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Pollen forecasting and its relevance in pollen allergen avoidance

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Abstract

Pollinosis and allergic asthma are respiratory diseases of global relevance, heavily affecting the quality of life of allergic subjects. Since there is not a decisive cure yet, pollen allergic subjects need to avoid exposure to high pollen allergens concentrations. For this purpose, pollen forecasting is an essential tool that needs to be reliable and easily accessible. While forecasting methods are rapidly evolving towards more complex statistical and physical models, the use of simple and traditional methods is still preferred in routine predictions. In this review, we summarise and explain the main parameters considered when forecasting pollen, and classify the different forecasting methods in two groups: observation-based and process-based. Finally, we compare these approaches based on their usefulness to allergic patients, and discuss possible future developments of the field.

Keywords: pollen, aeroallergens, pollen forecasting, pollinosis, allergen avoidance

Abbreviations:
AR: Allergic Rhinitis
APIn: Annual Pollen Integral
CAMS: Copernicus Atmosphere Monitoring Service
CI: Computational Intelligence
DA: Data Assimilation
FAR: False Alarm Ratio
GS: Gerrity Score
LAI: Leaf Area Index
LDD: Long Distance Dispersal
LiDAR: Light Detection and Ranging
LS: Lagrangian stochastic
POD: Probability of Detection
POFD: Probability of False Detection
QoL: Quality of Life
RMSE: Root Mean Squared Error
SPIn: Seasonal Pollen Integral

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1. Introduction

During the reproductive season, seed-plants produce and release male gametophytes in the form of pollen grains, that may carry allergenic molecules. Wind-pollinated plants in particular have to release huge amounts of pollen in the atmosphere to reach a successful reproduction, accidentally exposing the human population to high quantities of pollen allergens for several months of the year. During this period, the immune system of susceptible subjects might start to recognise the inhaled pollen molecules as antigens and produce a hypersensitivity reaction against them, a phenomenon called sensitisation (D'Amato et al., 2007; Erbas et al., 2012). Pollen sensitisation leads to pollen allergy, that can result in two types of symptomatology: an allergic rhinitis (AR) called "hay fever" or pollinosis, or less frequently, allergic asthma (D'Amato et al., 1991; Erbas et al., 2007).

According to the International Study of Asthma and Allergies in Childhood (ISAAC), the global prevalence of pollinosis at the beginning of this century was 22.1% in older children (13- to 14-yr-old) and 11.8% in younger ones (6- to 7-yr-old), with an overall increase per year around 0.3% in both age groups (Björkstén et al., 2008a). The incidence of pollen allergies however displays geographic variability, being influenced by bioclimatic conditions and allergenic plants distribution (Björkstén et al., 2008b).

The perspective of a constant increase in pollen allergy prevalence is concerning because, even if it is not life-threatening per se, AR can lead to illness and disability, and it can affect the quality of life (QoL) in general (Bousquet et al., 2008). According to their duration, severity and frequency, AR symptoms can compromise performance, quality of sleep, cognitive function and work productivity of the allergic subjects. Furthermore, anxiety and depression appear to be common comorbidities to AR, especially when the symptoms are persistent (Canonica et al., 2007). AR can also have indirect implications on apparently unrelated aspects of human health. For instance, epidemiological data show a link between osteoporosis and pollen allergy, along with other hyper-IgE syndromes, and common AR prescriptions can lead to other bone pathologies (Sirufo et al., 2020).

Allergic asthma has a similar effect to AR on mental health, but it causes a more severe inflammation of the lower airways, that may become fatal. Asthma in general is estimated to account for about 1 in every 250 deaths worldwide (Masoli et al., 2004), with an average of over 1300 deaths per day (European Respiratory Society, 2017). The causes behind asthma onset are often difficult to investigate; therefore the exact mortality of allergic asthma alone remains unknown.

Because of this deteriorating effect on QoL, and the high prevalence recorded in some countries, respiratory allergies costs in medical care for both individuals and society can be elevated (Canonica et al., 2007). The major monetary burden of these diseases, however, derives from productivity loss. In 2014, the Global Allergy and Asthma European Network evaluated the socio-economic damage provoked by AR in Europe, in terms of direct, indirect and intangible costs, and missed opportunities. According to the study, the European prevalence of airways allergies (between 20% and 35%) can lead to a loss in productivity from €55 to €151 billion per annum. These figures are higher than in other diseases, even if AR has milder consequences on health. This is because AR and asthma develop at an early age, therefore compromising the entire career of the sufferers through absenteeism or presenteeism (Zuberbier et al., 2014).

Due to this social burden, the possibility to cure and prevent pollen allergies would be beneficial for both the individual and the society. However, an effective therapy to treat the disease is yet to come. Currently, treatment of allergic rhinitis usually combines allergen avoidance, pharmacotherapy, immunotherapy and education (Bousquet et al., 2008). Pharmacotherapy aims to symptomatic treatment and inflammation reduction, and involves H1-anti-histamines, intranasal corticosteroids, topical cromoglycate and oral leukotriene-receptor antagonists (Roberts et al., 2018; Santos et al., 2015). Even severe allergic asthma symptoms can be soothed, using humanised monoclonal antibodies against IgE (Omalizumab) to reduce inflammation of the airway mucosa (Djukanović et al., 2004). Although there is evidence that these therapies can improve QoL of pollen allergies sufferers, patients taking these medications often do not consider their symptoms as completely under control (Canonica et al., 2007).

Allergen-specific immunotherapy is the only AR treatment that acts on the causes of the disease, having the potential to desensitise the patient (Roberts et al., 2018) and to prevent further allergic sensitisation and the development of asthma (Santos et al., 2015). Although it can substantially enhance patients QoL (Niederberger et al., 2018; Novakova et al., 2017; Pfaar et al., 2019), immunotherapy alone at the moment is not sufficient to treat every kind of pollinosis or to completely control AR symptoms (Demoly et al., 2016), so avoidance of the allergens is always required (Bastl et al., 2017c; Canonica et al., 2007; Mothes et al., 2004). An accurate allergic risk assessment is believed to help pollen allergy sufferers planning their movements, precautions and medications in order to avoid pollen allergens or at least mitigate their effect (Burge and Rogers, 2000). While aerobiological monitoring is common practice in several cities worldwide, it can only provide an estimation of allergenic pollen concentrations in retrospective, or in real-time at best (Huffman et al., 2019). Such information cannot be used for the prevention of allergy outbursts as it is, but it must be elaborated into forecasting models to predict the future pollen loads. To our knowledge, the last thorough review on pollen forecasting has been published in 2013 by Scheifinger and colleagues (Scheifinger et al., 2013). Since then, many progresses have been made in the fields of artificial intelligence, remote sensing, computer modelling, Mobile Health and Crowdsensing. This deeply contributed to the fast evolution of pollen and phenological forecasting, allowing to extend old models to new regions (Hall et al., 2020; Oteros et al., 2019), to create new models for wider geographic areas (Sofiev et al., 2020, 2017), and to improve the time resolution of the forecasting (Sofiev et al., 2017). This review aims to give a comprehensive overview on the forecasting models available, and to discuss whether and how they are useful to the allergic subjects in the management of their disease.

