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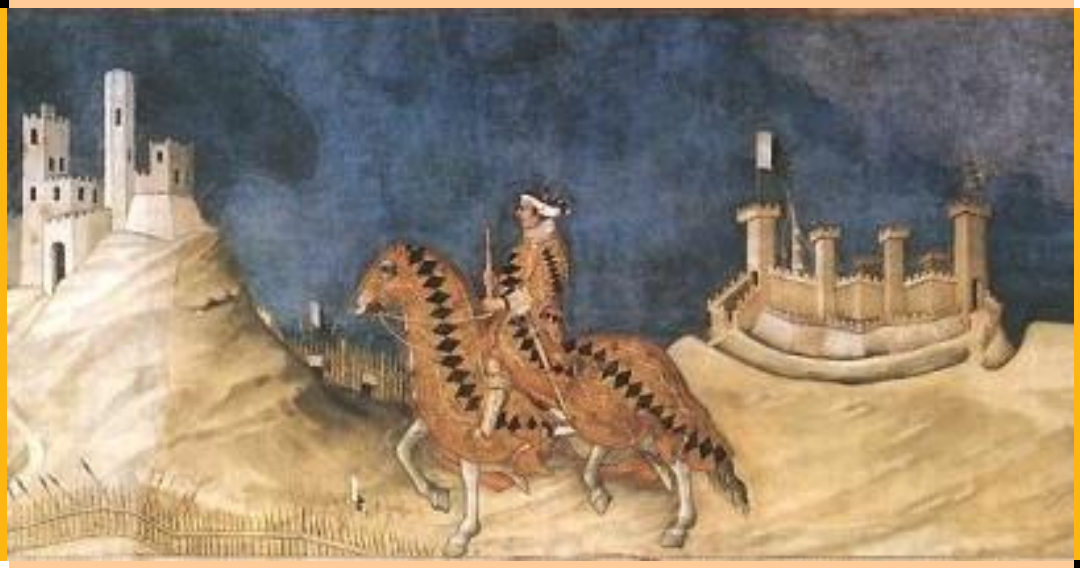

Fuzzy method for studying the relationships between allergies and socio-economic conditions

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ABSTRACT

The worrying increase of allergies in western lifestyle countries has not been explained to date, despite the great interest of the scientific community, a considerable part of which has unsuccessful sought the cause in their lifestyle and socio-economic conditions. In this article we show that there is sufficient evidence to say that the methodology used so far to investigate the link between allergies and living conditions is not adequate, because it does not allow to assess the multivariate and fuzzy nature of the phenomenon and leads to contradictory results. Moreover, for the first time we enunciate a theory able to link psychophysical stress to the onset of allergies, reporting empirical evidence in its support based on data provided by the italian *Istituto Superiore di Sanità* and providing the missing element in the construct already attempted by other authors that binds stress and allergies. The methodological solution that we propose and motivate with solid theoretical foundations is based on the fuzzy set theory, which allows to evaluate the impact of multifactorial phenomena with modalities similar to human perception schemes.

Keywords:

Allergy, fuzzy approach, socio-economic condition, stress, neuro-immune system, Weber-Fechner law.

1. Introduction

Allergy is considered a kind of immune system error, “an inappropriate and harmful response of the body’s defence mechanism to substances that are normally harmless. It involves the immune system and particularly the antibodies called immunoglobulins E (IgE)” [1]. Although the mechanism through which allergic disorders develop within an individual is widely known, it is not clear why a person becomes allergic. Within the last decades, there was a significant global increase in allergy prevalence [2], and the phenomenon has not been understood by the scientific community. The growth of allergic diseases have not been homogeneous in

