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# The Region-Specific Landscape of Sensitization to Respiratory Allergens in the Population of Kazakhstan Accord Based on Molecular Diagnostics

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**ABSTRACT**

**Introduction:** Allergic diseases still remain one of the most common and widespread chronic pathologies of our time, affecting up to 40% of the population. Due to its unique environment, which presents a combination of steppe, desert and mountain ecosystems, the Republic of Kazakhstan is of particular interest for studying regional sensitization features. The use of molecular diagnostic methods, such as ImmunoCAP ISAC, makes it possible to detect sensitization at the level of individual allergenic components and form personalized therapy strategies.

**Aim:** Evaluate epidemiological and regional features of sensitization to respiratory allergens in Kazakhstan for the period 2021-2024 using component allergy diagnostics.

**Methods:** The study embraces 4,745 patients with clinical manifestations of allergic diseases (allergic rhinitis, bronchial asthma, atopic dermatitis) who were tested against the ISAC panel (21 inhaled allergens). Descriptive statistics, Pearson's $\chi 2$ criterion, Monte Carlo simulation, and Fisher's exact criterion were used.

**Results:** During the observation period, the median number of sensitizations increased more than sixfold (from 18.0 in 2021 to 113.0 in 2024), indicating an increase in allergic load. The most frequently detected components were rFel d 1 (34.7%), rPhl p 1 (23.0%), nArt v1 (22.8%) and rBet v1 (21.5%).

Significant regional differences were identified ($p = 0.001$): weeds (Ambrosia, Artemisia) prevailed in the southern regions, tree allergens (Betula, Alnus) prevailed in the northern regions, polysensitization prevailed in the central and eastern regions, and a combination of steppe and household allergens prevailed in the western regions. Gender differences did not demonstrate any statistical significance ($p > 0.05$).

**Conclusion:** The study revealed a substantial increase in sensitization in Kazakhstan and a confirmed geographical stratification of the allergenic spectrum. The results obtained emphasize the need for introduction of regionally adapted diagnostic panels, development of personalized allergen-specific immunotherapy (ASIT) regimens and system monitoring of molecular profile of sensitization for realization of personalized medicine principles.

**Keywords:** sensitization, allergens, ImmunoCAP ISAC, Kazakhstan, component-resolution diagnostics, allergen-specific immunotherapy, epidemiology of allergy, regional peculiarities.

## Introduction

Allergic diseases are currently regarded as one of the most significant medical and social health problems worldwide. According to the World Health Organization (WHO), allergic disorders are detected in 20–30% of the population in industrialized countries, while in some regions the prevalence reaches up to 40%. The frequency and structure of allergic diseases largely depend on climatic, environmental, and botanical characteristics of a given territory, which determine the spectrum of aeroallergens and shape the pattern of sensitization in the population.

Kazakhstan is located at the intersection of steppe, desert, semi-desert, and mountainous ecosystems and is characterized by pronounced climatic and geographic diversity. The territory of the country includes arid, sharply continental, and mountainous zones, each with a specific composition of vegetation and distinct pollen exposure patterns. Such environmental heterogeneity creates conditions for the formation of a wide spectrum of inhalant allergens and contributes to the development of polysensitization in the population [1–3].

In Central Asian countries, pollen allergens from trees, grasses, and weeds belonging to the families Betulaceae, Poaceae, Asteraceae, and Amaranthaceae play a leading role in the structure of respiratory allergy. Among tree allergens, the most clinically relevant are species of the genera Betula (birch), Alnus (alder), and Corylus (hazel), which predominate in northern and eastern regions characterized by more humid and moderately continental climates. Pollen from grasses of the family Poaceae, including Phleum pratense (timothy grass), is widely distributed in steppe and forest-steppe zones and represents one of the most common causes of seasonal allergic rhinitis. In arid and semi-desert regions, weed species predominate, particularly Artemisia (mugwort), Ambrosia (ragweed), and Salsola (saltwort), which are considered major sources of aeroallergens under continental climate conditions. Pollen of Artemisia and representatives of the family Amaranthaceae is regarded as one of the main factors in the development of pollinosis in Central Asia and Eastern Europe [4–6].

Previous epidemiological studies have demonstrated that the structure of sensitization significantly depends on climatic conditions, vegetation patterns, and the degree of urbanization. In regions with dry continental climates, sensitization to weed pollen is more frequently observed, whereas in northern and forest-steppe areas reactions to tree pollen predominate. These differences emphasize the need for region-specific data when evaluating sensitization patterns and planning allergen-specific immunotherapy.

In recent years, significant progress in the study of allergic diseases has been associated with the introduction of component-based molecular allergodiagnostics. The ImmunoCAP ISAC technology allows detection of specific IgE not only to allergen extracts but also to individual molecular components, making it possible to distinguish primary sensitization from cross-reactivity and to identify clinically relevant allergens