2. Pollen indices

To date, monitoring airborne allergenic pollen concentrations is considered the most reliable way to assess the health hazard for pollinosis sufferers worldwide (Galán et al., 2014). Ideally, pollen monitoring networks should have the highest spatial density and temporal continuity possible. In fact, airborne pollen spectra show a spatial variation that depends on geographic position and bioclimatic features of the monitored area, and temporal variation throughout the year, according to plant phenology and pollen morphology. They are also influenced by weather conditions that can modify pollen productivity, emission and dispersion (Bastl et al., 2017c). Moreover, pollen spectra are likely to undergo interannual variations, for example because of irregular flowering cycles (masting), shifts in species composition or meteorological variability (Brennan et al., 2019; Burge and Rogers, 2000; Geller-Bernstein and Portnoy, 2019). To compare pollen data over time, daily pollen concentrations can be summarised into standard indices, such as the Annual Pollen Integral (APIn) and the Seasonal Pollen Integral (SPIn). They are expressed in pollen*day/m^3 and calculated as the sum of the average daily pollen concentrations over the chosen timespan, or the average pollen concentration over the chosen period multiplied by the period duration in

days (Galán et al., 2017). Comparison between these indices from different years allows to detect shifts in airborne pollen seasonality and concentrations for a specific region, helping for example to evaluate the effects of a changing climate on the air quality (Anderegg et al., 2021; Clò et al., 2016; Ziello et al., 2012).
Another important parameter derived from aeropalynological data is the pollen season, that positively correlates with pollen allergies outbursts (Erbas et al., 2018, 2012, 2007; Galan et al., 2010; Geller-Bernstein and Portnoy, 2019; Simunovic et al., 2020). There is no academic consensus over its definition, and according to the literature it can be calculated assuming as start and end day specific percentages of APIn or SPIn, considering threshold levels of daily pollen concentrations, or establishing a number of consecutive days during which a certain pollen type is detected (Bastl et al., 2018b; Pfaar et al., 2017).

However, since the majority of monitoring stations still rely on manual pollen counts, airborne pollen concentrations are provided with at least one day of delay and are not helpful for allergen avoidance. Hence, these data must be translated into a temporally resolved pollen forecast (Šikoparija et al., 2018).

3. Parameters for pollen forecasting

To accurately predict pollen trends, it is useful to consider not only aeropalynological data, but also phenological, meteorological and ecological ones.
Aeropalynological records usually derive from manual pollen counts, and can be accessed through local or international databases (Galán et al., 2014; Scheifinger et al., 2013). However, the majority of pollen and spore monitoring networks are privately owned and therefore their data might not be freely available (Buters et al., 2018). Moreover, monitoring methods have not been standardised between different networks yet, so pollen data from different regions are usually not directly comparable (Bastl et al., 2018b). Another issue with airborne pollen data collection is that monitoring stations are present only in few major cities, hence atmospheric pollen concentrations remain unknown for vast geographic areas. Furthermore, not all of the existing stations perform a continuous monitoring. To overcome these problems, some attempts have been made in the last years to infer airborne pollen concentrations from the number of internet searches and tweets about pollen allergy, but this field is still far from being accurate (Gesualdo et al., 2015; Hall et al., 2020; Kmenta et al., 2016). On one hand, the number of tweets and Google Trends searches on allergic rhinoconjunctivitis was proven to correlate with pollen concentrations, especially during the early pollen season, when there is also a clear causality between the two parameters (Gesualdo et al., 2015; Hall et al., 2020). On the other hand, this approach suffers from various biases associated with the exact geo-localisation of the allergic subject, the local internet consumption, and the keywords used to detect tweets and searches (Gesualdo et al., 2015). Moreover, when applying this method to sparsely populated areas, the sampled population might not be statistically relevant.

A more robust solution to fill in spatial gaps in pollen monitoring, not explored in Scheifinger's work, is to employ a group of statistic interpolation techniques, called kriging techniques. They are probabilistic methods that can model the spatial behaviour of pollen concentrations in unmonitored areas, using pollen records from adjacent monitoring stations. The high spatial autocorrelation of daily pollen concentrations in fact makes them fit for the application of these geostatistical methods (Della Valle et al., 2012; Oteros et al., 2019; Picornell et al., 2019). Multivariate kriging (cokriging) in particular has been used for this purpose, assuming as covariable a parameter that characterises sites with similar pollen emissions, such as the altitude or meteorological factors (Oteros et al., 2019; Picornell et al., 2019; Rojo and Pérez-Badia, 2015). Cokriging can also be combined with other models to weight in additional factors influencing the spatial distribution of airborne pollen, like the rainfall effect (Oteros et al., 2019). For each pollen type, internal validation of cokriging results can be performed calculating the determination coefficient R^2, the Root Mean Squared Error (RMSE), or the Mean Absolute Error (MAE); while external full cross-validation usually relies on Leave-one-out cross-validation (LOOCV) methods, and the results can be expressed as accuracy rates. According to these metrics, cokriging provides an accurate estimation of mean daily pollen concentrations in unmonitored areas, with relatively high spatial resolution (1 Km^2) but low time resolution (24-hour intervals). The atmospheric concentration of some pollen types however cannot be accurately described by cokriging, because the spatial distribution of their sources is driven by factors that are difficult to model (*e.g.* ruderal, ornamental or endemic species). For this reason, spatial interpolation could benefit from an accurate vegetation inventory of the region (Oteros et al., 2019; Picornell et al., 2019). Another promising approach for spatial interpolation of pollen data is the use of convolutional neural networks, that can predict pollen concentrations faster than kriging, and with similar or higher accuracy (Navares and Aznarte, 2019).

An interesting new source of aeropalynological data for pollen forecasting comes from the automatic pollen monitoring networks, that can provide real-time airborne pollen concentrations with high temporal resolution and continuity. Considered as a future possibility in Scheifinger and colleagues review (Scheifinger et al., 2013), in the last years automatic pollen sensors have been rapidly gaining accuracy and precision in pollen classification, and their results have already been employed in forecasting studies (Clot et al., 2020; Huffman et al., 2019; Sofiev, 2019).

As an alternative to aeropalynology, pollen forecasting can rely on phenological data providing the timing of pollen emission. Phenological data are collected worldwide by national networks using different technologies, from the traditional systematic observations *in situ* and *ex situ* (*e.g.* the International Phenological Gardens) to the most advanced techniques of citizen science and remote sensing (Scheifinger et al., 2013). Remote sensing in particular is a rapid-evolving field that allows to collect ecological vegetation data using satellites and unmanned aerial vehicles (Maes and Steppe, 2019). In fact, these instruments can be equipped with sensors that provide high resolution aerial photographs, multi-spectral or hyper-spectral composite images, or Light Detection and Ranging (LiDAR) data. The analysis of different spectral wavelengths and geometric features, often elaborated into ecological indices, allows to describe many aspects of the vegetation, such as the taxa composition or the plant physiological and phenological state. To date, the most advanced technology for remote species recognition is the combination of hyperspectral sensors and LiDAR sensors: the former can identify plant species by their spectral features even in areas with high plant diversity, while the latter analyse the plant structure and the geometry of its components. While this approach is still under development and improvement, several studies successfully employed it to create or update vegetation inventories (Pecero-Casimiro et al., 2020, 2019; Rocchini et al., 2018; Shi et al., 2018). This approach can also help overcoming the problems created by different national data collection approaches when forecasting pollen concentrations over vast geographic regions (Sofiev et al., 2006). Moreover, the possibility offered by the remote sensing to frequently monitor vast areas with a standard approach, gives the opportunity to better understand the relationship between variations in plant distribution and phenological state, and airborne pollen concentrations (Huete et al., 2019). Unfortunately, the remote monitoring of plant phenology is still problematic because it requires multi-seasonal satellite observations to match with ground-based visual analysis. The relationship between the phenology signature, derived from the spectral analysis of the leaves, and the actual phenological stage recorded in the filed, in fact, does not always hold true, and it requires specific expert knowledge to be interpreted (Tomaselli et al., 2017). However, it has been recently demonstrated that satellite data from the sensor MODIS, elaborated into the Enhanced Vegetation Index (EVI), tend to correlate with pollen concentrations on a local level, and that the use of Machine Learning techniques can help combining satellite data with ground-based data, with the potential to implement this relationship in pollen forecasting (Huete et al., 2019).

