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ORIGINAL PAPER

‘Pollen potency’: the relationship between atmospheric pollen counts and allergen exposure

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Abstract Pollen allergies are responsible for a considerable global public health burden, and understanding exposure is critical to addressing the health impacts. Atmospheric pollen counts are routinely used as a predictor of risk; however, immune responses are triggered by specific proteins known as allergens, which occur both within and on the surface of the pollen grain. The ratio between atmospheric pollen counts and allergen concentrations (‘pollen potency’) has been shown to be inconsistent, with potentially important implications for pollen monitoring practice. Despite this, there has been no previous synthesis of the literature and our understanding of the factors that influence pollen potency remains poor. We conducted a scoping review with the aim of deriving a current understanding of: (a) the factors that influence pollen potency; (b) its variation through time, between taxa and by location; and (c) the implications for pollen monitoring practice. Our synthesis found that pollen potency is highly variable within and between seasons, and between locations; however, much of this variability remains unexplained and has not been deeply investigated. We found no predictable pollen potency patterns relating to taxon, geography or time, and inconclusive evidence regarding possible driving factors. With respect to human health, the studies in our synthesis generally reported larger associations between atmospheric allergen loads and allergy symptoms than whole pollen counts. This suggests that pollen potency influences public health risk;

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however, the evidence base remains limited. Further research is needed to better understand both pollen potency variability and its implications for health.

Keywords Pollen · Aeroallergens · Allergens · Pollen potency · Aerobiology

1 Introduction

Allergic sensitisation to pollen poses a considerable individual and public health burden because it is a major cause of two common conditions: allergic rhinitis (AR, commonly referred to as hay fever) and allergic asthma. These conditions are common and globally pervasive. Asthma alone affects approximately 339 million individuals worldwide (Global Asthma Network, 2018), while it is estimated that AR affects 10–30% of the global adult population (Pawankar et al., 2013). The burden of both diseases is notable: allergic asthma can have serious health consequences including mortality (Thien et al., 2018), while AR symptoms result in reduced productivity, increased absenteeism from work and decreased quality of life (Katelaris et al., 2012). Overall, these impacts create a substantial economic burden. For example, the cost of absenteeism and presenteeism due to allergic diseases in the European Union was estimated to range from EUR€55 to €155 billion per annum (Zuberbier et al., 2014), while the indirect costs of AR and urticaria (allergic hives) in Asian countries have been estimated at USD $105.4 billion per annum (Kulthanan et al., 2018). AR and allergic asthma can be triggered by exposure to many different allergens, including those associated with plant pollen. A changing climate, increasing atmospheric carbon dioxide levels, the spread of exotic aeroallergen-producing species into new areas (Alan et al., 2020) and increasing geographic ranges of allergenic pollen taxa are all anticipated to increase pollen allergen exposure (Damialis et al., 2019), which will likely worsen the burden of these diseases in the future (Beggs, 2016). Thus, effective management and treatment of pollen allergy are a global health priority.

Symptoms of pollen allergies are typically seasonal because they are associated with the temporal patterns of pollen release into the atmosphere. In this context, atmospheric pollen monitoring networks have been established in many countries to provide individuals, clinicians and public health agencies with a means of tracking potential allergy risk (Alcázar et al., 2015; Haberle et al., 2014; Johnston et al., 2018). Pollen monitoring is typically undertaken with a volumetric spore trap, such as a Hirst-type trap (Hirst, 1952), that continuously samples air for periods of up to one week. Airborne bioaerosols and particles, including pollen, impact onto a microscope slide or tape that is covered with an adhesive. The deposited pollen grains are morphologically identified, and the atmospheric concentrations of different pollen taxa are then estimated (Buters et al., 2018). Pollen data can then be used by clinicians and patients to make informed decisions to minimise personal exposure and mitigate their risk. Many studies have supported the utility of providing publicly available atmospheric concentrations of whole pollen grains for this purpose, and they remain the ‘gold standard’ around the world (Buters et al., 2018).

However, one limitation of atmospheric pollen monitoring is that whole pollen grains are not the direct cause of allergy symptoms. Instead, symptoms arise when high molecular weight proteins, known as allergens, trigger an individual’s immune response by the binding of specific class E immunoglobulins (IgE). Allergens are located on the surface and within the cytoplasm of individual pollen grains (e.g. Behrendt et al., 1999; Süring et al., 2016) and are present on fine (< 2 μm) pollen fragments released into the atmosphere (e.g. Buters et al., 2010; Schäppi et al., 1997b; Taylor et al., 2002). Atmospheric allergen detection requires different sampling and laboratory infrastructure to regular pollen monitoring. This includes sampling air with a different device (for example, a High Volume Impactor) and immunochemical detection of the allergen with ELISAs instead of microscopic identification (Buters et al., 2010). Therefore, despite the close theoretical linkage between allergen concentrations and symptom severity, allergen concentrations are not routinely measured by pollen monitoring networks.

Importantly, there is evidence that atmospheric allergen concentrations are not directly related to trends in atmospheric pollen counts (Buters et al., 2012, 2015). There are two potential explanations for this: (a) there is variation in the amount of allergen carried by individual pollen grains and/or (b) there is variable release of allergen-carrying fragments into

the atmosphere (Schäppi et al., 1997a, 1997b, 1999). Schäppi et al., (1997a, 1999) were among the first to hypothesise that atmospheric allergen concentrations may be independent of atmospheric pollen counts, based on experiments demonstrating allergen-carrying particles being liberated from grass and birch pollen grains. More recently, the Health Impacts of Airborne Allergen Information (HIALINE) Network project (Buters et al., 2010) set out to investigate the relationship between atmospheric pollen counts and atmospheric allergen across a wide range of European environments. This group defined the ratio of pollen grains to allergen detected via immunoassay as 'pollen potency', and we follow this terminology here. The HIALINE project produced some of the first data showing significant variation in potency between taxa, within and between seasons, and between locations (Buters et al., 2010, 2012, 2015). Their findings suggest that the phenomenon of variable pollen potency might be more common than previously estimated.