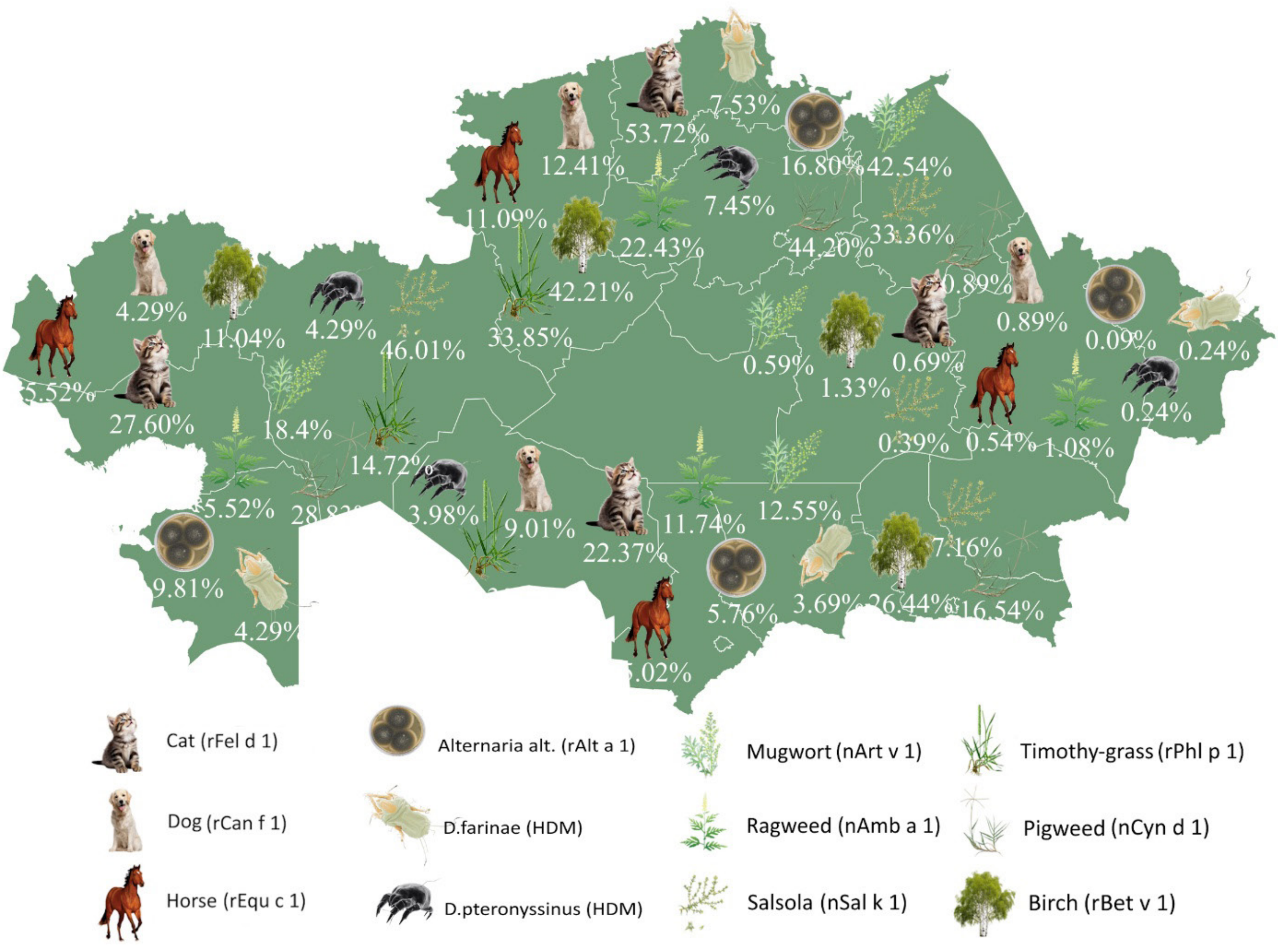


**Figure 1** –The landscape of sensitization spectrum of Republic of Kazakhstan

[26, 27]. This approach is particularly important in regions with high floristic variability, where conventional diagnostic methods may not accurately reflect the true structure of sensitization.

**Objective.** To evaluate the structure of sensitization to inhalant allergens among patients from different regions of Kazakhstan between 2021 and 2024 using component-based molecular allergy diagnostics.

## Methods

**Study design and population**

A retrospective, multicenter, observational study was conducted to evaluate the structure of molecular sensitization in patients from the Republic of Kazakhstan using component-resolved molecular allergodiagnostics.

Laboratory data obtained between January 2021 and December 2024 were included in the analysis. The final sample consisted of 4745 patients who underwent testing using the ImmunoCAP ISAC method.

Patients were referred for component-resolved diagnostics by allergists, pediatricians, pulmonologists, dermatologists, and general practitioners due to suspected IgE-mediated allergic diseases, presence of polysensitization, discrepancy between clinical manifestations and extract-based diagnostics, severe or systemic reactions, as well as during planning of allergen-specific immunotherapy (AIT). Thus, the study cohort represents a clinically selected population rather than a population-based sample.

**Inclusion and exclusion criteria**

Inclusion criteria:

1. Age of the patient from 1 to 80 years.
2. Availability of testing performed using the ImmunoCAP ISAC method during the period from January 2021 to December 2024.
3. Availability of a valid result of molecular allergy diagnostics with the possibility of analyzing inhalant allergen components.
4. Availability of the minimum required set of demographic data: age, sex, region, and year of testing.
5. Availability of a unique anonymized identifier allowing exclusion of repeated tests of the same patient.
6. Examination of the patient in medical institutions of the Republic of Kazakhstan / availability of data attributable to the population of the Republic of Kazakhstan.

Exclusion criteria:

1. Repeated testing of the same patient; only the first result was included in the analysis.
2. Incomplete laboratory data.
3. Incomplete or logically inconsistent demographic data.
4. Inability to perform unambiguous regional stratification of the patient.
5. Technically incorrect test results, including pre-analytical and analytical errors, as well as invalid internal controls.
6. Absence of results for key analyzed inhalant allergen components.
7. Age outside the established study range.

**Molecular allergodiagnostic method**

Molecular sensitization was assessed using the ImmunoCAP ISAC microarray platform (Thermo Fisher Scientific, Uppsala, Sweden), which allows semi-quantitative detection of specific IgE antibodies to 112 allergen components.

Serum samples were analyzed according to the manufacturer's instructions. Results were expressed in ISU-E (ISAC Standardized Units). The positivity threshold was defined as ≥ 0.3 ISU-E. Sensitization levels were interpreted as follows: 0.3–1 ISU-E — low level, 1–15 ISU-E — moderate level, 15 ISU-E — high level. Interpretation of molecular profiles was performed taking into account biochemical properties of allergens and known mechanisms of cross-reactivity.

**Clinical stratification**

Complete clinical data on confirmed diagnoses (allergic rhinitis, bronchial asthma, atopic dermatitis, food allergy, etc.) were not available for the entire study cohort.

The analysis was based on anonymized laboratory data extracted from the database of a clinical diagnostic laboratory and included only results of component-resolved molecular allergodiagnostics together with basic demographic parameters (age, gender, region of residence).

Due to complete data depersonalization, individual verification of clinical diagnoses, as well as the retrieval and analysis of medical records for each of the 4,745 patients at the level of healthcare institutions across the Republic of Kazakhstan, were not feasible from both organizational and ethical perspectives.

Therefore, the present study has primarily a laboratory-epidemiological design and is aimed at analyzing the structure of molecular sensitization rather than clinical phenotyping of patients.

**Statistical analysis**

Statistical analysis was performed using Microsoft Excel software (Microsoft Corp., USA).

The analysis was predominantly descriptive and aimed at evaluating the prevalence of molecular sensitization and comparing the frequency of detection of allergen components and panallergen families.

Quantitative values of specific IgE (ISU-E) were analyzed as continuous variables. Because of non-normal distribution, data were described using median (Me) and interquartile range (IQR).

Categorical variables (presence or absence of sensitization) were presented as absolute values and relative frequencies n (%). The prevalence of sensitization was calculated using the formula: $P (\%) = n / N \times 100$, where n is the number of patients with a positive result and N is the total number of examined patients (4745).

Comparison of proportions between allergen groups and panallergen families was performed using Pearson's $\chi^2$ test. When expected values in contingency tables were less than 5, Fisher's exact test was applied. The level of statistical significance was set at $p < 0.05$.

Since the analysis had a predominantly descriptive epidemiological character, correction for multiple comparisons was not performed; statistically significant differences were interpreted taking into account clinical and biological plausibility.

The analysis was performed using a complete-case approach; missing values were not imputed.

**Ethical considerations**

The study protocol was approved by the local ethics committee of NJSC "Astana Medical University", Astana, Kazakhstan. The study was based on retrospective analysis of anonymized laboratory data obtained from the database of "OLYMP Clinical Diagnostic Laboratory LLP" (Kazakhstan). Personal data were not available to the investigators. According to current legislation and local regulations, analysis of anonymized data did not require individual informed consent or additional ethical approval. The study was conducted in accordance with the principles of the Declaration of Helsinki.

## Results

A total of 4745 patients were included in the study: 364 were examined in 2021, 371 in 2022, 854 in 2023, and 3156 in 2024. An increase in the number of examined patients was observed over the study period, most pronounced in 2024, which may be related to increased awareness of molecular allergodiagnostics, improvement of diagnostic methods, and growing clinical interest in polysensitization [13, 14].

Since the distribution of quantitative variables was non-normal, the data were described using median (Me) and interquartile range (Q1–Q3): 2021 — Me = 18.0 (Q1–Q3: 10.5–49.0); 2022 — Me = 25.0 (11.0–52.0); 2023 — Me = 34.0 (18.5–87.5); 2024 — Me = 113.0 (61.0–280.5), max = 1009, as shown in Table 1.

