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Prevalence and Influencing Factors of Food Allergy in Global Context: A Meta-Analysis

Hua Feng[a, b] Xiujuan Xiong[c] Zhuo Chen[a] Qunying Xu[b] Zhongwei Zhang[b] Nan Luo[b] Yongning Wu[a, d]

[a]State Key Laboratory of Food Science and Technology, Nanchang University, Nanchang, PR China; [b]School of Public Health, Nanchang University, Nanchang, PR China; [c]Department of Pathology, Basic Medical College of Nanchang University, Nanchang, PR China; [d]NHC Key Laboratory of Food Safety Risk Assessment, Chinese Academy of Medical Science Research Unit (No. 2019RU014), China National Center for Food Safety Risk Assessment, Beijing, PR China

Keywords
Food allergy · Prevalence · Influencing factors · Meta-analysis

Abstract
Introduction: This study was conducted to evaluate the prevalence and influencing factors of food allergy (FA) in different regions and populations. ***Methods:*** The studies from January 2011 to December 2021 were searched through PubMed, Embase, Cochrane Library, and Web of Science databases. The prevalence of FA was evaluated by calculating the pooled effect estimates and their 95% confidence intervals (CIs). The odds ratio (OR) value was used to investigate the influencing factors of FA. Heterogeneity analysis among studies was performed using I^2 analysis. Sensitivity analysis was performed to assess the stability of the results, and Begg's test was used to assess publication bias. ***Results:*** A total of 105 published articles, including 3,318,608 participants, were involved in this study. The result indicated that the overall FA prevalence was 4.3% (95% CI: 0.038–0.047). The prevalence of FA was 4.2% in Asia (95% CI: 0.033–0.051), 3.2% in America (95% CI: 0.024–0.041), 4.8% in Europe (95% CI: 0.037–0.060), 1.6% in Africa (95% CI: 0.008–0.026), and 7.5% in Oceania (95% CI: 0.052–0.102). Milk (prevalence: 1.1%, 95% CI: 0.009–0.013) and egg (prevalence: 1.1%, 95% CI: 0.008–0.014) were the most common type of FAs. Male (OR: 1.289, 95% CI: 1.001–1.659), antibiotics exposure during pregnancy (OR: 1.221, 95% CI: 1.162–1.284), breastfeeding (OR: 1.349, 95% CI: 1.011–1.799), asthma (OR: 1.794, 95% CI: 1.443–2.230), eczema (OR: 5.121, 95% CI: 3.575–7.334), family history of atopic disease (OR: 1.893, 95% CI: 1.313–2.730), family history of FAs (OR: 2.096, 95% CI: 1.686–2.594), family history of atopic dermatitis (OR: 1.954, 95% CI: 1.645–2.322), family history of asthma (OR: 1.516, 95% CI: 1.370–1.678), and family history of allergic rhinitis/conjunctivitis (OR: 1.287, 95% CI: 1.191–1.392) increased the risk of FA. ***Conclusion:*** There were geographical differences in the prevalence of FA. Identification and nursing of FA high-risk populations should be strengthened to improve the quality of life.

Introduction

Food allergy (FA) is defined as adverse health effects arising from a specific immune response that occurs, reproducibly, on exposure to a given food [1]. There are

Edited by: H.-U. Simon, Bern

Karger@karger.com
www.karger.com/iaa

Correspondence to:
Yongning Wu, wuyongning@cfsa.net.cn

extensive data to suggest that FA is common, affecting up to 10% of the population in some countries [2], and has been increasing in prevalence in the last 2–3 decades [3, 4]. Clinical manifestations of FA may involve various organs and systems, including skin, gut and respiratory, and cardiovascular and nervous systems; moreover, symptoms variously embrace each other, giving rise to complex disease pictures [5, 6]. Following asthma and allergic rhinitis, FA has recently become another allergy epidemic [5]. FA poses a significant burden on the affected population and their families, resulting in dietary and social restrictions, fear of accidental reactions, high levels of anxiety related to the risk of severe reactions, fatalities, and, as a consequence, a reduced quality of life [1, 7, 8]. FA affects people of all ages, races/ethnicities, and socioeconomic strata and has become an important public health issue globally [9]. Nevertheless, there is presently no cure for FA [3]; thereby, adequate knowledge of prevalence, common allergenic foods, and potential risk factors are essential for the prevention of FA.

Previous studies have studied FA prevalence, but either focused on specific regions and populations or only on selected food allergens. A study [10] conducted in South Asia has found the overall incidence of FA was low. A study [11] evaluating the epidemiology of FA in Europe demonstrated discrepant FA prevalence from different diagnostic methods. Another study [12] suggested that peanut allergy is, however, much less prevalent in Asia compared to the West. Currently, studies estimating the incidence and prevalence of FA in different regions or populations are scanty. Furthermore, the epidemiology of FA, its risk factors are remarkably variable across different populations throughout the world due to geographic variations, differences according to age, race, and ethnicity, and other factors [13, 14]. Evaluating the scope of the FA burden among the different populations in various regions may be of importance to efficacious preventive measures.

Herein, this meta-analysis aimed to evaluate the prevalence of FA and potential influencing factors. Besides, we examined the prevalence of different food types and different diagnostic methods. This study may be necessary for the detection of FA to better understand the extent of the FA and its impact on health services.

Materials and Methods

This meta-analysis was performed with reference to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.

Search Strategy

From January 2011 to December 30, 2021, relevant available articles were identified by literature searching from PubMed, Embase, Cochrane Library, and Web of Science databases. The retrieval strategy was as follows: "Food Hypersensitivit*" OR "Hypersensitivit*, Food" OR "Allerg*, Food" OR "Food Allerg*" AND "Prevalenc*" OR "Period Prevalenc*" OR "Prevalenc*, Period" OR "Point Prevalenc*" OR "Prevalence, Point" OR "Facto*, Risk" OR "Risk Facto*" OR "Health Correlat*" OR "Correlat*, Health" OR "Risk Scor*" OR "Scor*, Risk" OR "Risk Factor Scor*" OR "Scor*, Risk Factor" OR "Populatio* at Risk". Full search strategy from PubMed is shown in online supplementary Table 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000527870).

Inclusion and Exclusion Criteria

The following inclusion criteria were applied: (1) populations with FA; (2) observational studies; (3) English articles about the subject of FA. The exclusion criteria were as follows: (1) animal experiments; (2) studies that fail to extract valid data; (3) conference reports, case reports, meta-analyses, reviews, editorial materials, letters, protocols, errata. We excluded studies on specific populations (e.g., asthma, eczema, allergic rhinitis, atopic dermatitis [AD], etc.) and specific patients (e.g., emergency department, surgical patients, allergy patients). However, populations with a history of asthma/eczema and other diseases in the general population were not excluded.

Data Extraction

The following information was extracted according to a predesigned extraction form by two independent authors (Feng Hua, Nan Luo): first author's name, publication year, the location where the study was carried out, study population, sample size, gender, age, history and diagnosis of FA, study quality score, and outcomes of studies.

Study Quality Assessment

The JBI scale (Joanna Briggs Institute, online clinical evidence evaluation system of the Australian Evidence-Based Nursing Center) was used for the quality evaluation of the cross-sectional studies; the scale has a total score of 20 points, with 0–14 as low quality and 15–20 as high quality. The Newcastle-Ottawa Scale (NOS) was recommended to assess the quality of the included case-control studies and cohort studies. For NOS, studies that scored 0–5 points, 5–10 points were classified as low, high quality in turn, respectively.

Definition of FA

FA in this study was clearly defined based on one of the following four ways: (1) FA diagnosed by a doctor (mainly obtained via a questionnaire); (2) oral food challenge of open food challenge (OFC)/the double-blind placebo-controlled food challenge was positive; (3) FA symptoms in combination with immunoglobulin E (IgE) ≥0.35kU/L; (4) symptoms of FA in combination with skin prick test (SPT) ≥3 mm.

Statistical Analysis

The prevalence of FA was evaluated by calculating the pooled effect estimates and their 95% confidence intervals (CIs). The odds ratio (OR) value was used to investigate the influencing factors of FA, and the effect size was expressed by 95% CI. RR represents the rate of rate 1/rate 2, where rate is the proportion in the group with the condition present. Heterogeneity analysis among studies was performed using I^2 analysis. $I^2 \geq 50\%$ indicated the existence of

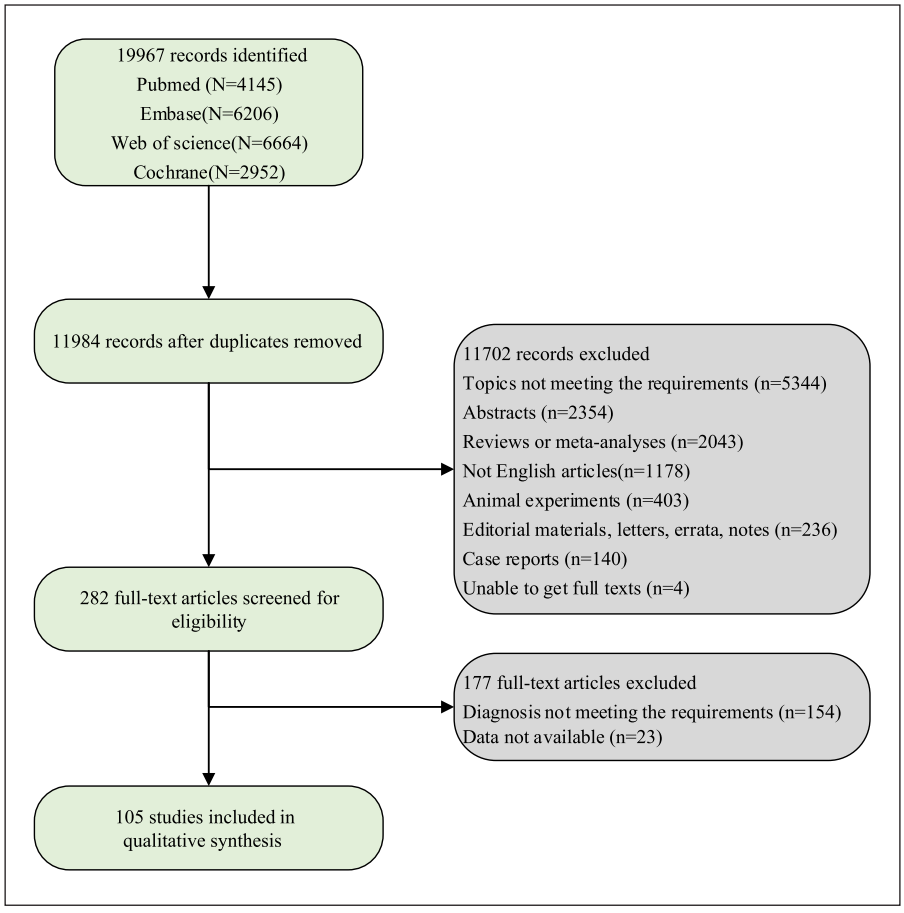

Fig. 1. Flowchart of literature search.

significant heterogeneity, and the random-effects model (REM) was used as the pooling method; otherwise, the fixed-effects model (FEM) was used. Differences were deemed statistically significant when $p < 0.05$. When heterogeneity $I^2 \geq 50\%$ and differences were statistically significant, subgroup analysis was performed by study region (Asia, America, Europe, Africa, Oceania), population (children <18 years old, adults ≥18 years old), and diagnosis modes (doctor, OFC, IgE, SPT, mixed), quality of literature (high quality, low quality). We used "METAPROP" command to perform fixed- and random-effects meta-analysis of proportions [15]. Sensitivity analysis was performed to assess the stability of the results. Funnel plots and Begg's test were used to assess publication bias, and the trim and fill method was used to assess the impact of bias on the results. All statistical analyses were performed using Stata (version 15.1; Stata Corp, College Station, TX, USA) software.

Results

Study Selection and Characteristics

A total of 19,967 records were initially retrieved from 4 databases, 11,984 studies were identified after duplicates were removed, and 282 full-text articles were screened. Our meta-analysis finally included 105 published articles [5, 16–119], including 3,318,608 participants. The flowchart of the literature search is shown in Figure 1. This meta-analysis involved 55 cross-sectional studies, 46 cohort studies, and 4 case-control studies. Study quality assessment indicated that 82 studies were of high quality, and 23 articles were of low quality. The characteristics of the eligible studies are summarized in Table 1.

Prevalence of FA

A total of 94 groups of data from 91 articles were included to assess the overall FA prevalence. The heterogeneity test results showed that $I^2 = 99.7\%$, so the REM was analyzed. The result indicated that the overall FA prevalence was 4.3% (95% CI: 0.038–0.047) (shown in Table 2 and Fig. 2a). Based on the quality of literature subgroup analysis, the FA prevalence was 3.6% (95% CI: 0.026–0.048), 5.3% (95% CI: 0.038–0.071), 4.2% (95% CI: 0.038–0.047) in high quality of cross-sectional studies, low quality of cross-sectional studies, and high quality of cohort studies, respectively (shown in Table 2).

Table 1. Baseline characteristics of included studies

Author	Year	Country	Region	Study design	Population	Number of patients	Number of males/ females	Age (years or months)	Allergic disorder (number of patients)	Family history of allergy	Diagnosis	QA	Outcomes
Aksoy [102]	2021	Turkey	Asia	Retrospective cohort study	Children	949	518/431	28±6 months	AD, respiratory allergy	–	OFC	7	Prevalence (food, milk, egg)
Bager [103]	2021	Sweden	Europe	Cohort study	Adult	2,215	–	24 years	–	–	IgE	6	Prevalence (nuts)
Beltrán-Cárdenas [104]	2021	Colombia	America	Cross-sectional study	Children	969	422/547	5–12 years	AR, AD, asthma, AC	–	doctor	14	Prevalence (food), influence (male)
Erhard [105]	2021	Germany	Europe	Prospective cohort study	Children	1,004	524/480	8.2±0.9 years	–	Maternal, paternal	OFC, SPT, IgE	7	Prevalence (nuts)
Garkaby [106]	2021	Israel	Asia	Cross-sectional study	Children	1,932	–	22.4 (18–30) months	–	–	OFC, SPT, IgE, doctor	16	Prevalence (food, milk, egg, nuts, peanut, fish)
He [107]	2021	China	Asia	Prospective cohort study	Children	741	385/355	0.5 years	–	–	OFC	7	Prevalence (food, milk, egg, peanut), influence (male, cesarean)
Kaneko [108]	2021	Japan	Asia	Retrospective cohort study	Children	23,969	–	0–6 years	–	–	Doctor	7	Prevalence (food, milk, egg, nuts, wheat, soya)
Lamminsalo [109]	2021	Finland	Europe	Population-based cohort study	Children	4,921	2,590/2,331	3 years	–	Maternal, paternal	Doctor	6	Prevalence (milk), influence (male, cesarean, family history of atopic disease, breastfeeding duration ≥6 months)
Ma [110]	2021	China	Asia	Cross-sectional study	Children	1,228	–	0–2 years	–	–	OFC	15	Prevalence (food, milk, egg)
Matsumoto [111]	2021	Japan	Asia	Cross-sectional study	All	2,688	1,555/1,133	18.4±0.8 years	AR, AD, asthma	–	Doctor	10	Prevalence (food)
Ontiveros [112]	2021	Paraguay	America	Cross-sectional survey	Adult	1,058	369/689	18–84 years	–	–	Doctor	13	Prevalence (food)
Rangkakulnuwat [113]	2021	Thailand	Asia	Cross-sectional study	Children	561	284/277	4.8±0.5 years	Asthma, AR, AD	Asthma (paternal, maternal, siblings), AR (paternal, maternal, siblings), AD (paternal, maternal, siblings)	OFC, SPT, IgE	17	Prevalence (food, milk, egg, shellfish, fish, wheat)
Suaini [114]	2021	Australia, Singapore	Mixed	Population-based cohort study	Children	1,192	627/565	14–18 months	Eczema	Father, mother, siblings	SPT, OFC	7	Prevalence (food), influence (male, breastfeeding, eczema, family history of atopic disease)
Sugiura [115]	2021	Japan	Asia	Cross-sectional study	Children	18,549	9,480/9,069	1.5 years	Eczema	AD (father, mother, siblings), asthma (father, mother, siblings), ARC (father, mother, siblings)	Doctor	12	Prevalence (food), influence (male, eczema, family history of FA/AD/asthma/ARC)

