Pavia). On average, the percentage of telephone interviews was equal to 20.4%, ranging from 7.9% (Ferrara) to 40% (Pisa).

The prevalence was significantly heterogeneous for all analysed symptoms (Table 3). The adjusted prevalence rates for most asthma-like symptoms were higher in the central and southern towns (Pisa, Sassari and Siracusa) with respect to the northern ones for most asthma-like symptoms (Fig. 2), while this was not true for 'allergic rhinitis' and 'chronic cough and phlegm' which did not show a particular trend.

Figure 3 shows regression lines of centre-specific logits for the main asthma-like symptoms on two of the climatic variables. The centre-specific logits (and, as a consequence, the prevalences) were higher at higher mean annual temperature, and lower at a greater temperature range. Robust estimates (dashed line) confirmed and, sometimes, even emphasized the results obtained by ordinary least square estimates. This trend is confirmed

Table 2. Number of eligible subjects, respondents and response rate by centre

Centre	Target*	Respondents	Response rate (%)
Udine (UD)	2936	2082	70.9
Verona (VR)	2927	2166	74.0
Pavia (PV)	2981	2444	82.0
Torino (TO)	2892	2266	78.4
Ferrara (FE)	3000	2106	70.2
Sassuolo (SL)	2869	2143	74.7
Pisa (PI)	2976	2411	81.0
Sassari (SS)	2925	2055	70.3
Siracusa (SR)	2463	1200	48.7
Total	25969	18873	72.7

* Number of eligible subjects = sample - (deaths + moved + wrong address).

Table 3. Variations in adjusted* prevalences (%) of the studied symptoms in Italian study of asthma in young adults (ISAYA)

	Min.	Median	Max.	Max./Min.	Heterogeneity test†
Wheezing	7.6	9.8	13.3	1.7	<0.001
Tightness in the chest	5.2	7.1	9.3	1.8	<0.001
Breathlessness	3.6	5.4	7.4	2.1	<0.001
Asthma attacks	2.6	3.5	5.2	2.0	<0.05
Medicines for asthma	2.0	2.3	4.1	2.0	<0.001
Allergic rhinitis	13.5	18.9	23.6	1.8	<0.001
Chronic cough and phlegm	7.6	9.2	13.0	1.7	<0.001

* Adjusted for sex, age, cumulative response rate, type of interview, smoke habits and social class.

† P-value of chi-square test for comparing proportion from independent populations. Min., minimum; Max., maximum.