**Table 1** Descriptive statistics of overall sensitization analysis

| Indicators | ME | $Q_1 - Q_3$ | n | MIN | MAX |
|---|---|---|---|---|---|
| 2021 | 18,00 | 10,50 – 49,00 | 55 | 1,00 | 159,00 |
| 2022 | 25,00 | 11,00 – 52,00 | 55 | 0,00 | 182,00 |
| 2023 | 34,00 | 18,50 – 87,50 | 55 | 0,00 | 295,00 |
| 2024 | 113,00 | 61,00 – 280,50 | 55 | 1,00 | 1009,00 |

The use of the median as a measure of central tendency ensures robustness of the analysis in the presence of asymmetric distributions, while the interquartile range reflects the variability of the sample.

At the same time, a progressive increase in both the interquartile range and the maximum values was observed, indicating changes in the distribution shape and an expansion of the variability range across the respective cohorts. Since the analysis was based on independent patient samples, these differences should be interpreted as inter-cohort variations reflecting differences in the composition of the examined groups, rather than as temporal trends at the individual level.

For analytical convenience, all identified allergens were conditionally grouped into three main categories: epidermal allergens, pollen allergens and indoor allergens.

Among epidermal allergens, the highest sensitization frequency was observed for the major cat allergen components rFel d 1 (34.7%) and Fel d 4 (10.2%).

Sensitization to major dog allergens was less frequent: rCan f 1 was detected in 9.1% of patients and rCan f 6 in 6.0%. The third most common epidermal allergen was the horse allergen rEqu c 1, detected in 6.8% of examined individuals. The lowest sensitization rates among epidermal allergens were observed for rodent allergens (mouse and hamster), not exceeding 2% of cases (Figure 2).

With regard to pollen allergens, the highest sensitization rates were detected for major components of timothy grass — rPhl p 1 (23.0%), rPhl p 2 (2.8%), rPhl p 4 (12.6%), rPhl p 5

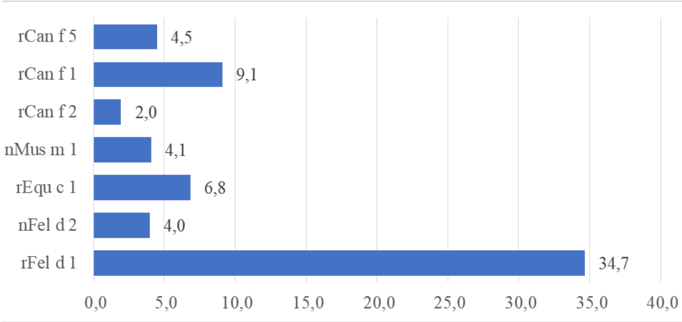


**Figure 2** – Spectrum of sensitization to epidermal allergens (%)

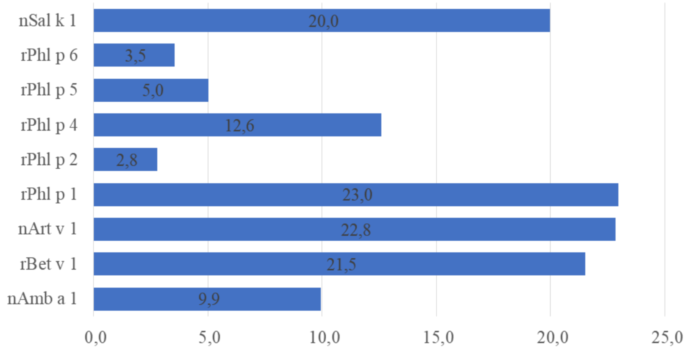


**Figure 3** – Spectrum of pollen sensitization (%)

(5.0%), and rPhl p 6 (3.5%); mugwort — nArt v 1 (22.8%); birch — rBet v 1 (21.5%); bermuda grass — nCyn d 1 (20.3%); and saltwort — nSal k 1 (20.0%).

Sensitization to the major allergen components of annual mercury — rMer a 1 was detected in 17.5% of patients, and to alder — rAln g 1 in 13.4%.

The identified components included allergens derived from trees, grasses, and weed pollen (Figure 3).

Regarding indoor allergens, the highest frequency of sensitization was observed for house dust mites, including Dermatophagoides pteronyssinus — nDer p 1 (4.4%) and Dermatophagoides farinae — nDer f 1 (4.5%).

With respect to fungal allergens, the most prevalent component was Alternaria alternata — rAlt a 1 (9.9%), whereas Aspergillus fumigatus (rAsp f 1, rAsp f 3, rAsp f 6) and Cladosporium herbarum were detected in 2–3% of cases (Figure 4).

Thus, the sensitization profile was characterized by a combination of high-frequency components (rFel d 1, rPhl p 1,

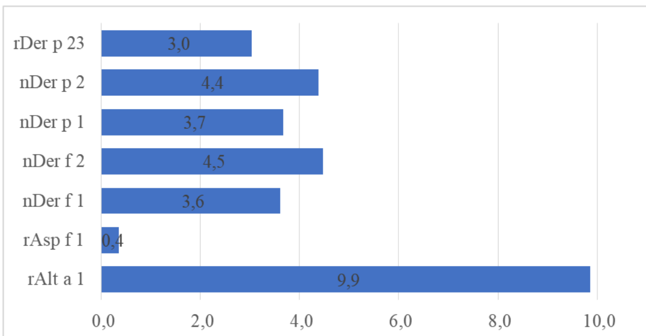


**Figure 4** – Spectrum of sensitization to indoor allergens (%)

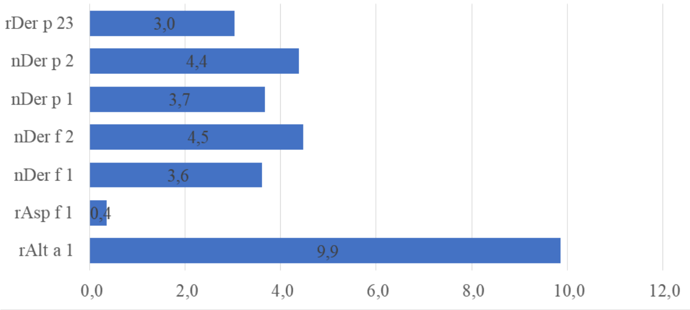


**Figure 5** – Dominant molecular allergen components

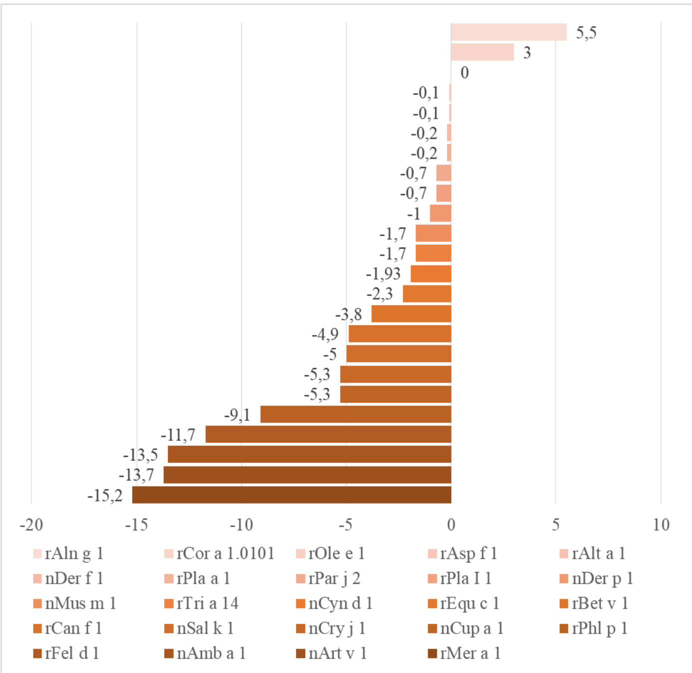


**Figure 6** – Changes of sensitization to allergen components (percentage points)

rBet v 1, nArt v 1) and a wide range of less prevalent allergens, which can be visually demonstrated by the Pareto chart shown in Figure 5.