Given the important role of allergens in precipitating allergy symptoms, variation in pollen potency may have important health implications. We hypothesised that varying pollen potency might be a factor underlying the significant global variation in the threshold of pollen grains that are required to trigger symptoms in sensitised individuals (de Weger et al., 2013). Further, if atmospheric allergen concentrations are decoupled from pollen counts, then atmospheric allergen concentrations could be a better predictor of risk of symptoms and may be more appropriate to monitor than concentrations of whole pollen grains (Cecchi, 2013). Although allergen monitoring implementing molecular and immunological approaches currently remains cost-prohibitive as standard practice, developing a better understanding of the relationship between whole pollen counts and atmospheric allergen loads may enable us to provide allergy patients with enhanced information about their personal risk.

To date, there has been no synthesis of the literature to investigate the characteristics of pollen potency and the implications for pollen monitoring practice and human health. We therefore undertook this scoping review with the aims of understanding: (a) taxonomic, temporal and geographic variation in pollen potency; (b) the factors that influence pollen potency; and (c) the implications for human health and pollen monitoring practice.

2 Methods

We sought peer-reviewed studies that evaluated the quantitative relationship between pollen and allergen (that is, pollen potency), published up to 5 February 2021. Our literature search strategy sought to capture studies that evaluated pollen potency in any way, including studies that considered the atmospheric ratio of allergen to whole pollen, as well as studies that quantified the relationship between pollen and allergen with pollen collected directly from plants. Given the interdisciplinary nature of the topic, we opted for a scoping review methodology as outlined in Munn et al. (2018). Search terms were developed to provide consistent results across three databases: Scopus, Web of Science and Medline via Ovid. The search terms used for each database and the number of results for each are listed in Table 1.

The results of the literature searches were exported into EndNote (Clarivate Analytics, Philadelphia, USA) then into Covidence (Veritas Health Innovation, Melbourne, Australia). Covidence native software detected and removed duplicates. We screened remaining studies for relevance by title and abstract, with two authors (LT and NB) using a key (Supplementary Figure 1) that was designed to only progress publications that investigated either (a) the ratio of atmospheric allergen to atmospheric whole pollen counts or (b) the amount of allergen present on/in a pollen grain or collection of pollen grains. Publications that received a *yes* or *maybe* were moved to full-text screening. LT then carried out full-text screening on all publications that were voted *yes* or maybe. Articles were deemed relevant if they quantified a relationship between allergen and pollen grains in the study design. We excluded review articles, conference proceedings, non-English language, non-peered reviewed articles and other non-article publications or publications that were inaccessible through reasonable searching protocols. We manually screened the reference lists of the final list of publications to obtain additional relevant publications. Publications that were deemed relevant were progressed to extraction. The relevant information was recorded from each study using a pre-designed data collection table: (i) title, (ii) first author, (iii) study location, (iv) study period, (v) taxa studied, (vi) allergen studied, (vii) methods of pollen and allergen sampling and

Table 1 Summary of each database, its search terms and number of results

Database	Term	Results
Web of Science	TS=(pollen NEAR/1 potency) OR TS=((monitor* OR predict* OR measur* OR count*) AND ("pollen allerge*" OR allerge* NEAR/1 pollen))	1272
Scopus	TITLE-ABS-KEY(pollen w/1 potency) OR TITLE-ABS-KEY((monitor! OR predict! OR measure! OR count!) AND ("pollen allerge*" OR allerge* w/1 pollen))	493
Medline via Ovid	((monitor* or predict* or measur* or count*) and (pollen allerge* or allerge* adj1 pollen) or (pollen adj1 potency)).ab,kw,ti.	728

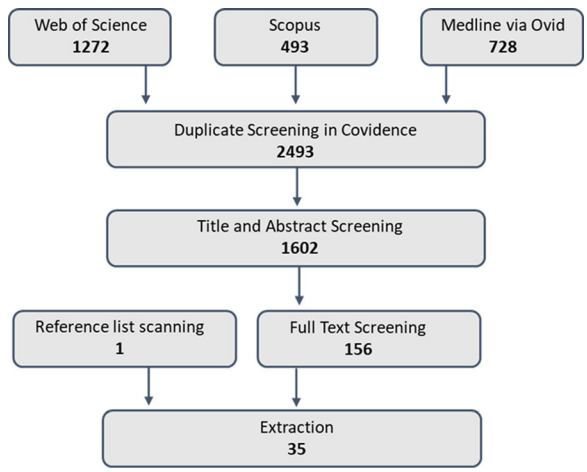

Fig. 1 Flow chart of publication selection

measurement, (viii) the metric used for measurement and (ix) the conclusions about pollen potency.

3 Results

A total of 35 peer reviewed articles met the inclusion criteria (Fig. 1). The majority of the studies were completed in locations across Europe (n = 28). Of the remaining studies, four were completed in Saitama, Japan, and three in Melbourne, Australia. Furthermore, Supplementary Figure 2 shows the number of articles in our extraction published per year. This demonstrates an increase in research frequency in the last decade but no substantial increase in the last few years.