different parts of the globe: in Western countries, the prevalence rates of asthma, allergic diseases and associated symptoms are generally higher than in other countries. Pearce et al. [3] concluded that the prevalence rate of asthma symptoms is particularly high in English-speaking countries, Western Europe and some of the more affluent Asian countries. One of the theories that attempts to explain this paradox, which sees countries with the best hygienic-sanitary conditions presenting the highest growth rate of allergies, is the "hygiene hypothesis of Strachan", according to which maternal exposure to microorganisms during pregnancy and early childhood exposure, which are thought to be higher in less "hygienic" and poorer environments such as farms and more crowded houses, would protect against the sensitisation to allergens later in life [4]. Despite its initial success, the hygiene hypothesis has shown numerous weaknesses and results for various types of exposure and in different populations contradict each other [5, 6]. Although the relationship between socio-economic position (SEP) and allergies is widely shared, contradictory results are found in the literature with both low and high SEP, and today there are no convincing results that can explain the observed epidemiological patterns. The incapacity of finding an explanation to the rapid growth of allergies in the Western lifestyle countries is, in our opinion, due to a wrong methodological approach. In this article, we provide solid evidence to support our thesis, showing how the results already present in literature provide, if properly evaluated, sufficient information to rebuild the relationship between SEP and allergies. We will also provide an appropriate methodology for the analysis of data from studies linking living conditions and allergies, illustrating for the first time a theory explaining the physiological mechanism underlying the relationship.

We retain that the proposed approach could help to relieve the suffering of people with allergies and make the social problem less burdensome. Even considering allergies inducing rhinitis, we know that runny or stuffy nose, teary eyes, or throat are associated with sleep-disordered breathing, mental health problems, psychiatric disorders, depression and anxiety; additionally, sleep-disordered breathing in childhood and adolescence is associated with increased disorders of learning performance, behaviour, and attention [7,8]. Thus, in general allergy rhinitis woes have negative impact on patients' quality of life and creates an important social problem. The total burden just of allergy rhinitis is not only related with physical and social functioning but also affect daily work and productivity, creating also economic problem for the individuals and for the society [8].

2. Main findings on the epidemiology of allergies

Epidemiological studies suggest that there are harmful as well as protective environmental and lifestyle factors. Beneficial factors include growing up in a rural environment with contact to farm animals ("farming effect"), [9,10] and early contact with siblings or peers [11], that is, children who grow up in a rural environment and with siblings or in contact with peers, are less likely to develop allergic sensitizations as adults. Obesity, lack of physical exercise [12–14], a diet rich in industrially processed foods, growing up as singlet in an urban home, are instead reported as risk factors [4, 15]. In hygiene hypothesis these elements were related to a favourable (for protective factors) or unfavourable (risk factors) effect on development of a highly diverse microbiota on the bodies′ barrier organs that is the skin and the mucosa of the respiratory, urogenital, and gastrointestinal tract [4,16]. This interpretation is in our view wrong; indeed it leads to contradictory results as amended earlier. If contacts with animals can be linked to a different development of the human microbiome, it is difficult to consider that contacts with peers or siblings have the same effects. Instead, it would be more reasonable to consider the different social dimension of having or not siblings, which (as well as the overall family environment), has been shown to affect cognitive and psychological development, on how child will perceive social stress in future and on the risk of stress-dependent diseases in future life [17-21]. Furthermore, also with regard to the effect of pet ownership in childhood, on allergic sensitisation, contradictory results were reported [22-28], coming in some cases to report opposite effects of the contact with the same animal depending on the environment in which the contact takes place [29]. However, the most surprising evidence supporting the relationship between SEP and allergies is the "involuntary social experiment" that was the fall of the Berlin Wall, which had opened up a unique opportunity to compare the effects of lifestyles of the East and West. Throughout the 1990s, researchers realized a high prevalence of allergies in the former West Germany compared with a very low prevalence in the East. Indeed, immediately after German reunification, the different incidence of allergic diseases in the East and West Federal countries of Germany has varied considerably [30], gradually decreasing over only 30 years [31] as the environmental conditions become more similar. This short-term development cannot be attributed to a drift in gene pool of the population nor at a different rate of pollution, considering that a wall is not suitable to screen environmental pollutants. In conclusion, it can be said that decades of research on the ethology of allergies have brought theories abstractly plausible with weak and contradictory evidences. Although the acquisitions of allergy immunology have been

of no small importance, if considered individually, scientific research has not so far been able to unify and understand in a general theory such results, in order to appreciate the phenomenon in its complexity.