Differences in sensitization frequency to individual allergen components were observed between yearly patient cohorts. The corresponding data are presented in Table 2, with visualization shown in Figure 6.

For comparative analysis of the sensitization structure, the results are presented as the proportion of sensitized patients (%) and the difference between 2021 and 2024 expressed in percentage points (pp), which allows comparison of independent samples without interpreting the observed differences as temporal changes.

The largest differences between yearly cohorts for pollen allergens were observed for the following components: annual mercury (rMer a 1): −15.2 percentage points (from 32.7% to 17.5%); mugwort (nArt v 1): −13.7 pp (from 36.5% to 22.8%); timothy grass (rPhl p 1): −9.1 pp (from 32.1% to 23.0%); ragweed (nAmb a 1): −13.5 pp (from 20.9% to 7.4%).

Relatively stable values were observed for birch (rBet v 1), where the difference was −3.8 pp (from 25.3% to 21.5%), as well as for bermuda grass (nCyn d 1), for which the sensitization

**Table 2** Changes in sensitization to allergen components by year (percentage points)

| Allergen | | 2021 | 2022 | 2023 | 2024 | Change (p.p.) |
|---|---|---|---|---|---|---|
| Ragweed *Ambrosia artemisiifolia* | nAmb a 1 | 20,9 | 18,3 | 10,5 | 7,4 | -13,5 |
| Birch *Betula verrucosa* | rBet v 1 | 25,3 | 26,4 | 17,1 | 21,5 | -3,8 |
| Cypress *Cupressus sempervirens* | nCup a 1 | 11,3 | 13,2 | 5,7 | 6 | -5,3 |
| Salsola (saltwort) *Salsola kali* | nSal k 1 | 25 | 27,7 | 23,1 | 20 | -5 |
| Bermuda grass *Cynodon dactylon* | nCyn d 1 | 8 | 7,1 | 11,8 | 6,07 | -1,93 |
| Alder *Alnus glutinosa* | rAln g 1 | 7,9 | 8,1 | 8,1 | 13,4 | 5,5 |
| Plane tree *Platanus acerifolia* | rPla a 1 | 0,3 | 0,5 | 0,1 | 0,1 | -0,2 |
| Plantain *Plantago lanceolata* | rPla I 1 | 2,2 | 2,5 | 1,3 | 1,5 | -0,7 |
| Mugwort *Artemisia vulgaris* | nArt v 1 | 36,5 | 31,2 | 23,7 | 22,8 | -13,7 |
| Wall pellitory *Parietaria officinalis* | rPar j 2 | 1,4 | 2,3 | 0,6 | 0,7 | -0,7 |
| Annual mercury *Mercurialis annua* | rMer a 1 | 32,7 | 29,7 | 17,8 | 17,5 | -15,2 |
| Wheat *Triticum aestivum* | rTri a 14 | 4,9 | 7,1 | 4,8 | 3,2 | -1,7 |
| Olive tree *Olea europaea* | rOle e 1 | 0,5 | 1 | 0,4 | 0,5 | 0 |
| Hazel *Corylus avellana* | rCor a 1.0101 | 9,3 | 10,7 | 10,7 | 12,3 | 3 |
| Timothy grass *Phleum pratense* | rPhl p 1 | 32,1 | 30,5 | 20,3 | 23 | -9,1 |
| Japanese cedar *Cryptomeria japonica* | nCry j 1 | 10,7 | 15,5 | 5,2 | 5,4 | -5,3 |
| *Alternaria alternata* | rAlt a 1 | 10 | 9,9 | 0 | 9,9 | -0,1 |
| *Aspergillus fumigatus* | rAsp f 1 | 0,5 | 1,3 | 0 | 0,4 | -0,1 |
| *D.farinae* (HDM) | nDer f 1 | 3,8 | 3,6 | 3,6 | 3,6 | -0,2 |
| *D. pteronyssinus* (HDM) | nDer p 1 | 4,7 | 4,6 | 3,1 | 3,7 | -1 |
| Cat | rFel d 1 | 43,7 | 46,2 | 34,7 | 32 | -11,7 |
| Horse | rEqu c 1 | 9,1 | 9,1 | 7,3 | 6,8 | -2,3 |
| Mouse | nMus m 1 | 5,8 | 2,8 | 4 | 4,1 | -1,7 |
| Dog | rCan f 1 | 14 | 10,7 | 8,3 | 9,1 | -4,9 |

frequency remained close to 20% in all cohorts. Some tree pollen allergens demonstrated higher values in 2024 compared with 2021, including rAln g 1 (+5.5 pp) and rCor a 1.0101 (+3.0 pp).

For animal-derived allergens, the highest sensitization frequency in all cohorts was observed for cat allergen rFel d 1. The proportion of sensitized patients was 43.7% in 2021, 46.2% in 2022, 34.7% in 2023, and 32.0% in 2024, corresponding to a difference of −11.7 pp between 2021 and 2024. Sensitization to dog allergen rCan f 1 decreased from 14.0% to 9.1% (−4.9 pp).

Among fungal allergens, the most pronounced difference was observed for Alternaria alternata (rAlt a 1), with an increase of +5.8 pp (from 4.1% to 9.9%). For Aspergillus fumigatus (rAsp f 1), absolute values remained low in all cohorts. House dust mite allergens demonstrated relative stability: nDer f 1 — approximately 3.6% (−0.2 pp), nDer p 1 — approximately 3.7% (−1.0 pp).

To assess possible differences in gender distribution between yearly cohorts, statistical analysis was performed using Pearson's $\chi^2$ test. Of the 4745 examined patients, 2483 were male (52.3%) and 2262 were female (47.7%). The data are detailed in Table 3 and graphically represented in Figure 7.

The gender distribution of patients across the yearly cohorts showed only minor differences. Statistical analysis using Pearson's $\chi^2$ test yielded the following results: $\chi^2 = 5.92$; df = 3; p = 0.116. These findings indicate no statistically significant differences in gender distribution between yearly cohorts ($p > 0.05$).