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Table 1 (continued)

Author	Year	Country	Region	Study design	Population	Number of patients	Number of males/females	Age (years or months)	Allergic disorder (number of patients)	Family history of allergy	Diagnosis	QA	Outcomes
Tezuka [116]	2021	Japan	Asia	Prospective birth cohort study	Children	80,408	41,125/39,283	1 year	Eczema	Maternal	Physician	7	Prevalence (milk)
Vassilopoulou [117]	2021	Greece	Europe	Cross-sectional study	Children	202	107/95	8.7±1.7 years	–	–	Physician	13	Prevalence (food, milk, egg, nuts, peanut, fish, wheat, soya), influence (family history of atopy disease/FA)
Venter [118]	2021	USA	America	Longitudinal pre-birth cohort study	Children	1,261	660/601	5 years	Asthma, AD/eczema, wheeze	Maternal asthma, maternal AR	Physician	6	Prevalence (food)
Warren [119]	2021	USA	America	Cross-sectional study	Adult	40,443	–	–	–	–	Physician	16	Prevalence (peanut)
Arancibia [87]	2020	Chile	America	Prospective cohort study	Children	411	209/202	1 year	–	Mother, father	OFC	7	Prevalence (milk)
Chen [88]	2020	USA	America	Prospective cohort study	Adult	1,574	455/1,108	21.9±0.62 years	–	–	Doctor	7	Prevalence (food, milk, nuts, peanut, shellfish)
Dai [5]	2020	China	Asia	Cross-sectional study	Children	4,151	2,174/1,977	3.99±0.824 years	Eczema, AR, wheeze	–	Doctor, SPT, IgE, OFC	15	Prevalence (food, milk, egg, peanut, shellfish, fish)
Grabenhenrich [89]	2020	Europe	Europe	Prospective birth cohort study	Children	6,069	–	8.3±0.9 years	–	–	Doctor, SPT, DBPCFC	7	Prevalence (food, milk, egg, nuts, peanut, shellfish, wheat, soya)
Hassan [90]	2020	Saudi Arabia	Asia	Cross-sectional study	Adult	5,497	1,962/3,535	22.60±4.96 years	AD, asthma, AR, AC	–	Physician	14	Prevalence (food)
Le [91]	2020	Vietnam	Asia	Cross-sectional survey	All	9,039	2,955/6,084	≥16 years	–	–	Doctor	15	Prevalence (food, milk, egg, nuts, peanut, shellfish, fish, wheat, soya)
Levin [92]	2020	South Africa	Africa	Cohort study	Children	1,583	847/736	1–3 years	Asthma, AR, AD	–	OFC	7	Prevalence (food), influence (cesarean, antibiotics exposure in the first year)
Li [93]	2020	China, India, Russia	mixed	Cross-sectional study	Children	35,549	17,785/17,764	7–10 years	–	–	SPT, IgE	16	Prevalence (food, milk, egg, peanut, shellfish, fish, wheat)
Lozoya-Ibáñez [94]	2020	Portugal	Europe	Cross-sectional study	All	1,702	648/1,054	14.9±2.1 (10–23) years	–	–	SPT, IgE, OFC	11	Prevalence (food, milk, egg, nuts, peanut, shellfish)
Molloy [95]	2020	Australia	Oceania	Prospective birth cohort study	Children	1,074	557/517	1 year	Eczema	Asthma, eczema	OFC	6	Prevalence (food)

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Table 1 (continued)

Author	Year	Country	Region	Study design	Population	Number of patients	Number of males/females	Age (years or months)	Allergic disorder (number of patients)	Family history of allergy	Diagnosis	QA	Outcomes
Morillo-Argudo [96]	2020	Ecuador	America	Cross-sectional study	Children	1,338	673/665	13±0.9 years	–	–	Doctor	15	Prevalence (food, nuts, peanut, shellfish, soya)
Samady [97]	2020	USA	America	Cross-sectional study	Children	38,408	19,626/18,782	0–17 years	Asthma, eczema	–	Physician	17	Prevalence (egg)
Shourick [98]	2020	Brazil, China, Russia, USA, France	mixed	Cross-sectional study	Adult	9,399	4,612/4,787	40.9±14.5 years	Respiratory allergies, skin allergies	–	Doctor	9	Prevalence (food)
Skoczylas [99]	2020	Poland	Europe	Cross-sectional study	Children	1,008	516/492	6–18 years	AR, asthma, AD	–	Doctor	15	Prevalence (food)
Wang [100]	2020	USA	America	Cross-sectional study	Children	38,408	19,626/18,782	0–17 years	asthma, eczema, AR	Asthma, eczema	Physician	17	Prevalence (shellfish)
Yamamoto-Hanada [101]	2020	Japan	Asia	Prospective birth cohort study	Children	92,945	47,680/45,247	3 years	Asthma, AD, AC	Asthma (father, mother), AD (father, mother), AC (father, mother)	Physician	7	Prevalence (food)
Adeyeye [78]	2019	USA	America	Longitudinal, prospective birth cohort	Children	5,753	–	3 years	Wheeze	Maternal	Doctor	8	Prevalence (food)
Botha [79]	2019	South Africa	Africa	Cross-sectional study	Children	1,583	847/736	1–3 years	AR, AD	Asthma, AR, AD	OFC	15	Prevalence (milk, egg, peanut, fish)
Davisse-Paturet [80]	2019	France	Europe	Birth cohort study	Children	11,720	5,965/5,755	2 months	Eczema, wheeze, asthma	–	Doctor	6	Prevalence (food)
de Jong [81]	2019	The Netherlands	Europe	Population-based prospective cohort study	Children	5,471	2,724/2,747	10 years	Eczema, asthma	Mother, father	Doctor	7	Prevalence (food, nuts, peanut)
Le [82]	2019	Vietnam	Asia	Cross-sectional study	Children	8,620	4,294/4,326	2–6 years	–	–	Doctor	15	Prevalence (food, milk, egg, nuts, peanut, shellfish, fish, wheat, soya)
Mathias [83]	2019	USA	America	Prospective birth cohort	Children	1,387	688/698	6 years	–	–	Doctor	7	Prevalence (food)
Metzler [84]	2019	Austria, Finland, France, Germany, Switzerland	Europe	Birth cohort study	Children	1,133	560/530	6 years	Asthma, AD, AR	–	Doctor	7	Prevalence (food), influence (antibiotics exposure during pregnancy/antibiotics exposure in the first year)
Nachshon [85]	2019	Israel	Asia	Cohort study	All	12,592	5,855/6,737	17–18 years	–	–	OFC	7	Prevalence (food, milk, egg, nuts, peanut, shellfish, fish)

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Table 1 (continued)

Author	Year	Country	Region	Study design	Population	Number of patients	Number of males/females	Age (years or months)	Allergic disorder (number of patients)	Family history of allergy	Diagnosis	QA	Outcomes
Rentzos [86]	2019	Sweden	Europe	Cross-sectional study	Adult	1,042	480/562	51.0±30.0 years	–	–	IgE	14	Prevalence (food, milk, egg, peanut)
Alkazemi [68]	2018	Kuwait	Asia	Case-control study	Children	200	122/78	0–13 years	Eczema, asthma, rhinitis	–	IgE, SPT	7	Influence (antibiotics exposure in the first year, breastfeeding, breastfeeding duration ≥6 months)
Cabrera-Chávez [69]	2018	El Salvador	America	Population-based cross-sectional survey	Children	508	260/248	9.2 (4–12) years	AD, asthma, AR, AC	–	Physician	13	Prevalence (food)
Clausen [70]	2018	Iceland	Europe	Prospective birth cohort study	Children	1,304	668/636	–	–	–	IgE, DBPCFC	6	Prevalence (food, milk, egg, peanut, fish, wheat, soya)
Mehaudy [71]	2018	Argentina	America	Retrospective cohort study	Children	14,710	–	0–1 year	–	–	Doctor	6	Prevalence (milk)
Mitre [72]	2018	USA	America	Retrospective cohort study	Children	792,130	396,915/395,215	4.6 years	AD, asthma, AR, AC	–	Doctor	7	Prevalence (food, milk, egg, peanut), influence (antibiotics exposure in the first year)
Mitselou [73]	2018	Sweden	Europe	Prospective cohort study	Children	1,086,378	528,431/557,947	0.2–12.8 years	–	–	Doctor	8	Prevalence (food), influence (male, cesarean)
Palmu [74]	2018	Finland	Europe	Cross-sectional study	Children	1,937	990/947	6–7 years	–	–	Doctor	16	Prevalence (food, milk, egg, nuts, fish, wheat, soya)
Sardecka [75]	2018	Poland	Europe	Case-control study	Children	239	126/113	7.9±6.8 years	AD, asthma, AR	AD, asthma, AR	OFC	7	Influence (male, cesarean, breastfeeding, family history of FA/AD/asthma/AR, antibiotics exposure in the first year)
Tham [76]	2018	Singapore	Asia	Birth cohort study	Children	1,152	–	–	–	–	SPT	6	Prevalence (food, egg, peanut, shellfish)
Venkataraman [77]	2018	UK	Europe	Prospective birth cohort study	Adult	1,456	–	18 years	Asthma, eczema, AR	–	SPT	7	Prevalence (food)
Gil [64]	2017	Spain	Europe	Retrospective, observational case-control study	All	422	256/166	14.5±4.80 years	–	–	Doctor	3	Influence (cesarean, breastfeeding duration ≥6 months, family history of atopy disease)
Jorge [65]	2017	Portugal	Europe	Population-based cross-sectional study	Children	2,474	1,235/1,239	7.1±1.9 years	–	–	IgE, SPT	16	Prevalence (food, milk, egg, nuts, shellfish, fish)

Table 1 (continued)

Author	Year	Country	Region	Study design	Population	Number of patients	Number of males/ females	Age (years or months)	Allergic disorder (number of patients)	Family history of allergy	Diagnosis	QA	Outcomes
Peters [6]	2017	Australia	Oceania	Population-based cohort study	Children	5,276	2,683/2,593	1.05±0.06 years	Eczema, wheeze	Eczema, asthma	OFC	6	Prevalence (food, egg, peanut)
Yamamoto-Hanada [67]	2017	Japan	Asia	Birth cohort study	–	149,004	49,991/ 99,013	–	Asthma, AR/ hay fever, AC, AD	–	Doctor	7	Prevalence (food)
Doğruel [50]	2016	Turkey	Asia	Birth cohort study	Children	1,377	731/646	1 year	AD	Maternal, paternal, sibling	OFC	8	Prevalence (food, milk, egg), influence (male, breastfeeding duration ≥6 months, family history of atopic disease)
Fujimori [51]	2016	Japan	Asia	Cross-sectional study	Adult	1,130	–	18–24 years, 51–87 years	–	–	Physician	13	Prevalence (food)
Gonçalves [52]	2016	Brazil	America	Cross-sectional study	Children	3,897	–	4–59 months	–	–	Physician	17	Prevalence (food, milk, egg, peanut, fish, wheat, soya)
Grimshaw [44]	2016	UK	Europe	Birth cohort study	Children	1,140	583/557	2 years	–	Maternal, paternal	DBPCFC	8	Prevalence (food, milk, egg, peanut, fish, wheat, soya), influence (cesarean, antibiotics exposure during pregnancy, family history of atopic disease)
Gupta [53]	2016	USA	America	Cross-sectional study	All	1,359	765/594	0–20 years	Asthma, eczema	Mother, father, both	SPT, IgE	16	Influence (male, cesarean, breastfeeding, asthma, eczema, family history of FA)
Hwang [54]	2016	Korea	Asia	Cross-sectional study	Children	3,344	1,703/1,641	8.79±1.84 years	Asthma, AR, AD	Asthma, AR, AD	Doctor	14	Prevalence (food)
Lozoya-Ibáñez [55]	2016	Portugal	Europe	Population-based cross-sectional survey	Adult	840	409/431	48 years	–	–	SPT, IgE, OFC	16	Prevalence (food, nuts, peanut, shellfish, fish)
Okada [56]	2016	Japan	Asia	Cross-sectional study	Children	284	152/130	–	Asthma, AD, AR	–	Doctor	14	Prevalence (food)
Ontiveros [57]	2016	Mexico	America	Population-based cross-sectional survey	Children	1,049	508/541	8.6 (5–13) years	AR, AD, asthma, AC	–	Doctor	13	Prevalence (food)
Panjari [58]	2016	Australia	Oceania	Cohort study	Children	57,005	28,476/27, 169	4.9±0.44 years	–	–	Doctor	5	Prevalence (food, milk, egg, nuts, peanut, wheat, soya), influence (male)

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Table 1 (continued)

Author	Year	Country	Region	Study design	Population	Number of patients	Number of males/females	Age (years or months)	Allergic disorder (number of patients)	Family history of allergy	Diagnosis	QA	Outcomes
Papathoma [59]	2016	Greece	Europe	Prospective birth cohort study	Children	459	246/213	3 years	AD	Maternal, paternal	SPT, IgE	7	Prevalence (food, milk, egg, nuts, peanut, fish)
Protudjer [60]	2016	Sweden	Europe	Birth cohort study	Children	2,572	1,278/1,294	16 years	Asthma, eczema, rhinitis	–	Doctor	6	Prevalence (food)
Venter [61]	2016	UK	Europe	Birth cohort study	Children	969	–	10 years	Asthma, eczema, hay fever	–	SPT, OFC	7	Prevalence (peanut), influence (breastfeeding, asthma, eczema, family history of atopy disease)
Venter [62]	2016	UK	Europe	Birth cohort study	Children	969	–	10 years	–	–	OFC	7	Prevalence (wheat)
Xepapadaki [63]	2016	Europe	Europe	Prospective birth cohort study	Children	12,049	6,193/5,856	2 years	–	Mother, father	DBPCFC	7	Prevalence (egg)
Baççioğlu [40]	2015	Turkey	Asia	Cross-sectional study	Children	494	–	11–12 years	Asthma, AR, AD	–	Doctor	12	Prevalence (food)
Baricic [41]	2015	Croatia	Europe	Cross-sectional study	Children	702	–	0.5–4 years	–	–	Physician	14	Prevalence (food)
Basera [42]	2015	South Africa	Africa	Cross-sectional study	Children	512	268/244	1–3 years	–	Asthma, eczema	OFC	16	Prevalence (food, milk, egg, peanut, fish)
Dyer [43]	2015	USA	America	Cross-sectional study	Children	38,480	–	0–17 years	–	–	Doctor	15	Prevalence (food, peanut)
Ju [45]	2015	Korea	Asia	Cross-sectional study	All	543	271/272	–	–	–	Doctor	13	Prevalence (food, milk, egg, peanut, shellfish, wheat, soya)
Schoemaker [46]	2015	Europe	Europe	Prospective birth cohort study	Children	12,049	6,193/5,856	2 years	–	Mother, father	DBPCFC	7	Prevalence (milk)
Verrill [47]	2015	USA	America	Cross-sectional study	Adult	4,568	–	–	–	–	Doctor	13	Prevalence (food, egg, nuts, peanut, shellfish, fish, soya)
Winberg [48]	2015	Sweden	Europe	Population-based cohort study	Children	2,612	–	11–12 years	–	–	IgE, DBPCFC	6	Prevalence (food, milk, egg, wheat)
Zeng [49]	2015	China	Asia	Cross-sectional study	Children	2,540	1,331/1,209	4.6±1.1 years	AD, asthma, AC, AR	AD (father, mother, siblings), asthma (father, mother, siblings), AC (father, mother, siblings), AR (father, mother, siblings)	Physician	14	Prevalence (food, egg, nuts, peanut, shellfish, fish, wheat, soya)