Full-text screening revealed that most studies (n = 32) measured the relationship between atmospheric concentrations of pollen and allergen. Two

Fig. 2 Reported seasonal average pollen potency measurements by pollen taxon from all studies that provided a measurement in picograms of allergen per pollen grain (n = 16). Year denotes year of measurement. Country denotes the country where sampling occurred. Pollen denotes the method of pollen collection (A = Hirst-type continuous flow volumetric sampler). Allergen denotes the method of allergen collection (C = Cyclone Sampler (Burkard) or D = high-volume Impactor). The bars show the average pollen potency across that season measured in picograms of allergen per pollen grain rounded to two figures. Note that the scale for potency measurements differs by taxon. Records for Ash and Privet are listed with Olive because they share the Ole e 1 antibody used for allergen quantification; Alder records are listed with Birch for the same reason. Within each taxon, measurements from same sampling location are grouped to facilitate comparison of between-season variation. Summary statistics for each taxon are provided in the bottom right; these statistics are based on all reported seasonal average pollen potency measurements for that taxon

Reference	Pollen	Allergen	Country	Year	Average pollen potency for season (picograms of allergen per pollen grain)
Grass					
Buters 2015	A	D	Austria	2010	3.5
Buters 2015	A	D	Austria	2011	2.9
Buters 2015	A	D	Finland	2009	1.6
Buters 2015	A	D	Finland	2010	2.0
Buters 2015	A	D	Finland	2011	1.5
Buters 2015	A	D	France	2009	2.4
Buters 2015	A	D	France	2010	2.4
Buters 2015	A	D	France	2011	2.9
Buters 2015	A	D	Germany	2009	3.0
Buters 2015	A	D	Germany	2010	2.1
Buters 2015	A	D	Germany	2011	2.1
Jochner 2015	A	D	Germany	2009	0.7
Jochner 2015	A	D	Germany	2010	1.5
Jochner 2015	A	D	Germany	2010	5.7
Buters 2015	A	D	Italy	2009	1.5
Buters 2015	A	D	Italy	2010	2.9
Buters 2015	A	D	Italy	2011	0.8
Buters 2015	A	D	Poland	2009	2.7
Buters 2015	A	D	Poland	2010	3.4
Buters 2015	A	D	Poland	2011	2.0
Buters 2015	A	D	Portugal	2009	2.1
Buters 2015	A	D	Portugal	2010	1.5
Buters 2015	A	D	Portugal	2011	1.5
Fernández-González 2019 a	A	C	Portugal	2018	15
Buters 2015	A	D	Spain	2009	2.3
Buters 2015	A	D	Spain	2010	4.1
Buters 2015	A	D	Spain	2011	2.4
Rodríguez-Rajo 2011	A	C	Spain	2007	4.7
Rodríguez-Rajo 2011	A	C	Spain	2007	8.9
Buters 2015	A	D	Turkey	2010	3.1
Buters 2015	A	D	UK	2009	5.9
Buters 2015	A	D	UK	2010	3.6
Buters 2015	A	D	UK	2011	4.2
Ščevková 2020	A	C	Slovakia	2020	5.7
Olive					
Galan 2011	A	D	Portugal	2009	0.8
Fernández-González 2019 a	A	C	Portugal	2018	4.0
Brito 2011	A	D	Spain	2004	0.1
Galan 2011	A	D	Spain	2009	3.9
Plaza 2016	A	C	Spain	2012	8.7
Plaza 2016	A	C	Spain	2013	3.6
Plaza 2016	A	C	Spain	2014	1.6
Vara 2016	A	C	Spain	2011	1.3
Álvarez-López 2020	A	C	Spain	2017	0.4
Álvarez-López 2020	A	C	Spain	2018	0.5
Ash					
Vara 2016	A	C	Spain	2011	1.3
Álvarez-López 2020	A	C	Spain	2017	4.0
Álvarez-López 2020	A	C	Spain	2018	1.9
Privet					
Vara 2016	A	C	Spain	2011	0.5

Reference	Pollen	Allergen	Country	Year	Average pollen potency for season (picograms of allergen per pollen grain)
Birch					
Buters 2012	A	D	Finland	2009	2.6
Buters 2012	A	D	France	2009	3.1
Buters 2010	A	D	Germany	2004	1.0
Buters 2010	A	D	Germany	2005	1.2
Buters 2010	A	D	Germany	2006	1.3
Buters 2010	A	D	Germany	2007	2.2
Buters 2012	A	D	Germany	2009	3.9
Jochner 2015	A	D	Germany	2009	3.3
Jochner 2015	A	D	Germany	2009	3.7
Jochner 2015	A	D	Germany	2010	1.1
Jochner 2015	A	D	Germany	2010	1.8
Albertini 2012	A	D	Italy	2009	2.6
Buters 2012	A	D	Italy	2009	2.6
Fernández-González 2019 a	A	C	Portugal	2018	8.0
Buters 2012	A	D	UK	2009	2.3
Álvarez-López 2020	A	C	Spain	2017	3.1
Álvarez-López 2020	A	C	Spain	2018	1.0
Fernández-González 2020 a	A	C	Spain	2016	1.0
Fernández-González 2020 a	A	C	Spain	2017	3.0
Fernández-González 2020 a	A	C	Spain	2018	1.0
Fernández-González 2020 a	A	C	Spain	2019	2.2
Alder					
Álvarez-López 2020	A	C	Spain	2017	3.4
Álvarez-López 2020	A	C	Spain	2018	1.2
Álvarez-López 2020	A	C	Spain	2016	1.0
Álvarez-López 2020	A	C	Spain	2017	3.0
Álvarez-López 2020	A	C	Spain	2018	1.0
Álvarez-López 2020	A	C	Spain	2019	3.0
Platanus					
Rodríguez-Rajo 2011	A	C	Spain	2007	0.0
Rodríguez-Rajo 2011	A	C	Spain	2007	0.1
Alcazar 2015	A	C	Spain	2011	0.5
Alcazar 2015	A	C	Spain	2012	0.4
Álvarez-López 2020	A	C	Spain	2017	1.9
Álvarez-López 2020	A	C	Spain	2018	0.9
Urticaceae					
Fernández-González 2019 a	A	C	Portugal	2018	1.0
Rodríguez-Rajo 2011	A	C	Spain	2007	0.2
Rodríguez-Rajo 2011	A	C	Spain	2007	1.2
Ragweed					
Celenk 2019	A	D	Turkey	2014	2.6