**Table 3** Observed frequencies of patients by gender and year

| Gender | 2021 | 2022 | 2023 | 2024 | Total |
|---|---|---|---|---|---|
| Males | 204 | 210 | 448 | 1621 | 2483 |
| Females | 160 | 161 | 406 | 1535 | 2262 |
| Total | 364 | 371 | 854 | 3156 | 4745 |

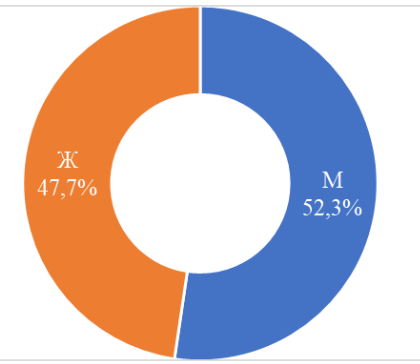


**Figure 7** – Pie chart showing the distribution of examined patients by gender (%)

For the analysis of age distribution, patients were divided into six age categories: 1–3 years, 4–6 years, 7–10 years, 11–14 years, 15–18 years, and ≥18 years, as presented in Table 4.

The distribution of patients across age groups was uneven, with the largest proportion observed in the adult category (≥18 years).

The number of patients in the age groups was as follows: 1–3 years — 523 patients (11.02%), 4–6 years — 669 (14.1%),

**Table 4** Age structure of examined patients with respiratory allergy

| Age (years) | 2021 | 2022 | 2023 | 2024 | Total |
|---|---|---|---|---|---|
| 1-3 | 27 | 31 | 120 | 345 | 523 |
| 4-6 | 45 | 55 | 111 | 458 | 669 |
| 7-10 | 59 | 67 | 163 | 555 | 844 |
| 11-14 | 46 | 53 | 91 | 339 | 529 |
| 15-18 | 33 | 31 | 67 | 194 | 325 |
| 18 and over | 154 | 134 | 302 | 1265 | 1855 |

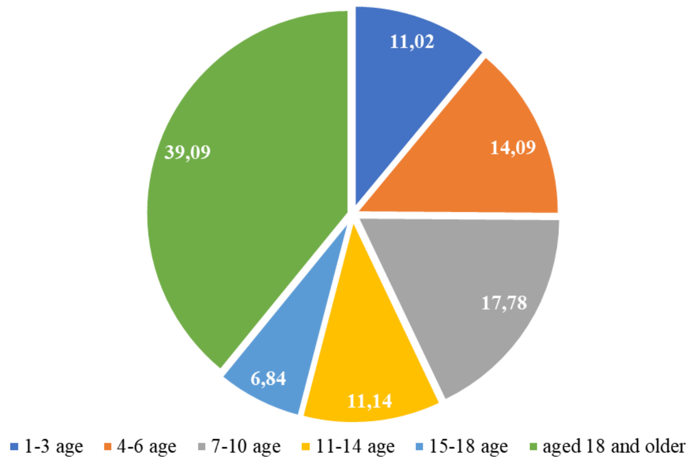


**Figure 8** – Sensitization to respiratory allergens by age groups (%)

7–10 years — 844 (17.8%), 11–14 years — 529 (11.2%), 15–18 years — 325 (6.8%), ≥18 years — 1855 (39.1%), as shown in Figure 8.

In all yearly cohorts, the adult group remained the largest, with proportions ranging from 40.6% to 42.3%. Among pediatric age categories, the highest representation was observed in the 7–10 years group, followed by the 4–6 years and 1–3 years groups.

The 15–18 years group was the least represented among all age categories. The distribution of patients by age differed between yearly cohorts, as reflected in the contingency table.

To assess the statistical significance of differences in age distribution between yearly cohorts, Pearson's $\chi^2$ test was applied. The analysis demonstrated statistically significant differences in the distribution of age categories between yearly cohorts: $\chi^2 = 351.44$; df = 15; $p < 0.00001$.

These findings indicate heterogeneity of the age composition of examined patients across different years, while the predominance of the adult age group remained consistent in all cohorts.

The analysis conducted also demonstrated that patients sensitized to inhalant allergens were identified across all age groups; however, the frequency of detection of individual components varied depending on the age category. In younger age groups, sensitization to food and cross-reactive components was more frequently observed, whereas in older age groups inhalant allergens predominated, including pollen, epidermal, and household components.

In adult patients, multiple sensitization involving several allergen groups simultaneously was observed more often.

Climatogeographical characteristics of sensitization were analyzed by comparing the frequency of inhalant allergen detection in patients residing in different regions of Kazakhstan, as presented in Table 5.

In the southern regions, the highest sensitization frequency was observed for grass and weed allergens. The most frequently detected components were birch — rBet v 1 (26.44%), hazel pollen — rCor a 1.0101 (18.02%), timothy grass — rPhl p 1 (17.35%), bermuda grass — nCyn d 1 (16.54%), mugwort — nArt v 1 (12.55%), and ambrosia — nAmb a 1 (11.74%). Sensitization to tree pollen allergens was also detected, although its frequency was lower compared with the northern region.

In the central-eastern region, the sensitization frequency for most allergen components was substantially lower and

