ABSTRACT

Airborne pollens are one of the common causative and triggering agents of respiratory allergy in a changing planetary environment. A growing number of people worldwide are contracting allergic diseases caused by pollens. The seasonal variations in pollens have occurred everywhere and the sensitization rate to pollens has increased in children as well as in adults. Moreover, allergenic plants, such as ragweed and Japanese hop, grow in soil damaged by human's activities and deforestation with air pollution. It is impossible to avoid plants that cause allergies, because pollens can travel many kilometers in the breeze or wind. Hence, it is essential to survey and forecast pollens for the management of pollen allergy. Weather conditions may alter pollen concentrations. A number of studies have shown that increases in CO$_2$ concentration and atmospheric temperature raise pollen concentration. Hence most of the studies on the impact of climate change on aeroallergens must include the amount and allergenicity of pollens. It is yet unknown whether complex interactions with pollens, meteorological variables, and air pollutants in the changing environment. Considering the effect of climate change on the long-term trends in pollen levels and emerging viral infection, it is crucial to forecast and eliminate the associated risk for human health in future and take appropriate measures to reduce it.

Keywords: Pollen allergy; climate change; calendar; forecast; respiratory allergy; air pollution; sensitization rate; aeroallergens; viral infection

INTRODUCTION

A growing number of people are recently suffering from allergic diseases caused by pollens because of climate change in the world. Moreover, seasonal and regional variations in pollens have changed in the Asia Pacific region as well as in Europe and America.$^{1-4}$ As the sensitization rate to pollens has recently increased in children, rapidly proliferating allergenic plants have emerged as a dangerous element to allergic children.$^{5,6}$

Plants causing allergies are difficult to identify because they seldom have prominent flowers. The rapid proliferation of weeds and trees, as well as air pollution by greenhouse gases caused by the increase in traffics as well as by the construction of modern buildings and factories, constitute harmful conducive to allergies. Nobody can be protected from allergy.
Plants by staying in the cities or rural areas. Allergenic plants grow abundantly in areas where people are damaging the natural environment due to their houses, roadways, highway, and agricultural activities.\(^7\) The allergenic plants, such as ragweed, grow best in soil damaged by human activities and deforestation with a changing world. It is almost impossible to avoid plants that cause allergies, because pollens can travel many kilometers in the breeze or wind.\(^9\) However, avoiding large doses of plant pollens is critical for sensitive people. The intensity of allergic reactions differs according to the amount of exposure. Weather conditions, including rainfall, atmospheric temperature, humidity, and wind speed and direction, may alter the concentrations of plant pollens and other allergens, subsequently influencing the occurrence of allergic diseases.

Most of the studies on the impact of climate change on aeroallergens can be divided into a number of distinct areas, including the effect on the amount, allergenicity, and season of pollens, as well as on the distribution of allergenic plants.\(^11,12\) Studies of the impact of climate change on the distribution of allergenic pollens have focused typically on the analysis of observed pollen counts, and their regression relationships with local meteorological and climatic factors.\(^13,14\) The onset, duration, and intensity of the pollen season vary annually. Weather variables and CO\(_2\) are among the main factors affecting phenology and pollen production by plants.\(^16,17\) In addition, weather patterns influence the movement and dispersion of aeroallergens like pollen and mold in the atmosphere through the action of wind and rainfall, depending on atmospheric stability.\(^18,19\)

**POLLEN AS AN AEROALLERGEN**

The size and weight of pollen as aeroallergens fall in the 20- to 60-μm range of most of the particulate matter particles, and their allergenic constituents are protein with a molecular weight between 10,000 and 40,000 Da. Protective mechanisms in the nasal mucosae and upper tracheobronchial passages remove most of the larger particles, so only those with a size of 5 μm or smaller reach the alveoli of the lungs. These are considerations in the pathogenesis of allergic rhinitis, bronchial asthma, and hypersensitivity pneumonitis, as well as in the irritant effects of chemical and particulate pollutants.\(^20\)

The development of asthma after pollen exposure is enigmatic because pollen grains are deposited in the upper airways due to their large particle size. Experimental evidence suggests that rhinitis, but not asthma, is caused by the inhalation of the whole pollen in naturally encountered amounts. Pollen asthma may be caused by the inhalation of pollen debris that are small enough to access the bronchial tree. Evidence supports the hypothesis that extracts of materials are collected on an 8-μm filter, except for ragweed.\(^20\)