3. A new reading of the nature of allergies

3.1. Multifactorial nature of allergies and neuro-immune system

The multifactorial nature of allergic disease is currently evident [32]. It is linked to biological factors, such as the physiological conditions of the sensitised subject, the nature and characteristics of the allergens, the environmental factors such as pollution and exposure conditions, and evidently to SEP, although we do not know how. The apparent contradiction of the results in the literature arises precisely from the not overall assessment of the variables involved in the pathology's ethology. Above all, the most often neglected element in epidemiological studies of allergies is the link between the immune and neurological system. As authoritatively argued such relationship is so close that one should talk about the neuro-immune system [33,34]. There are studies that even indicate elements in support of a coevolution between the immune system and language [35]. Thus, we believe that stress is the key latent variable to understand the allergy epidemics. Indeed, it has been pointed out, that the mammalian immune system has memory of socially stressful events [36, 37], consequently, the psychological factors, such as general well-being or perceived stress level, are configured as a largely unappreciated pathophysiological component in allergy. The key element we need, to gain a better understanding on the relationship between stress and allergies is to consider the two compartments, the immune and neurological system, as unique one, or at least as directly communicating, as is now clear from the acquisitions in the newly born field of neuroimmunology. This would help to explain the high subjectivity in allergic sensitization.

Here, we provide an indirect proof of our hypothesis.

In early 2020, the coronavirus disease 2019 (COVID-19) pandemic led to a series of sudden and profound increases in reported psychiatric symptoms and changes in mental health care delivery methods. Recent surveys have also found higher rates of depressive and anxiety symptoms among adults in the initial months of the pandemic compared with previous years, [38] increased rates of serious psychological distress during

the pandemic compared with the previous years, [39] and increased rates of depressive and anxiety symptoms during the pandemic. However, during 2020, medication fills for antidepressants were stable or changed only modestly after accounting for prior-year patterns. Let as consider the case of Italy (Table 1), when compared to prior-years Defined Daily Doses (DDDs) per 1000 inhabitants day, there was a slight increase.

If we look at analogous data for antihistamines, we can observe (Table 2) a relevant increasing rate between 2019 and 2020 DDDs /1000 inhabitants Day. It seems strange, considering that in Mediterranean area, the main pollination period covers about half the year, from spring to autumn, and in 2020, Italy during the worst months for allergies was under lockdown order: this implies that the population could not be exposed to environmental allergens. The reason could be therefore the hypothesis advanced in this paper: the relationship between stress and allergies.

Table 1: Consumption of antidepressant drugs subject to medical prescriptions expressed as DDD/1000 ab die weighed in the period 2016-2020. In the last two columns on the right, the percentage change rate for the years 2019-2020 (Δ % 20-19) and the Compound Annual Growth Rate (CAGR) for the years 2016-2020 are presented respectively. Source: Istituto Superiore di Sanità.

Geographic area	2016	2017	2018	2019	2020	Δ % 20-19	CAGR % 16-20
Italy	37.93	38.04	38.79	39.36	40,18	2,11	1,16
North-West	39,64	40,00	40,80	41,37	42,26	2,15	1,29
North-East	37.88	38.28	39.21	39.78	40.53	1.91	1.36
Center	43.57	43.68	44.46	45.05	46.07	2.26	1.12
South	32.27	31.95	32.57	33.17	33.93	2.29	1.01
Islands	34.80	34.57	35.07	35.46	36.05	1.65	0.71

Table 2: Consumption of Antihistamines, subject to medical prescriptions expressed as DDD/1000 ab die weighed in the period 2016-2020. In the last two columns on the right, the percentage change rate for the years 2019-2020 (Δ % 20-19) and the Compound Annual Growth Rate (CAGR) for the years 2016-2020 are presented respectively. Source: Istituto Superiore di Sanità.

Geographic area	2016	2017	2018	2019	2020	Δ % 20-19	CAGR % 16-20
Italy	9.28	8.98	9.34	9.42	9.79	3.94	1.07
North-West	7.14	6.94	7.20	7.27	7.52	3.39	1.04
North-East	7.12	6.82	6.99	7.21	7.65	6.09	1.45
Center	9.13	9.00	9.38	9.35	9.61	2.69	1.03
South	13.29	12.76	13.39	13.49	14.00	3.76	1.06
Islands	10.73	10.32	10.72	10.72	11.24	4.80	0.92