**Table 5** Geographical patterns of sensitization (%)

| Allergen | | Region | | | |
|---|---|---|---|---|---|
| | | Western | Northern | Central-Eastern | Southern |
| Ragweed *( Ambrosia artemisiifolia)* | nAmb a 1 | 5,52 | 22,43 | 1,08 | 11,74 |
| Birch *(Betula verrucosa)* | rBet v 1 | 11,04 | 42,21 | 1,33 | 26,44 |
| | rBet v 2 | 9,20 | 24,83 | 0,09 | 6,05 |
| | rBet v 4 | 3,06 | 5,21 | 0,19 | 3,02 |
| Cypress *(Cupressus sempervirens_* | nCup a 1 | 37,42 | 20,44 | 1,08 | 6,12 |
| Salsola (saltwort) *(Salsola kali)* | nSal k 1 | 46,01 | 33,36 | 0,39 | 7,16 |
| Lamb's quarters *(Chenopodium album)* | rChe a 1 | 13,49 | 16,63 | 0,24 | 2,80 |
| Alder *(Alnus glutinosa)* | rAln g 1 | 0,61 | 21,35 | 0,04 | 16,02 |
| Plane tree *(Platanus acerifolia)* | rPla a 1 | 1,84 | 3,64 | 0,29 | 1,55 |
| | rPla a 3 | 1,84 | 6,78 | 0,04 | 3,39 |
| Plantain *(Plantago lanceolata)* | rPla I 1 | 13,49 | 17,05 | 1,18 | 6,57 |
| Mugwort *(Artemisia vulgaris)* | nArt v 1 | 18,40 | 42,54 | 0,59 | 12,55 |
| | nArt v 3 | 6,74 | 13,99 | 0,09 | 4,50 |
| Wall pellitory *(Parietaria officinalis)* | rPar j 2 | 10,42 | 12,33 | 1,28 | 5,90 |
| Annual mercury *(Mercurialis annua)* | rMer a 1 | 14,72 | 28,89 | 0,19 | 7,16 |
| Wheat *(Triticum aestivum)* | rTri a 14 | 2,45 | 4,05 | 0 | 0,88 |
| | rTri a 19 | 3,06 | 1,57 | 0,09 | 0,73 |
| | nTri a aA_TI | 0,61 | 1,15 | 0 | 0,66 |
| Olive tree *(Olea europaea)* | rOle e 1 | 1,22 | 1,49 | 0,24 | 1,03 |
| | nOle e 7 | 3,68 | 3,31 | 0,14 | 1,77 |
| | rOle e 9 | 3,06 | 12,25 | 0,24 | 2,95 |
| Hazel *(Corylus avellana)* | rCor a 1.0101 | 11,04 | 32,11 | 0,89 | 18,02 |
| Bermuda grass *(Cynodon dactylon)* | nCyn d 1 | 28,83 | 44,20 | 0,89 | 16,54 |
| Timothy grass *(Phleum pratense)* | rPhl p 1 | 14,72 | 33,85 | 0 | 17,35 |
| | rPhl p 2 | 7,36 | 12,00 | 0,99 | 5,68 |
| | rPhl p 4 | 12,26 | 21,44 | 0,19 | 7,82 |
| | rPhl p 5 | 1,22 | 8,44 | 0,14 | 6,64 |
| | rPhl p 6 | 2,45 | 5,29 | 0,04 | 3,24 |
| | rPhl p 7 | 2,45 | 2,40 | 0,09 | 1,03 |
| | rPhl p 11 | 6,13 | 14,56 | 1,03 | 6,05 |
| | rPhl p 12 | 11,04 | 26,40 | 0,24 | 8,71 |
| Japanese cedar *(Cryptomeria japonica)* | nCry j 1 | 9,81 | 11,34 | 0,39 | 5,02 |
| *Alternaria alternata* | rAlt a 1 | 9,81 | 16,80 | 0,09 | 5,76 |
| | rAlt a 6 | 2,45 | 3,06 | 0,04 | 0,73 |
| *Aspergillus fumigatus* | rAsp f 1 | 0,61 | 0,91 | 0 | 0,29 |
| | rAsp f 3 | 1,84 | 1,98 | 0,24 | 0,81 |
| | rAsp f 6 | 4,29 | 4,80 | 0,34 | 1,32 |
| *D. farinae (HDM)* | nDer f 1 | 4,29 | 7,53 | 0,24 | 3,69 |
| | nDer f 2 | 4,29 | 9,18 | 0,29 | 4,50 |
| *D. pteronyssinus (HDM)* | nDer p 1 | 4,29 | 7,45 | 0,24 | 3,98 |
| | rDer p 2 | 2,45 | 8,19 | 0,14 | 4,06 |
| | nDer p 10 | 4,90 | 5,38 | 0,34 | 1,55 |
| | rDer p 23 | 24,53 | 25,91 | 2,52 | 9,82 |
| Cat | rFel d 1 | 27,60 | 53,72 | 0,69 | 22,37 |
| | nFel d 2 | 5,52 | 11,92 | 1,08 | 4,35 |
| | rFel d 4 | 7,97 | 20,03 | 0,54 | 7,60 |
| Horse | rEqu c 1 | 5,52 | 11,09 | 0,54 | 5,02 |
| | nEqu c 3 | 3,06 | 6,20 | 0,29 | 2,58 |
| Mouse | nMus m 1 | 2,45 | 12,25 | 0,89 | 4,35 |
| Dog | rCan f 1 | 4,29 | 12,41 | 0,04 | 9,01 |
| | rCan f 2 | 1,22 | 2,98 | 0,29 | 4,13 |
| | rCan f 4 | 2,45 | 5,29 | 0,54 | 4,06 |
| | rCan f 3 | 3,68 | 7,86 | 0,19 | 4,43 |
| | rCan f 5 | 3,06 | 9,43 | 0,74 | 6,12 |
| | rCan f 6 | 1,84 | 7,53 | 0 | 4,87 |

generally did not exceed 1–2%. The most frequently detected components were plane tree— rPla l 1 (1.18%), hazel pollen — rCor a 1.0101 (0.89%), bermuda grass — nCyn d 1 (0.89%), mugwort — nArt v 1 (0.59%), and birch — rBet v 1 (1.33%). The low values may reflect the distribution of examined patients and the limited representation of the sample in this region.

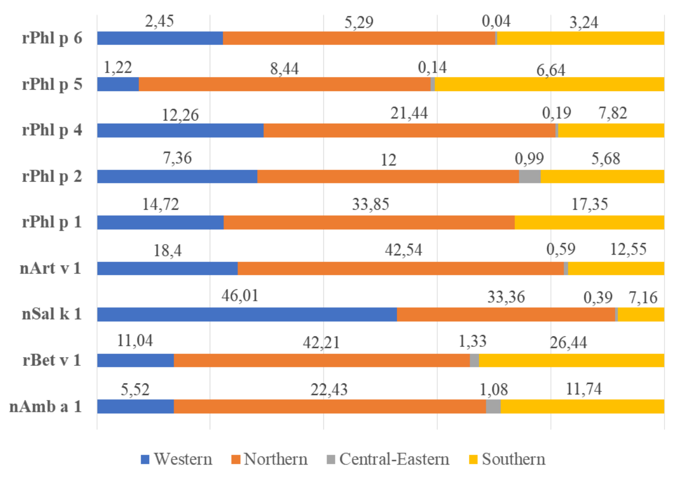


**Figure 9** – Geographical features of sensitization (%)

In the northern regions, the highest sensitization frequency was observed for tree and grass allergens. The most frequently detected major components were bermuda grass — nCyn d 1 (44.20%), mugwort — nArt v 1 (42.54%), birch — rBet v 1 (42.21%), timothy grass — rPhl p 1 (33.85%), saltwort — nSal k 1 (33.36%), hazel pollen — rCor a 1.0101 (32.11%), and annual mercury — rMer a 1 (28.89%). A high sensitization frequency was also observed for minor molecules, including timothy grass — rPhl p 12 (26.40%) and birch — rBet v 2 (24.83%).

In the western regions, the highest sensitization frequency was observed for weed allergens and representatives of the family Amaranthaceae. The most frequently detected components were saltwort — nSal k 1 (46.01%), bermuda grass — nCyn d 1 (28.83%), mugwort — nArt v 1 (18.40%), annual mercury — rMer a 1 (14.72%), timothy grass — rPhl p 1 (14.72%), lamb's quarters — rChe a 1 (13.49%), and birch — rBet v 1 (11.04%). This region was also characterized by a high sensitization frequency to cypress pollen — nCup a 1 (37.42%).

Indoor and epidermal allergens were detected in all regions, with sensitization frequency varying between macroregions. The highest sensitization rates to epidermal allergens were observed in the northern regions, where rFel d 1 was detected in 53.72% of patients, rDer p 23 in 25.91%, rCan f 1 in 12.41%, and nMus m 1 in 12.25%.

In the western and southern regions, sensitization to these allergens was lower but remained at a notable level (rFel d 1 — 27.60% and 22.37%, respectively; rDer p 23 — 24.53% and 9.82%; rCan f 1 — 4.29% and 9.01%).