Pollen grains induce positive skin test results in ragweed-sensitive subjects. Using an immunochemical method for identifying atmospheric allergens, Amb a 1 was found to exist in ambient air in the absence of ragweed pollen grains. A positive bronchial challenge test is induced with pollen grains fragmented in a ball mill, but not by the inhalation of whole ragweed pollen grains. The exposure of grass pollen grains to water causes their rupture into smaller, respirable-size starch granules with intact group V allergens, possibly explaining the phenomenon of thunderstorm asthma during grass pollen seasons. However, despite the generally accepted limitations, the examination of tracheobronchial aspirates and surgical lung specimens has revealed large numbers of whole pollen grains in the lower respiratory tract.\(^21,22\)
Another consideration is the rapidity of which various allergens are leached out of whole pollen grains. The mucous blanket of the respiratory tract has been estimated to transport pollens into the gastrointestinal tract in less than 10 minutes. However, Amb a 1, a ragweed allergen, is extracted slowly, and only a small percentage of the total extractable Amb a 1 is released from the pollen grain at this time. This observation has not been reconciled with the presumed importance of Amb a 1 in clinical allergy, although absorption may be more rapid in more alkaline mucus found in allergic rhinitis.  

Factors influencing the clinical significance of pollen  
Pollens are frequently encountered aeroallergens. In general, entomophilous (insect-pollinated) plants produce scant, heavy, or sticky pollens that do not become airborne because of their heavy molecular weight. Depending on their season, anemophilous (wind-pollinated) grains can remain airborne for days and be carried hundreds of miles from their point of origin. Anemophilous plants possess large stamens borne on long, well-exposed filaments, often organized as catkins. Their flowers usually lack color, scent, and nectar and release large quantities of pollen in warm, dry weather. The size is a critical physical attribute to aeroallergens and an important consideration in the pathogenesis of allergic rhinitis, asthma, and hypersensitivity pneumonitis. Pollen grains range in size from 15 to 75 μm. Thus, the conjunctiva and upper respiratory tract are exposed to the highest dose of these aeroallergens.

Effects of weather on allergen load and pollen potency  
Both climate and weather play a key role in the production, release, and bioavailability of pollen-derived allergens. Plants discriminate day from night by means of photoreceptors, that is, pigments that capture different wavelengths that may promote or inhibit flowering. These pigments synchronize with biological activities at the day and night cycle. Plants may respond to day lengths exceeding a critical threshold in late spring or early summer, securing time for seed maturation. Increasing light intensity during springtime and early summer is likely to affect flowering in summer-flowering plants and modify the effect of the photoperiod.

The variation in pollen potency can be attributed to the synthesis of allergens in pollen during its ripening. In the week before pollination, no allergens are found in pollen, which otherwise is ready to release. Subsequently, a rapid increase in pollen allergen content occurs along with the development of anthers. Anthers react to weather conditions, and when the conditions are optimal for pollination, they open and release pollens. If the weather conditions are favorable for early pollination, ripe anthers will release less mature pollens with less allergens. Otherwise, when the weather conditions delay the opening of the anthers, more mature pollens with more allergens are released.

A pollen season is defined as one in which pollen is present in the air. The term is used for pollens either collectively from any plant taxon or separately from each taxon. The pollen season in a specific area is related to the local flowering season, because pollens present in the air are produced and released by mature flowers. However, pollen seasons and flowering seasons usually do not fully coincide because of the effects of mid- and/or long-range transport. In the temperate regions, the main pollination period covers approximately half the year, from spring to autumn. The effect of temperature on pollination is greater in spring- and early summer-flowering plants, whereas pollination of plants that flower in late summer and fall is generally correlated with their photoperiod. The complex relationship between weather and pollen concentration in the atmosphere plays a crucial role in modulating allergen levels.
IMPACT OF CLIMATE CHANGE

Climate change is a constant process that affects allergy, and its impact on pollen may be one of the most important consequences for human health. There are multiple interrelated consequences of climate change on plant phenology. Because the influence of climate change is complex, there is no predictable quantitative assessment of how climate change may affect pollen allergy in the future.15,28