Table 1 (continued)

Author	Year	Country	Region	Study design	Population	Number of patients	Number of males/ females	Age (years or months)	Allergic disorder (number of patients)	Family history of allergy	Diagnosis	QA	Outcomes
Bunyavanich [33]	2014	USA	America	Pre-birth cohort study	Children	1,277	645/632	7.93±0.82 years	Asthma, AR, AD	Asthma (paternal, maternal), AR (paternal, maternal), AD (paternal, maternal)	IgE, doctor	7	Prevalence (food, milk, egg, peanut, wheat, soya)
Burney [34]	2014	Europe	Europe	Cross-sectional study	Adult	17,366	7,884/9,482	37.2±9.7 years	–	–	Doctor	14	Prevalence (food)
Ezell [35]	2014	USA	America	Birth cohort study	Children	590	312/278	–	–	–	Physician	6	Prevalence (food, milk, egg, peanut)
Gupta [36]	2014	USA	America	Cross-sectional study	All	402,788	202,337/ 200,451	–	–	–	Physician	18	Prevalence (food)
Järvenpää [37]	2014	Finland	Europe	Cross-sectional study	Children	1,653	830/823	6–7 years	–	–	Physician	17	Prevalence (food, milk, egg, nuts, fish, wheat, soya)
Park [38]	2014	Korea	Asia	Cross-sectional study	Children	16,749	8,758/7,991	0–6 years	–	–	Physician	15	Prevalence (food)
Stelmach [39]	2014	Poland	Europe	Birth cohort study	Children	501	–	12 (10–18) months	AD	–	Doctor	6	Prevalence (food)
Kaya [26]	2013	Turkey	Asia	Cross-sectional study	Children	10,096	5,019/5,077	12.9±0.9 years	Asthma, AR, eczema	Asthma, AR, AD	SPT, IgE, OFC, DBPCFC, physician	16	Prevalence (food, nuts, peanut)
Kijima [27]	2013	Japan	Asia	Cross-sectional study	Adult	3,321	2,209/1,112	18.40±0.85 years	AD, asthma, AR	–	Doctor	11	Prevalence (food)
Metsälä [28]	2013	Finland	Europe	Case-control study	Children	32,474	19,094/13,380	–	–	–	Physician	6	Influence (antibiotics exposure during pregnancy)
Mustafayev [29]	2013	Turkey	Asia	Cross-sectional study	Children	6,963	3,572/3,391	10.83±0.01 years	Wheeze, rhinitis, eczema	–	SPT, OFC	14	Prevalence (food, egg, peanut)
Nissen [30]	2013	Denmark	Europe	Birth cohort study	Adult	276	126/150	26 years	Eczema, asthma, ARC	–	OFC	6	Prevalence (food)
Pelé [31]	2013	France	Europe	Prospective cohort study	Children	1,500	772/727	2 years	Wheeze, eczema	–	Doctor	7	Prevalence (food, milk)
Warren [32]	2013	USA	America	Cross-sectional study	Children	38,480	19,625/18,855	0–17 years	–	–	Doctor	15	Prevalence (milk)
Ahn [21]	2012	Korea	Asia	Population-based cross-sectional study	Children	7,882	3,916/3,966	6–7 years, 12–13 years	–	–	IgE	15	Prevalence (food, milk, egg, nuts, peanut, shellfish, fish, soya)

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Table 1 (continued)

Author	Year	Country	Region	Study design	Population	Number of patients	Number of males/females	Age (years or months)	Allergic disorder (number of patients)	Family history of allergy	Diagnosis	QA	Outcomes
Kavaliunas [22]	2012	Lithuania	Europe	Cross-sectional study	Children	3,084	1,531/1,553	8.2±1.2 years	–	–	Doctor, IgE	15	Prevalence (food)
Lao-araya [23]	2012	Thailand	Asia	Cross-sectional study	Children	452	234/218	5.3±1.0 years	Asthma, AR, AD	Asthma (paternal, maternal, siblings), AR (paternal, maternal, siblings), AD (paternal, maternal, siblings)	OFC	17	Prevalence (food, shellfish, fish)
Lau [24]	2012	USA	America	Cross-sectional study	Children	38,480	–	0–17 years	–	–	Doctor	15	Prevalence (shellfish)
Wu [25]	2012	China	Asia	Cross-sectional study	All	30,018	14,899/15,119	–	–	–	Physician	16	Prevalence (food, milk, egg, peanut, shellfish, fish, soya)
Chen [16]	2011	China	Asia	Cross-sectional study	Children	497	270/227	0–1 year	–	–	OFC	16	Prevalence (food, milk, egg)
Obeng [17]	2011	Ghana	Africa	Cross-sectional study	Children	1,714	–	5–16 years	–	–	SPT	15	Prevalence (food)
Osborne [18]	2011	Australia	Oceania	Cross-sectional study	Children	2,848	1,488/1,330	12.7±0.8 months	Eczema	Father, mother	OFC	17	Prevalence (food, egg, peanut), influence (family history of FA)
Pyrhönen [19]	2011	Finland	Europe	Population-based cohort study	Children	5,920	3,025/2,892	0–4 years	–	Father, mother, both	IgE, SPT, OFC, physician	7	Prevalence (food, milk)
Pyrhönen [20]	2011	Finland	Europe	Population-based cohort study	Children	3,800	–	0–4 years	–	Asthma (father, mother, both), AD (father, mother, siblings)	OFC	7	Influence (family history of FA/AD/asthma)

SPT, skin prick test; OFC, oral food challenge; DBPCFC, double-blind, placebo-controlled food challenge; FA, food allergy; AD, atopic dermatitis; AR, allergic rhinitis; AC, allergic conjunctivitis; ARC, allergic rhinoconjunctivitis; QA, quality assessment.

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Table 2. Prevalence of FA

Outcomes	Indicators	Total			Cross-sectional (high)			Cross-sectional (low)			Cohort (high)		
		studies	prevalence (95% CI)	I^2	studies	prevalence (95% CI)	I^2	studies	prevalence (95% CI)	I^2	studies	prevalence (95% CI)	I^2
FA	Overall	94	4.3% (0.038–0.047)	99.7	32	3.6% (0.026–0.048)	99.8	21	5.3% (0.038–0.071)	98.9	41	4.2% (0.038–0.047)	99.5
	Sensitivity analysis		4.3% (0.038–0.047)										
	Region												
	Asia	34	4.2% (0.033–0.051)	99.5	15	3.4% (0.020–0.053)	99.5	11	5.9% (0.032–0.093)	99.4	8	3.4% (0.024–0.045)	99.4
	Children	24	3.4% (0.023–0.046)	99.5	12	2.8% (0.014–0.046)	99.4	6	4.0% (0.008–0.093)	99.6	6	4.1% (0.033–0.049)	94.4
	Adult	5	5.6% (0.038–0.078)	99	1	6.4% (0.060–0.068)	NA	3	5.8% (0.027–0.100)	NA	1	4.2% (0.041–0.043)	NA
	America	20	3.2% (0.024–0.041)	99.8	6	1.3% (0.005–0.027)	99.8	5	5.0% (0.036–0.068)	88.4	9	3.9% (0.026–0.055)	98.7
	Children	16	2.9% (0.021–0.039)	99.8	5	1.4% (0.003–0.032)	99.9	3	4.9% (0.040–0.058)	NA	8	3.6% (0.023–0.051)	98.7
	Adult	4	4.4% (0.012–0.094)	99.4	1	1.3% (0.012–0.014)	NA	2	6.2% (0.056–0.069)	NA	1	7.6% (0.063–0.090)	NA
	Europe	31	4.8% (0.037–0.060)	99.3	7	5.7% (0.017–0.119)	99.6	5	4.2% (0.026–0.062)	93.5	19	4.6% (0.033–0.061)	99.3
	Children	25	5.4% (0.041–0.069)	99.4	6	6.8% (0.019–0.142)	99.6	2	5.5% (0.041–0.071)	NA	17	5.0% (0.035–0.066)	99.3
	Adult	5	2.9% (0.015–0.046)	92.5	1	1.1% (0.005–0.021)	NA	2	4.4% (0.041–0.047)	NA	2	2.0% (0.012–0.030)	NA
	Africa	3	1.6% (0.008–0.026)	NA	2	1.3% (0.008–0.019)	NA	–	–	–	1	1.8% (0.012–0.026)	NA
	Children	3	1.6% (0.008–0.026)	NA	2	1.3% (0.008–0.019)	NA	–	–	–	1	1.8% (0.012–0.026)	NA
	Oceania	5	7.5% (0.052–0.102)	97.7	1	10.4% (0.093–0.116)	NA	–	–	–	4	6.6% (0.048–0.086)	95
	Children	5	7.5% (0.052–0.102)	97.7	1	10.4% (0.093–0.116)	NA	–	–	–	4	6.6% (0.048–0.086)	95
Food FA													
	Milk	45	1.1% (0.009–0.013)	98.8	20	0.6% (0.003–0.009)	97.5	4	0.8% (0.000–0.024)	92	21	1.8% (0.013–0.024)	99.3
	Children	37	1.2% (0.010–0.016)	99	17	0.6% (0.003–0.010)	97.8	1	2.0% (0.005–0.050)	NA	19	2.0% (0.015–0.026)	99.3
	Adult	3	0.4% (0.002–0.007)	NA	1	0.5% (0.004–0.006)	NA	1	0.1% (0.000–0.005)	NA	1	0.7% (0.003–0.012)	NA
	Egg	45	1.1% (0.008–0.014)	99	22	0.9% (0.006–0.013)	98.1	7	0.7% (0.002–0.016)	95.7	16	1.5% (0.008–0.023)	99.5
	Children	37	1.3% (0.009–0.017)	99.2	19	1.0% (0.006–0.016)	98.4	3	1.1% (0.000–0.039)	NA	15	1.7% (0.010–0.026)	99.5
	Adult	3	0.3% (0.002–0.004)	NA	1	0.3% (0.002–0.004)	NA	2	0.2% (0.001–0.003)	NA	–	–	–
	Peanut	41	0.7% (0.005–0.009)	98.9	20	0.4% (0.002–0.006)	98.7	7	0.7% (0.002–0.015)	94.5	14	1.3% (0.008–0.020)	99.2
	Children	30	0.7% (0.004–0.010)	99	15	0.3% (0.001–0.007)	98.7	3	0.9% (0.000–0.027)	NA	12	1.4% (0.008–0.022)	99.3
	Adult	6	0.7% (0.003–0.013)	97.1	3	0.6% (0.001–0.013)	NA	2	0.2% (0.001–0.004)	NA	1	2.6% (0.019–0.035)	NA
	Nuts	23	0.8% (0.005–0.013)	98.6	10	0.3% (0.001–0.007)	95.5	4	0.6% (0.001–0.014)	91.4	9	1.7% (0.009–0.027)	98.9
	Children	16	0.7% (0.004–0.012)	98.5	8	0.4% (0.001–0.008)	96.5	2	0.2% (0.000–0.004)	NA	6	1.2% (0.006–0.019)	97.9
	Adult	4	1.9% (0.000–0.066)	99.2	1	0.1% (0.000–0.007)	NA	1	0.3% (0.001–0.005)	NA	2	5.7% (0.049–0.064)	NA
	Shellfish	23	0.9% (0.005–0.015)	99.2	15	1.0% (0.004–0.016)	99.3	4	1.4% (0.002–0.038)	97.8	4	0.3% (0.000–0.009)	95.5
	Children	13	0.7% (0.003–0.012)	98.8	10	0.5% (0.002–0.010)	98.9	1	4.4% (0.036–0.053)	NA	2	0.3% (0.001–0.004)	NA
	Adult	4	1.2% (0.002–0.031)	98.4	2	3.0% (0.028–0.033)	NA	1	0.6% (0.004–0.008)	NA	1	1.1% (0.006–0.017)	NA

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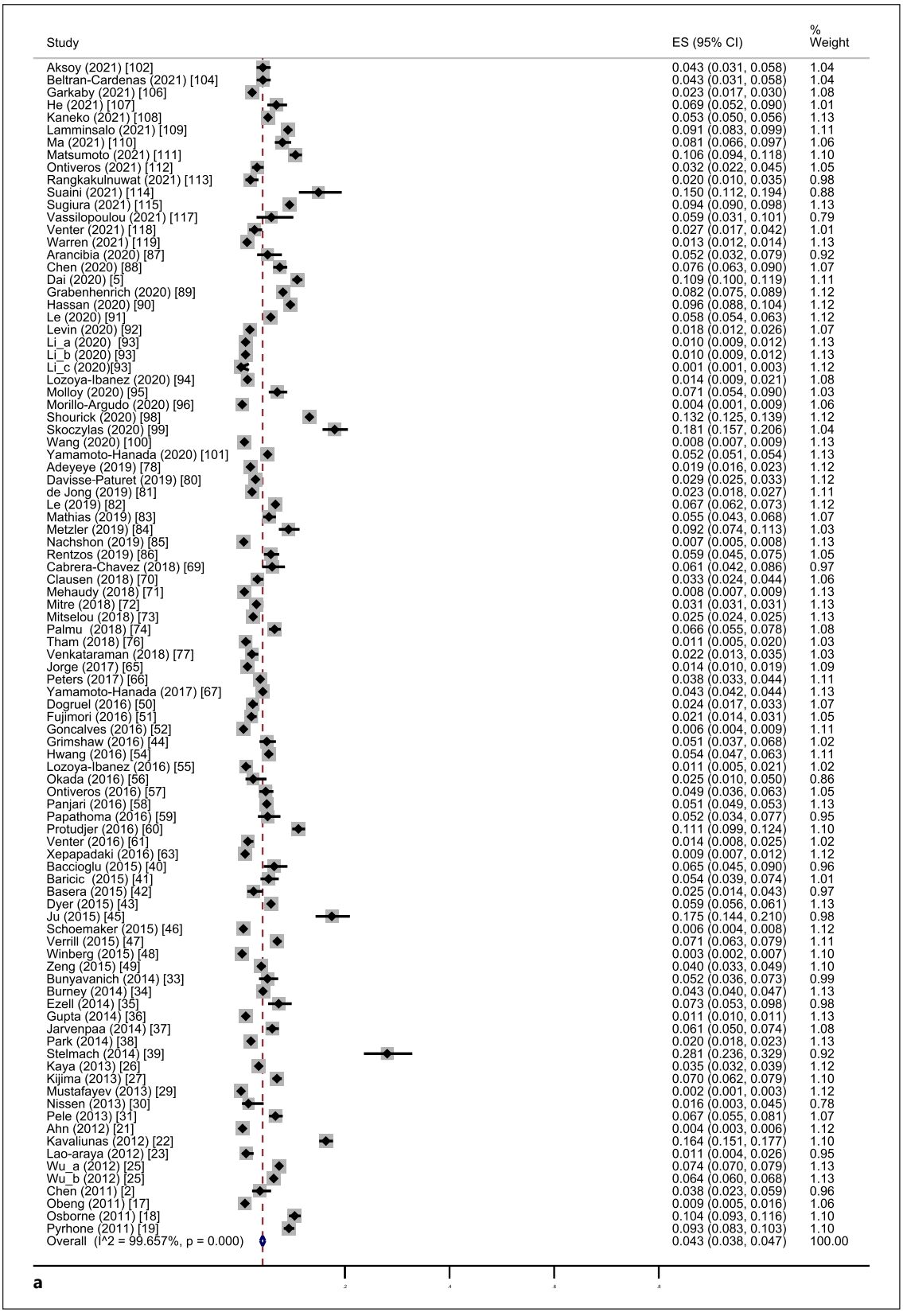
Table 2 (continued)