Both phenology and plant species composition vary between different sites, therefore forecasting models are usually developed for specific plant groups and regions (Levetin and Van de Water, 2003). Since phenology networks have more densely distributed stations and older records than air quality networks, they can supply to spatial and temporal gaps in the airborne pollen data series. Besides, the independent evolution of the two networks implies that their monitoring is not coordinated, with palynological records accounting for a higher botanical diversity than phenological ones (Scheifinger et al., 2013). Pollen production and dispersion is also influenced by environmental factors, that are accounted for by many forecasting approaches. Meteorological parameters for pollen forecasting can be either actual values from historical records or real-time monitoring, collected by meteorological stations, or future values estimations (Norris-Hill, 1995). These parameters are usually evaluated individually, but they can also be elaborated into bioclimatic indices. Bioclimatic indices could be more useful than individual meteorological variables when forecasting the pollen pre-season, since in this period they show a better correlation with mean daily pollen concentrations (Valencia-Barrera et al., 2002). Furthermore, since bioclimatic features modify plants phenology, it is important to assess bioclimatic similarity when comparing pollen forecasting models applied in different regions (Valencia-Barrera et al., 2001).

4. Observation-based forecasting

Pollen forecasting is based on two broad categories of models: observation-based and process-based. The proportion of papers mentioning the different types of forecasting are represented in the Supplementary Figure 1. Observation-based models, sometimes referred as empirical models, are statistic elaborations of real aeropalynological, phenological and environmental data, collected in a specific region for several years (Tab. 1, Fig. S1A). They are also called receptor-oriented models, because they aim to estimate pollen concentrations that pollen traps (receptors) will record, without making assumptions on their sources and atmospheric dynamics (Norris-Hill, 1995; Ranzi et al., 2003; Scheifinger et al., 2013; Šikoparija et al., 2018). Depending on the application, these predictions can be short-term, seasonal, or long-term. Short-term pollen forecasting is performed during the main pollen season, when meteorological conditions can cause daily variations. Seasonal forecasts are the most common, and they calculate start date, severity and peak levels of pollen season. Long-term forecasts aim to detect trends in seasonal pollen levels due to large-scale environmental modifications, and they require at least 20-years records of airborne pollen (Levetin and Van de Water, 2003).

The most popular and simple observation-based model is the calendar forecast. It uses flowering seasonality or aeropalynological data from the past years to find a medium trend. Pollen calendars are commonly presented as graphical descriptions of airborne concentrations for different pollen types during the year, outlining the shape and the duration of pollen seasons (Ranzi et al., 2003; Šikoparija et al., 2018). For a more accurate forecasting, records of meteorological parameters can be included in the calculation. Factors that could affect pollen trends are for example temperature, rainfall, hours of sunshine, cloud cover, relative humidity, wind speed and wind direction. Depending on the context and the pollen type, variations in one of these parameters may explain most of the pollen concentrations variability (Norris-Hill, 1995). The simplest way to evaluate these relations are regression and correlation analysis, that model past pollen concentrations relationship with one or more meteorological factors. Correlation or regression coefficients are then used to estimate future pollen concentrations. The same approach can be used to forecast the pollen season based on shifts in plant phenology (Scheifinger et al., 2013). However, calendar models seem to be nearly as efficient (Šikoparija et al., 2018).

A downside of the all the previous models is that they do not consider the timescale. When focusing on this aspect, time-series models are generally preferred. The Box-Jenkins method, an autoregressive moving average (ARMA) model, is regarded as a standard time-series model in aerobiology. Nonetheless, more advanced approaches are available, such as the Holt-Winters method (Aznarte et al., 2007; Ranzi et al., 2003; Scheifinger et al., 2013). However, because of the chaotic component in pollen time-series, Computational Intelligence (CI) will probably be the turning point for the observation-based models since it appears to better describe complex and non-linear phenomena than statistical models. Common CI applications in pollen forecasting are machine learning models such as the neural networks or the random forests. Neural nets can also be combined with fuzzy-rule based systems to obtain neuro-fuzzy models. Neural and neuro-fuzzy models a higher forecasting accuracy than traditional linear approaches in the comparison between predicted and measured pollen concentrations, especially with pollen concentrations higher than 50 grains/m^3 (Aznarte et al., 2007). To date, different machine learning and advanced machine learning models are available for pollen forecasting, considering phenological and environmental parameters as well, often measured via satellite (Aznarte et al., 2007; Huete et al., 2019; Zewdie et al., 2019). Another innovative approach is the Hidden Markov Model (HMM), a stochastic model that uses the current state of the system to predict the probability of different future scenarios. The peculiarity of this method is to contemplate stochastic variations caused by mast cycling, particularly useful in *Betula* pollen forecasting (Levetin and Van de Water, 2003; Tseng et al., 2020).

	Observation-based forecasting						
Approach	**Simple statistical analysis**		**Time-series analysis**			**Stochastic approach**
Method	Calendar	Regression analysis, correlation	ARMA	Time-series decomposition	Machine-learning	Hidden Markov Model (HMM)
Examples	Pollen calendar, phenological calendar	-	Box-Jenkins method	Holt-Winters method	Neural networks, Random forests, Neuro-fuzzy models	-

Input	Past pollen concentrations, Past phenological observations	Past pollen concentrations, Past phenological observations, Meteorological parameters (past or forecasted)	Past pollen concentrations, seasonality	Past pollen concentrations, seasonality, cycle, random perturbation	Past pollen concentrations, Past phenological observations, Meteorological parameters and their thresholds	Past pollen concentrations, plant phenology, Past meteorological parameters
Output	Shape and duration of future pollen season	Shape and duration of future pollen season	Future atmospheric concentrations of some pollen types	Future airborne pollen concentrations	Probability of future scenarios	Future SPIn, considering mast cycle
Applicability	Routine seasonal forecasting	Seasonal forecasting when there is strong inter-annual meteorological variability	Pollen forecasting for specific studies where the timescale is important				Seasonal forecasting when pollen concentrations are influenced by stochastic variations
Bibliography	(D'Amato et al., 1991; Šikoparija et al., 2018)	(Norris-Hill, 1995; Scheifinger et al., 2013)	(Ranzi et al., 2003; Scheifinger et al., 2013)	(Aznarte et al., 2007)	(Arizmendi et al., 1993; Aznarte et al., 2007; Huete et al., 2019; Lops et al., 2020; Ranzi et al., 2003; Zewdie et al., 2019).	(Tseng et al., 2020)

Table 1 *Main features of observation-based pollen forecasting models*

5. Process-based forecasting

Process-based models, also known as simulation models, are built on a-priori assumptions about pollen dispersal and plant phenological responses to environmental factors. These models aim to forecast pollen production and release by the source plant and to reconstruct its journey from the source to the air sampler, therefore they are also defined source-oriented (Ranzi et al., 2003; Scheifinger et al., 2013; Šikoparija et al., 2018).

5.1 Process-based phenological models

Some process-based methods start from the assumption that pollen season overlaps with flowering season. They are defined process-based phenological models, and predict the beginning, the peak and the end of the pollen season as a function of environmental factors (Tab. 2, Fig. S1B) (Scheifinger et al., 2013). Two main events are thought to influence flowering season entrance: chilling temperature, that breaks bud dormancy, and forcing temperature (or thermal forcing), that stimulates bud development. The timing of these events can be elaborated into bud-burst models to produce a phenological forecast. While temperature appears to be the main driver of flowering for temperate climate trees, pollen season of herbaceous taxa and tropical and Mediterranean trees tends to correlate more with precipitations and photoperiod instead. Photoperiod in particular can be assumed to determine the moment when temperatures start to affect bud development (Migliavacca et al., 2012; Siniscalco et al., 2015). More flexible and generalised models, able to detect the principal

phenological control in a certain dataset, are also available (Scheifinger et al., 2013).
These process-based models
Phenological projections hold some degrees of uncertainty, associated to parameters, structure and drivers of the model (Migliavacca et al., 2012). Since each species has its peculiar environmental requirements, specific models and parameters should be selected for different plant groups (Scheifinger et al., 2013; Siniscalco et al., 2015). Nevertheless, different studies have observed interannual changes in environmental requirements for the same species, underlining how the relations between phenology and environment are yet to be fully understood (Siniscalco et al., 2015). The less controllable and quantifiable uncertainty associated to phenological models however is due to model drivers, and it is mainly caused by unpredictable changes in the future climate. All these problems can be minimised by using a model-data fusion approach that accounts for the overall model uncertainty (Migliavacca et al., 2012). Another major issue of phenological forecasting is that local flowering and pollen seasons match only when long distance dispersal (LDD) contribution to the pollen records is negligible (Scheifinger et al., 2013).