At present, the basis for this necessary energy production is the burning of fossil fuels. Oxidation of carbon sources (fossil fuels) results in increased atmospheric levels of carbon dioxide. Estimates of total carbon emissions from all human activities, including agriculture and land use, are expected to be about 43 billion tons in 2019. As carbon dioxide absorbs infra-red radiation (heat), an increase in atmospheric concentrations will elevate surface temperature. Since 1970, average surface air temperature has increased by approximately 1.6°F (up to 1.0°C).29 The term ‘global warming’ is generally understood in the context of an average increase in surface temperature.30 An altered climate will affect the range of allergenic plant species and the length of the pollen season, and elevated atmospheric CO₂ levels may increase plant productivity and pollen production affecting plant ecology.31

Elevated CO₂ levels increase pollen production

Weeds: common ragweed

Many studies reported a significant increase in allergenic protein Amb a 1 in comparison to the pre-industrial, current, and future atmospheric CO₂ levels based on the climate chamber experiments.17,32 Choi et al.33 also performed CO₂ concentration experiments using climate chambers and evaluated the on-site difference between urban and suburban sites. The chamber experiments showed 230% and 272% increases of Amb a 1 concentration under 2 future CO₂ scenarios (600 and 1,000 ppm) from the current (380 ppm). The mean observed CO₂ concentration was 440 and 320 ppm at the urban and suburban sites, respectively. The mean Amb a 1 concentration was higher at the urban site than at the suburban site.

Trees: oak

Pollen production experiments of trees by altering CO₂ concentration are limited by canopy size and exposure time. Kim et al.34 used open-top CO₂ chambers to maintain CO₂ concentrations at ambient (400 ppm), ×1.4 (560 ppm), and ×1.8 (720 ppm) levels for more than 7 years. The production of pollen grains and the allergen Que a 1 by oak trees in the chambers were quantitatively assessed (Fig. 1). Total pollen counts per tree of the ×1.4 and ×1.8 levels significantly increased to 353% and 1,299%, respectively, compared to the ambient level. The allergenic protein content at the ×1.4 and ×1.8 levels showed a significant increase to 12% and 11%, respectively.

In the future, people will be exposed to higher allergen levels at higher CO₂ concentrations. However, the actual level of elevated allergy risk is difficult to predict due to underlying plant physiology and ecology resulting from complex impacts of planetary environment changes including air temperature, rainfall, soil nutrition, and changing flowering periods.

Changes in pollen seasons

Weather conditions, including rainfall, humidity, wind speed, and air temperature, may alter pollen concentrations. Increased temperature may lead to earlier pollination of many plants and longer duration of pollination. Additionally, climate change is thought to increase the
quantity of allergenic protein in individual pollen grains. The changes also involve plants producing allergenic pollens, with expected consequences on allergic individuals. Long pollen seasons increase the duration of exposure, potentially resulting in more sensitization. Longer pollen seasons also result in longer symptom periods in patients with allergic disease, and higher pollen concentrations may cause more severe symptoms. An earlier start of the pollen season was confirmed in studies focused on allergenic plants. Due to earlier onset, pollen seasons are altered more often by weather conditions in late autumn or early spring. Ziska et al. have recently demonstrated a clear positive correlation between recent global warming and increase in seasonal duration/pollen concentrations for multiple allergenic plant species on a decadal basis in the northern hemisphere. This study demonstrated a significant increase in pollen season duration over time, increasing by 0.9 days per year on average (Table). These data indicate that recent climatic changes, especially temperature, affect pollen concentrations as well as season duration and timing in the northern hemisphere.

**Table.** Temporal changes in the start and end dates as well as in the duration of the pollen season for 17 locations in the northern hemisphere