Outcomes	Indicators	Total			Cross-sectional (high)			Cross-sectional (low)			Cohort (high)		
		studies	prevalence (95% CI)	I^2	studies	prevalence (95% CI)	I^2	studies	prevalence (95% CI)	I^2	studies	prevalence (95% CI)	I^2
	Fish	25	0.4% (0.002–0.007)	97	19	0.4% (0.002–0.007)	97.5	3	0.4% (0.001–0.008)	NA	3	0.4% (0.000–0.012)	NA
	Children	19	0.3% (0.002–0.005)	93.5	15	0.3% (0.001–0.005)	95.6	2	0.5% (0.003–0.009)	NA	2	0.7% (0.003–0.011)	NA
	Adult	3	0.5% (0.001–0.013)	NA	2	1.1% (0.009–0.013)	NA	1	0.3% (0.002–0.005)	NA	–	–	–
	Soya	19	0.3% (0.002–0.004)	91.7	10	0.2% (0.001–0.003)	82.3	4	0.7% (0.001–0.020)	93.6	5	0.7% (0.004–0.011)	94.6
	Children	14	0.4% (0.002–0.006)	93.1	7	0.2% (0.000–0.003)	83.3	2	0.3% (0.001–0.005)	NA	5	0.7% (0.004–0.011)	94.6
	Adult	2	0.1% (0.001–0.002)	NA	1	0.2% (0.001–0.002)	NA	1	0.0% (0.000–0.002)	NA	–	–	–
	Wheat	18	0.3% (0.002–0.005)	91.8	8	0.2% (0.001–0.004)	89.3	3	1.0% (0.000–0.040)	NA	7	0.4% (0.003–0.006)	86.5
	Children	16	0.3% (0.002–0.005)	92.7	7	0.2% (0.001–0.004)	87	2	0.2% (0.000–0.004)	NA	7	0.4% (0.003–0.006)	86.5
Diagnosis													
	Doctor	61	5.2% (0.046–0.058)	99.8	21	4.3% (0.031–0.058)	99.8	18	6.1% (0.048–0.075)	97.6	22	5.2% (0.046–0.059)	99.7
	Children	46	4.7% (0.041–0.054)	99.8	16	3.8% (0.026–0.052)	99.8	10	5.4% (0.038–0.072)	95.9	20	5.2% (0.045–0.059)	99.7
	Adult	11	5.6% (0.038–0.077)	99.7	3	6.0% (0.009–0.150)	NA	6	5.3% (0.035–0.075)	98.1	2	4.2% (0.041–0.043)	NA
	OFC	26	2.3% (0.014–0.033)	98.6	7	2.9% (0.002–0.084)	99.4	1	0.2% (0.001–0.003)	NA	18	2.2% (0.015–0.031)	97.3
	Children	24	2.4% (0.014–0.036)	98.6	7	2.9% (0.002–0.084)	99.4	1	0.2% (0.001–0.003)	NA	16	2.4% (0.015–0.035)	97.2
	Adult	1	1.6% (0.003–0.045)	NA	–	–	–	–	–	–	1	1.6% (0.003–0.045)	NA
	IgE	8	3.9% (0.016–0.071)	99.2	3	2.7% (0.007–0.058)	NA	1	5.9% (0.045–0.075)	NA	4	3.9% (0.013–0.079)	98.5
	Children	6	2.9% (0.011–0.057)	99	3	2.7% (0.007–0.058)	NA	–	–	–	3	2.9% (0.007–0.065)	NA
	Adult	2	7.2% (0.063–0.081)	NA	–	–	–	1	5.9% (0.045–0.075)	NA	1	7.9% (0.068–0.091)	NA
	SPT	7	1.1% (0.004–0.022)	96.9	2	0.2% (0.001–0.003)	NA	1	1.0% (0.008–0.013)	NA	4	1.7% (0.010–0.027)	79.2
	Children	6	1.0% (0.003–0.020)	97.2	2	0.2% (0.001–0.003)	NA	1	1.0% (0.008–0.013)	NA	3	1.6% (0.007–0.028)	NA
	Adult	1	2.2% (0.013–0.035)	NA	–	–	–	–	–	–	1	2.2% (0.013–0.035)	NA
	Mixed	16	2.2% (0.013–0.032)	98.2	9	1.0% (0.005–0.015)	96.5	1	1.4% (0.009–0.021)	NA	6	5.4% (0.028–0.086)	94.4
	Children	14	2.3% (0.014–0.035)	98.4	8	1.0% (0.005–0.015)	96.9	–	–	–	6	5.4% (0.028–0.086)	94.4
	Adult	1	1.1% (0.005–0.021)	NA	1	1.1% (0.005–0.015)	NA	–	–	–	–	–	–

FA, food allergy; CI, confidence interval; NA, not available; OFC, open food challenge; IgE, immunoglobulin E; SPT, skin prick test.



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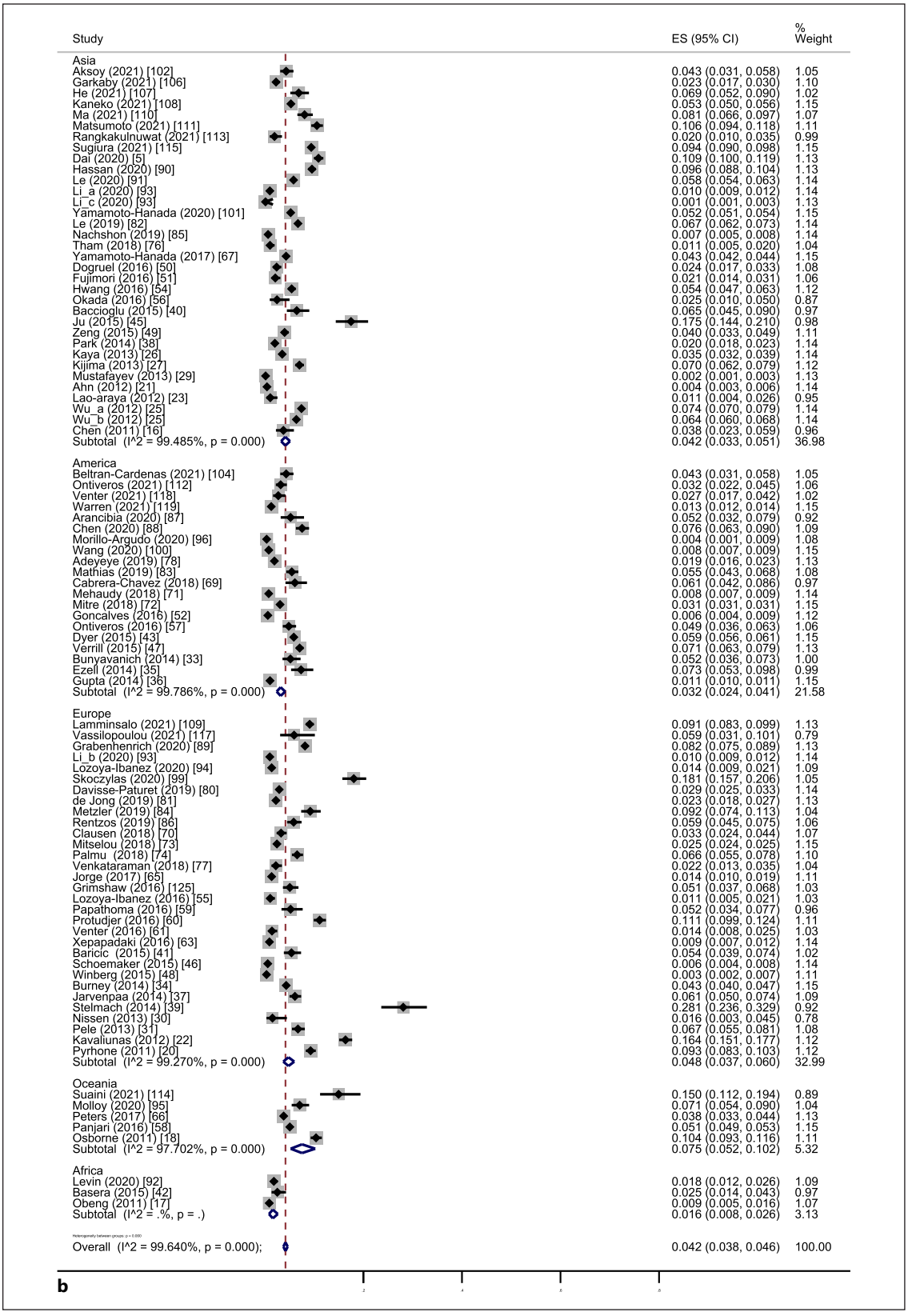


Fig. 2. Prevalence of FA. **a** Overall prevalence. **b** Prevalence in Asia, America, Europe, Africa, and Oceania.

FA in Asia

Thirty-two studies including 34 sets of data investigated the FA prevalence in Asia. The REM analysis result showed that FA prevalence in Asia was 4.2% (95% CI: 0.033–0.051) (shown in Table 2; Fig. 2b). Regarding the quality of study, 15 studies were high-quality cross-sectional studies, with the FA prevalence being 3.4% (95% CI: 0.020–0.053); 11 studies were low-quality cross-sectional studies, with the FA prevalence being 5.9% (95% CI: 0.032–0.093); 8 studies were high-quality cohort studies, with the FA prevalence being 3.4% (95% CI: 0.024–0.045). When grouping by population, the FA prevalence in children (3.4%, 95% CI: 0.034–0.046, I^2 = 99.5%) was lower than adults (5.6%, 95% CI: 0.038–0.078, I^2 = 99.0%) (shown in Table 2).

FA in America

The FA prevalence in America was evaluated in 20 studies. The prevalence of FA in the Americas was 3.2% (95% CI: 0.024–0.041, I^2 = 99.8%) (shown in Table 2; Fig. 2b). Concerning the quality of literature subgroup analysis, the prevalence of FA in America from high-quality cross-sectional studies was 1.3% (95% CI: 0.005–0.027), lowering the prevalence of FA in low-quality cross-sectional studies (5.0%, 95% CI: 0.036–0.068) and high-quality cohort studies (3.9%, 95% CI: 0.026, 0.055). Based on the population group, the prevalence of FA in children in the Americas was 2.9% (95% CI: 0.021–0.039, I^2 = 99.8%), and the prevalence of FA in adults in the Americas was 4.4% (95% CI: 0.012–0.094, I^2 = 99.4%) (shown in Table 2).

FA in Europe

Thirty-one studies investigated FA prevalence in Europe. The prevalence of FA in Europe was 4.8% (95% CI: 0.037–0.060, I^2 = 99.3%) (shown in Table 2 and Fig. 2b). With regard to the quality of study, FA prevalence in high-quality cross-sectional studies was higher (5.7%, 95% CI: 0.017–0.119) than low-quality cross-sectional studies (4.2%, 95% CI: 0.026–0.062) and high-quality cohort studies (4.6%, 95% CI: 0.033–0.061). Concerning the population group, FA prevalence in children was higher (5.4%, 95% CI: 0.041–0.069, I^2 = 99.4%) than adults (2.9%, 95% CI: 0.015–0.046, I^2 = 92.5) (shown in Table 2).

FA in Africa

Three studies were included to evaluate the prevalence of FA in the African population, all of whom were children. The REM result showed that the prevalence of FA in the African children was 1.6% (95% CI: 0.008–0.026) (shown in Table 2; Fig. 2b). Based on the literature quality, 2 studies were regarded as high-quality cross-sectional studies, and 1 study was a high-quality cohort study; the prevalence of FA was 1.3% (95% CI: 0.008–0.019) and 1.8% (95% CI: 0.012–0.026) (shown in Table 2).

FA in Oceania

Five studies only involving the children population were included to evaluate the prevalence of FA in Oceania. The result showed that the prevalence of FA in Oceania among children was 7.5% (95% CI: 0.052–0.102, I^2 = 97.7%) (shown in Table 2; Fig. 2b). Regarding the subgroup analysis of literature quality, the prevalence of FA in Oceania from the high-quality cross-sectional studies was 10.4% (95% CI: 0.093–0.116) and the prevalence of FA in Oceania from the high-quality cohort was 6.6% (95% CI: 0.048–0.086).

Prevalence of FA in Different Food Types

Milk

A total of 45 sets of data from 43 articles evaluated the allergy prevalence of milk. The REM analysis result showed that allergy prevalence of milk was 1.1% (95% CI: 0.009–0.013) (shown in Table 2 and Fig. 3). According to the subgroup analysis of literature quality, comparing with high-quality cross-sectional studies (0.6%, 95% CI: 0.003–0.009) and low-quality cross-sectional studies (0.8%, 95% CI: 0.000–0.024), high-quality cohort studies (1.8%, 95% CI: 0.013–0.024) had a higher prevalence of milk FA. Regarding the population group, milk allergy prevalence was higher in children (1.2%, 95% CI: 0.010–0.016, I^2 = 99.0%) than in adults (0.4%, 95% CI: 0.002–0.007) (shown in Table 2).

Egg

Egg allergy prevalence was assessed in 45 sets of data from 42 articles. The overall allergy prevalence was 1.1% (95% CI: 0.008–0.014, I^2 = 99.0%) (shown in Table 2; Fig. 3). When stratifying by the quality of study, high-quality cohort studies had higher egg allergy prevalence (1.5%, 95% CI: 0.008–0.023) compared with high-quality cross-sectional studies (0.9%, 95% CI: 0.006–0.013) and low-quality cross-sectional studies (0.7%, 95% CI: 0.002–0.016). The egg allergy prevalence in children (1.3%, 95% CI: 0.009–0.017, I^2 = 99.2%) was higher than in adults (0.3%, 95% CI: 0.002–0.004) (shown in Table 2).

Peanut

A total of 41 groups of data were included in 38 studies to assess the allergy prevalence of peanuts. The overall

allergy prevalence was 0.7% (95% CI: 0.005–0.009, I^2 = 98.9%) (shown in Table 2; Fig. 3) and was similar among children (0.7%, 95% CI: 0.004–0.010, I^2 = 99.0%) and adults (0.7%, 95% CI: 0.003–0.011, I^2 = 97.1%). According to the subgroup analysis of the quality of the literature, high-quality cohorts had a higher prevalence of peanut FA (1.3%, 95% CI: 0.008–0.020) (shown in Table 2).