Taxa	Min	Q1	Q2	Q3	Max	n
Grass	0.7	2.0	2.6	3.6	15.0	34
Olive	0.1	0.6	1.4	3.8	8.7	10
Ash	1.3	*NA*	1.9	*NA*	4	3
Privet	*NA*	*NA*	0.5	*NA*	*NA*	1
Birch	1.0	1.2	2.3	3.1	8.0	21
Alder	1.0	1.1	2.1	3.0	3.4	6
Platanus	0.0	0.1	0.4	0.8	1.9	6
Urticaceae	0.2	*NA*	1.0	*NA*	1.2	3
Ragweed	*NA*	*NA*	2.6	*NA*	*NA*	1

methods were employed to demonstrate this relationship: (a) average weight of atmospheric allergen in picograms (pg) per pollen grain for a continuous period (e.g. year or season) and/or (b) as a graphical depiction of disaggregated daily data of coupled atmospheric pollen and allergen concentrations through time. Sixteen publications used both methods, two used only the former and 14 used only the latter. Figure 2 summarises the results from all publications that used the first method ($n = 16$) to provide a quantitative comparison of average pollen potency between taxa, locations and seasons. Figure 2 also summarises the methods used to collect atmospheric allergen and pollen grains, respectively. While all of these studies collected whole pollen grains using Hirst-type samplers, allergens were collected via a mixture of High Volume Cascade Impactors and cyclone samplers.

The three remaining articles measured the relationship between pollen and allergen using pollen collected from plants rather than atmospheric measurements; these studies included an average measurement of weight of allergen in pg per weight of pollen in micrograms (Beck et al., 2013; Behrendt et al., 1999; Buters et al., 2008). These papers primarily investigated environmental factors that affect the amount of allergen borne by pollen grains, with the denominator being weight of pollen, rather than individual pollen grains. Therefore, results from these studies are not directly comparable with the more common approach of monitoring atmospheric concentrations of pollen or pollen allergens. No studies investigated the specific amount of allergen associated with singular pollen grains, meaning we were not able to investigate pollen potency relating to variable allergen content of individual pollen grains. For a full summary of extracted information, see Supplementary Table 1.

Ten pollen taxa were investigated across the 35 studies, with numerous studies investigating more than one taxon. Thirteen papers studied *Betula* (birch) pollen, ten studied Poaceae (grass) pollen, nine studied *Olea* (olive) pollen, four studied *Cryptomeria japonica* (Japanese cedar) pollen, five studied *Platanus* (Plane tree) pollen, four studied Urticaceae (pellitory) pollen, two each studied *Ambrosia* (ragweed), *Fraxinus* (ash) and *Alnus* (alder) pollen and one study investigated *Ligustrum* (privet) pollen. In most instances, studies investigated pollen potency with respect to the allergen most commonly evaluated in clinical practice (for example Bet v 1 for birch). However, several studies investigated potency with respect to additional or alternative allergens for a respective pollen taxon (full details in Supplementary Table 1).

3.1 Temporal variation in pollen potency

Temporal variation in pollen potency was examined in 29 publications, with most exploring temporal variation across a single pollen season. Of these, 19 publications displayed disaggregated daily data graphically; all demonstrated that atmospheric pollen and allergen concentrations became decoupled across one single season. However, fluctuations in potency were irregular, and neither the individual studies themselves, nor our subsequent synthesis of these studies found any predictable patterns as to when in a season potency would be greatest. For example, measurements of olive pollen potency in Córdoba (Spain) from 2012 to 2014 indicated that potency was at its highest at the mid-point of the 2012 season; however, it was moderate or low at the same point of the season in 2013 and 2014 (Plaza et al., 2016). Overall, almost all studies that tracked within-season variation in pollen potency recorded large and often sharp fluctuations. For example, Buters et al. (2010) demonstrated a more than ten-fold difference in birch pollen potency within a single season, while Buters et al. (2015) reported up to 17-fold differences within seasons for grass pollen potency. Overall, we found no consistent patterns of within-season variation across taxa and seasons.

Ten studies compared variation across multiple seasons. One method for evaluating between-season variation is the comparison of average pollen potency values across multiple seasons. As shown in Fig. 2, studies that investigated potency across multiple seasons in a single location found differing magnitudes of variation in season-average values. For example, Buters et al. (2015) found that average grass pollen potency differed little across three seasons at one location in France, recording 2.4 pg/pollen grain in 2009 and 2010 and 2.9 pg/pollen grain in 2011. Conversely, the same study found that average potency varied over threefold over the same three seasons in one location in Italy, with average measurements of 1.5, 2.9 and 0.8 pg/pollen grain, respectively (Buters et al., 2015).

3.2 Taxonomic variation in pollen potency

Pollen potency measurements in pg/pollen grain were reported for nine of the ten taxa investigated across the included studies (only graphical disaggregated daily data were reported for Japanese cedar). Across the nine taxa with measurements in pg/pollen grain, median season-average pollen potency ranged from 0.4 to 2.6 pg of allergen per pollen grain (Fig. 2). The two most widely studied taxa, grass and birch, demonstrated similar medians (2.6 and 2.3 pg/pollen grain, respectively), similar minima (0.7 and 1.0 pg/pollen grain) and similar maxima (15 and 21 pg/pollen grain). Furthermore, grass, birch and olive pollen demonstrate similar magnitudes of variation in season-average potency measurements, with inter-quartile ranges of 2.0–3.6 pg/pollen grain, 1.2–3.1 pg/pollen grain and 0.6–3.8 pg/pollen grain, respectively. Season-average potency measurements for *Platanus* and Urticaceae have typically been substantially lower (Fig. 2).