| Location, Country       | Start time | P value | End time | P value | Season length | P value |
|-------------------------|------------|---------|----------|---------|---------------|---------|
| Amiens, France          | -0.61      | 0.007   | 0.19     | 0.330   | 0.86          | 0.004   |
| Brussels, Belgium       | -0.62      | 0.003   | 0.16     | 0.229   | 0.78          | 0.003   |
| Busan, Korea            | -1.17      | 0.0004  | -0.05    | 0.890   | 1.13          | 0.010   |
| Fairbanks, USA          | -0.68      | 0.129   | 1.68     | 0.005   | 0.92          | 0.124   |
| Geneva, Switzerland     | -0.45      | 0.204   | 0.74     | 0.010   | 1.64          | 0.014   |
| Kevo, Finland           | -0.62      | 0.014   | 0.19     | 0.211   | 0.81          | 0.013   |
| Krakow, Poland          | -0.47      | 0.542   | 1.04     | 0.009   | 1.50          | 0.065   |
| Legnano, Italy          | -0.30      | 0.531   | -0.65    | 0.403   | -0.36         | 0.710   |
| Minneapolis, USA        | -0.58      | 0.116   | 1.30     | 0.003   | 1.85          | 0.001   |
| Moscow, Russia          | -0.47      | 0.294   | 0.53     | 0.067   | 1.04          | 0.036   |
| Papillion, USA          | 0.13       | 0.560   | 0.75     | 0.047   | 0.61          | 0.084   |
| Reykjavik, Iceland      | -1.51      | 0.010   | 0.01     | 0.942   | 1.22          | < 0.0001 |
| Saskatoon, Canada       | -0.23      | 0.487   | 0.51     | 0.025   | 0.73          | 0.077   |
| Seoul, Korea            | -0.85      | 0.007   | -0.12    | 0.844   | 0.74          | 0.294   |
| Thessaloniki, Greece    | -0.41      | 0.135   | 0.52     | 0.081   | 0.93          | 0.018   |
| Turku, Finland          | -0.67      | 0.0009  | 0.17     | 0.044   | 0.84          | 0.011   |
| Winnipeg, Canada        | -0.90      | 0.010   | 0.35     | 0.114   | 1.24          | 0.010   |

A negative value indicates an earlier start or end time, a positive value a later start or end time. Permitted from Ziska et al.40
Increased pollen sensitization rates

Sensitization to pollen plays a crucial role in the development of allergic disorders. However, the effect is less pronounced in individuals sensitized to only one type of pollen than in those sensitized to many types of pollen. Since different pollens are released at different periods of pollen season, atopic individuals sensitized to more than one type of pollen have a longer period of exposure. The duration of the pollen season is also influenced by factors affecting pollen dispersal. A longer pollen season and larger amounts of atmospheric pollen may enhance human exposure to allergenic pollens, potentially leading to an increase in allergic sensitization. A recent study demonstrated a positive correlation between changes in the pollen season over 20 years and sensitization rates to major tree pollens among children. With climate change, a continuous increase in the concentrations of tree pollens and thus in sensitization rates, especially in younger children, can be expected (Figs. 2 and 3).
**POLLEN CALENDAR**

Pollen season, a specific period with many region-specific pollen grains in the air, is a yearly phenomenon. A pollen calendar, which indicates the region, period, and species of abundant pollens, is developed based on this recurrence. The methods used to develop a pollen calendar include temporal averaging and statistical derivation from a probability density function (PDF).

The first pollen calendar in Korea was developed in 2004 using observational data from 1997 to 2000. It presented the national average pollen seasons of 21 species. The regional pollen characteristics were analyzed after 10 years of observation. Hence, pollen calendars were revised. Although pollen species in Korea are mostly similar throughout the country, there are regional differences in the representative species and their peak concentrations. Several key points are identified from the calendar with warning levels of pollen standardized for trees, grasses, and weeds.

With continuous monitoring of the pollen calendar, accumulated data on vegetation distribution, land use, and regional climate are tracked. The pollen calendar must reflect these changes using newly collected data. The daily mean of data collected over 11 years was smoothed using PDFs, Julian days were fitted as X (independent variable) and pollen concentration as Y (dependent variable) for individual species and stations. The risk benchmarks according to pollen concentration were also determined using the fitted probability distribution for each pollen species. Consistent benchmarks were able to compare pollen concentrations across the nation despite the high spatial variability. The highest magnitudes among the stations studied in South Korea were considered the benchmark concentrations for each pollen species. The actual risk levels were determined from the cumulative distribution curves of the fitted distribution. The periods of yearly cumulative pollen, less than 2.5% or more than 97.5%, were removed from the calendar to prevent unnecessary lengthening of the pollen season. Thus, the pollen risk information was consistently developed and delivered for each city. The revised calendar shows regional risks with continuous pollen periods more clearly than the older version (Fig. 4).

**POLLEN FORECAST**

To reduce the exposure to pollen, it is crucial to provide a reliable aerobiological forecast to patients with pollen allergies. Although the quality of the weather forecast has improved substantially in the last decade, the effects of weather variables on aeroallergen load are not completely understood. For instance, rainfalls clear the pollen from the air, thus reducing the risk of exacerbation of allergic rhinitis and asthma.