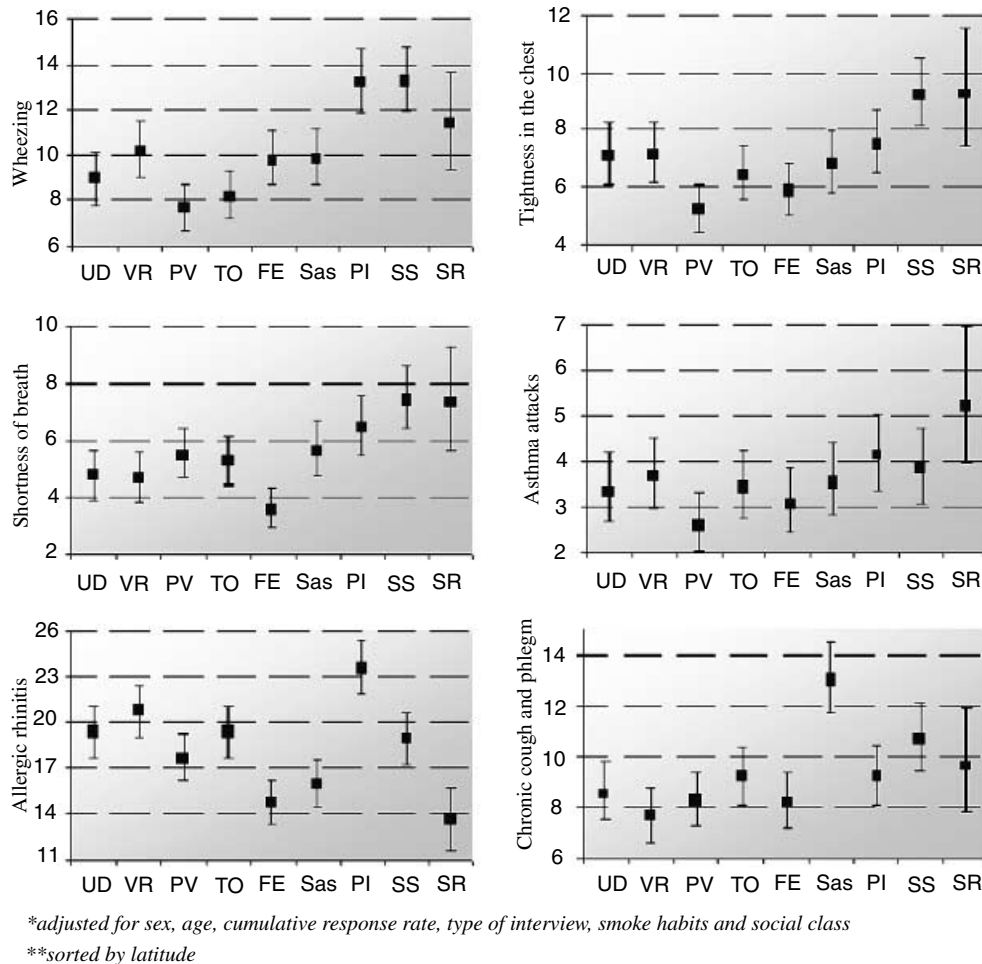


Figure 2. Adjusted* prevalences and 95% confidence intervals of symptoms by centre**.

for all of the asthma-like symptoms and for latitude and distance from the sea (Table 4). The ORs of asthma and asthma-like symptoms were significantly different from the unit for all of the geo-climatic variables considered (Table 4): the risk of having symptoms increases at decreasing latitudes, at a minor distance from the sea and at a slighter temperature range, and at increasing annual mean temperatures.

The same is not true for allergic rhinitis and chronic cough and phlegm that present ORs which are not significantly different from the unit (Table 4): they do not seem to be influenced, at least not in the same way, by the considered geo-climatic variables.

When performing stepwise multiple regression analysis on asthma-like symptoms, variables retaining significance varied according to the symptom considered (Table 5). Temperature range was the most important climatic variable that accounted for differences in the prevalence of the symptoms; it was kept as the first variable in the model for three of the five symptoms (*wheezing*, *tightness in the chest* and *breathlessness*). Distance from the sea was kept as the second variable in two models (*tightness in the*

chest and *breathlessness*). Variations in the prevalence of *asthma attacks* were explained only by differences in mean temperature, whereas *medicine for asthma* was influenced by latitude.

Discussion

Italian Study of Asthma in Young Adults is an extensive epidemiological survey on adult asthma in Italy: it is the first to collect data in southern Italy and to make a direct comparison among prevalence rates from the different geographical and climatic regions in Italy.

As partially seen in a previous analysis on climate and pollution (5), our results further strengthen the finding of a relationship between climate and asthma prevalence; there is an increasing prevalence of asthma where temperature range is slighter and the mean annual temperature is higher. Even if to a minor extent, geographical factors, such as distance from the sea and latitude, also influenced symptom prevalence. Our analysis showed substantial variations among centres for allergic rhinitis albeit with

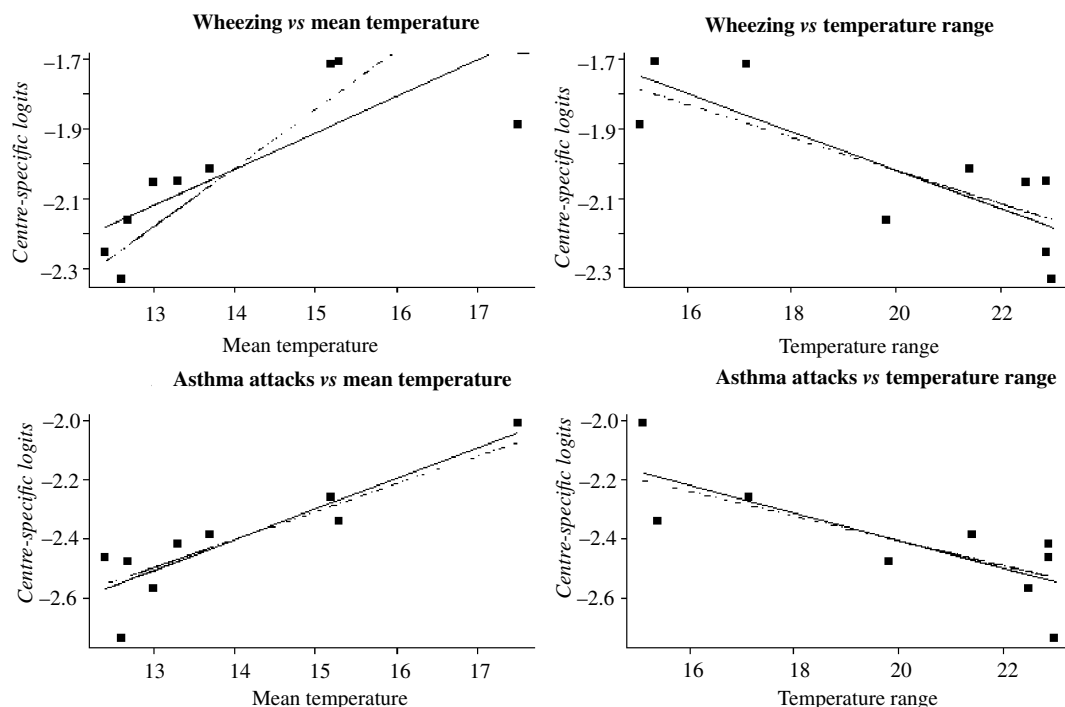


Figure 3. Regressions of centre-specific logits on climatic variables: main asthma-like symptoms. Solid line: ordinary least square; dashed line: robust estimate.