5.2 Process-based dispersal models

Although around 90% of wind-borne (anemophilous) pollen grains falls within 100 m and 2.7 km from its source, the remaining 10% might travel from hundreds to thousands of kilometres (Green et al., 2018). Pollen dispersion is promoted by air masses movements and turbulences, opposed by gravity (dry deposition) and rain (wet deposition), and it is influenced by the chemico-physical modifications pollen can undergo during the process. In dry atmospheric conditions, around 50% of the total pollen emitted by anemophilous species is estimated to be transported more than 10000 km further from its source, with a half-lifetime of at least 1 day (Sofiev et al., 2006). In some cases, this LDD component can significantly alter local pollen records, for example when wind-pollinated species have dense extra-regional populations (Sofiev et al., 2006; Zink et al., 2012).
Thus, to better approximate future pollen concentrations, it is useful to model pollen emission and pollen dispersion as separate events (Kawashima and Takahashi, 1995; Sofiev et al., 2006).
First emission models developed for this type of process-based forecasting estimate pollen emission based on the relationship between weather conditions and quantity of pollen released into the atmosphere, derived from experimental data (Cai et al., 2019). Kawashima and Takahashi (Kawashima and Takahashi, 1999) pioneered this approach, calculating the potential pollen emission of a uniformly flowering source, based on its correlation with hourly measures of air temperature and wind speed, and on the number of male flowers estimated from the variations in summer temperatures. Similarly, Schueler and Schlünzen (Schueler and Schlünzen, 2006) considered the pollen emission as a function of the pollen production over a certain period. The pollen production in this case was estimated from the relationship between actual pollen concentrations in the tree crown, and three meteorological parameters (wind speed, relative humidity, and temperature), measured with a two-hour resolution. Comparison with actual pollen levels recorded at the source site proved this estimation acceptable, although not very precise. More articulate emission models based on empirical data have been developed, that pay more attention to the biological and biometric features of the source plant. An early example of this approach is provided by Hidalgo and colleagues (Hidalgo et al., 2002), who employed neural networks to calculate the emission sub-model, based on three parameters: (I) the characteristics of the previous pollen seasons,

formulated as the relationships between past pollen counts and meteorological data; (II) the dispersion factors, that included meteorological conditions, source plants abundance and distribution, and local topography; (III) the total pollen production, estimated empirically as the number of flowers per tree, anthers per flower, and pollen grains per anther. Another empirical emission model was proposed by Helbig and collaborators in 2004 (Helbig et al., 2004), that has the advantage to be very general, so that it can be adapted to different plant species. This model starts from the definition of pollen production as the maximum number of pollen grains recorded for a plant species during the pollen season. This maximum quantity is emitted in time by the source plant, according to the characteristics of the species, and in particular: (I) the likelihood to bloom in a certain day of the season; (II) the maximum pollen quantity that can be emitted from a certain area minus the pollen already emitted, that depends on the LAI and the height of the canopy; (III) the friction velocity required for the pollen release; (IV) the threshold temperature, humidity and wind speed required for pollen emission (Cai et al., 2019; Helbig et al., 2004). Starting from the same inputs, a semi-mechanistic emission model based on the mass balance of pollen emission fluxes from all the sides of the crown has been recently proposed (Cai et al., 2019). Some of the parameters and assumptions of this model however are associated with significant uncertainties, and the modelled emissions have only a medium correlation with actual pollen records for the area.

Emission models can also be based on long-term phenological observations (Sofiev et al., 2006) and on the aforementioned phenological models (Duhl et al., 2013; Siljamo et al., 2013; Sofiev et al., 2015a, 2006). For instance, the “double-threshold air temperature sum” is a phenological emission model built on the direct proportionality between the flowering stage and the heat sum accumulation occurred between two temperature thresholds, and it allows to model the probability of an individual tree to enter the flowering stage. It takes into account other meteorological factors as well: ambient humidity and precipitations, that decrease the pollen emission; wind speed, that promotes it; and atmospheric turbulence, that has significant positive impact on pollen emission only in a scenario close to free convection. The accuracy of this method varies according to the study area (Sofiev et al., 2015a). Phenological emission models can also be calculated by CI, using for example the Random Forest machine learning technique, that was proven to explain 50% of the variance when comparing the predicted and recorded pollen concentrations over a missing test year (Huete et al., 2019).

Atmospheric pollen dynamics instead are described by dispersal models, considering both environmental factors and pollen features, such as shape, density, dimension, and viability (Tab. 3, Fig. S1C) (Sofiev et al., 2006; Zhang et al., 2014). Distant pollen sources can be mapped using vegetation inventories or solving the inverse dispersion problem. In the latter case, when a pollen monitoring station records a possible LDD event, the source is identified by reconstructing the pollen trajectory from the source to the air sampler (Sofiev et al., 2013, 2006).

First pollen dispersion models were based on statistic elaborations (Helbig et al., 2004; Kuparinen, 2006). They can be integrated as sub-models in more complex, fully mechanistic dispersion models. The latter derive from the atmospheric physics principles that describe the motion of airborne particles. They consider factors such as gravity, wind speed, and turbulence, to explain pollen dynamics based on concurrent environmental conditions. More specifically, they are based on the advection-diffusion equation, that is an accurate approximation of pollen noninertial motion, approached with Eulerian or Lagrangian methods (Kuparinen, 2006; Nguyen et al., 1997; Sofiev et al., 2006).

In general, inputs required by mechanistic dispersal models are: a map of the source plants distribution, the pollen emission sub-model, knowledge on the features of the past pollen seasons, and the meteorological forecasting (Sofiev et al., 2013).

In the Eulerian approach, airborne particles are treated as a continuum (Zhang and Chen, 2007), and they are modelled as concentration fields on a grid that is fixed in space and time (Jia et al., 2021; Nguyen et al., 1997; Young et al., 2000). This method allows to predict the mean concentration of airborne particles for each point of the grid by solving the advection-diffusion equation, mainly using one of the following advection schemes: flux-form finite volume, that calculates the particles transport by mass fluxes at the borders of the grid cells; semi-Lagrangian, that considers the transport from departure points of the grid to an arrival point, and calculates the particle concentrations at the grid points closest to the arrival; or expansion-function, that calculates the solution of the equation using different sets of basis functions (Sofiev et al., 2015b).

Eulerian models for pollen forecasting are usually adapted from existing mesoscale models for air pollutants dispersal, combined with meteorological models. A valid example of the Eulerian approach is the KAMM/DRAIS/MADEsoot, a comprehensive mesoscale model system for aerosol dispersion that produces a three-dimensional forecasting of temporal and spatial distribution of pollen grains (Helbig et al., 2004). Perquisites of this method are to take into account geomorphological heterogeneity, meteorological spatial variability, species-specific pollen emissions, wet deposition and resuspension. Other examples of Eulerian models are mentioned in Table 3. A multi-model ensemble has been published as well, calculated as the arithmetic average and median of the results from seven Eulerian models fields per hour. This ensemble, now implemented in the Copernicus Atmosphere Monitoring Service (CAMS) forecast (www.regional.atmosphere.copernicus.eu), showed higher correlation coefficients with observed daily mean pollen concentrations than the individual models alone (Sofiev et al., 2015a).

However, the Eulerian approach requires a number of simplifications that can limit the use of the model in many occasions (Kuparinen, 2006). For example, they do not take into account the effect of tree canopies. In fact, variations in leaf-area index and the foliage shedding of deciduous trees have been proven to strongly influence the turbulences within the canopy and therefore to affect pollen dispersion (Nathan and Katul, 2005). Furthermore, the application of Eulerian models is still hindered by their huge computational costs, and by the numerical diffusion effect produced by the grid system (Jia et al., 2021).