Nuts

Twenty-three studies assessed the allergy prevalence of nuts. The overall allergy prevalence was 0.8% (95% CI: 0.005–0.013, I^2 = 98.6%) (shown in Table 2; Fig. 3). Nut allergy prevalence was lower in children (0.7%, 95% CI: 0.004–0.012, I^2 = 98.5%) than in adults (1.9%, 95% CI: 0.000–0.066, I^2 = 99.2%). Literature quality subgroup analysis showed that high-quality cohorts had a higher prevalence of nuts FA (1.7%, 95% CI: 0.009, 0.027) (shown in Table 2).

Shellfish

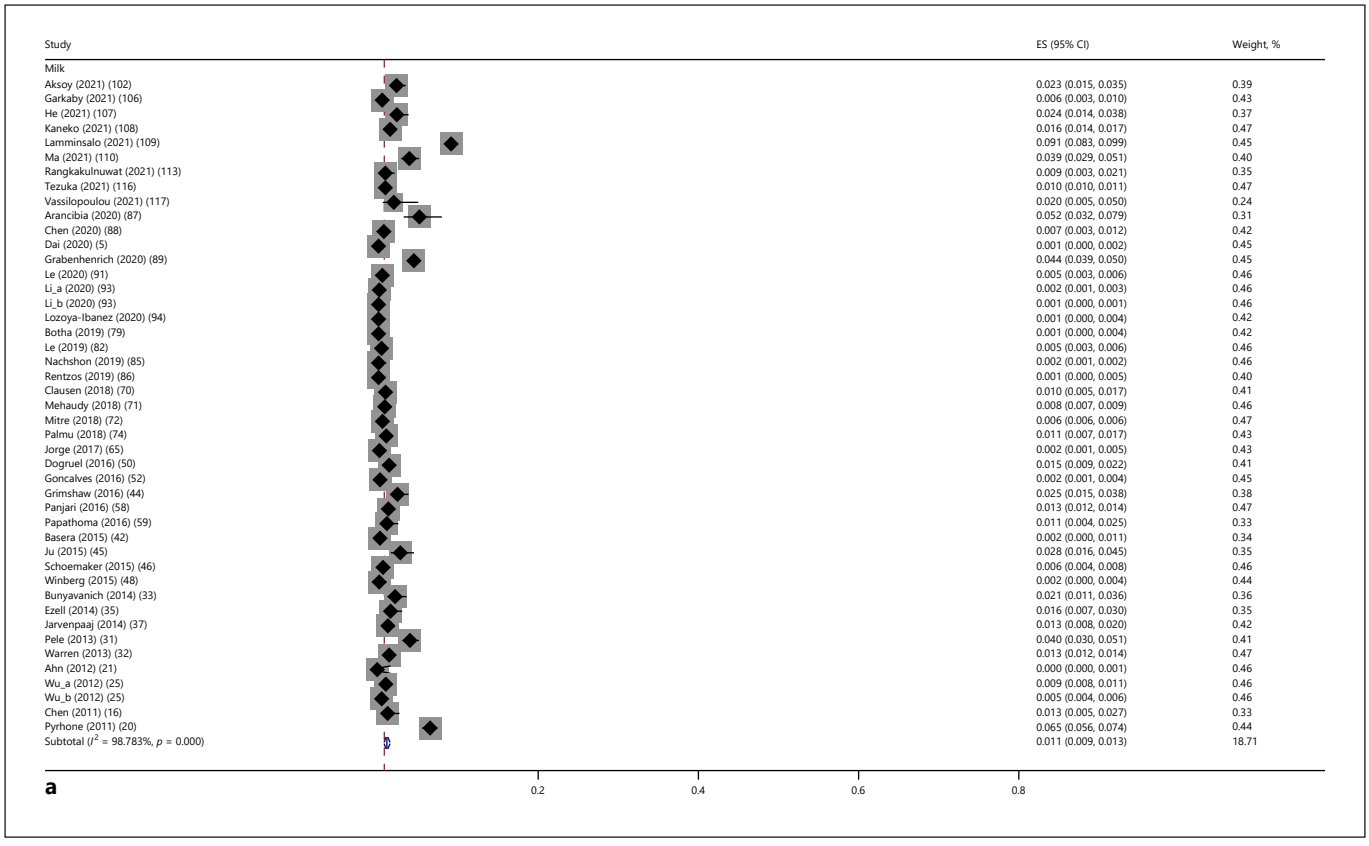
The allergy prevalence of shellfish was assessed in 23 sets of data from 21 articles. The overall allergy prevalence was 0.9% (95% CI: 0.005–0.015, I^2 = 99.2%) (shown in Table 2; Fig. 3). The allergy prevalence was 0.7% in children (95% CI: 0.003–0.012, I^2 = 98.8%), lower than in adults (1.2%, 95% CI: 0.002–0.031, I^2 = 98.4%). Literature quality subgroup analysis suggested that high-quality cohorts (0.3%, 95% CI: 0.000–0.009) had a lower prevalence of shellfish FA compared to high- and low-quality cross-sectional studies (shown in Table 2).

Fish

The overall allergy prevalence of fish was 0.4% (95% CI: 0.002–0.007, I^2 = 97.0%) (shown in Table 2; Fig. 3). The allergy prevalence in children (0.3%, 95% CI: 0.002–0.005, I^2 = 93.5%) was lower than in adults (0.5, 95% CI: 0.001–0.013). The results of the literature quality subgroup analysis are shown in Table 2.

Soya

A total of 19 groups of data from 18 studies were included to assess the allergy prevalence of soya. The REM showed that the allergy prevalence of soya was 0.3% (95% CI: 0.002–0.004, I^2 = 91.7%) (shown in Table 2; Fig. 3). The allergy prevalence of soya in children (0.4%, 95% CI: 0.002–0.006, I^2 = 93.1%) was higher than in adults (0.1%,



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95% CI: 0.001–0.002). Literature quality subgroup analysis revealed that the soya FA was 0. 2%, 0.7%, and 0.7%, respectively, in high-quality cross-sectional studies, low-quality cross-sectional studies, and high-quality cohort studies (shown in Table 2).

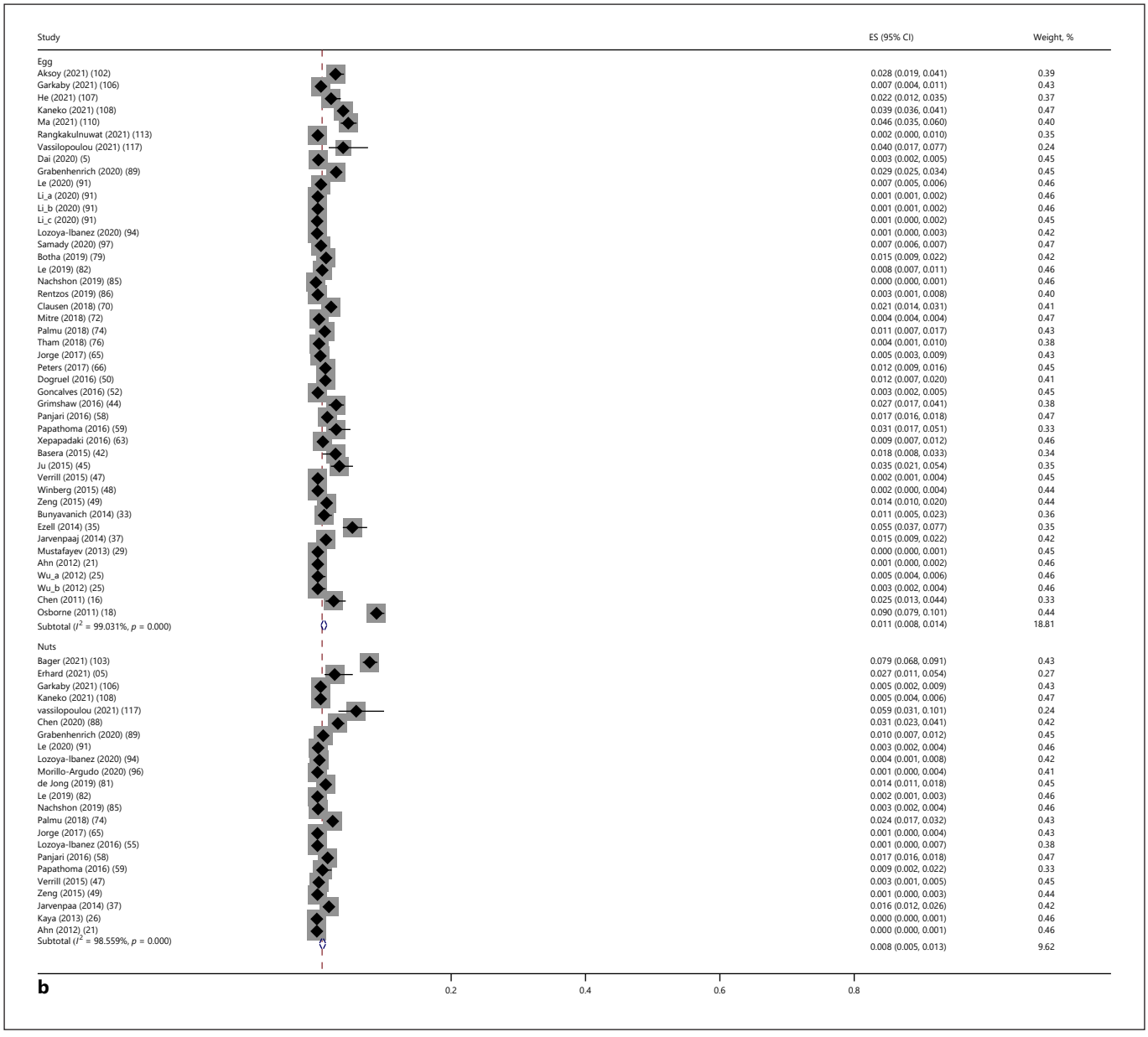
Wheat

The allergy prevalence of wheat was assessed in 18 articles. The result showed that the allergy prevalence of wheat was 0.3% (95% CI: 0.002–0.005, I^2 = 91.8%) (shown in Table 2; Fig. 3). And the allergy prevalence of wheat in children was also 0.3% (95% CI: 0.002–0.005, I^2 = 92.7%). Based on the literature quality subgroup analysis, low-quality cross-sectional studies had a higher prevalence of wheat FA (1.0%, 95% CI: 0.000–0.040) (shown in Table 2).

Prevalence of Different Diagnostic Modalities

FA Diagnosed by Doctor

The overall prevalence of FA by doctor diagnosis was 5.2% (95% CI: 0.046–0.058, I^2 = 99.8%) (shown in Table 2; Fig. 4). The prevalence among children (4.7%, 95% CI: 0.041, 0.054, I^2 = 99.8%) was lower than among adults (5.6%, 95% CI: 0.038–0.077, I^2 = 99.7%) (shown



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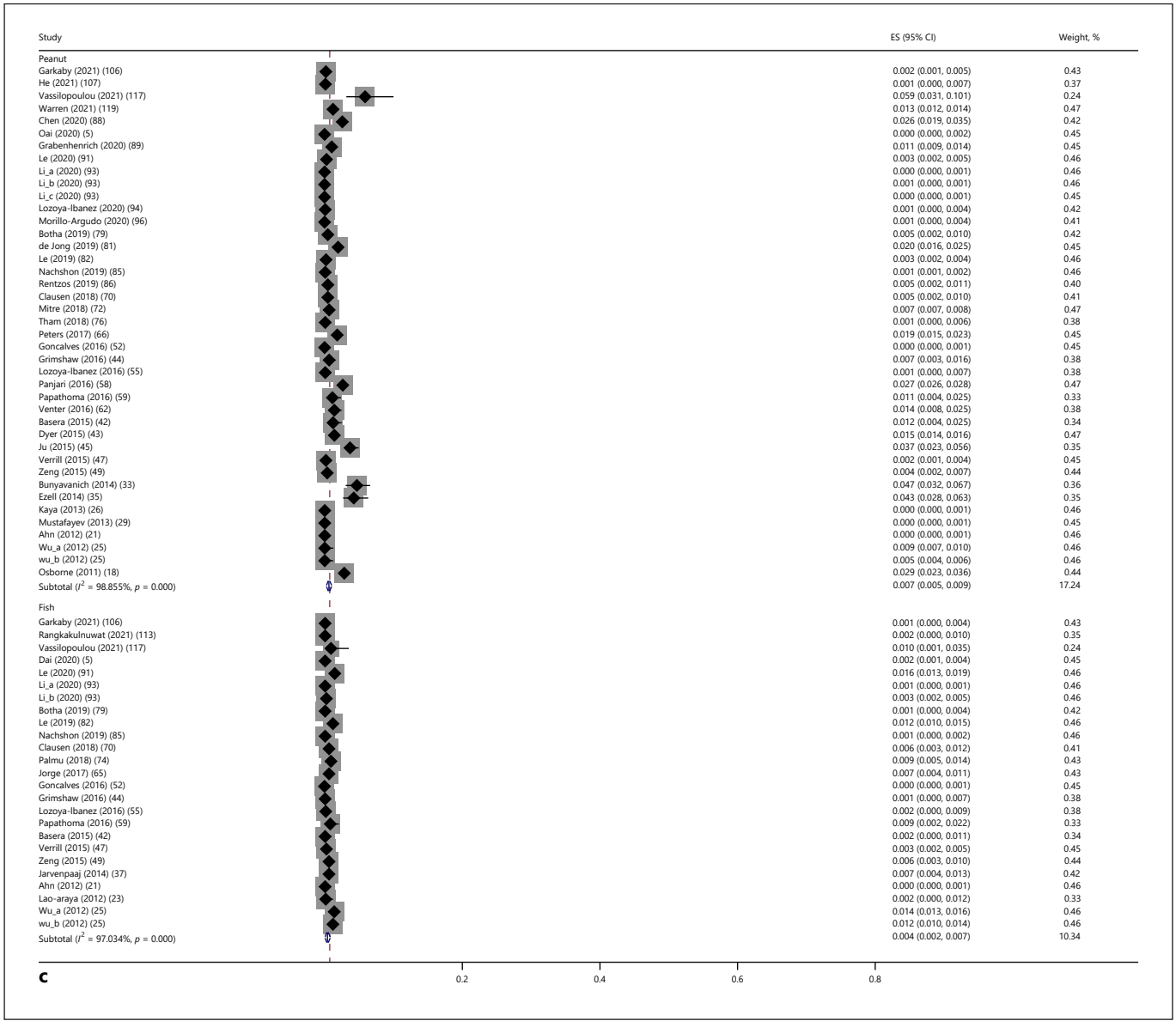
in Table 2). Regarding the literature quality subgroup analysis, the FA diagnosed by doctor in high-quality cross-sectional studies, low-quality cross-sectional studies, and high-quality cohort studies was 4.3% (95% CI: 0.031–0.058), 6.1% (95% CI: 0.048–0.075), and 5.2% (0.046–0.059) (shown in Table 2).

FA Diagnosed by OFC

The overall prevalence of FA by OFC test was 2.3% (95% CI: 0.014–0.033, $I^2 = 98.6\%$) and higher among children (2.4%, 95% CI: 0.014–0.036, $I^2 = 98.6\%$) than among adults (1.6%, 95% CI: 0.003–0.045) (shown in Table 2). According to the literature quality subgroup analysis, high-quality cross-sectional studies had a higher prevalence of FA diagnosed by OFC (2.9%, 95% CI: 0.002–0.084) (shown in Table 2).