Table 4. Bootstrap estimates of the association between symptoms and geo-climatic variables [odds ratio (OR) and 95% CI]

Symptoms and treatments	OR (95% CI)			
	Latitude	Distance from the sea*	Mean temperature	Temperature range
Wheezing	0.96 (0.92–0.99)	0.90 (0.85–0.96)	1.11 (1.05–1.17)	0.95 (0.93–0.97)
Tightness in the chest	0.95 (0.92–0.98)	0.92 (0.86–0.97)	1.11 (1.06–1.15)	0.95 (0.93–0.97)
Breathlessness	0.94 (0.91–0.98)	0.93 (0.87–0.99)	1.11 (1.03–1.17)	0.95 (0.92–0.97)
Asthma attacks	0.95 (0.93–0.98)	0.93 (0.86–0.98)	1.11 (1.06–1.14)	0.95 (0.93–0.98)
Medicines for asthma	0.92 (0.89–0.94)	0.90 (0.83–0.98)	1.14 (1.09–1.24)	0.94 (0.92–0.99)
Allergic rhinitis	1.03 (0.99–1.07)	1.00 (0.91–1.10)	0.98 (0.91–1.07)	0.99 (0.95–1.05)
Chronic cough and phlegm	0.98 (0.93–1.01)	1.00 (0.94–1.14)	1.03 (0.97–1.11)	0.99 (0.97–1.05)

* OR for a 30-km interval.

Table 5. Geo-climatic agents mainly influencing asthma-like symptoms; for each symptom, the factor(s) explaining the greatest variability throughout Italy is shown

Asthma-like symptoms	Main factor	Additional factor
Wheezing	Temperature range	–
Tightness in the chest	Temperature range	Distance from the sea
Breathlessness	Temperature range	Distance from the sea
Asthma attacks	Mean temperature	–
Medicines for asthma	Latitude	–

no particular pattern. This held true when we investigated chronic cough and phlegm.

Deeper insight into the climatic variables and the consideration of strictly geographical factors in our

analysis pointed out that temperature range has the greatest influence on asthma-like symptoms, which explains the variations in prevalence for three of five symptoms. This is followed by the distance from the sea. Mean temperature was the only climatic variable explaining *asthma attacks* and the use of *medicines for asthma* was linked to latitude.

Until now, climate has been mainly studied for its short-term effects: storms and other sudden atmospheric changes often cause an increase in asthma attacks, because of the sudden temperature decrease and the increase in ozone concentration (4, 17, 18).

On the contrary, there are very few studies on the long-term effects of climate on the variability of asthma prevalence; their results (3, 6, 19–21) support our findings

that coastal and milder climates could favour the onset of asthma and asthma-like symptoms.

Similarly, very little has been published on the relationship between climate and allergic rhinitis, and chronic cough and phlegm. Allergic rhinitis seems to be more frequent in dry areas with respect to temperate ones (22); chronic cough and phlegm are also exacerbated in dry environments where inorganic powders are more easily spread (23).

One possible explanation for the positive association between asthma prevalence and milder climatic areas could be the ozone concentration in the atmosphere: ozone is known to reach higher levels at higher temperatures. High ozone levels seem to be noticeably linked to asthma and asthma-symptoms both for the short-term (24, 25) and long-term effects (26–28). In the long-term, continuous exposure to high ozone levels gives rise to an impaired respiratory function (26) and airway inflammation in atopic asthmatics (27) and increase the number of new asthma cases (28). Moreover, there could be an interaction between pollution and climatic factors, so that a particular climate could elicit a pollution effect on health (5, 17, 24, 27–29).

As asthma is predominantly found in association with immediate hypersensitivity to inhaled allergens, the different exposure to outdoor and indoor allergens in the two geo-climatic areas should be considered. In fact, pollinosis in southern, Mediterranean Italy differs from pollinosis in more northern parts of Europe (30). The higher annual mean temperature and the slighter temperature range of Mediterranean areas favour the production of pollens throughout the year, while in continental areas, which are colder and have a wider temperature range, pollination is usually limited to the period spring–summer (31). In particular, there can be dense concentrations of airborne grass over many months in southern and coastal region of Italy, whereas they are only present in the spring and summer in northern Italy and in continental Europe (30–32). Concentrations of airborne pollens of the *Parietaria* genera – typical of Italian flora – and of *Olea europea* are particularly high in southern Italy (including the islands) and along the coasts; in these parts of Italy, *Parietaria* airborne pollen is present at different levels practically all year around (30, 32). Remarkably, the literature has ascertained that these two particular pollens deserve special attention in the southern coastal region, because they have been found to be a major cause of allergy and the high prevalence of asthma in sensitized subjects (30, 33).