Another way to predict mean pollen concentrations in a specific area is the Lagrangian approach, that considers airborne particles as a discrete phase, and models their individual paths in a continuous space by applying a deformation to either the grid or the coordinates of a fixed grid (Nguyen et al., 1997; Young et al., 2000; Zhang and Chen, 2007). Lagrangian models for pollen forecasting are usually based on the “Lagrangian particle random-walk” method, that calculates the trajectory of thousands to millions particles, with the advection modelled on the wind dynamics and the diffusion simulated by random relocation (Nguyen et al., 1997; Sofiev et al., 2013). In particular, the Lagrangian Stochastic (LS) turbulence model is considered to give a realistic simulation of temporary airflows. An example of LS model for pollen dispersal is the SMOP-2D, that simulates individual pollen grains path from their emission to their deposition, considering wind turbulence, pollen aerodynamic features, canopy structure and landscape heterogeneity (Jarosz et al., 2004; Kuparinen, 2006). Using surface pollen spectra and vegetation data as input, it has been proven that LS models can give a more accurate approximation of the observed pollen concentration than some classical Eulerian models when considering long-range events of pollen dispersal (Theuerkauf et al., 2016). Other examples of Lagrangian models are listed in Table 3. In general, Lagrangian models account for different factors that drive LDD events, including the irregular and autocorrelated turbulent fluctuations, and this tends to give a better approximation of the dispersal curve (Kuparinen, 2006). However, the potential of this approach is hampered by the topographical complexity of the study area, that can significantly complicate the modelling of the particles path (Sofiev et al., 2013).

There is not common agreement over the better approach to choose when forecasting pollen concentrations based on their dispersal. While some authors consider Lagrangian models to be more realistic in describing pollen atmospheric dynamics (Kuparinen, 2006; Theuerkauf et al., 2016), others prefer a more comprehensive Eulerian approach that seems a better fit especially in areas where airflow movements are difficult to predict, such as the mountains (Sofiev et al., 2013). In general, all the models have some limits, and the model choice is guided by the features of the study area or the data available. It is interesting to notice that SILAM, a global-to-meso-scale model for pollen forecasting, has been developed with both Eulerian and Lagrangian approaches, allowing to choose the better option for the study (Sofiev et al., 2015b; Veriankaitė et al., 2010).

Quasi-mechanistic models have also been proposed to explain pollen dispersion. They consider pollen dynamics to be probabilistic, describing pollen dispersion as a Brownian motion with drift, integrated with biological and aerodynamic factors (Klein et al., 2003).

While pollen dispersal can be approximated with a certain accuracy, however, this type of forecasting is still limited by the uncertainties associated with the emission sub-model. In fact, unpredictable changes in the future weather or in the plant physiology can substantially modify the starting day of the flowering season, or the pollen productivity, compromising pollen forecasting reliability. While the knowledge of the characteristic of the past pollen season can be useful to train the model, long-term averages of past observed data are not good predictors of the future pollen concentrations (Ranta et al., 2006; Sofiev et al., 2006). This problem can be approached by calculating the probability of the pollen produced by a certain source (*e.g.* forests, prairies) to affect a receptor area, with the source considered constant in time, and not taking into account the seasonality and the variations in pollen production and release. This way, it is possible to define areas of risk that are likely to be reached by allergenic pollen via LDD. This information is then manually integrated with updated qualitative data on the phenological state of the plant sources: if the flowering has started, then the probability is converted into forecasted pollen concentrations. This approach was proven to better approximate the observed pollen concentrations than the deterministic approach to pollen emission, although it still was not very accurate in some cases (Sofiev et al., 2006). Other options to improve the predictions of mechanistic forecasting models could be the use of either the “dynamic phenological emission” approach, that is an observation-based phenological model including real-time meteorological data, or the “emission data assimilation” approach, that relies on real-time phenological or aeropalynologycal data assimilation (DA) (Sofiev, 2019; Sofiev et al., 2006). The latter option has been recently tested using real-time aerobiological records for data assimilation in the SILAM model. DA is a relatively recent technology that allows to bring the model predictions closer to the observations, and it could be potentially used to improve the pollen forecasting quality throughout the season, predicting accurate airborne pollen concentrations several days ahead. Unfortunately, the atmospheric lifetime of pollen grains turned out to be too short for DA corrections, making them ineffective in a few hours when applied to forecasting (Sofiev, 2019).

	Process-based phenological models					
Model type	Thermal forcing only	Chilling only	Forcing temperature and chilling	Models including photoperiod	Models including photoperiod and water availability	Generalised Phenological Models
Examples	Spring warming (SW), Growing Degree Day (GDD)	-	Sequential, Parallel, Alternating, Deepening Rest, Four Phases	-	-	Unified model, Promotor-Inhibitor model
Input	Starting day of temperature accumulation, Spring daily temperatures, Plant phenology, Plant distribution	Starting day of temperature accumulation, Winter daily temperatures, Plant phenology, Plant distribution	Starting day of temperature accumulation, Winter and spring daily temperatures, Plant phenology, Plant distribution	Winter and spring daily temperatures, Plant phenology, Photoperiod, Plant distribution	Winter and spring daily temperatures, Plant phenology, Photoperiod, Soil water availability, Plant distribution	Environmental and phenological data, plant dataset
Assumptions	Pollen season begins when the sum of forcing units reaches a threshold value	Pollen season begins a certain time after the sum of chilling units reaches a threshold value	Pollen season start is defined by a combination of chilling and forcing units	Photoperiod defines the starting day of temperature accumulation, pollen season start is defined by a combination of chilling and forcing units	Photoperiod defines the starting day of temperature accumulation, pollen season start is defined by a combination of meteorological factors	Plant responses to a combination of environmental factors can be calculated with flexibles models
Best fit	Late-flowering trees in temperate regions	*Olea europaea* and *Alnus glutinosa* in Mediterranean reagions	Early-flowering trees in temperate regions (*e.g. Alnus* sp., *Acer* sp.)	Tropical and Mediterranean trees	Herbaceous species, tropical and Mediterranean trees	Complex datasets
Output	Starting date, peak and end of the next pollen season					
Bibliography	(Scheifinger et al., 2013; Siniscalco et al., 2015)					

Table 2 *Description of the principal process-based phenological models used in pollen forecasting*

	Pollen dispersion models			
Model type	**Numerical models**	**Fully mechanistic models**		**Quasi-mechanistic models**
Approach	Statistic	Eulerian	Lagrangian	Probabilistic
Examples	Multiple regression equation	ADMS, CHIMERE, COSMO-ART, EURAD-IM, KAMM/DRAIS/MADEsoot, Kawashima & Takahashi model, LOTOS-EUROS, MATCH, METRAS, MOCAGE, SILAM Eulerian, WRF-MEGAN-CMAQ	CALMET/CALPUFF, HYSPLIT, PAPPUS, SILAM Lagrangian, SMOP-2D	-
Input	Past pollen concentrations, Meteorological parameters	Source plants distribution, Information on plant phenology and pollen season characteristics, Emission model, Meteorological model, Boundary layer, diffusion intensity, turbulent mixing.	Source plants distribution, Information on plant phenology and pollen season characteristics, Emission model, Meteorological model, Horizontal and vertical dimensions of the grid.	Male flowers height, Pollen settling velocity, Wind direction and speed, Turbulence
Principle	Pollen dispersion is modelled from the relation between pollen concentrations and meteorological factors.	Analytical approach. Pollen is modelled as a continuum, and its future concentrations in a certain point of a fixed grid are calculated by analytically resolving an advection-diffusion equation with Eulerian approach.	Simulation approach. Pollen dispersion is modelled by simulating the trajectories of individual particles.	Pollen dispersion is modelled as a three-dimensional Brownian motion with drift.
Output	Future pollen concentrations in a certain area	Future pollen concentrations in a certain area		Probability that a pollen grain falls in a certain point
Limits	Useful as sub-models for more complex models	Problems in evaluating pollen emissions, difficulties in simplifying biological factors, high computational costs, numerical diffusion effect.	Problems in evaluating pollen emissions, difficulties in modelling pollen trajectories in areas with complex topography.	Designed to model pollen dispersion in pollination events
Bibliography	(Helbig et al., 2004; Kuparinen, 2006; Scheifinger et al., 2013)	(Helbig et al., 2004; Hunt et al., 2001; Kawashima and Takahashi, 1999, 1995; Müller-Germann et al., 2015; Schueler and Schlünzen, 2006; Siljamo et al., 2013; Sofiev et al., 2015a, 2015b; Veriankaitė et al., 2010; Zhang et al., 2014; Zink et al., 2012)	(Hidalgo et al., 2002; Jarosz et al., 2004; Kuparinen, 2006; Müller-Germann et al., 2017; Sofiev et al., 2013, 2006; Zhang and Han, 2008)	(Klein et al., 2003)