3.2. Immunological stress-induced overload

If it is true that the immune and neurological systems are so related and communicating that they can be considered as a single system, it follows that the same stimulus can be perceived by both systems. This condition opens up the possibility of considering allergic sensitization as a pathology potentially induced by a perceptive overload, regulated by the well-known Weber-Fechner law [40, 41]. According to this law of psychophysics, the function that expresses the sensory perception depending on the stimulus administered is not linear but logarithmic and goes towards a plateau that corresponds to perceptual saturation. In other words, the quality of perception worsens as the stimulus increases, resulting in an overload of the perceptual channel and phenomena of erroneous perception. Moreover, when a sensory channel is polymodal (sensitive to different types of energy), confusion becomes possible between stimuli of a different nature, both perceivable by the same receptor [42-44]. An example is the confusion of extreme heat and extreme cold, linked to the stimulation of nociceptors (pain receptors) present on human skin, which are sensitive to both extremely low and extremely high temperatures [45,46]. Since allergic sensitization is nothing more than the erroneous perception of a harmless agent as a pathogen, we propose that the perceived psychophysical stress can induce and aggravate the pathology, as the stimuli felt by the neurological system can be communicated to the immune system, producing, in the presence of exposure to environmental allergens, a perceptual overload with a consequent deterioration of the quality of recognition of the immune system. It is known that stress can generate inflammatory states like those found in allergic reactions, with the involvement of the same mediators

(e.g. Histamine and cytokines) [47-51], it is therefore likely that in the presence of an inflammatory state and a perceptual overload, the immune system is misled. Although today′s knowledge on neuroimmunology in allergy is mostly sporadic, results on allergic sensitisation in humans and animal models aggravated or induced by social stress already exist [47-51] and it is known a significant rate of comorbidity between allergies and mental pathologies [52-54], as well as evidence of immune memory of social stress [36,37]. It is important to note that currently, in the clinical field, SEP is considered an important predictor of a range of health and illness outcomes [52, 55]. Therefore, allergies are an example in a wider framework of chronic diseases for which research seeking to identify the extent to which this often-reported effect is due to protective benefits of higher SEP or to toxic elements of lower social status without consistent or conclusive findings [52]. For other chronic diseases, research has already borne fruit, advancing the relatively novel hypothesis according to which these effects are due to chronic stress associated with SEP [52, 56]. To get a correct assessment of the link between SEP and allergies (and probably also for other chronic diseases) we do still need an appropriate analytical methodology, which we propose in this paper. Our hypothesis is that through an appropriate analysis it would be possible to demonstrate that behind the sharp rise in allergic diseases in the occidental lifestyle countries, there is a perceptive overload.

4. A framework for allergies' epidemiology analysis

In the light of the above, we believe that a key issue in the study of the relationship between SEP and allergies is to measure how stress is felt. The stressful impulse is generated by a plurality of situations of different nature. It is therefore not possible to measure the relationship between stress and a chronic disease, claiming to quantify only one or more of the stressful sources, moreover separately. The correct approach for studying it, should measure the amount of stress experienced by the subjects, encompassing the several sources of stress. We emphasize the concept of stress felt, since it is necessary to take into account the subjective nature of perception, from which it is not possible to disregard, for a correct analysis of a disease, which is assumed to be linked to physiological mechanisms of relationship with the environment peculiar to individual subjects. To obtain a subjective measure of perceived stress, that is, a quantification as relative as possible and considering the conditions actually experienced by the individual, it is necessary to adopt a perspective as similar as possible to human perception. More precisely we can say, a function that evaluates continuously and