Expanding from season averages to comparative trends in temporal pollen potency variation, four publications tracked temporal variation in more than one taxon across one or multiple seasons (Table 2). These studies found that different taxa exhibited substantially different within- and between-season pollen potency trends. For example, Rodríguez-Rajo et al. (2011) displayed seasonal pollen potency trends for grass, *Platanus* and Urticaceae pollen in three cities in Spain. Each taxon demonstrated distinct pollen potency dynamics within single seasons, which in turn were inconsistent across the three study locations (for details see Supplementary Table 1). Overall, our synthesis did not identify any consistent patterns in within- or between-season variation related to taxon.

3.3 Geospatial variation in pollen potency

Twelve studies compared pollen potency across locations (Table 2). We found that there were sometimes substantial differences in season average measurements across locations, even within the same country. For example, Rodríguez-Rajo et al. (2011) found that in Spain, grass pollen potency was on average almost twice as high (8.7 pg/pollen) in the city of Ourense in 2007 compared to the city of León (4.7 pg/pollen). In addition, some studies explored

Table 2 List of conclusions extracted from selected publications related to the types of variation in pollen potency

Type of variation	Conclusion	References
Temporal	Pollen potency varies within a single season as a dynamic decoupling of atmospheric pollen and allergen concentrations	Publications that only evaluate a single season: Albertini et al. (2013), Buters et al. (2012), Celenk (2019), De Linares et al. (2007, 2010), Fernández-González et al. (2013, 2019a, b), Galan et al. (2013), Gong et al. (2017), Porcel Carreño et al. (2020), Schäppi et al. (1997a, b, 1999), Riediker et al. (2000), Rodríguez-Rajo et al. (2011), Ščevková et al. (2020), Vara et al. (2016) and Wang et al. (2013a)
	Pollen potency varies between seasons, both in terms of season-average potency and within-season potency dynamics	Publications that evaluate more than one season: Alan et al. (2020), Alcazar et al. (2015), Álvarez-López et al. (2020), Buters et al. (2010, 2015), De Linares et al. (2019), Fernández-González et al. (2020), Jochner et al. (2015), Plaza et al. (2016) and Wang et al. (2013b)
Taxonomic	Both point-in-time pollen potency and temporal patterns in pollen potency vary by taxon	Álvarez-López et al. (2020), Fernández-González et al. (2019a, 2020), Jochner et al. (2015), Porcel Carreño et al. (2020), Rodríguez-Rajo et al. (2011) and Vara et al. (2016)
Geographical	Both point-in-time pollen potency and temporal patterns in pollen potency vary by location	Alan et al. (2020), Beck et al. (2013), Buters et al. (2008, 2012, 2015), Fernández-González et al. (2019b), Galan et al. (2013), Jochner et al. (2015) and Rodríguez-Rajo et al. (2011)

Table 3 List of conclusions extracted from reviewed publications related to the factors that influence pollen potency and/or of its components (whole pollen counts and allergen concentration)

Conclusion	References
Meteorological factors including temperature (daily maximum and minimum), wind speed and humidity affect pollen potency	Alan et al. (2020), Álvarez-López et al. (2020), Beck et al. (2013), Brito et al. (2011), Buters et al. (2008, 2010, 2012, 2015), De Linares et al. (2010, 2019), Fernández-González et al. (2013, 2019a, b, 2020), Galan et al. (2013), Gong et al. (2017), Jochner et al. (2015), Plaza et al. (2016), Rodríguez-Rajo et al. (2011), Schäppi et al. (1997b, 1999), Wang et al. (2013a, b)
Meteorological factors are not associated with potency	Alcazar et al. (2015)
Altitude affects pollen potency	Jochner et al. (2015)
Proximity to ocean affects pollen potency	Fernández-González et al. (2019a)
Long distance dispersal of pollen can affect pollen potency because potency varies in pollen from different locations	Alan et al. (2020), Álvarez-López et al. (2020), Buters et al. (2012), Fernández-González et al. (2019a), Galan et al. (2013) and Jochner et al. (2015)
Ozone exposure increases pollen potency	Beck et al. (2013)

whether temporal dynamics in pollen potency across a season were similar or different across multiple locations. For example, Buters et al. (2015) graphically displayed the relationship between atmospheric grass pollen and the allergen Phl p 5 for the 2009–2011 seasons for ten separate locations across Europe. They found stark differences in temporal patterns of pollen potency across locations.

3.4 Factors influencing pollen potency

Twenty-five publications investigated potential drivers of pollen potency (Table 3). No single variable was consistently identified as strongly influential. Only one publication investigated the factors that affected pollen potency directly by testing the association between environmental variables and the ratio of pollen allergen to whole pollen counts (Jochner et al., 2015). This study reported a significant negative correlation between pollen potency and humidity (but no correlation between pollen potency and sunshine duration or precipitation). Since there are no other studies that investigate this directly, one can investigate the factors that affect the individual components of pollen and allergen. Thus, the remaining publications made inferences about driving factors by investigating the relationship between environmental variables and one or both of these components.