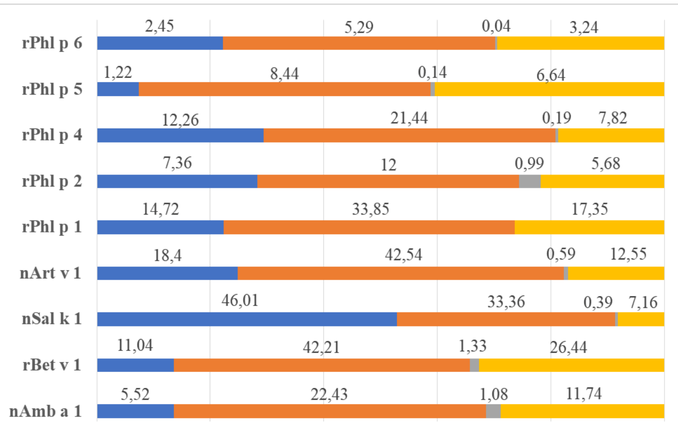


**Figure 10** – Geographical features of sensitization (%)

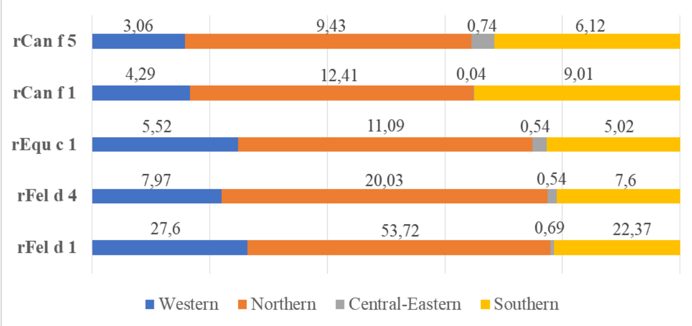


**Figure 11** – Geographical features of sensitization (%)

In the central-eastern region, sensitization rates for most indoor and epidermal allergens were minimal and generally did not exceed 1–3%.

The most pronounced regional differences were observed for pollen allergens, which served as the basis for the main comparative analysis focused on plant-derived components.

Overall, the regional distribution of sensitization was characterized by varying representation of tree, grass, and weed allergens. The frequency of epidermal and indoor allergens also varied between regions; however, differences were more pronounced for pollen components and accounted for the main interregional patterns of sensitization.

## Discussion

The spectrum of sensitization in patients ranges from monosensitization, when the immune system reacts to a single antigen, to polysensitization, characterized by reactivity to multiple allergens [1,2]. Polysensitized patients represent a clinically more complex category, in whom the disease often follows a more severe course and requires an individualized diagnostic and therapeutic approach [3,4].

The use of molecular diagnostic methods, including ImmunoCAP ISAC, makes it possible to define the sensitization profile at the level of individual allergen components and to identify clinically relevant molecules, which is crucial for the selection of allergen-specific immunotherapy and for assessing the risk of cross-reactivity [5–7]. In patients with multiple sensitization, a combined approach that includes allergen-specific immunotherapy and symptomatic pharmacotherapy is increasingly used [8,9].

The present study was based on ISAC molecular allergodiagnostic data obtained in Kazakhstan during 2021–2024. The analysis included age-related, gender-related, and geographic characteristics, allowing assessment of sensitization patterns in different regions of the country [10–12].

A high frequency of sensitization to epidermal allergens, particularly rFel d 1, is consistent with international studies indicating the widespread prevalence of cat allergy in populations with high urban density and continuous household exposure to animal allergens [12]. The components rFel d 1 and rCan f 1 are considered major allergens and more often reflect primary sensitization, whereas Fel d 4 and Can f 6 may participate in cross-reactive immunological responses [16]. A high frequency of sensitization to cat epithelium is regarded as one of the markers of atopic statu

In contrast to indoor allergens, which tend to be more universal in distribution, pollen components reflect regional differences in flora and climatic conditions. The most relevant pollen allergens in the present study were rPhl p 1, rBet v 1, nArt v 1, and nSal k 1, which is consistent with studies conducted in countries with continental climates and pronounced pollen seasons [18–22]. The broad spectrum of identified pollen allergens, including tree, grass, and weed components, supports the need for a comprehensive approach to seasonal diagnosis and individualized selection of allergen-specific immunotherapy, particularly in regions with diverse vegetation.

The relatively low frequency of sensitization to house dust mites may be related to the climatic features of Kazakhstan, particularly low humidity, which can limit the proliferation of Dermatophagoides spp. [23]. At the same time, the observed frequency of sensitization to Alternaria alternata confirms the importance of fungal allergens as risk factors for severe allergic disease, including bronchial asthma and chronic allergic rhinitis [24].

Overall, the sensitization structure in the study population was determined by a combination of universal indoor allergens and region-dependent pollen components, which should be taken into account when developing diagnostic panels, selecting allergen-specific immunotherapy, and designing region-oriented clinical recommendations.

Presenting the data in percentage points allowed a clearer comparison of sensitization frequencies for individual allergen components between independent yearly cohorts. This approach is more informative for descriptive analysis, as it allows assessment of absolute differences without the influence of unequal sample sizes.

The largest differences were observed for pollen allergens, particularly rMer a 1, nArt v 1, nAmb a 1, and rPhl p 1. This indicates greater variability in sensitization frequencies to seasonal allergens compared with indoor components. Epidermal allergens, particularly rFel d 1, remained highly prevalent across all cohorts, confirming their importance as stable components of the inhalant sensitization profile. At the same time, such allergens have a more universal distribution and reflect regional allergen patterns to a lesser extent.

By contrast, pollen components demonstrated greater variability between yearly cohorts, which may be related to differences in the composition of examined patients, regional distribution, and clinical indications for molecular diagnostics. Sensitization to fungal allergens, particularly Alt a 1, also showed noticeable differences between cohorts, confirming the clinical relevance of this component in patients with respiratory allergy.

It is important to emphasize that the analysis was performed on independent patient groups examined in different years; therefore, the observed differences should not be interpreted as temporal trends in sensitization. They should more appropriately be regarded as inter-cohort variations reflecting the characteristics of the examined groups.

The findings support the need for component-resolved diagnostics to refine sensitization profiles and to individualize the selection of diagnostic panels and allergen-specific immunotherapy.

Gender is considered one of the biological factors capable of influencing the immune response and the characteristics of sensitization [7,8]. According to epidemiological studies, allergic diseases, including bronchial asthma and atopic dermatitis, are more often diagnosed in boys during childhood, which has been linked to features of innate and adaptive immunity as well as differences in hormonal profiles during early development [9].

In adolescence and in adult women, the frequency of allergic diseases may increase, which is associated with hormonal changes and fluctuations in gender hormone levels that can modulate inflammatory responses [10]. Physiological conditions such as the menstrual cycle, pregnancy, and menopause are known to influence symptom severity and susceptibility to allergens [14]. In men, a relative decrease in allergic reactions after puberty has been described, which is attributed to stabilization of hormonal balance and features of immune regulation [15].

A number of authors emphasize the need to consider gender-related features when studying allergic diseases and choosing therapeutic strategies [16]. In particular, the influence of hormonal status on the efficacy of allergen-specific immunotherapy and the formation of immune tolerance has been discussed, along with the role of social factors that may affect healthcare-seeking behavior and treatment adherence [17].

In the present study, no statistically significant gender-related differences were found between yearly cohorts, indicating comparability of the study groups with respect to this parameter and allowing interpretation of the results without adjustment for gender composition.

Age is considered one of the key factors influencing the development of sensitization and the clinical manifestations of allergic diseases [9,19]. It is well known that immune response patterns, duration of allergen exposure, hormonal status, and immune system maturation may determine differences in sensitization profiles across age groups.