accumulates all the possible elements influencing the onset of the pathology, also evaluating their interactions. An optimal mathematical tool, which has already been successfully tested with regard to sensory perception (of physical stimuli) is the fuzzy set theory [57]. It has been used, with excellent results, in the measurement of heat and cold [58]: these are concepts that cannot be simply quantified by a temperature, instead concern a perceived state that is a function of several elements such as wind, humidity and shadow. On the other hand, it is impossible to say that a temperature of 18 °C belongs to the domain of heat or cold, or that a certain income level is associated with a stressful social condition, or not, without considering other factors involved in determining this stress condition. Someone considers cold a condition corresponding to 18 °C with given humidity and wind, while someone else considers it warm, the same can be applied to any social condition, in other words there are no clear and objective boundaries in what is perceived by the humans. The fuzzy set theory was created to treat and measure a phenomenon by considering its imprecision, uncertainty, and vagueness and does not assign an object or a condition to a set but treats it according to degrees of membership. The fuzzy set theory get optimal result to model human perception [59, 60]. The human brain can cope with the surrounding world, which is imprecise, uncertain, and adaptive. His own author writes, "Humans have a remarkable capability to perform a wide variety of physical and mental tasks without any measurements and any computations…. Reflecting the bounded ability of the human brain to resolve detail, perceptions are intrinsically imprecise" [59]. On the other hand, an individual copes with imprecise and uncertain surrounding environment and tries to adapt to it. From a clinical point of view, this implies a concept, properly expressed in the field of toxicology and environmental medicine: the bioavailability of a toxic agent [61], namely the fraction of a toxic or potentially toxic substance, present in a given environmental compartment, which can be absorbed by the living organisms on which it exerts its action. Considering exposure to an environmental allergen and the same stress as a harmful agent, their potential damage cannot be calculated by ignoring the conditions that can make it effective, such as their concomitance, the social environment and the resources available to the subject exposed. Therefore, we propose a completely new approach in the field of allergies, a fuzzy model that allows to take into account the exposure to the allergen, concomitant pathologies, lifestyle, SEP and living conditions measured with appropriate fuzzy indices [62] and relate them to an objective measure of the disease, namely the level of specific IgE present in the serum of the subject analysed. To illustrate our methodology, we will follow the example of one of the most common allergies, that to pollen.

An analysis planning to assess the relationship between pollinosis and SEP should, as mentioned above, examine living, socio-economic and physiological conditions (relevant to the disease under consideration), the actual exposure to the allergen, the perception of stress and symptoms of the experimental subjects and the clinical response to tests for the presence of pollinosis. To do that, we refer to the fuzzy set theory, already used in ecology and ecophysics, indeed, it has proven to be a powerful tool for modelling and predicting animal species behaviour in response to complex external stimuli, such as climate change [63], as suitable to capture the cumulative effect of many variables such as environmental, biological, historical factors, the interaction between species together with the uncertainty that characterizes the animal action. The phenomenon of human's pathological response to socio-environmental conditions is the same, so we can believe that the fuzzy approach brings the same benefits, if not greater, given the highest degree of uncertainty and complexity of human social action.

Here, three orders of reasons for supposing the primacy of fuzzy approach in the study of the epidemiology of allergies.

1. The first is that the dependence between the onset of a disease and living conditions (in a broad sense) is one of those complex and non-linear phenomena that appear stochastic due to the many variables that are involved and the lack of knowledge of their ruling laws. Being phenomena that involves the interactions of humans with the complex environment in which they live, these are cases that can be modelled by the Langevin equation [64], in which the stochastic variables change more quickly than the other controlled variables. In recent years, the trust in the application of Fuzzy Logic System to such phenomena has widely grown, thanks to the demonstration of their potential in the specific case [65-68].
2. Many studies have shown that phenomenon like poverty/wealth, social status, well-being, [69] are by their nature fuzzy and the quality of life measurement, which covers the above-mentioned aspects, has indeed already been successfully addressed using the fuzzy set approach [70]; this approach has proven to be superior to other so called "traditional" approaches in several socio-economic phenomena, such as marital disruption [71], educational mismatch [72], violence against women [73], relationship between covid-19 pandemic and vulnerability [74].

3. The object that we want to measure, in studying the dependence of allergies on lifestyle and the environment, is the effect that these aspects produce on humans. It is therefore necessary to measure such variables as the humans' psyche and physical does. The mammals' cerebral cortex is organized into functional units of information processing called cortical columns, that as experimentally proven have functional boundaries which are not sharp, i.e., binary, but gradual, i.e., fuzzy [75]. More generally it has been shown that the human perceptive experience is physiologically fuzzy [76-78]. From this it is possible to deduce two things: i) the approach to the measure of the variables involved with the epidemiology of allergies must be fuzzy; ii) the demonstrated characteristics of fuzzy poverty measures to have smaller sampling error, compared with traditional poverty measures [79], it is confirmed in the human physiology of the social phenomena perception, that the solutions adopted by nature are almost always the most efficient ones.

In the following subsection, the pillars we need to structure our framework.

4.1 The data

Data and information are necessary to feed the framework: environmental data for allergen's exposure, clinical, socio-economic and stress data. The following subsections explain the survey plans.