Weather conditions, including rainfall, atmospheric temperature, humidity, wind speed, and wind direction, may alter the concentrations of plant pollens and other allergens, which can subsequently influence the occurrence of allergic diseases such as asthma, allergic rhinitis, allergic conjunctivitis, and even atopic dermatitis. Many studies have demonstrated that a rise in CO$_2$ concentration and atmospheric temperature increase pollen concentration. Most of the studies on the impacts of climate change in aeroallergens can be divided into several distinct areas, including the effects on pollen amount, pollen allergenicity, pollen season, and plant and pollen distribution. Meteorological factors, such as mean temperature,
wind speed, humidity, amount of sunlight, and degree-days, can directly affect the biological and chemical components of this interaction.\textsuperscript{15,28} The accumulation of daily sunshine and other meteorological factors, such as humidity and precipitation, should be considered to improve further the accuracy of the modeled start dates and season lengths of birch and oak pollen and to develop regression models for pollen prediction. Daily fluctuations in pollen concentrations are linked to a variety of meteorological factors such as temperature, rainfall, and the duration of sunshine. Temperature and rainfall are especially important in determining pollen concentrations, although the relationships are complex and influenced by other variables.\textsuperscript{32}

The Korea Meteorological Administration (KMA) operates a daily pollen-monitoring network, develops forecast models, and provides daily pollen forecast.\textsuperscript{33} The KMA along with the Korean Academy of Pediatric Allergy and Respiratory Disease established the National Pollen Observational Network in Korea in 1997. As of 2020, the network is composed of 12 stations with Burkard traps. Using 7-day recording drums and an optical microscope, daily pollen concentrations of all species are collected, identified, and counted at each site every week. This constitutes real observational data on which both model development and validation are based. All diagnostic and forecasting models are basically developed using these data.\textsuperscript{4,28}

\textbf{Fig. 4.} Pollen calendars for (A) Seoul, (B) Gangneung, (C) Daejeon, and (D) Jeonju stations. At the Seoul station, the peak concentrations of pine, oak, ginkgo and Japanese hop pollens are high (A). At the Gangneung station, the peak concentration of pine pollen is particularly high, while those of birch, oak, elm and mugwort pollens are moderate (B). The peak concentrations of oak and pine pollens are very high at the Daejeon station (C). At the Jeonju station, the peak concentration of pine pollen is very high and those of oak and elm pollens are high (D). Permitted from Shin et al.\textsuperscript{44}
For the prediction of allergy risks by pollen, pollen concentrations have long been observed at many places worldwide. The threshold levels for symptom development of pollinosis vary among studies and countries, which has only one benchmark for a given pollen species. Thus, patients can compare pollen risks and reversely find their hazardous periods based on the personal symptom history. The symptom index can be calculated and the data were analyzed using a decision tree. Revising the threshold levels for the risk index for pollen allergies may be useful for developing pollen prediction models in Korea.

The daily pollen concentration is highly dependent on weather conditions such as air temperature, relative humidity, solar radiation, and precipitation. Diagnostic forecast models, developed from the observed data, can predict daily pollen concentration using the daily weather forecast. The development and improvement of forecast model for pollen must be crucial to prevent patients with pollen allergies from being exposed to allergenic pollens.

**Regional regression model**

Regional pollen risk forecast using regression models is performed in 3 steps: 1) identifying the weather variables that affect pollen variability, 2) developing regression models for pollen concentration using the weather variables, 3) estimating pollen concentration from the model and determine the pollen risk based on the concentration. The KMA developed monthly pollen concentration models and provided tree/weed pollen risks in spring and autumn. The pollen risk forecast reflects daily weather conditions by assimilating output from operational numerical weather forecasts. The weather variables selected are daily air temperature, temperature range, relative humidity, wind speed, precipitation hours, total precipitation, and 7-day accumulated sunshine hours. The risk grade is determined using pollen concentration, estimated from regression models, and provided on a daily basis.