Moulds, particularly *Alternaria*, deserve attention too, because they are considered to be both indoor and outdoor risk factors for asthma and asthma-like symptoms (34). Moulds thrive in warm and humid climates, and the release of the spores is elicited by sunny and windy weather, typically found along the coastal areas; nonetheless, wide variations in the prevalence of

Alternaria sensitization have been reported among the southern coastal towns in Italy (35). Moreover, *Alternaria* is also frequent in northern inland towns in Italy (35), so this explanation could not be sufficient, in our national context, to explain such differences.

For some years house dust mites have been recognized as the main source of allergens in dust, in most temperate humid areas of the world. Besides closed buildings, heating, carpets and upholstered furniture, great numbers of house dust mites are due to particularly favourable climate conditions (36). Some studies have shown significantly higher levels of mites or mite allergens in house near the coast than inland, both in Australia (37) and in the Mediterranean area (38–41). Moreover, house dust mites were found to be very common in Sardinian houses (42). Cockroach allergens and animal dander should also be considered among indoor allergens; however, cockroach allergy in southern Italy seems to be quite low (43) and it is unlikely that there is a variation in pet exposure among the different geographical areas.

Our findings seem contradictory to the finding of ISAAC and ECRHS in that these studies had the highest prevalence of asthma in northern Europe and the lowest in eastern and southern Europe (1–2). However, when taking the whole world into account, the highest prevalence of asthma was found mainly in English-speaking countries, including New Zealand and Australia, which suggests that there are other risk factors involved in the development of asthma, besides climate and geographical areas. In Italy however, where there is a rather low prevalence of self-reported respiratory symptoms (1, 2, 44), atopy (45) and bronchial hyperresponsiveness (46), the SIDRIA, with an extended ISAAC protocol, showed the same geographical trend among children, with significantly higher prevalence of asthma in central than in northern Italy (47).

Contrary to asthma, allergic rhinitis does not seem to have a geographical trend across the peninsula. Thus, our results seem to suggest that the geo-climatic determinants of asthma are different from those of allergic rhinitis. It seems unlikely that this result could be due to some methodological bias: in fact, the response rate was quite high, except for Siracusa, where usually people are culturally more reluctant to participate in surveys. In our analysis we adjusted for the potential bias which could have occurred because of the differences among centres, either in the way the study was performed (response rate, type of interview) or because of individual characteristics (age, sex, smoking habits and social class). Moreover, when regressing the centre-specific logits on the climatic variables, we considered the different number of subjects and the unusual values using weighted least square and robust regression methods, respectively.

Another potential source of bias could be that subjects tend to recognize as ‘allergic rhinitis’ only seasonal rhinitis or hay fever; however a good reliability of the mailed questionnaire on allergic rhinitis with the clinical

diagnosis was found (48). This raises the important question of the reason for the difference between subjects with allergic rhinitis and those with asthma or wheezing. With respect to allergic rhinitis, subjects with asthma may be characterized by the continuous exposure for most months of the year to the allergens (49) and the total burden of aeroallergens (50). Both these features are prevalent in the Mediterranean areas with respect to the northern ones (51, 52).

Although it is questionable that allergen exposure is a primary and major cause of asthma (53), it is well established that allergen exposure can trigger asthma attacks in sensitized asthmatic subjects and prolonged exposure can lead to the persistence of symptoms (54–56). As asthma prevalence in a population reflects both asthma incidence and the average duration of the condition, the higher allergen exposure that prolongs or exacerbates asthma symptoms may thereby increase current asthma prevalence in the central-southern coastal towns in Italy.

Other reasons for the higher asthma prevalence in central-southern Italy, such as the migration of asthmatic patients to coastal areas, are very unlikely.

The fact that *medicine for asthma* is particularly linked to latitude could also be due, apart from the higher prevalence, to different attitudes towards prescribing drugs and their use, which is generally more frequent in southern Italy.

Contrary to asthma, chronic bronchitis does not seem to be influenced by geo-climatic factors, but rather, it is more linked to chemical pollutants and individual etiologic factors (smoking).

In conclusion, characteristic geo-climatic factors of southern Italian areas increase the risk of having active asthma. It could be very interesting to collect data from other centres in central-southern Italy to support these findings and to further investigate the effect of climate on asthma prevalence.

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