Twenty-four publications, primarily derived from European network studies, have described associations between meteorological factors and pollen counts, allergen concentrations and/or pollen potency. However, our synthesis found no consistent patterns. For example, three studies found a positive relationship between rainfall and atmospheric allergen concentration (Schäppi et al., 1997a, 1997b; Wang et al., 2013a), while four studies showed the inverse (Beck et al., 2013; De Linares et al., 2010; Schäppi et al., 1997b; Wang et al., 2013b). Two studies demonstrated a negative correlation between rainfall and atmospheric pollen concentration (Jochner et al., 2015; Schäppi et al., 1997b), while one study did not find any correlation (Rodríguez-Rajo et al., 2011). Our synthesis found likewise conflicting results regarding associations between allergen and/or whole pollen concentrations and other possible meteorological drivers, such as humidity (Buters et al., 2015; Fernández-González et al., 2019a) and temperature (Beck et al., 2013; Galan et al., 2013).

Other environmental variables that were associated with one or both components of pollen potency were altitude, proximity to the ocean and prevalence of long-distance dispersed pollen (Table 3). Few studies discussed the potential influence of plant physiology and genetics [for an exception see Buters et al. (2008)]. Aside from climatic conditions, factors such as soil composition and tree health have been identified as likely to influence the quantity of allergen released from pollen (Buters et al., 2008); however, these have not been directly studied. Ozone levels have also been

Table 4 Summary of characteristics of studies investigating relationship between health outcomes and allergenic exposure

Study	Exposure metrics	Health outcome metric/s	Statistical analysis	Key results
Schäppi et al. (1999)	Atmospheric group 5 grass allergen concentration (Phl p 5 and cross-reactive allergens) in both respirable and non-respirable particle fractions, grass pollen counts, total allergen, rainfall and temperature	Hospital attendance for patients whose diagnosis was classified on admission or discharge as either asthma or chronic obstructive airways disease	Spearman's rank correlation coefficient	There was a significant correlation between the 4-day running mean of group 5 grass allergens in respirable fractions and the 4-day running mean of asthma attendances (with a 2-day delay): $r^2 = 0.334$, $p < 0.001$
	Location: Melbourne, Australia			There was no significant correlation between asthma attendances and whole grass pollen concentrations or any other meteorological variables (statistics not reported)
Porcel Carreño et al. (2020)	Atmospheric concentrations of: grass pollen, group 5 grass allergen concentration (Phl p 5), group 1 grass pollen allergen (Phl p 1), olive pollen and group 1 olive pollen allergen (Ole e 1)	Emergency Department (ED) visits for which the cause of admission was determined to be an asthma exacerbation	Pearson rank correlation coefficient	There was a significant correlation between whole grass pollen counts and asthma ED visits that increased over lags 1–3 ($r = 0.313$ same day, 0.488 1-day lag, 0.575 3-day lag; in all cases $p < 0.005$)
	Location: Cáceres, Spain			Three measures of grass pollen allergen (Phl p overall, Phl p1, Phl p5) were more weakly associated with asthma ED visits, excepting lag 3, when Phl p overall ($r = 0.644$) and Phl p 5 ($r = 0.670$) were slightly more strongly associated with ED visits than whole pollen. On the same day, only Phl p overall was significantly associated with ED visits; at lag 1 lag Phl p overall and Phl p 5 were significantly associated, at lag 3 all allergen measures were significantly associated ($p < 0.001$)
				For olive, neither whole pollen nor allergen were significantly associated with ED visits on the same day. Associations with lags were measured at different points for whole pollen and allergen (Ole e 1); however, the association between whole pollen at lag 4 ($r = 0.716$) and Ole e 1 at lag 6 (0.720) are similar

Table 4 continued

Study	Exposure metrics	Health outcome metric/s	Statistical analysis	Key results
Brito et al. (2011)	Atmospheric olive pollen grain concentration and olive pollen allergen concentration (Ole e 1) Location: Ciudad Real, Spain	Hay fever and asthma symptom reports in twenty olive-monosensitised individuals	Forward stepwise Poisson multiple regression model	The daily number of symptoms was correlated with olive pollen count (with a 4-day lag) ($r = 0.700$, $p < 0.001$) However, the daily number of symptoms was more strongly correlated with olive pollen allergen concentration (Ole e 1; with a 2-day lag): $r = 0.803$, $p < 0.001$
Buters et al. (2012)	Birch pollen concentration and birch pollen allergen concentration (Bet v 1) in locations across France, the United Kingdom, Germany, Italy and Finland	Degranulation of humanised rat basophil sensitised to birch pollen	Linear regression goodness of fit statistic	The release of β-hexosaminidase (marker of histamine release) was more strongly correlated with Bet v 1 ($r^2 = 0.95$) than with birch pollen: ($r^2 = 0.71$)
Buters et al. (2015)	Grass pollen concentration and grass pollen allergen concentration (Phl p 5) from ten sites across ten European countries	Degranulation of humanised rat basophil sensitised to grass pollen	Linear regression goodness of fit statistic	The release of β-hexosaminidase (marker of histamine release) was more strongly correlated with grass pollen allergen concentration (Phl p 5) ($r^2 = 0.80$) than grass pollen concentration ($r^2 = 0.61$)

Details on exposure, health outcome, statistical analysis, results and p value are presented for each study

NA not applicable, *n.s.* not significant

proposed as a possible driving factor, with some support from the very limited data available: Beck et al. (2013) found a weak positive relationship between ozone levels and Bet v1 atmospheric concentrations (Beck et al., 2013; Buters et al., 2008).

3.5 Pollen potency and health

Five publications investigated the relevance of pollen potency for human health by testing the relationship between allergen and pollen with a health outcome related to asthma or allergies (Table 4). Four of these were undertaken in Europe; the other was undertaken in Melbourne, Australia. All but one of the studies found that allergen concentrations had a slightly higher correlation with human health outcomes than whole pollen concentrations; the fifth (Porcel Carreño et al., 2020) reported mixed results, with whole grass and olive pollen sometimes appearing more strongly associated with asthma emergency department attendances than allergen, depending on the lag and allergen metric used (for details see Table 4). However, across all studies, differences were generally not substantive and the correlation between the health proxy and whole pollen counts was still high: for example, Brito et al. (2011) reported a value of $r = 0.7$ for the relationship between whole olive pollen counts and daily symptom counts, but a value of $r = 0.8$ for the relationship with Ole e 1 allergen concentrations.