Table 3 *Description of principal pollen dispersion models used in process-based pollen forecasting*

6. Pollen loads and forecasting skills

To be disseminated to the public, predicted pollen concentrations must be translated into discrete categories indicating the allergenic risk they pose. This is not an easy task, because the physical response to aeroallergens exposure depends on many factors: aeroallergens concentrations, air pollution levels, meteorological parameters, and other environmental factors (Caillaud et al., 2014; Cecchi, 2013; D'Amato et al., 2007; Karatzas et al., 2013; Mothes et al., 2004). Genetics and epigenetics of the subject also play an important role in the manifestation of allergic symptoms. Thus, even when considering pollen exposure alone, *e.g.* exposing the subjects to fixed pollen concentrations in a controlled environment (pollen chamber), there is a certain subjectivity in the timing and the intensity of the allergic reaction (De Weger et al., 2013; Mothes et al., 2004).

Threshold values for symptom development have been defined throughout the years, to help allergic patients and medical personnel to understand pollen information and manage allergy symptoms. These thresholds have been established by evaluating the reactions of allergic patients to pollen exposure in "real life" conditions (De Weger et al., 2013). The most common method to achieve this is by asking the subjects to record their symptoms in a diary, and then correlating these symptoms to daily pollen levels (Bastl et al., 2014; De Weger et al., 2013; Kmenta et al., 2014). In some cases, this correlation is corroborated by weekly information provided by a network of allergologists (De Weger et al., 2013). During the last decade, interactive symptom diaries accessible to allergic patients and their physicians have been developed. They can be websites, such as www.pollendiary.com, www.airrater.org, www.allergymap.gr, and www.allergieradar.nl (Bastl et al., 2020, 2018a; Jones et al., 2020; Kalogiros et al., 2018; Pfaar et al., 2017); or specific apps like ARIA, MASK-air, and Allergy Diary (Bousquet et al., 2019; Caimmi et al., 2018; Clot et al., 2020; Kalogiros et al., 2018). While this Crowdsensing approach provides real-time and standardised data, the determination of pollen threshold levels for symptoms development remains problematic, and there is no general consensus on how they should be calculated (De Weger et al., 2013). Moreover, although there is a proven correlation between allergic symptoms and mean daily pollen concentrations, personal exposure of the subject likely differs from the pollen concentrations recorded by the monitoring station (Berger et al., 2014; De Weger et al., 2013; Levetin, 2004). The variability in pollen monitoring approaches adopted by different stations also represents an important limit to the standardisation of pollen risk thresholds (Levetin, 2004). Moreover, the exposure level that can cause an allergic reaction also depends on the pollen type. In general, average daily airborne pollen concentrations that can trigger an allergic reaction range from 0 to 100 pollen grains/m^3 (Pfaar et al., 2017), but there is a variety of scales and categories that can be used to describe the airborne pollen concentrations and their associated risk. These values are accurately described and summarised by de Weger and colleagues (De Weger et al., 2013). Hence, while it is common to classify pollen loads using "Very Low", "Low", "Medium", "High", and "Very High" (or "Extreme") categories, it is important to acknowledge that the pollen concentration range included in the same level might variate among monitoring and forecasting providers, and aeroallergen considered (De Weger et al., 2013; Gehrig et al., 2018; Silver et al., 2020; Sofiev et al., 2020).

Another problem to address when disseminating pollen forecast for health managing purposes is its accuracy.

When estimating a model performance, the most common statistics employed to compare observed and predicted pollen concentrations are the correlation coefficients and the RMSE. Some authors also applied other metrics like Theil's U statistic, to obtain a scale-free measure, or MAE that is less sensitive to large errors than RMSE (Aznarte et al., 2007; Dennis et al., 2009; Picornell et al., 2019; Sofiev et al., 2017; Valencia-Barrera et al., 2002). Another useful metric is the accuracy rate or model accuracy (MA), that can be calculated as the relationship between the number of correct forecasts and the number of total forecasts (Picornell et al., 2019; Siljamo et al., 2013).

When the aim of the forecast is to inform the public on the allergic risk, however, it is important to evaluate mode accuracy and consistency in predicting different pollen levels. While the aforementioned statistics can also be applied to categorical pollen concentrations, for this purpose probabilistic skill-based indices and threshold-based statistics are preferred (Emmerson et al., 2019; Ritenberga et al., 2016; Siljamo et al., 2013; Zink et al., 2013). These metrics can be calculated for all the pollen load levels estimated by the forecast (Bastl et al., 2017b), or they can be based on a single threshold separating low and high daily pollen concentrations (De Weger et al., 2013; Siljamo et al., 2013).

When considering just one threshold, the Hit Rate (HR) or Probability of Detection (POD) is used to estimate the fraction of high pollen levels predictions that are correct (high predicted and high observed), while the False Alarm Ratio (FAR) identifies the fraction of incorrect high-level predictions (high predicted and low observed). A complementary measure is the Probability of False Detection (POFD), that calculates the fraction of observed low-concentration days predicted as high. To evaluate the reliability of the predicted high-level days more comprehensively, the relationship between POD and POFD can be estimated through the Odds Ratio (OR) or the Hansen-Kuiper (or True Skill) Score, estimating the chances to observe a high-concentration day when it has been predicted (Emmerson et al., 2019; Gerrity, 1992; Siljamo et al., 2013). Some metrics also evaluate the performance of the forecasting against the probability to obtain the correct prediction by chance. Examples are the Equitable Threat Score (ETS), that measures the skill of a forecast to correctly predict high pollen days, adjusted for the probability to randomly obtain correct forecasts (Emmerson et al., 2019); and the Peirce Skill Score (PSS), that compares the performance of the model to that of a random forecast (Peirce, 1884; Zink et al., 2013).

When evaluating forecasting skills for more than two categories of pollen concentrations, all these metrics should be calculated for each category, considering the occurrence of the desired category as an event, and the occurrence of any other category as a non-event. This means that, when a non-event is both predicted and observed (correct negative), the prediction cannot be automatically assumed as correct (Emmerson et al., 2019; Zink et al., 2013). In this case, the Threat Score (TS) can be applied to evaluate the fraction of correct forecasts, ignoring the correct negatives (Zink et al., 2013).

A limit of these threshold-based metrics is that they do not consider how close the incorrect forecast was to the observed pollen level, in terms of pollen concentrations. For this reason, categorical forecasting evaluation is usually supported by the aforementioned non-categorical evaluation methods (Zink et al., 2013). To avoid low performance estimations of a model due to slight differences between predicted and observed concentrations, it is possible to assume an interval of tolerance around the threshold values, so that the categories have a slight overlap (Bastl et al., 2017b).
Another useful metric is the Gerrity Score (GS) (Gerrity, 1992), that attributes different weights to incorrect predictions, depending on how much they differ from the observed

values. This score also evaluates the forecasting skill relative to the random chance, by rewarding the correct prediction of rare events more than the correct prediction of common events (Emmerson et al., 2019; Gerrity, 1992).

To be useful for allergic patients, pollen forecasting should have high POD and GS, accurately predicting days with high or very high pollen loads, that can cause relevant allergic reactions (Zink et al., 2013). On the other hand, the FAR of the forecasting model should be low, since incorrectly predicting high pollen loads can lead allergic patients to assume unnecessary medications or to avoid outdoor activities (Bastl et al., 2017a).