4.1.1. Allergens' exposure data

It is known that the average airborne pollen concentration is an exposure parameter of interest to be monitored for its incidence on pollinosis but plants, being organisms not endowed with motility, have developed a surprising ability to adapt to changes in the environment through biochemical modifications [80], therefore, environmental stress and availability of nutrients in the soil can, significantly influence the allergen content and allergy-relevant substances in pollen [81-83]. For this reason, the concentration allergens in pollen (not evaluated in aerobiological monitoring studies) in the regions covered by the study will be assessed as an effective exposure parameter estimated on data collected by an *ad-hoc* sample survey. Pollen samples will be collected adopting a two-phase strategy (tessellation stratified sampling or systematic grid sampling), suitably compatible with the most adopted sampling designs in large-scale forest inventories [84, 85]. In the first phase, the area covered by vegetation is partitioned into a grid of quadrats and a sample of quadrats is randomly

selected. In the second phase a point is drawn according to a scheme appropriate to the nature of the area (randomized or systematic way depending on the chosen strategy) within the quadrats selected. Alternatively, the pollen sample could be collected by specially developed devices for the individual estimation of pollen exposure [86], where it is possible to have a sufficiently large sample of subjects willing to cooperate in this regard. The allergens in the sampled pollen grains should then be determined using chemical analytical techniques such as High-Performance Liquid Chromatography (HPLC) coupled with Diode Array Detector (DAD) and Mass Spectrometer detector (MS) [87-89].

4.1.2. Pollinosis clinical evidence and data

Allergies are characterized by a immunoglobulins of type E (IgE)-dominated inflammation, so for the diagnosis of allergy it is necessary to quantify the IgE and for the understanding of the physiological mechanism underlying pathology it is also significant the determination of the levels of immunoglobulins of type G (IgG) [90]. The skin prick tests (SPT) are widespread, for the diagnosis of pollen allergy, but these tools return only a qualitative assessment; the proposed approach need a quantitative assessment, therefore we plan to quantify specific IgE in the serum of the experimental subjects, by immunochemical assay (for example ELISA) [90]. To get it, we plan to conduct a survey of patients in medical facilities who treat and diagnose pollen allergies, recording IgE levels detected on patients selected for the survey.

4.1.3. SEP, living conditions, and stress data

The most accurate way to detect data on patients about living conditions, demographics characteristics, health condition, other pathologies (other than allergy), lifestyle, income, time use, stressful events and so on, is surely a face-to-face interview by a structured questionnaire constructed ad hoc for the purpose and scientifically validated. The appropriate strategy would be to choose one or more geographical areas of interest, within which to select a sample of patients in the pollinosis diagnosis centres and to submit the questionnaire to them. For the validity of the study would be required two distinct surveys design. Specifically, we need to plan a matching case control design [91], with a sample survey on patients of the allergy clinic (treated group), and the other sample survey on a matched control group, to ensure internal validity of the study. To create such group, we must ensure that the members of the treatment group have a similar counterpart in the matched

control group, outside of the allergy problems. As for the design of sampling, systematic sampling could be adopted [92].

4.2 Fuzzy and multidimensional methods

To the best of our knowledge there is no studies or research on the relationships between allergies and stressing factors conducted by using multidimensional indicators defined according to the fuzzy set theory.

The fuzzy set theory seems to be very satisfactory approach to measure phenomenon that cannot be adequately described by the conventional true-false binary logic. In fuzzy set theory, an item may belongs to a set with partial degrees of membership between 0 and 1. According to Zimmermann (1996) [93], "*if X is a collection of objects denoted generically by x, then a fuzzy set A in X is a set of ordered pairs* $A = \{(x, \mu_A(x) | x \in X\}$ *where* $\mu_A(x)$*is called the membership function or grade of membership/degree of truth of x in A. It maps each element of X to a membership value between 0 and 1*".

According to the multidimensional approach, individual's stress conditions assumed to affect the pathology of pollen, such as health, poverty, etc. are characterised by different type of items being such phenomenon's concerning a plurality of dimensions. Indeed, factors generating stress are interrelated, in the sense that they influence each other to produce a cumulative and complex effect on people. It is not possible to relegate the effect of an event, such as the loss of work, to the economic dimension only; it is clear that through a series of reflections on aspects not directly monetary, such as change of habits, less propensity to relax in leisure, emotional impact, the event is likely to be evaluated even within different dimensions. Thus, a relevant key point in our multidimensional analysis is selecting the relevant information. The fuzzy multidimensional approach has been largely developed in the last fifteen years; from Betti and Verma (2008) [94] until Betti et al. (2015) [95], a step-by-step procedure has been set up to define the fundamental actions in order to construct a multidimensional index; these could be summarised as follows.