Two additional publications amongst those returned by our search investigated factors other than pollen potency that contributed to the magnitude of the human immune response. Beck et al. (2013) found that birch pollen extracts prepared from environments higher in ozone were more strongly correlated with components of a stronger allergic response (e.g. skin prick test wheal measurements, cytokine secretion and neutrophil migration). This study also described weak positive correlations between higher ozone and higher Bet v 1 concentrations ($r = 0.37$, $p < 0.05$); however, it did not directly assess the relationship between Bet v 1 and health outcomes. Behrendt et al. (1999) showed

that grass, birch and pine pollen all secrete the eicosanoid prostaglandin E2 and leukotriene B4, which are initiators of innate and inflammatory responses. These two studies suggested that there are factors beyond allergen content that could additionally contribute to the human immune response to pollen.

4 Discussion

The results of this scoping review demonstrate inconsistent findings with respect to all facets of pollen potency across the peer reviewed literature. Consequently, there is insufficient evidence to support clear conclusions about the factors that influence pollen potency, nor explain the large degree of variation between taxa, across time and between locations. However, this review identified several key gaps in the existing literature, and on this basis we generate recommendations to inform the pollen potency research agenda. The implications of the review results are discussed in further detail below, stratified by our research aims: (a) variation in pollen potency, (b) factors influencing pollen potency and (c) pollen potency and health outcomes.

4.1 Variation in pollen potency

Our synthesis revealed a large degree of temporal, taxonomic and geographic variation in pollen potency measurements. With respect to temporal variation, a key implication of the degree and sporadic nature of the variation reported both within and between seasons is that it is difficult to either (a) predict pollen potency at any stage in the season or (b) extrapolate potency trends from 1 year to another. This greatly limits the capacity to forecast pollen potency for a season, let alone days during a season, based on previous observations. One caveat is that the maximum number of seasons over which pollen potency was tracked was three: it is possible that patterns may become evident with longer time series. With respect to variation between taxa, this review identified similar ranges in average pollen potency measurements reported for birch, grass and olive, but substantially lower average measurements for *Platanus* and Urticaceae. Further research is required to establish whether the lower potency of the latter taxa is a consistent trend or simply an artefact of the low number of studies carried out on these taxa to date. Further, disaggregated daily data [e.g. as reported by Fernández-González et al. (2010) and De Linares et al. (2010)], revealed that different pollen taxa displayed distinct within-season pollen potency dynamics. This further highlights the difficulty of transferring pollen potency research: trends observed in one taxon in a given location cannot be extrapolated to any other. Further, due to the limited taxonomic resolution of current pollen detection methods for grass (Campbell et al., 2020; Jones et al., 2020), overlapping seasons of cross-reactive species and the presence of more than one major allergen (Lol p 1 and Phl p 5) further confound the conclusions that can be drawn about grass pollen potency (Buters et al., 2015; Jochner et al., 2015; Ščevková et al., 2020). Finally, given the substantial and non-systematic geospatial variation in pollen potency, we also conclude that findings cannot be extrapolated geospatially, nor by climatic region. With the caveat that most studies were conducted in Europe, we also found insufficient evidence to conclude that particular locations exhibit more or less potent pollen. This implies that it is not possible at this time to support the hypothesis that pollen potency variation is the driver of different symptom thresholds in different locations (de Weger et al., 2013).

4.2 Factors influencing pollen potency

The results of this review highlight several major gaps in our understanding of the factors that influence pollen potency. Our synthesis suggests that meteorological factors including temperature and humidity may influence temporal and/or geographic variation in pollen potency, as numerous studies have reported associations between pollen potency and meteorological variables (see Table 3). However, no study found a decisive influence of any one variable, the direction and magnitude of effects were inconsistent across studies, and the mechanisms remain unclear. For example, it is unclear whether the effects of meteorological variables relate primarily to their impacts on allergen production and/or free allergen release due to pollen fragmentation. In addition to meteorological variables, a small number of studies also reported associations between pollen potency and geographic factors such as altitude and proximity to coast (Table 3); however, again the predictability and mechanisms behind these associations remain unclear.

Our review suggests that pollen potency is most likely determined by a complex web of interacting factors, which we are currently unable to reconcile using available data. A systematic and standardised methodological approach to investigating pollen potency drivers may be required to provide greater clarity (discussed further below).

4.3 Pollen potency and health

Our synthesis suggests that atmospheric allergen counts might be more correlated with allergic symptoms than pollen counts. All but one of the publications that investigated this relationship showed that allergen concentrations had a greater magnitude in the size of the association between allergy symptoms than pollen concentrations, although the differences were not always substantial. This finding suggests that although allergen concentrations may generally better predict health outcomes than whole pollen counts, the substantially higher cost of obtaining information about allergen concentrations might not be justified by a modest improvement in correlations with clinical outcomes.