**Probability-regression model**

This is a unified model based on the analysis of probability distribution. Simple regression models are developed from the data on individual sites and are able to predict pollen concentration at specific sites. For the development of a nationwide service for pollen risks, a unified model must be developed for pollen prediction that explains the weather conditions commonly observed during the pollen outbreak. The PDF-regression model was developed using daily weather variables and the daily pollen concentration of oak in spring and Japanese hop in autumn from 1997 to 2009. The daily pollen concentration is represented on a histogram according to each weather variable. The histogram is the sum of the probability of pollen appearance at a specific weather event and is fitted to the Weibull PDF. Regression models are developed using the PDFs of individual weather variables as the independent variables and pollen concentration at all observational sites as a dependent variable. Regional regression models were simplified in the PDF-regression model, which can also predict the nationwide distribution of pollen risks using the operational numerical weather forecast because of its sole dependence on weather conditions.

**Probability-machine learning model**

Previous models were mainly caused by the characteristics of the dataset utilized in the development of a model using a large number of low concentration days. Additionally, the relationship between weather conditions and pollen concentrations was not linear. To solve these problems, the probability of pollen appearance was estimated from weather data before machine learning models were programmed to predict pollen concentration. Additionally, the bootstrap aggregating-type ensemble model was developed to prevent people from
overfitting the deep neural network (DNN) model to training data and from underestimating the concentration. Nine stations with sufficient data collected from 2007 to 2014 were selected for the training data. Several weather input variables were transformed into the daily probability of pollen appearance. As the accuracy of this model is greater than that of conventional models, DNN models have been implemented as an operational service by the KMA since 2017.

Pollen dispersal model
Detailed mid- and long-range pollen forecast can be achieved by simulating dissemination-transportation-deposition with dispersal models like the Asian dust forecast. Pollen dispersal and risk models can be developed over a large area based on vegetation distribution and phenological flowering models, despite insufficient observational data for probability-regression or machine learning models. The birch and the Japanese cedar forecasts of Finland and Japan, respectively, have incorporated dispersal forecast models.

POLLEN AND RESPIRATORY VIRUS
A number of recent studies have reported that pollen exposure weakens immunity against certain seasonal respiratory viruses by diminishing the antiviral interferon response. A recent, large cohort study from South Korea reported that asthma exacerbations in school-aged children are associated with co-exposure to multiple seasonal environmental factors, that is, ozone, rhinovirus, and tree pollen. Another study has recently reported that pollen grains of various plant taxa release as yet unidentified compounds that suppress the production of antiviral $\lambda$-interferons in respiratory epithelial cells, and provided evidence from human and mouse models that pollen exposure enhances susceptibility to infection by 2 different respiratory viruses, human rhinovirus and respiratory syncytial virus. Damialis et al. demonstrated that 44% of the infection rate variability increased after higher pollen concentrations most frequently during the previous 4 days. Without pollination lockdown, an increase in pollen abundance by 100 pollen/m$^3$ resulted in a 4% increase of infection rate. Their dataset is the most comprehensive, based on the worldwide data from 130 stations across 31 countries including Korea, and 5 continents. This study suggested that 2 mechanisms for the innate immune response, inflammasome activation and antiviral interferon response of pollen, appear to be modulated toward the same direction by pollen and severe acute respiratory syndrome coronavirus 2.

CONCLUSION
This review summarized recent studies regarding the impact of environmental change like climate on pollen allergy and pollen calendar with forecast, particularly in Korean peninsula as follows: 1) pollen as an aeroallergen and the effects of weather on pollen bioavailability; 2) changes in pollen load and potency due to CO$_2$ gas which is one of the major greenhouse gases as well as in pollen season, and increased pollen sensitization rate in the perspective of changing climate environment; 3) the revision of pollen calendar; and 4) the development of prediction model to prevent the patients with pollen allergy from being exposed to allergenic pollens. Finally, coronavirus disease 2019 (COVID-19) pandemic is very crucial worldwide issue since the beginning of 2019, and this review focused on the correlation between pollen exposure and COVID-19 transfer.
Looking to the future, it is yet unknown whether complex interactions among pollens, meteorological variables, and air pollutants may play a role in a changing planetary environment. Even though there is published evidence for the effects of various environmental parameters, these usually refer to preliminary results and the investigation of only a single factor. If we consider the huge effect of climate change on the long-term trends of airborne pollen levels and emerging viral infections, it is of utmost importance to forecast and warn the associated risk for human health in future pandemics and take appropriate measures to reduce it as much as possible.

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