FA Diagnosed by IgE Test

The overall prevalence of FA by IgE test was 3.9% (95% CI: 0.016–0.071, $I^2 = 99.2\%$) (shown in Table 2; Fig. 4). And the prevalence of FA by IgE test was significantly lower in children (2.9%, 95% CI: 0.011–0.057, $I^2 = 99.0\%$) than in adults (7.2%, 95% CI: 0.063–0.081). Concerning the literature quality subgroup analysis, low-quality cross-sectional studies had a higher prevalence of FA diagnosed by IgE test (5.9%, 95% CI: 0.045–0.075) (shown in Table 2).



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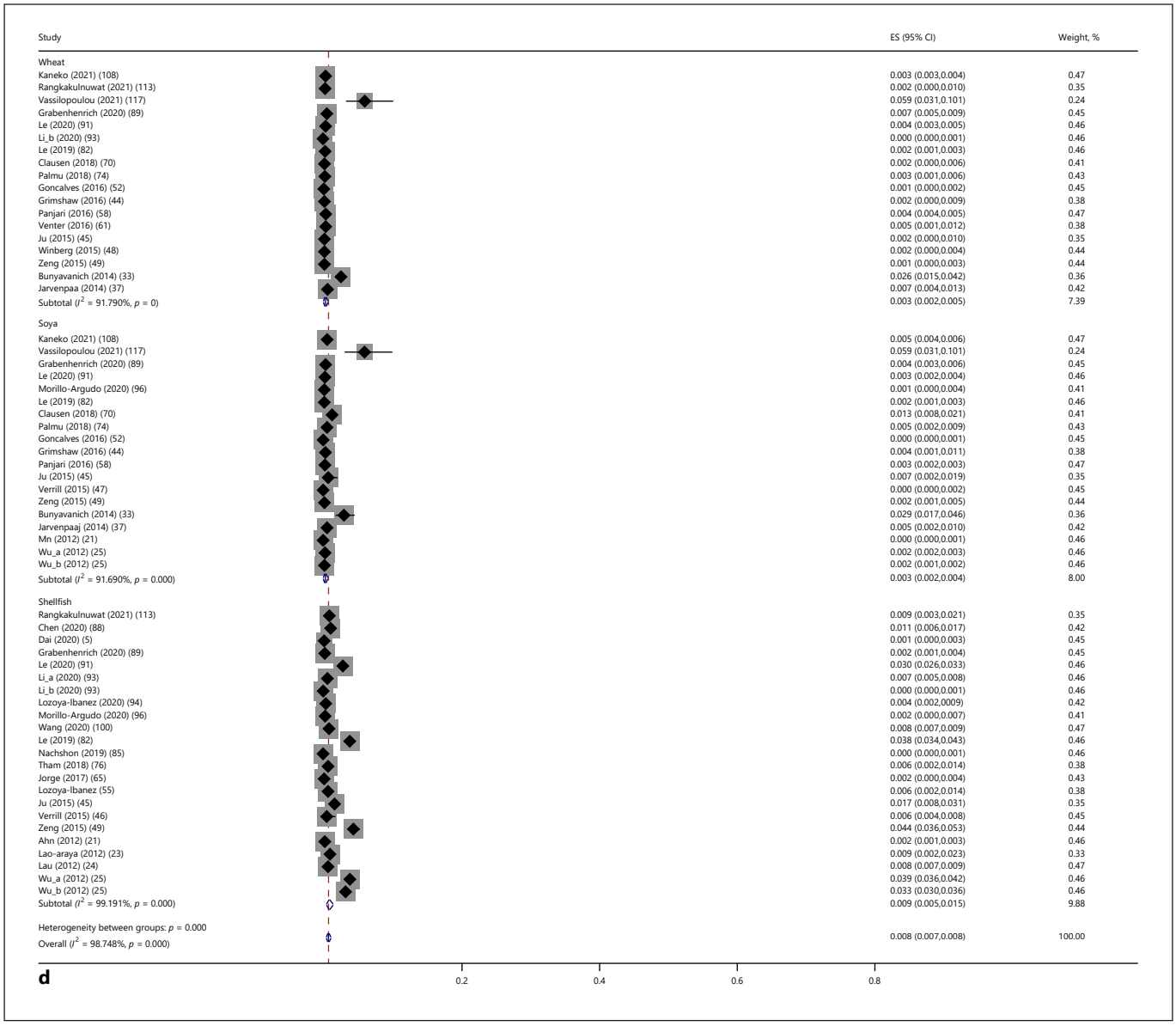

Fig. 3. a–d Prevalence of different food types.

FA Diagnosed with Positive SPT

The overall prevalence of FA by positive SPT was 1.1% (95% CI: 0.004–0.022, I^2 = 96.9%) (shown in Table 2; Fig. 4). And the prevalence of FA by positive SPT was 1.0% in children (95% CI: 0.003–0.020, I^2 = 97.2%) and 2.2% in adults (95% CI: 0.013–0.035). The literature quality subgroup analysis results are described in Table 2.

FA Diagnosed by Mixed Test

The overall prevalence of FA by mixed test was 2.2% (95% CI: 0.013–0.032, I^2 = 98.2%) (shown in Table 2; Fig. 4). And the prevalence of FA was higher in children (2.3%, 95% CI: 0.014–0.035, I^2 = 98.4%) than in adults (1.1%, 95% CI: 0.005–0.021). Table 2 shows the literature quality subgroup analysis results.

Comparison of the FA Prevalence in Different Regions, Different Food Types, and Different Diagnostic Modalities

America (RR: 0.515, 95% CI: 0.507–0.524, $p < 0.0001$), Europe (RR: 0.555, 95% CI: 0.545–0.565, $p < 0.0001$), and Africa (RR: 0.338, 95% CI: 0.253, 0.443, $p < 0.0001$) had a

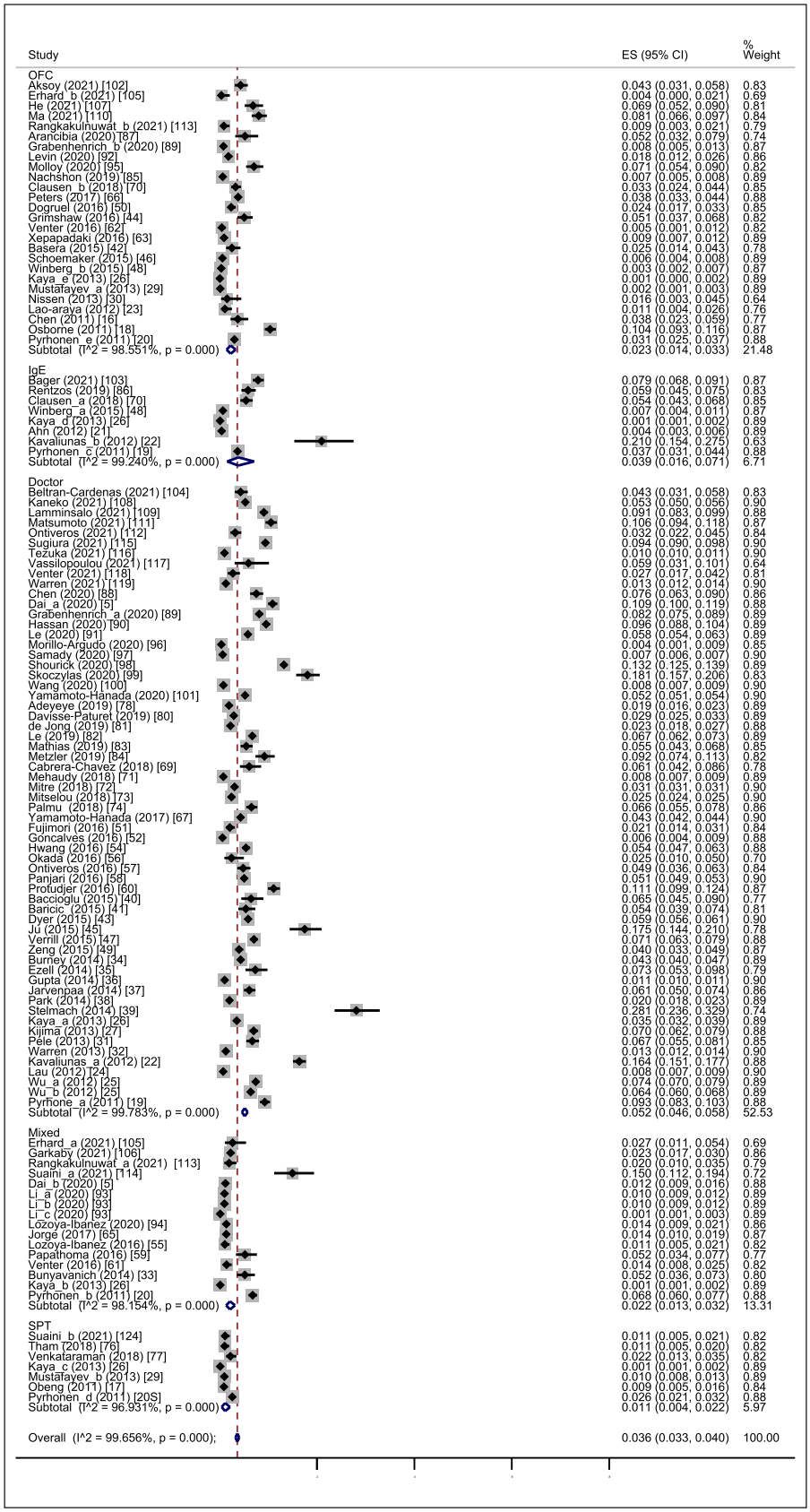

Fig. 4. Prevalence of different diagnostic modalities.

lower prevalence of FA compared with Asia. However, Oceania (RR: 1.119, 95% CI: 1.079–1.160, $p < 0.0001$) had a higher prevalence of FA than Asia (shown in Table 3). Europe (RR: 1.076, 95% CI: 1.060–1.093, $p < 0.0001$) and Oceania (RR: 2.171, 95% CI: 2.096–2.249, $p < 0.0001$) had a higher FA prevalence than America. Nevertheless, Africa (RR: 0.656, 95% CI: 0.491–0.859, $p = 0.0011$) had a lower FA prevalence than America. Africa (RR: 0.610, 95% CI: 0.457–0.798, $p = 0.0001$) had a lower FA prevalence compared with Europe while Oceania (RR: 2.017, 95% CI: 1.947–2.089, $p < 0.0001$) had a higher FA prevalence compared with Europe. Oceania had a higher FA prevalence compared with Africa (RR: 3.309, 95% CI: 2.524–4.426, $p < 0.0001$) (shown in Table 3).

Peanut (RR: 1.119, 95% CI: 1.086–1.152), nuts (RR: 1.321, 95% CI: 1.252–1.392, $p < 0.0001$), shellfish (RR: 1.709, 95% CI: 1.636–1.785, $p < 0.0001$) had a higher FA prevalence than milk. However, egg (RR: 0.789, 95% CI: 0.764–0.815, $p < 0.0001$), fish (RR: 0.849, 95% CI: 0.789–0.912, $p < 0.0001$), soya (RR: 0.385, 95% CI: 0.350–0.422, $p < 0.0001$), and wheat (RR: 0.475, 95% CI: 0.432–0.520, $p < 0.0001$) had a lower FA prevalence than milk. Comparing with egg, peanut (RR: 1.418, 95% CI: 1.374–1.464, $p < 0.0001$), nuts (RR: 1.674, 95% CI: 1.585–1.768, $p < 0.0001$), shellfish (RR: 2.167, 95% CI: 2.070–2.268, $p < 0.0001$), and fish (1.076, 95% CI: 1.001–1.157, $p = 0.047$) had a higher FA prevalence while soya (RR: 0.488, 95% CI: 0.443–0.535, $p < 0.0001$) and wheat (RR: 0.602, 95% CI: 0.548–0.660, $p < 0.0001$) had a lower FA prevalence. Nuts (RR: 1.181, 95% CI: 1.120–1.244, $p < 0.0001$) and shellfish (RR: 1.528, 95% CI: 1.463–1.596, $p < 0.0001$) had a higher prevalence of FAs and fish (RR: 0.759, 95% CI: 0.706–0.815, $p < 0.0001$), soya (RR: 0.344, 95% CI: 0.313–0.377, $p < 0.0001$), wheat (RR: 0.424, 95% CI: 0.386–0.465, $p < 0.0001$) had a lower prevalence of FAs compared to peanut. Compared to nuts, only shellfish (RR: 1.294, 95% CI: 1.216–1.378, $p < 0.0001$) had a higher prevalence of FA, while fish (RR: 0.643, 95% CI: 0.590–0.699, $p < 0.0001$), soya (RR: 0.291, 95% CI: 0.262–0.323, $p < 0.0001$), and wheat (RR: 0.359, 95% CI: 0.324–0.398, $p < 0.0001$) all had lower prevalence. The fish (RR: 0.497, 95% CI: 0.459–0.537, $p < 0.0001$), soya (RR: 0.225, 95% CI: 0.204–0.248, $p < 0.0001$), and wheat (RR: 0.278, 95% CI: 0.252–0.306, $p < 0.0001$) had a lower prevalence of FA compared with shellfish. Soya (RR: 0.453, 95% CI: 0.404–0.508, $p < 0.0001$) and wheat (RR: 0.559, 95% CI: 0.499–0.626, $p < 0.0001$) had a lower prevalence of FAs than fish. Wheat had a higher FA prevalence than soya (RR: 1.234, 95% CI: 1.085–1.404, $p = 0.0011$) (shown in Table 3).

FAs diagnosed by the OFC (RR: 0.616, 95% CI: 0.5824–0.6499, $p < 0.0001$), IgE (RR: 0.652, 95% CI: 0.598–0.710, $p < 0.0001$), SPT (RR: 0.317, 95% CI: 0.276–0.362, $p < 0.0001$), and mixed (RR: 0.469, 95% CI: 0.438–0.502, $p < 0.0001$) were lower than FA diagnosed by the doctor. FA diagnosed by IgE was higher than FA diagnosed by OFC (RR: 1.059, 95% CI: 0.956–1.173, $p = 0.2633$) while FAs diagnosed by the SPT (RR: 0.515, 95% CI: 0.444–0.595, $p < 0.0001$) and mixed (RR: 0.762, 95% CI: 0.698–0.832, $p < 0.0001$) were lower than FA diagnosed by OFC. FA diagnosed by the SPT (RR: 0.486, 95% CI: 0.413–0.570, $p < 0.0001$) and mixed (RR: 0.720, 95% CI: 0.645–0.803, $p < 0.0001$) was lower than FA diagnosed by the IgE. FA diagnosed by the mixed test was higher than FA diagnosed by the SPT (RR: 1.480, 95% CI: 1.274–1.725, $p < 0.0001$) (shown in Table 3).

Influencing Factors for FA

Gender

A total of 11 groups of data from 10 studies were included to assess the effect of gender on the FA. REM analysis results demonstrated that males had a higher risk of FA than females (OR: 1.289, 95% CI: 1.001–1.659, $p = 0.049$). Then, subgroup analysis was performed based on regions. Male was associated with a higher risk of FA in the Asian population (OR: 1.220, 95% CI: 1.108–1.343), $p < 0.001$) while there were no differences between the male and female groups in America (OR: 1.176, 95% CI: 0.487–2.840, $p = 0.718$), Europe (OR: 1.056, 95% CI: 0.667–1.670, $p = 0.817$), and Oceania (OR: 1.783, 95% CI: 0.879–3.613, $p = 0.109$). Regarding diagnostic modes, for mixed diagnosis, the risk of FA was higher in male group than female group (OR: 1.966, 95% CI: 1.325–2.916, $p = 0.001$) (Table 4). However, based on the literature quality subgroup analysis result, male was only associated with FA in high-quality cross-sectional studies (OR: 1.755, 95% CI: 1.407–2.188, $p < 0.001$) (shown in Table 5).