Importantly, the results also highlight that allergen concentrations do not fully explain trends in health outcome responses as a degree of residual variance remains (Table 4). This suggests that factors other than pollen allergen load impact the prevalence and magnitude of allergic response (Beck et al., 2013; Behrendt et al., 1999). While outside the scope of this review, these factors might include plant fibres and trichomes (Sercombe et al., 2011), other environmental allergen sources that patients may be co-sensitised to [e.g. fungal as shown in Tham et al. (2017)], and/or other compounds associated with pollen, often referred to as non-allergenic pollen-derived compounds (Gilles et al., 2012). With respect to the latter, the most commonly investigated are pollen-associated lipid mediators (PALMs), which are molecules that can interact with the immune system, impacting the immune system response (Beck et al., 2013; Behrendt et al., 1999; Gilles et al., 2012). Resident bacteria on pollen grains are also believed to enhance the immune response, or in some situations, act as an immune sensitiser and activate the immune system (Obersteiner et al., 2016; Oteros et al., 2019). Further potential contributing factors include the immune adjuvant effect of pollution on pollen grains [reviewed in Senechal et al. (2015)], as well as Adenosine and NADPH-oxidase levels in pollen, both of which have been associated with a stronger immune response (Beck et al., 2013; Gilles et al., 2012; Wimmer et al., 2015). We suggest that to achieve a more holistic understanding of pollen allergy risk, the influence of PALMs and other non-allergenic compounds on health outcomes should be further explored in future research.

4.4 Implications for pollen monitoring practice and future research

The results of this review have important implications for pollen monitoring and allergy risk communication. Our results highlight that the understanding of pollen potency remains too rudimentary for its application in public health practice. The degree of unsystematic and unexplained variability in pollen potency diminishes predictive capacity. Further, we are not yet able to measure atmospheric allergen content (and thus pollen potency) routinely and in real time, in part due to the high cost of molecular and immunological approaches to airborne allergen measurement. This means that on a day-to-day basis, we are not able to use pollen potency information to supplement the allergy risk information provided by whole pollen counts.

In relation to future research, these results highlight the need to better understand and characterise pollen potency, as well as the broader range of factors that contribute to an immune response to pollen. While Supplementary Figure 2 suggests an increase in research effort in the last decade, there has not been a considerable increase in the last few years. Consequently, we recommend an increase in research effort and that future studies work towards standardised methodologies that systematically examine pollen potency drivers. Specifically, we suggest the standardisation of approaches to allergen collection and measurement: across the studies included in this review, a diversity of collection and measurement approaches were utilised (details in Supplementary Table 1). Although analysis of Fig. 2 does not suggest a systematic difference in results generated by the two main methods used for atmospheric allergen collection (cyclone and High Volume Impactor samplers), methodological differences could nevertheless potentially contribute to some of the inconsistency in conclusions found here. We were unable to explicitly

assess this due to the difficulty of controlling for other differences between studies and suggest the literature would benefit from a direct experimental comparison of results generated by different methods to generate a single recommended sampling approach. In addition to greater methodological homogeneity, longer time series of single taxa across one or multiple locations would also be highly valuable in order to provide data sets with greater power to discern potentially complex patterns and trends. Further, we recommend that future research incorporates size-fractioned sampling to facilitate a better understanding of the relative role of pollen fragmentation versus variation in allergen per original pollen grain in driving pollen potency variation.

Further, in addition to meteorological variables, we highlight the need to consider a broader range of potential pollen potency drivers, such as herbivory (e.g. Lommen et al., 2017), land disturbances (e.g. Kernerman et al., 1992) and pollution (e.g. Beck et al., 2013; Kim et al., 2018; Singer et al., 2005; Ziska, 2020; Ziska et al., 2019). Such factors have been shown to increase allergen content and have high potential to act as strong drivers of pollen potency because some allergens are plant defence proteins (Matricardi et al., 2016), which are commonly upregulated during plant stress (Tashpulatov et al., 2004). Agriculture or other activities that disturb vegetation could also play a role, for example via the re-aerosolisation of deposited pollen (and pollen fragments) (e.g. Kernerman et al., 1992; Taylor et al., 2002). Factors related to plant physiology and genetics also remain under-explored; further investigation of the size distribution of atmospheric allergen could also help resolve the degree to which pollen fragmentation contributes to pollen potency variation (e.g. Buters et al., 2012; De Linares et al., 2010; Wang et al., 2012). Finally, future research should also investigate the role of pollen-derived factors such as PALMs, Adenosine, NADPH-oxidase, bacterial LPS and pollutants in modulating the immune response (Beck et al., 2013; Gilles et al., 2009, 2012; Oeder et al., 2015).

5 Strengths and limitations of the review

To our knowledge, this scoping review represents the first to synthesise published research summarising findings on pollen potency and the implications for human health. This has enabled us to highlight key gaps in the existing literature, supporting an evidence-based agenda for the ongoing characterisation of the relationship between atmospheric pollen and allergen concentrations, and their implications for individual and public health outcomes. It is, however, important to acknowledge certain limitations in our approach. First, we only included studies published in English. Second, as a scoping review, we did not systematically assess studies for data quality or risk of bias. These limitations are unlikely to substantially affect our core finding that there is substantive and frequently un- or poorly explained variability in pollen potency results.

6 Conclusion

The published literature reveals considerable taxonomic, temporal and geographic variation in pollen potency. The inconsistent and largely unexplained variation in pollen potency identified in this review makes it challenging to draw definitive conclusions about the factors that may influence pollen potency and to what extent. Similarly, insufficient evidence exists to be able to predict allergen levels in the air by extrapolating potency data onto pollen counts. Results from this review confirm that further research is needed to better understand what is a highly complex system of factors that determine pollen potency. To aid the comparison of work in this field, we recommend that the field adopts more consistent methodologies to enable standardised characterisation of pollen potency. A better understanding of the factors driving pollen potency will in turn improve our understanding of allergic disease and offer insights to direct effective management options for sufferers in future. We also recommend the future research agenda investigates the characteristics of free allergen caused by pollen fragmentation, methods of detection and non-allergen pollen-derived molecules in order to enhance our understanding of the full range of factors that determine the intensity of human allergic response.

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Declaration

Conflict of interest The authors declare that there is no conflict of interests.

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