Cumulative Pollen Concentration Curves for Pollen Allergy Diagnosis

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In the Mediterranean area, patients with seasonal allergic rhinitis are often sensitized to a wide array of grasses, trees, and weeds [1] due to pollen types that are prominent in regions with a Mediterranean climate [2]. Global warming has further increased the duration of pollen seasons, resulting in wide overlaps between several clinically relevant taxa [3].

Given this scenario, pollen calendars are becoming more and more complex as a tool for aerobiologists and physicians [4,5]. Daily symptom monitoring via e-Diaries and graphical representations of airborne pollen data are increasingly used to improve the precision of diagnostic work-ups for pollen allergy [6]. Unfortunately, diagrams illustrating daily pollen concentrations from many different sources in parallel make the interpretation of each of these curves very difficult, ultimately hampering clinicians' attempts to identify the culprit pollen and, therefore, the prescription of specific allergen immunotherapy [7]

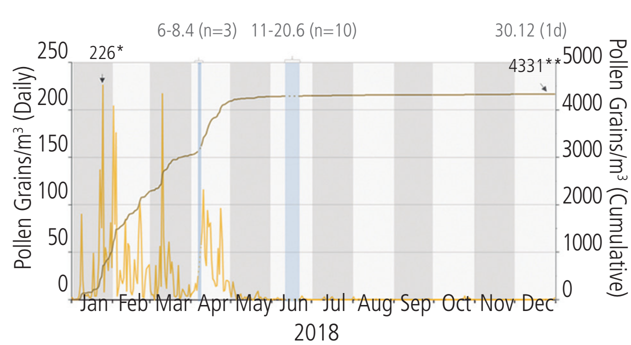
This problem may be solved by using curves based on the cumulative transformation of pollen data. Cumulative pollen concentrations were described over 40 years ago [8], although they are rarely used in aerobiology [9]. To our knowledge, the use of cumulative pollen concentration curves in clinical practice has not been reported to date.

In this study, we aimed to investigate whether the graphical representation of cumulative pollen concentrations over time helps to identify single pollen concentrations in a complex diagram and whether this is perceived as clinically useful by physicians. To this end, we constructed pollen concentration curves as daily cumulative vs absolute values based on pollen data collected during the @IT.2020 study, a multicenter project on pollen allergy and allergen immunotherapy in 9 southern European cities. In this context, aerobiological monitoring was performed from January 1 to December 31, 2018 on pollen from the Cupressaceae, Fagales, Oleaceae, Poaceae, and Urticaceae families, as well as from *Ambrosia* and *Artemisia* species. Complete aerobiological data were available for 6 cities (Valencia, Marseilles, Rome, Messina, Istanbul, and Izmir) during the study period (Tables e1 and e2). Data from the coordinating study center for aerobiological monitoring in Rome were used as a reference (Figure).

The graphical representation of pollen concentrations was based on 2 approaches. First, individual daily pollen concentration values were represented for 7 taxa in 1 diagram. Second, the cumulative pollen concentration was calculated for each day by adding the daily average concentration to the sum of previously counted pollen from the same source.

A workshop with specialized allergists and physicians undergoing training in allergology (Table e3) was held in 4 locations (Rome, Lisbon, Ankara, and Tirana) between March and May 2019. In the framework of the workshop, participants completed a survey on the clarity and usability of absolute and cumulative pollen concentration curves, based on the airborne pollen data obtained in Rome during the year 2018 (Figure and Figure e1). After a short training session on the correct interpretation of graphs based on absolute and cumulative data, physicians completed a questionnaire structured according to the individual perception of daily and cumulative pollen concentration curves, the usability of both curves, and usefulness in a clinical setting.

Overall, 112 physicians completed the survey. Most physicians correctly interpreted information on daily absolute and cumulative pollen concentrations taken from both curves (n_{abs}=94, 83.9%; n_{cum}=90, 80.4%) (Table e4). When asked to evaluate the usefulness of the curves in combination for clinical decision-making, over two-thirds (n=80, 71.4%) of the local physicians judged the information provided as useful from a clinical standpoint. By interpreting each curve alone, only 4 of the physicians (3.6%) judged the information provided by the cumulative values to be useful, while 28 (25%) considered the information given by the diagram portraying only daily absolute values as useful (Table e4). Information on the highest peak daily pollen concentration was sought and found using a combination of both curves. However, the cumulative curve was considered



*Highest peak
**Cumulative pollen concentration in 2018

Figure. Daily absolute (yellow) and cumulative (brown) pollen concentrations of Cupressaceae in Rome 2018. Blue areas indicate linearly interpolated data for missing values.

the only graphical tool able to identify the highest annual cumulative pollen concentration.

In summary, we found that the graphical representation of cumulative pollen concentrations in addition to daily absolute concentration curves was intuitively interpretable for most study participants with regard to the start of the pollen season, trend, and conclusion, as well as for monthly growth and annual cumulative levels (annual total integral). In addition, the curves were clearly differentiated, even when those for various pollen types with overlapping seasons were represented together in the same diagram

Our results make it possible to visualize pollen data for many allergenic pollen types in aerobiologically complex areas by combining detailed information easily and effectively in a single diagram. This is particularly relevant for the management of patients with IgE to pollen extracts whose seasons overlap. Given that pollen-allergic patients are often polysensitized [10], our data suggest a wide area of application for these complementary methodologies in clinical practice. The characteristics of cumulative pollen concentrations open up a range of possible uses in the analysis of the interaction between exposure to allergenic pollen and data recorded in clinical practice, such as patients' symptom curves acquired via e-Diaries [11].

The present study is subject to several limitations. Despite having data from 6 Mediterranean centers, we selected Rome as a reference, even though it is not representative of all aerobiological conditions in the participating centers. This strategy aimed to keep the physician assessment short, thus limiting attrition and tiredness, which could have lowered answer quality if data from all cities had been assessed independently. Moreover, although we acknowledge that aerobiological conditions differ between centers/cities and that this could lead to diverse perceptions on the usefulness of daily absolute or cumulative pollen curves, our proof-of-concept study is the first to compare these 2 data representations and show that both provide relevant information to physicians caring for pollen-allergic patients. Furthermore, the study was performed based on pollen data for 1 year exclusively. However, we believe that the conclusions reached by our study are relatively independent of the year of data collection.

Altogether, our study shows that in southern European countries, the graphical representation of pollen data based on cumulative pollen concentrations is efficient, informative, and perceived as useful in the diagnostic work-up of pollen-allergic patients. Our approach can act at the basis for future investigations, for example, on the role of individual thresholds of absolute and cumulative pollen concentrations eliciting symptoms in most sensitized patients.

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Conflicts of Interest

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The remaining authors declare that they have no conflicts of interest.

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