How these metrics could be clearly communicated to the public along with the forecast, however, is still debated (Bastl et al., 2017b).

7. Dissemination of pollen forecasts

Allergic symptoms can be exacerbated by different environmental and genetic components, but pollen exposure is certainly the most important risk factor for pollen allergic subjects (Bousquet et al., 2019). Aeroallergen monitoring and avoidance in fact represent a primary and secondary prevention strategy respectively for an individual decrease of the risks to develop allergic illnesses (Reid and Gamble, 2009). Knowledge of future pollen loads is perceived by pollen allergy sufferers to be useful for prevention and avoidance, as well as preparation and planning, highlighting a public demand for pollen information (Medek et al., 2019). This information is usually integrated with weather or air quality forecasting, and provided to the public via newspapers and television on a national scale, by websites on a regional scale, and by smartphone applications (apps) on a personal scale (Karatzas et al., 2013). Public consumption of pollen forecasting during the pollen season, recorded by forecasting websites, underlines the concern pollen allergy causes to sensitive subjects, and their need to monitor the situation (Kmenta et al., 2016).
While public access to air quality information is ensured by Governments and international organisations (Karatzas et al., 2013; Monfort et al., 2002) both as ordinary monitoring and incident-event alerts, pollen monitoring and forecasting tend to be overlooked by these regulations (Karatzas et al., 2013).

Nonetheless, in the last decades different Countries have joined efforts in common aerobiology networks and projects, with the creation of national and international websites designed for pollen allergic subjects, that provide daily pollen counts and pollen forecast at different time and spatial resolutions. Examples are www.polleninfo.org for Eurasian countries (Kmenta et al., 2016), www.pollen.com for the USA (Geller-Bernstein and Portnoy, 2019), and www.pollenforecast.com.au for Australian regions. Smartphone apps providing daily pollen forecasts and monitoring allergy symptoms are also available in many countries (Bastl et al., 2017b; Bousquet et al., 2019; Jones et al., 2020; Kmenta et al., 2016), and many weather forecasting websites offer pollen information. All these tools are part of the Electronic Health (eHealth) and Mobile Health (mHealth), defined by the WHO as the medical and public health practice supported by information and communication technologies, and by wireless mobile devices, respectively (Bastl et al., 2020; WHO, 2018).

During the last century, the pollen calendar has been the main source of pollen forecasting available to the public (Fig. S1A), with the advantage to be intuitive and clearly understandable (D'Amato et al., 1991; Gehrig et al., 2018), but with the downsides of a low time resolution and the impossibility to predict uncommon and swift events. Pollen calendars are still employed to disseminate general, long-term information about the future pollen seasons by pollen-monitoring networks, patient organizations, and for medical information purposes (Gehrig et al., 2018), but they are progressively being substituted or flanked by more comprehensive approaches. To better exploit the informative potential of the pollen calendar, a recent study (Gehrig et al., 2018) developed a new form of it, intended for the public consumption as complementary to other forms of forecast. This pollen calendar is based on users' expectation to know the possible occurrence of high pollen levels during a certain period, instead of the mean pollen season. For this purpose, it is not calculated as an average value, but as the 90% quantile of the daily pollen concentrations for each day of the year, in a moving 9-day time window, over 20 years of data. These pollen concentrations are automatically calculated and regularly updated on the website (www.meteoswiss.ch/pollen-calendar), presented as pollen loads levels (low, moderate, high, very high), and can be visualised for individual monitoring stations, regions, or pollen type (Gehrig et al., 2018). Another way to disseminate long-term pollen information is a table with the starting date of the pollen season for the major pollen allergens, obtained by past pollen data and phenological observations. This information is embedded only in few pollen apps, e.g. Pollen and Pollen News, but it tends to be more accurate than daily or hourly forecasts (higher POD), and may help pollen allergic patients to prepare for the pollen season (Bastl et al., 2017b).

However, in the last decades a broad variety of pollen forecasting models have been proposed, in the attempt to obtain more accurate and precise predictions (Fig. S1), although just some of them have been made available for public consumption. Observation-based forecasting methods other than pollen calendars have been employed to disseminate short-term pollen forecasts: for instance, the Spanish Aerobiology Network (REA) offers three-day forecasts generated on a national scale by the University of Cordoba using time-series (Fernández-Rodríguez et al., 2016; Oteros et al., 2019), that are available on the website www.uco.es/investiga/grupos/rea or on the Pollen REA app. Within the possible observation-based approaches, CI seems to give the best approximation of future pollen concentrations, in particular when using machine learning models with a non-linear behaviour, such as neural nets (Aznarte et al., 2007). This approach has been preferred by some pollen forecasting providers, such as the Danish patient association Asthma-Allergy, with their smartphone app Dagens Pollental.

Unfortunately, due to their regional and empirical nature, observation-based models cannot be generalised to wide geographic areas. Furthermore, they rely on real pollen records, usually expressed as mean daily pollen concentrations. This limits the time resolution of these approaches, since they can predict at best the daily concentrations or the starting, peak and end date of the pollen season, but they cannot give detailed information to pollen allergic subjects on the variations of the risk they are exposed to throughout the day (Scheifinger et al., 2013).

Process-based forecasting models instead have higher temporal and spatial resolution than the observation-based ones, and some of them can even weight in the effect of LDD events (Ranzi et al., 2003). In particular, some process-based dispersal models can now estimate future concentrations of 6 pollen types up to 5 days, for wide geographic regions (Sofiev et al., 2020). On the other hand, these models are associated with various uncertainties (Migliavacca et al., 2012), they do not run operationally and are not calculated for all the allergic pollen types (Maya-Manzano et al., 2021). This reduces the value of these forecasts for pollen allergic subjects, making this approach mainly limited to scientific research applications.

Nevertheless, some process-based dispersal models are starting to be employed by forecasting providers as informative tools to alert the public about possible future pollen concentrations, even with hourly resolution. For example, Swiss Federal Office of Climatology and Meteorology MeteoSwiss offers both the aforementioned user-oriented pollen calendar, and hourly three-day pollen forecasts calculated using COSMO-ART model. Similarly, Austrian website www.pollenwarndienst.at allows to choose among various pollen forecasts elaborated by the Medical University of Vienna: phenological calendars indicating the starting date of the pollen season, three-day forecasts in the form of daily pollen concentration maps or daily pollen loads estimated by COSMO-ART, and daily forecasts with hourly resolution created with SILAM. Some of these forecasts are also available for other European countries at the website www.polleninfo.org. Furthermore, the ensemble model embedded in the CAMS website offers a 5-day global pollen forecasting and a 3-day forecasting on a European scale (Sofiev et al., 2020, 2017). CAMS also provides 3-day pollen forecasts to several apps designed for pollen allergic patients, such as BreezoMeter and MeteoPollen (Tab. 4) (Bousquet et al., 2019). The app PASYFO recently developed for Lithuania and Latvia by The Copernicus Project combines SILAM model and CAMS forecasts (Sofiev et al., 2020), while the Austrian app Pollen relies on the SILAM model for daily forecasts (Kmenta et al., 2014), achieving hit rates of 60% on the predicted pollen loads (Bastl et al., 2017b).

These examples, listed in Table 4, are excellences in their field. In fact, many pollen forecasting sources do not specify the method applied, nor they are associated to scientific publications or official institutions. This makes it difficult to evaluate their factual utility to allergic patients. In fact, pollen information disseminated by private or unofficial entities might be subject to conflict of interest or affected by poor data quality (Bastl et al., 2017a, 2017b). Health-related mobile apps in particular often lack of clinical evidence and validation (Matricardi et al., 2020a), and their pollen forecasts tend to have low performance and to be discontinuous, especially when they are published by private companies (Bastl et al., 2017b). Deliberate inaccuracy in pollen forecasting leads to avoidable under- and overestimations of the allergenic risk, because the public is not aware of the forecast performance, resulting in what can be considered a physical injury of the allergic subjects (Bastl et al., 2017a; Bousquet et al., 2019).