Cesarean

Cesarean was regarded as a potential risk factor of FA in 9 studies. The result showed that there was no difference in the risk of FA between the cesarean group and the vaginal group (OR: 1.214, 95% CI: 0.890–1.656, $p = 0.221$). Based on regional subgroup analysis, the result indicated that among African groups, cesarean had a higher risk of having FA (OR: 2.318, 95% CI: 1.107–4.854, $p = 0.026$). Concerning the diagnostic modes, for doctor diagnosis, cesarean was associated with higher risk of FA (OR: 1.571, 95% CI: 1.051–2.347, $p = 0.028$) (Table 4). Based on the literature quality subgroup analysis, cesarean was a potential risk factor of FA in high-quality cohort studies

Table 3. Comparison of the FA prevalence in different regions, different food types, and different diagnostic modalities

Outcomes	Comparisons	Total (RR [95% CI])	*p*	Children (RR [95% CI])	*p*	Adult (RR [95% CI])	*p*
Region							
	versus Asia						
	America	0.515 (0.507–0.524)	<0.0001	0.563 (0.551–0.576)	<0.0001	0.455 (0.425–0.486)	<0.0001
	Europe	0.555 (0.545–0.565)	<0.0001	0.561 (0.548–0.573)	<0.0001	0.902 (0.839–0.969)	0.0041
	Africa	0.338 (0.253–0.443)	<0.0001	0.345 (0.258–0.452)	<0.0001	–	–
	Oceania	1.119 (1.079–1.160)	<0.0001	1.142 (1.099–1.187)	<0.0001	–	–
Food							
	versus milk						
	Egg	0.789 (0.764–0.815)	<0.0001	0.795 (0.769–0.822)	<0.0001	0.601 (0.419–0.857)	
	Peanut	1.119 (1.086–1.152)	<0.0001	1.104 (1.071–1.138)	<0.0001	2.196 (1.736–2.810)	<0.0001
	Nuts	1.321 (1.252–1.392)	<0.0001	1.325 (1.250–1.404)	<0.0001	5.440 (4.20–7.109)	<0.0001
	Shellfish	1.709 (1.636–1.785)	<0.0001	1.114 (1.048–1.183)	0.0005	5.088 (4.007–6.534)	<0.0001
	Fish	0.849 (0.789–0.912)	<0.0001	0.472 (0.416,0.535)	<0.0001	1.953 (1.491–2.577)	<0.0001
	Soya	0.385 (0.350–0.422)	<0.0001	0.419 (0.377–0.464)	<0.0001	0.272 (0.165–0.434)	<0.0001
	Wheat	0.475 (0.432–0.520)	<0.0001	0.468 (0.425–0.515)	<0.0001	–	–
Diagnosis							
	versus doctor						
	OFC	0.616 (0.582–0.650)	<0.0001	0.721 (0.680–0.762)	<0.0001	0.350 (0.114–1.077)	0.067
	IgE	0.652 (0.598–0.710)	<0.0001	0.425 (0.378–0.476)	<0.0001	1.633(1.430–1.859)	<0.0001
	SPT	0.317 (0.276–0.362)	<0.0001	0.312 (0.270–0.358)	<0.0001	0.503 (0.303–0.786)	0.0009
	Mixed	0.469 (0.438–0.502)	<0.0001	0.488 (0.455–0.523)	<0.0001	0.245 (0.112–0.466)	<0.0001

RR, rate of rate 1/rate 2; FA, food allergy; CI, confidence interval; NA, not available; OFC, open food challenge; IgE, immunoglobulin E; SPT, skin prick test.

(OR: 1.237, 95% CI: 1.201–1.275, $p < 0.001$) and low-quality case-control studies (OR: 4.334, 95% CI: 2.735–6.865, $p < 0.001$). However, in high-quality case-control studies, cesarean was associated with a decreased risk of FA (OR: 0.218, 95% CI: 0.125–0.380, $p < 0.001$) (shown in Table 5).

Antibiotics Exposure

FEM analysis results showed that antibiotics exposure during pregnancy increased the risk of FA (OR: 1.221, 95% CI: 1.162–1.284, $p < 0.001$) (Table 4). Both high-quality cohort (OR: 1.539, 95% CI: 1.003–2.362, $p = 0.049$) and case-control studies (OR: 1.218, 95% CI: 1.158–1.281, $p < 0.001$) found that antibiotics exposure during pregnancy was associated with an increased risk of FA (shown in Table 5).

Breastfeeding

Our result demonstrated that the risk of FA in a breastfeeding group was higher than that in a nonbreastfeeding group (OR: 1.349, 95% CI: 1.011–1.799, $p = 0.042$) (Table 4). However, when the breastfeeding was ≥6 months, breastfeeding could not be considered to be the factor associating with the risk of FA (OR: 1.040, 95% CI: 0.501–2.156, $p = 0.917$, $I^2 = 85.7\%$).

Allergic Disorder

Asthma

Two studies were used to evaluate asthma as an influencing factor of FA. FEM analysis result demonstrated that asthma increased the risk of FA (OR: 1.794, 95% CI: 1.443–2.230, $p < 0.001$) (shown in Table 4). Table 5 shows the subgroup analysis of literature quality. The result demonstrated the same results in both high-quality cross-sectional studies (OR: 1.755, 95% CI: 1.407–2.188, $p < 0.001$) and high-quality cohort studies (OR: 4.240, 95% CI: 1.203–14.937).

Eczema

A total of 5 groups of data from 4 studies were included, and the difference was statistically significant ($I^2 = 72.4\%$), so REM was used for analysis. The result showed that the population with eczema was at a higher risk of FA (OR: 5.121, 95% CI: 3.575–7.334, $p < 0.001$). According to our subgroup analysis, eczema increased the risk of FA in Asia (OR: 5.988, 95% CI: 5.341–6.714, $p < 0.001$), America (OR: 3.624, 95% CI: 2.838–4.627, $p < 0.001$), Europe (OR: 11.431, 95% CI: 2.486–52.555, $p = 0.002$), Oceania (OR: 4.858, 95% CI: 2.422–9.741, $p < 0.001$). Regarding diagnostic modes analysis, the risk of

Table 4. Analysis of influencing factors of FAs

Variables	Indicators	OR (95% CI)	*p*	I^2
Male	Overall	1.289 (1.001–1.659)	0.049	96.1
	Sensitivity analysis	1.289 (1.001–1.659)		
	Publication bias	$Z = 0.62$	0.533	
	Region			
	Asia	1.220 (1.108–1.343)	<0.001	0
	America	1.176 (0.487–2.840)	0.718	85.3
	Europe	1.056 (0.667–1.670)	0.817	94
	Oceania	1.783 (0.879–3.613)	0.109	76.4
	Diagnosis			
	Doctor	1.089 (0.795–1.493)	0.594	97.9
	OFC	1.229 (0.876–1.724)	0.234	0
	SPT	2.157 (0.554–8.398)	0.267	NA
	Mixed	1.966 (1.325–2.916)	0.001	36.8
Cesarean	Overall	1.214 (0.890–1.656)	0.221	89
	Sensitivity analysis	1.214 (0.890–1.656)		
	Publication bias	$Z = 1.36$	0.175	
	Region			
	Asia	1.231 (0.696–2.176)	0.475	NA
	America	1.060 (0.850–1.322)	0.607	11.9
	Europe	1.142 (0.640–2.036)	0.654	95.5
	Africa	2.318 (1.107–4.854)	0.026	NA
	Diagnosis			
	Doctor	1.571 (1.051–2.347)	0.028	89.7
	OFC	0.955 (0.320–2.851)	0.934	90.9
	Mixed	0.982 (0.772–1.249)	0.882	NA
Antibiotics exposure	During pregnancy			
	Overall	1.221 (1.162–1.284)	<0.001	30.6
	Sensitivity analysis	1.221 (1.162–1.284)		
	In the first year			
	Overall	1.213 (1.175–1.253)	<0.001	32.4
	Sensitivity analysis	1.213 (1.175–1.253)		
Feeding	Breastfeeding			
	Overall	1.349 (1.011–1.799)	0.042	0
	Sensitivity analysis	1.349 (1.011–1.799)		
	Breastfeeding duration ≥6 months			
	Overall	1.040 (0.501–2.156)	0.917	85.7
	Sensitivity analysis	1.040 (0.501–2.156)		
Allergic disorder	Asthma			
	Overall	1.794 (1.443–2.230)	<0.001	45.3
	Sensitivity analysis	1.794 (1.443–2.230)		
	Eczema			
	Overall	5.121 (3.575–7.334)	<0.001	72.4
	Sensitivity analysis	5.121 (3.575–7.334)		
	Region			
	Asia	5.988 (5.341–6.714)	<0.001	0
	America	3.624 (2.838–4.627)	<0.001	NA
	Europe	11.431 (2.486–52.555)	0.002	NA
	Oceania	4.858 (2.422–9.741)	<0.001	NA
	Diagnosis			
	Doctor	5.976 (5.328–6.703)	<0.001	NA
	SPT	7.690 (2.141–27.621)	0.002	NA
	Mixed	4.140 (2.839–6.040)	<0.001	23.7

Table 4 (continued)

Variables	Indicators	OR (95% CI)	*p*	I^2
Family history	*Atopic disease*			
	Overall	1.893 (1.313–2.730)	0.001	78.6
	Sensitivity analysis	1.893 (1.313–2.730)		
	Publication bias	*Z* = 0.66	0.511	
	Region			
	Asia	3.593 (2.007–6.431)	<0.001	35.4
	Europe	1.200 (0.773–1.865)	0.416	80.4
	Oceania	3.192 (2.032–5.016)	<0.001	0
	Diagnosis			
	Doctor	1.528 (1.297–1.801)	<0.001	0
	OFC	2.962 (1.407–6.237)	0.004	72.2
	SPT	1.937 (0.230–16.319)	0.543	76.5
	Mixed	0.991 (0.161–6.082)	0.992	93.8
	FA			
	Overall	2.093 (1.688–2.594)	<0.001	77.9
	Sensitivity analysis	2.093 (1.688–2.594)		
	Region			
	Asia	2.427 (2.015–2.923)	<0.001	70.7
	America	1.462 (1.164–1.837)	0.001	NA
	Europe	2.515 (1.827–3.462)	<0.001	0
	Oceania	1.273 (0.850–1.906)	0.242	NA
	Diagnosis			
	Doctor	2.441 (2.054–2.900)	<0.001	57.2
	OFC	1.907 (1.144–3.180)	0.013	68
	Mixed	1.462 (1.164–1.837)	0.001	NA
	AD			
	Overall	1.954 (1.645–2.322)	<0.001	69.6
	Sensitivity analysis	1.954 (1.645–2.322)		
	Region			
	Asia	1.795 (1.608–2.005)	<0.001	43.6
	Europe	3.086 (2.196–4.336)	<0.001	0
	Diagnosis			
	Doctor	1.795 (1.608–2.005)	<0.001	43.6
	OFC	3.086 (2.196–4.336)	<0.001	0
	Asthma			
	Overall	1.516 (1.370–1.678)	<0.001	26.9
	Sensitivity analysis	1.516 (1.370–1.678)		
	Allergic rhinitis/conjunctivitis			
	Overall	1.287 (1.191–1.392)	<0.001	34.9
	Sensitivity analysis	1.287 (1.191–1.392)		

OR, odds ratio; FA, food allergy; CI, confidence interval; OFC, open food challenge; SPT, skin prick test.

FA in the eczema group was higher than that of the no eczema group when FA was diagnosed by doctor (OR: 5.976, 95% CI: 5.328–6.703, $p < 0.001$), SPT (OR: 7.690, 95% CI: 2.141–27.621, $p = 0.002$), mixed mode (OR: 4.140, 95% CI: 2.839–6.040, $p < 0.001$) (shown in Table 4). According to our subgroup analysis of literature quality, eczema was found to be associated with an increased risk of FA in high-quality cross-sectional studies (OR: 3.624, 95% CI: 2.838–4.627, $p < 0.001$), low-quality of cross-sectional studies (OR: 5.976, 95% CI: 5.328–6.703, $p < 0.001$), and high-quality cohort studies (OR: 6.016, 95% CI: 3.407–10.624, $p < 0.001$) (shown in Table 5).

Family History

Atopic Disease

Family history of the atopic disease was regarded as a potential factor for FA. REM results showed that the population who had a family history of atopic disease was at

Table 5. Analysis of influencing factors of FAs based on the literature quality

Variables	Indicators	OR (95% CI)	*p*	I^2
Male	Overall	1.289 (1.001–1.659)	0.049	96.1
	QA			
	Cross-sectional (high)	1.755 (1.407–2.188)	<0.001	NA
	Cross-sectional (low)	1.023 (0.630–1.663)	0.926	61.1
	Cohort (high)	1.360 (0.965–1.916)	0.079	96.1
	Case control (high)	1.090 (0.652–1.822)	0.744	NA
Cesarean	Overall	1.214 (0.890–1.656)	0.221	89
	QA			
	Cross-sectional (high)	0.982 (0.772–1.249)	0.882	NA
	Cohort (high)	1.237 (1.201–1.275)	<0.001	0
	Case control (high)	0.218 (0.125–0.380)	<0.001	NA
	Case control (low)	4.334 (2.735–6.865)	<0.001	NA
Antibiotics exposure	During pregnancy			
	Overall	1.221 (1.162–1.284)	<0.001	30.6
	QA			
	Cohort (high)	1.539 (1.003–2.362)	0.049	38.4
	Case control (high)	1.218 (1.158–1.281)	<0.001	NA
	In the first year			
	Overall	1.213 (1.175–1.253)	<0.001	32.4
	QA			
	Cohort (high)	1.215 (1.177–1.255)	<0.001	0
	Case control (high)	0.667 (0.359–1.240)	0.2	49.4
Feeding	Breastfeeding			
	Overall	1.349 (1.011–1.799)	0.042	0
	QA			
	Cross-sectional (high)	1.439 (0.996–2.080)	0.053	NA
	Cohort (high)	0.609 (0.264–1.404)	0.244	0
	Case control (high)	1.603 (0.928–2.767)	0.09	0
	Breastfeeding duration ≥6 months			
	Overall	1.040 (0.501–2.156)	0.917	85.7
	QA			
	Cohort (high)	1.110 (0.907–1.358)	0.311	0
	Case control (high)	2.667 (1.233–5.768)	0.013	NA
	Case control (low)	0.391 (0.238–0.643)	<0.001	NA
Allergic disorder	Asthma			
	Overall	1.794 (1.443–2.230)	<0.001	45.3
	QA			
	Cross-sectional (high)	1.755 (1.407–2.188)	<0.001	NA
	Cohort (high)	4.240 (1.203–14.937)	0.025	NA
	Eczema			
	Overall	5.121 (3.575–7.334)	<0.001	72.4
	QA			
	Cross-sectional (high)	3.624 (2.838–4.627)	<0.001	NA
	Cross-sectional (low)	5.976 (5.328–6.703)	<0.001	NA
	Cohort (high)	6.016 (3.407–10.624)	<0.001	0
Family history	Atopic disease			
	Overall	1.893 (1.313–2.730)	0.001	78.6
	QA			
	Cross-sectional (low)	1.728 (0.499–5.985)	0.388	NA
	Cohort (high)	1.992 (1.302–3.047)	0.001	80.8
	Case control (low)	1.235 (0.841–1.814)	0.282	NA
	FA			
	Overall	2.093 (1.688–2.594)	<0.001	77.9
	QA			
	Cross-sectional (high)	1.417 (1.162–1.727)	0.001	0