i) *Identification of items to be included in the analysis and their transformation into the [0, 1] interval according a membership function*

Our primary data sources will be the surveys introduced in section 4 particularly the sample survey on patients about living conditions, demographics characteristics, health condition, other pathologies (other than allergy), lifestyle, income, time use, stressful events and so on.

ii) Exploratory and confirmatory factor analysis to identify dimensions of deprivation

These steps concern the implementation of multivariate statistical techniques to identify hidden dimensions of stressing factors. This means that the different latent dimensions h (h=1…H) of the stressing factors are computed directly from the items chosen at the previous step, and they are not attributed a priori by following any arbitrary and subjective rule. By dimension, we intend a group of items, ideally independent from other

dimensions, which should describe a particular facet of the stressing factors. The procedure will begin with an exploratory factor analysis (EFA) to give a preliminary framework of the underlying dimensions. In the fuzzy approach is common an arrangement of some of the factors within the dimensions identified to create more meaningful groups is necessary after EFA. The new latent structure can be validated using a confirmatory factor analysis (CFA) by using goodness of fit indices ([95, 96] Betti et al., 2015; Potsi et al., 2016).

iii) Calculation of scores for each dimension and aggregation over dimensions

These steps concern the construction of the weights to be assigned to each single item within each dimension and then the aggregation over such dimensions. There are several methods for calculating weights for aggregating different items within dimensions ([97] Filippone et al., 2001). According to the approach proposed by Betti and Verma (1999) [98], within each identified dimension h, the weight wj to attribute to each single item j is computed, as the product between the "prevalence weights" and the "correlation weights": the former depending only on the distribution of item j in the population is defined as a decreasing function of the proportion of deprived in this item; the latter depending on the correlation between item j and the other items (in the dimension concerned) in order to reduce the redundancy produced by highly correlated items. Accordingly, a total index aggregating those of all the dimension can be computed.

The relationship between the computed measures computed for the different dimensions and the IgE level collected for each subject can be analyses, focusing to the identification of the dimensions presenting a closer relationship with pollinosis. A great advantage and a novelty with respect to approaches used so far in the field of allergy [65] is the possibility of identifying equivalent stress levels (identified by the same overall index value) generated by different combinations of the dimensions, potentially accounting for apparently contradictory results already present in the literature. Furthermore, in a second step, to evaluate the relationship between the various dimensions and the pollen allergy, it would be possible to perform fuzzy regressions [99], in which the dependent variables are the fuzzy measures for the various dimensions and the response variable the collected IgE for each patient.

5. Conclusion

The impressive increase in allergy cases in Western lifestyle countries has generated, in recent decades, considerable interest in the study of the relationships between SEP and allergies. However, the results achieved have been contradictory, although the dependence between allergies and individual socio-economic, environmental or lifestyle factors has been clearly shown in different fields of research, including at the physiological level. In this article we have shown through elements already present in literature but previously

not considered in unitary way, that the weakness in the research on the epidemiology of allergies is given by three elements: the lack of an overall assessment of all the variables involved and their relationships; the lack of a methodology allowing the assessment of the multivariate effect of SEP, lifestyle and environment on pathology; the absence of a scientific rationale on the physiological mechanism linking the impact of the above factors and allergies. By identifying psychophysical stress as a lost element in the dependence between SEP and allergy, for the first time we have outlined a physiological mechanism that can bind the two elements, based on the qualification of allergy as a perceptual overload, subject to the Weber-Fechner law. In the light of already known findings, we have outlined an optimal methodology of analysis for the study of the relationships between allergies and SEP, environmental, biological and lifestyle factors. This methodology is based on the use of fuzzy set theory for the assessment of the factors involved, as this is primarily the closest approach to the human cortical column assessment system and, moreover, it allows an optimal quantification of the variables involved, by their fuzzy nature. The illustrated methodology, allowing the evaluation of all the variables involved and being likely to be extended to other factors, opens new perspectives in social and health research, in particular on chronic diseases related to living conditions. To the best of our knowledge, the approach presented here is a novelty in the field of allergy, which, although it had already known the application of soft computing, has never been investigated in the ways suggested here.

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