Another problem when evaluating the utility of pollen forecasting for allergic patients is the subjectivity of the symptoms, that partly depends on the personal exposure to the allergen. This problem has been addressed with the development of interactive symptom diaries, that allow to produce individual, user-specific symptom forecasting using CI to model the relationship between recorded symptoms, associated pollen counts, and concurrent environmental parameters (Bastl et al., 2014; Kmenta et al., 2014; Voukantsis et al., 2013). A continuous personal monitoring of allergic symptoms and pollen exposure could be the key to improve pollen forecasting in a way that is useful to allergy sufferers, and that can also help health workers to foresee pollen allergy outbreaks and emergency room accesses (Bastl et al., 2014; Pfaar et al., 2017). For this reason, many apps providing pollen information have also integrated a symptom monitoring and forecasting service (Tab. 4) (Kmenta et al., 2016, 2014; Sofiev et al., 2020). It is however important to investigate whether the knowledge of pollen forecasts can have the psychological effect of anticipating pollen symptoms (Pfaar et al., 2017). Moreover, it is challenging to evaluate the real benefits provided by mobile apps to allergy sufferers, especially because of their discontinuous engagement with the app and the impossibility to detect subjective biases in their perception of the symptoms (Bousquet et al., 2019).

App	Website	Availability	Observation-based forecast	Process-based forecast	Day forecasted	Symptoms forecast	Pollen types	Bibliography
BreezoMeter	www.breezometer.com	International	No	CAMS ensemble	3	No	13+	(Bousquet et al., 2019)
Dagens Pollental	www.astma-allergi.dk/dagenspol	Denmark	Neural Networks	No	5	No	6	(Bousquet et al., 2019)
Meteo Allergie	http://www.pollinieallergia.net/	Italy	Pollen calendar, time series	No	7	No	11	(Mateo Pla et al., 2016)
MétéoPollen	www.meteopollen.com	France	No	CAMS ensemble	3	No	Not specified	(Bousquet et al., 2019)
PASYFO	https://atmosphere.copernicus.eu	Lithuania, Latvia	Pollen calendar	CAMS ensemble, SILAM	CAMS: 4 SILAM: 2	Yes	Calendar: 23 CAMS: 4 SILAM: 6	(Sofiev et al., 2020)
Pollen	www.pollenwarndienst.at www.polleninfo.org	Europe	Starting date of the pollen season	SILAM	3	Yes	25	(Bastl et al., 2017b; Bousquet et al., 2019; Kmenta et al., 2014)
Pollenflug Vorhersage	www.wetteronline.de	Germany	Pollen calendar, algorithms	No	7	No	14	(Bastl et al., 2017b)
Pollen-News	www.aha.ch/swiss-allergy-centre	Switzerland	No	COSMO-ART	3	No	14	(Bastl et al., 2017b)
	www.meteoswiss.ch	Switzerland	Pollen calendar	COSMO-ART	3	No	4	(Gehrig et al., 2018)
	www.polleninfo.org	Europe	Starting date of the pollen season	COSMO-ART, SILAM	3	No	COSMO-ART: 4 SILAM: 6	(Bousquet et al., 2019; Sofiev et al., 2006)
	www.regional.atmosphere.copernicus.eu	International	No	CAMS ensemble	5	No	5	(Sofiev et al., 2017)
	https://silam.fmi.fi	Europe	No	SILAM	4	Yes	6	(Sofiev et al., 2017)
	www.uco.es/investiga/grupos/rea	Spain	Time series	No	3	No	14	Rodríguez et al., 2016; Oteros et al., 2019)

Table 4 *Description of mobile applications and websites cited in literature, that provide pollen forecasting to the public specifying the forecasting method applied.*

8. Conclusions

Pollen forecasting is an active research ground that conjugates aerobiology, engineering, physics, and informatics to approximate the complex phenomena of pollen emission and dispersion. To date, many approaches and models are available to forecast future pollen concentrations and the risk they pose to pollen allergic subjects. Observation-based models are the first type of pollen forecasting developed, based on past pollen concentrations and phenological observations (Fig. S1A). They are still employed to provide accurate pollen calendars and pollen season starting dates, allowing allergic subjects to plan in advance their movements and medications. On the other hand, the information is local, averaged, and expressed as weekly or daily values (Scheifinger et al., 2013). In the last two decades there has been a great effort to model the complex relationships between plants and the environment, that influence pollen emission and dispersal (Fig. S1B, C). This approach, called process-based, allows to simulate future pollen dynamics, given the initial conditions of the system. On a direct comparison, process-based models have more potential than the observation-based ones, and some of them can even weight in the effect of LDD events. Nonetheless, their use may be hindered by the computational effort and the amount of data they require (Ranzi et al., 2003). In fact, they need detailed information on geographical and meteorological features of the study area, and a deep knowledge of plant phenology and distribution (Norris-Hill, 1995; Šikoparija et al., 2018; Skjøth et al., 2010). This problem could be partially solved by preparing local or global allergenic plant inventories (Skjøth et al., 2010; Sofiev et al., 2006). Another major issue of process-based models is the uncertainty associated with pollen emission modelling, due to both a lack of knowledge about the process and the unpredictability of future climate scenarios (Migliavacca et al., 2012).

A common problem to all these forecasting approaches is that the airborne pollen data they elaborate are temporally and spatially scattered, and they do not accurately reflect individual exposure. Furthermore, since pollen sampling and counting methods may vary between different monitoring stations (Buters et al., 2018), real and forecasted pollen concentrations calculated in different areas might not be comparable. Comparability issues also arise from the long data collection and the massive computational effort these models require, that discourage the comparison between different models on the same dataset.

Because of all these issues, high forecasting accuracy is difficult to achieve. Complex dispersal models are not run routinely for many pollen types and locations yet, and their application is often limited to scientific research purposes. Process-based dispersion models like SILAM, COSMO-ART, and the CAMS ensemble, are being used by forecasting websites and mobile apps to inform the public on the allergenic risk, often with hourly resolution (Bousquet et al., 2019; Sofiev et al., 2020). Nonetheless, the usefulness of these instruments to pollen allergic subjects is still uncertain. On one hand, pollen information consumption is perceived as important and beneficial by allergic patients, because Electronic Health can help them self-manage their disease and reduce the symptom severity, a crucial issue especially for those living in rural or remote areas (Kmenta et al., 2016; Matricardi et al., 2020b; Sofiev et al., 2020). On the other hand, forecasting pollen levels in remote and underpopulated areas, where no pollen monitoring is in place, is still problematic (Hall et al., 2020; Oteros et al., 2019; Sofiev et al., 2020; Wakamiya et al., 2019). Furthermore, it is difficult to evaluate the reliability of the pollen forecast provided by many apps and websites, since they do not indicate their sources, their data are not be scientifically validated, and they tend to have temporal gaps (Bastl et al., 2017b). If the allergic subject relies on these instruments for his wellbeing, unaware of their probabilistic nature, unreliable pollen forecasting might be even detrimental to his health (Bastl et al., 2017a).

To enhance the value of pollen forecasting, more epidemiological studies correlating allergic symptoms and pollen concentrations are needed, because the severity of the allergic reaction also depends on other factors (Bastl et al., 2018a; Caillaud et al., 2014; De Weger et al., 2013; Sofiev et al., 2020). These studies need to be performed on a global scale, since pollination varies with plant abundance and microclimate, resulting in regionally differences in pollen emission that could affect both the pollen forecasting models and the individual exposure (Bastl et al., 2017b; Reid and Gamble, 2009). For these reasons, a portfolio of quality criteria for pollen monitoring and forecasting was recently suggested in the interest and for the protection of people affected by a pollen allergy (Bastl et al., 2017a).

9. Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

10. Author Contributions

CS, IA, DFG, SDD contributed to the design of the work as well as drafting the work and revising it critically for important intellectual content; then they made the final approval of the version to be published. They agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. In details, the idea to write a review on pollen forecasting was proposed by CS and SDD. CS performed the thorough literature search, designed and wrote the article, with the contribution of all authors.

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