Table 5 (continued)

Variables	Indicators	OR (95% CI)	*p*	I^2
	Cross-sectional (low)	2.441 (2.054–2.900)	<0.001	57.2
	Cohort (high)	2.464 (1.734–3.502)	<0.001	NA
	Case control (high)	2.528 (0.971–6.580)	0.057	NA
	AD			
	Overall	1.954 (1.645–2.322)	<0.001	69.6
	QA			
	Cross-sectional (low)	1.808 (1.670–1.957)	<0.001	43.6
	Cohort (high)	2.917 (2.022–4.207)	<0.001	NA
	Case control (high)	4.398 (1.755–11.024)	0.002	NA
	Asthma			
	Overall	1.516 (1.370–1.678)	<0.001	26.9
	QA			
	Cross-sectional (low)	1.508 (1.359–1.674)	<0.001	0
	Cohort (high)	1.131 (0.640–1.997)	0.672	NA
	Case control (high)	3.418 (1.428–8.182)	0.006	NA
	Allergic rhinitis/conjunctivitis			
	Overall	1.287 (1.191–1.392)	<0.001	34.9
	QA			
	Cross-sectional (low)	1.290 (1.147–1.452)	<0.001	50.4
	Cohort (high)	1.002 (0.520–1.932)	0.996	NA

OR, odds ratio; FA, food allergy; CI, confidence interval; QA, quality assessment.

higher risk of FA (OR: 1.893, 95% CI: 1.313–2.730, p = 0.001). Subgroup analysis result demonstrated that FA was associated with a family history of atopic disease among Asian (OR: 3.593, 95% CI: 2.007–6.431, $p < 0.001$) and Oceanian population (OR: 3.192, 95% CI: 2.032–5.016, $p < 0.001$). And the group with a family history of atopic disease had a higher risk of FA when FA was tested by doctor (OR: 1.528, 95% CI: 1.297–1.801, $p < 0.001$) and OFC (OR: 2.962, 95% CI: 1.407–6.237, p = 0.004) (Table 4). However, only high-quality cohort studies found that family history of atopic disease was an influencing factor of FA (OR: 1.992, 95% CI: 1.302–3.047, p = 0.001) (shown in Table 5).

FAs

Six studies assessed the family history of FAs on the risk of FA. Our result showed that the population with a family history of FAs was more likely to develop FA (OR: 2.096, 95% CI: 1.686–2.594, $p < 0.001$). In Asia (OR: 2.427, 95% CI: 2.015–2.923, $p < 0.001$), America (OR: 1.462, 95% CI: 1.164–1.837, p = 0.001), and Europe (OR: 2.515, 95% CI: 1.827–3.462, $p < 0.001$), FA was associated with a family history of FAs. However, in Oceania, there was no difference in FA risk between the group with a family history of FA and the group without FA (OR: 1.273, 95% CI: 0.850–1.906, p = 0.242). Higher risk of FA was observed when FA was tested by doctor (OR: 2.441, 95% CI: 2.054–2.900, $p < 0.001$), OFC (OR: 1.907, 95% CI: 1.144–3.180), p = 0.013), mixed (OR: 1.462, 95% CI: 1.164–1.837, p = 0.001) (shown in Table 4).

Atopic Dermatitis

Family history of AD was assessed in 3 articles. REM results demonstrated that the risk of FA was higher in the group with a family history of AD than in the group without (OR: 1.954, 95% CI: 1.645–2.322, $p < 0.001$). The subgroup analysis showed that among Asian (OR: 1.795, 95% CI: 1.608–2.005, $p < 0.001$), European (OR: 3.086, 95% CI: 2.196–4.336, $p < 0.001$) population, family history of AD increased the risk of FA, and FA tested by a doctor (OR: 1.795, 95% CI: 1.608–2.005, $p < 0.001$), OFC (OR: 3.086, 95% CI: 2.196–4.336, $p < 0.001$) was associated with higher risk of FAs (shown in Table 4).

Asthma

Three studies were used to assess the effect of family history of asthma on the risk of FA. It was found that a family history of asthma increased the risk of FA (OR: 1.516, 95% CI: 1.370–1.678, $p < 0.001$) (shown in Table 4).

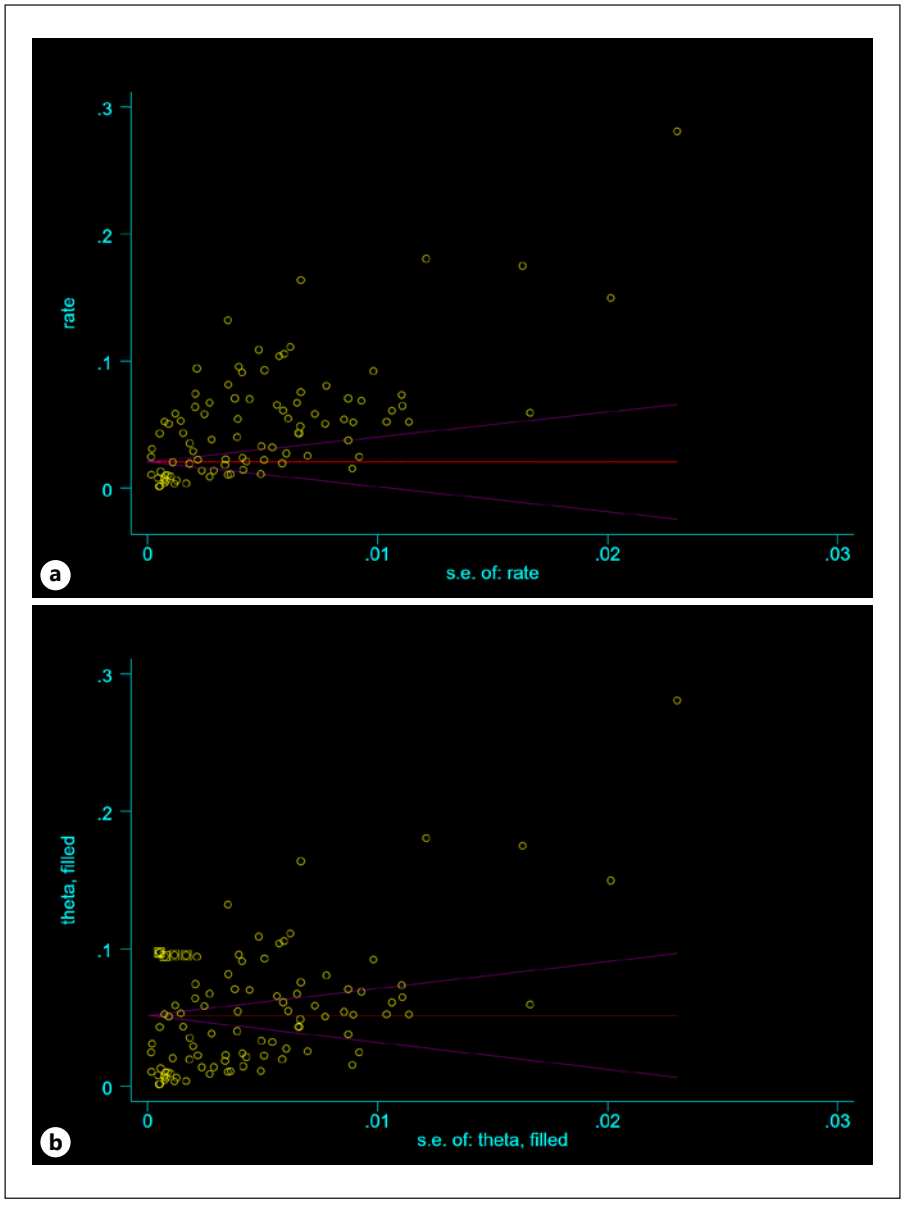

Fig. 5. Publication bias of FA. **a** Unadjusted. **b** Adjusted.

Allergic Rhinitis/Conjunctivitis

The effect of allergic rhinitis/conjunctivitis on FA was assessed in 2 studies. The FEM demonstrated that population with a family history of allergic rhinitis/conjunctivitis may be considered to have a higher risk of FA (OR: 1.287, 95% CI: 1.191–1.392, $p < 0.001$) (shown in Table 4).

Sensitivity Analysis and Publication Bias

The results of sensitivity analysis suggested that our result was relatively stable. The result of publication bias showed that FA ($Z = 2.04$, $p = 0.042$) had publication bias. The combined result of the effect estimate obtained from the REM before "trim and fill" was 0.043 (95% CI: 0.038–0.047). The REM was used to estimate the number of missing studies after 5 iterations. Meta-analysis was conducted again for all studies. The combined result of the effect estimate obtained from the REM after the "trim and fill" was 0.051 (95% CI: 0.046–0.057), and there was no significant change before and after the result, indicating that publication bias had little influence and the conclusion in the literature was relatively robust. The publication bias of FA is shown in Figure 5.

Discussion

FA is an important atopic disease although its precise burden is unclear. In this meta-analysis, we evaluated the prevalence of FA and potential influencing factors in global context. The present evidence indicates that the overall prevalence of FA is 4.3%, with 4.2% in Asia, 3.2% in America, 4.8% in Europe, 1.6% in Africa, and 7.5% in Oceania. Milk, eggs, and shellfish were the main food allergens. Our meta-analysis concluded that FA was associated with male, antibiotics exposure during pregnancy, breastfeeding, asthma, eczema, family history of atopic disease, FAs, AD, asthma, and allergic rhinitis/conjunctivitis.

In this study, the overall prevalence of FA in Asia was 4.2% with 3.4% among children, 5.6% among adults. Some studies reported the prevalence of FA in northern Asian countries, such as Japan with a prevalence of 5–10% [120] and Korea with a prevalence of 5.3% [38]. A study suggests that in Central and East Asian countries, the prevalence of pediatric FA is highly variable. Countries further south such as Hong Kong, China, the Philippines, and Singapore reported prevalence of less than 5% [49, 76]. A pervious study [11] conducted in 2013 in Europe has found that the point prevalence of FA assessed by specific IgE was 10.1% and by SPT was 2.7% and by FC positivity was 0.9%. Using methodology identical to that in adults, prevalence estimate of FA, ranging from 1.0% to 5.6%, was found in school-age children across Europe [121]. Lyons et al. [122] conducting a study evaluating FA in adults across Europe found that the prevalence of FA reaches almost 6% in parts of Europe. The FA prevalence in the American population is 3.2%, with 2.9% in children and an estimated 4.4% in adults in our findings. A study demonstrated the prevalence of FA to any food is 3.5% in Mexican schoolchildren [57]. Mehaudy et al. [71], conducting prevalence of cow's milk protein allergy among children in Argentina, has found a percent increase of 0.4% in 2004 to 1.2% in 2014 in the number of cases per year. Arancibia et al. [87] found the overall prevalence of cow's milk protein allergy was 5.2%, with a 6 times higher prevalence in the high-income cohort (9.2%) compared with the low-income group (1.5%) in Chilean. Our study demonstrated that the prevalence of FA was 7.5% in Oceania, mainly conducted in Australia. Australia reports the highest prevalence of IgE-mediated FA, with 10% of infants demonstrating challenge-confirmed allergies to one or more food allergens [123]. In another study, 15.0% FA prevalence was reported in Australia [124]. In this study, the African population had the lowest prevalence of FA (1.6%). A study [79], investigating rural and urban FA prevalence in the South African, demonstrated that the prevalence of FA was 2.5% in urban and 0.5% prevalence in the rural African children. Nutritional factors have been associated with differing FA risk, particularly the timing of introduction of potentially allergenic foods, micronutrient intake during early life, ingestion of prebiotics, variety of foods ingested during the first year of life, and ingestion of fast foods high in advanced glycation end products (AGEs) [125]. The Western dietary pattern is high in advanced glycation end products, which are found in cooked meat, oil, cheese, and high-sugar diets [126]. This may be the possible explanations for the lower risk of FA prevalence in Africa.

In our study, shellfish, milk, and eggs had higher prevalence of FA. In a previous study, the prevalence of egg was 0.35–1.8%, peanut was 0.1–0.3%, and shellfish was 0.2–0.9% [76]. The types of foods responsible for causing reactions differ depending on the age-group. We found that milk, eggs, and soya had high prevalence of FA in children compared with adults. Other studies also showed that allergy to cow's milk and egg more common among younger children and allergy to peanut, tree nuts, fish, and shellfish is more common in older children and adults [66, 127].

Numerous epidemiological studies suggest that early-life antibiotic exposure may increase the risk of developing FA [128, 129]. Maternal intake of antibiotic during pregnancy increases the risk of allergy in children [128]. Sasaki et al. [130] found early-onset eczema was associated with an increased risk of FA. Disrupted skin barrier function in infant eczema might cause allergen sensitization through environmental exposure via the skin (rather than orally), but given the trend to avoid allergenic solid foods, the induction of oral tolerance fails and FA develops [123]. A common risk factor for FA in infancy was parental history of allergy [131]. Sasaki et al. [130] found that a family history of allergic disease was associated with an increased risk of FA. Children with a parent or sibling with the allergic disease are at increased risk of allergic disease [132]. An immature gut of the infant has been hypothesized as a possible route of sensitization. Breastfeeding until at least 6 months of age has been shown to have protective factors for the newborn and may possibly improve gut permeability [133]. Although exclusive breastfeeding is universally recommended for all mothers, there is no specific association between exclusive breastfeeding and the primary prevention of any specific FA [134]. In our study, breastfeeding increased the risk of FA. The effect of breastfeeding on FA needs to be further elucidated.

A previous meta-analysis in 2007 [135] assessed the food FA and found that self-reported prevalence of FA varied from 1.2% to 17% for milk, 0.2–7% for egg, 0–2% for peanuts and fish, 0–10% for shellfish, and 3–35% for any food. However, there is marked heterogeneity in the prevalence of FA that could be a result of the differences between populations. Our study is a meta-analysis to evaluate the prevalence of FA across the global context. The present study had several limitations. First, data were unevenly distributed across different regions, which may affect the reliability of our results. In addition, the study population also mainly focused on children. Second, data on FA only focus on the last 10 years. More research is needed in the future to further investigate the prevalence of FA in a global context, among different populations.

Conclusions

The result suggested there are geographic differences in the prevalence of FA, with highest prevalence in Oceania and lowest prevalence in Africa. Male, antibiotics exposure during pregnancy, breastfeeding, asthma, eczema, family history of atopic disease, FAs, AD, asthma, and allergic rhinitis/conjunctivitis were associated with increased the risk of FA. Regional FA prevention and treatment strategies should be implemented, and identifying high risk of FA populations is necessary.

Statement of Ethics

An ethical statement is not applicable because this study is based on published literature.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Hua Feng and Yongning Wu designed the study. Hua Feng wrote the manuscript. Xiujuan Xiong, Zhuo Chen, Qunying Xu, Zhongwei Zhang, and Nan Luo collected, analyzed, and interpreted the data. Yongning Wu critically reviewed, edited, and approved the manuscript. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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