In the present study, the largest proportion of examined patients belonged to the adult category, which is consistent with epidemiological data indicating a high prevalence of allergic diseases among the working-age population. The greater representation of adults may reflect longer allergen exposure and a higher likelihood of developing multiple sensitization in the course of chronic allergic disease.

A considerable number of examined patients was also observed in the younger age groups, confirming the importance of early diagnosis of sensitization. In early childhood, the immune system is still developing, which is accompanied by increased susceptibility to new antigens and more frequent development of IgE-mediated responses. During this period, sensitization to PR-10 proteins, LTPs, and other cross-reactive components that may contribute to subsequent polysensitization is often detected [23].

In preschool and younger school-age children, sensitization to inhalant allergens is more frequently detected, including components of grasses, weeds, house dust mites, and epidermal animal allergens. This is consistent with the literature indicating that this period is characterized by a shift from predominantly food sensitization to inhalant sensitization, reflecting a broadening of allergen exposure [24].

In adolescents and adults, combined sensitization to several allergen groups, including pollen, indoor, and epidermal components, is more frequently observed. Such a profile is regarded as a manifestation of the polysensitized phenotype, which is associated with a more complex disease course and may require an individualized diagnostic and therapeutic approach. Prolonged allergen exposure, repeated contact with multiple antigen sources, and features of immune regulation may contribute to an expansion of the sensitization spectrum with age.

The findings confirm that the age composition of examined patients can substantially influence the detected sensitization structure and should be taken into account when interpreting component-resolved diagnostic results. Differences between age groups may be determined by both biological features of the immune response and differences in clinical indications for molecular testing.

An important practical implication is the need for a stratified approach to the assessment of sensitization according to patient age. The use of component-resolved diagnostics makes it possible to more accurately identify clinically relevant allergens, assess the risk of cross-reactivity, and rationally select allergen-specific immunotherapy.

Thus, consideration of age-related features is essential for correct interpretation of molecular allergodiagnostic results and optimization of clinical management in patients with allergic diseases.

It is well known that the spectrum of sensitization to inhalant allergens may vary substantially depending on climatogeographic conditions, vegetation characteristics, and the nature of allergen exposure in a given region [11–13]. In the present study, comparison of sensitization frequencies across macroregions of Kazakhstan revealed heterogeneous distribution of pollen, epidermal, and indoor allergens, with the most pronounced differences observed for plant-derived components.

In the southern regions, sensitization to weed and grass allergens, including nAmb a 1, nArt v 1, nCyn d 1, and rPhl p 1, was registered more frequently. This profile is consistent with the literature describing the predominance of weed and grass allergens in regions with continental and arid climates, where representatives of the families Amaranthaceae and Poaceae are widespread and prolonged pollen seasons are observed.

In the northern regions, a high frequency of sensitization to tree and grass allergens was observed, particularly rBet v 1, rCor a 1, rMer a 1, and rPhl p 1, as well as to components associated with cross-reactivity, such as rBet v 2 and rPhl p 12. This profile is consistent with epidemiological studies indicating the predominance of sensitization to tree and meadow grass pollen in regions with more humid climates and pronounced spring–summer pollen seasons.

In the western regions, a high frequency of sensitization to nSal k 1, belonging to allergens of the Amaranthaceae family, as well as to nCyn d 1, nArt v 1, and rMer a 1, was observed, which is characteristic of steppe and semi-desert territories. At the same time, reactions to grass and tree allergens were also detected in this group, indicating a mixed pattern of allergen exposure.

In the central-eastern region, sensitization frequencies for most allergen components were substantially lower than in the other macroregions. This likely reflects the characteristics of the examined patient distribution and the limited representation of the sample, which should be considered when interpreting regional differences.

Sensitization to indoor and epidermal allergens was detected in all regions, although its frequency also varied. The highest rates were observed in the northern regions, where reactions to rFel d 1, rDer p 23, and rCan f 1 were more frequent. This may reflect differences in living conditions, contact with domestic animals, and microclimatic features of indoor environments, although the present study did not include direct assessment of environmental factors.

The results suggest that the sensitization structure in Kazakhstan is shaped by a combination of factors, including climatic conditions, regional flora, and patterns of allergen exposure. The predominance of sensitization to weeds in the southern and western regions, the high frequency of reactions to tree and grass allergens in the northern regions, and the mixed sensitization profile observed in some regions reflect the diversity of the country's natural zones.

These findings are consistent with international studies demonstrating that regional flora, climatic conditions, and the degree of urbanization exert a substantial influence on the structure of allergic diseases. Component-resolved molecular allergodiagnostics allows more precise characterization of sensitization profiles, identification of clinically relevant allergens, and optimization of allergen-specific immunotherapy selection with consideration of regional features.

It should be taken into account that the study had a retrospective laboratory-epidemiological design and was based on anonymized data obtained from a clinical diagnostic laboratory. More accurate evaluation of regional patterns requires prospective studies including clinical information, more balanced patient distribution across regions, and expanded analysis of environmental factors.

## Limitations

Several limitations should be considered when interpreting the results. The study had a retrospective design and was based on laboratory data obtained from the database of a clinical diagnostic laboratory. Due to the anonymized nature of the sample, information on clinical diagnosis, disease severity, and follow-up was not available in all cases.

The sample was not random and included patients referred for molecular allergodiagnostics, which may have introduced selection bias toward individuals with suspected polysensitization or more severe allergic disease.

Regional analysis was based on the location where laboratory testing was performed, which does not always coincide with the patient's region of permanent residence. Some examined individuals may have sought testing in large diagnostic centers located in other regions, including the capital region, which could potentially reduce the accuracy of geographic stratification. An additional limitation is possible migration of patients between regions, including recent changes of residence, which complicates interpretation of the observed regional differences as reflecting the true population structure of sensitization.

Despite these limitations, the large number of examined patients and the use of component-resolved allergodiagnostics provide a reliable overview of sensitization structure across different climatogeographic regions.

## Conclusion

The present study demonstrates that the sensitization profile in Kazakhstan is shaped by a combination of ubiquitous indoor allergens and region-specific pollen components, reflecting the influence of climatic, ecological, and botanical factors.

Component-resolved allergodiagnostics enabled precise characterization of sensitization patterns across different demographic and geographic groups, highlighting the predominance of polysensitization and the heterogeneity of allergen exposure. Regional analysis revealed distinct pollen sensitization patterns corresponding to environmental conditions, whereas indoor allergens showed broader and more universal distribution.

The absence of significant sex-related differences and the heterogeneous age structure indicate that demographic factors should be considered when interpreting sensitization profiles, particularly in clinically selected populations.

Importantly, the identified variability between independent cohorts underscores the need for cautious interpretation of cross-sectional data and supports the use of standardized approaches when comparing sensitization patterns.

Overall, the findings emphasize the clinical value of molecular allergodiagnostics for improving diagnostic accuracy, enabling personalized selection of allergen-specific immunotherapy, and supporting the development of region-adapted diagnostic panels in patients with respiratory allergy.

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## References

1. LandzaatLJ, BroughHA, BurksAW, Ballmer-WeberBK, NilssonC, GiselssonM, BorresMP, SastreJ, ValentaR, MatricardiPM. Early inhalant allergen sensitization at component level using multiplex microarray analysis. Clinical and Translational Allergy. 2023;13(7):e12271. https://doi.org/10.1002/clt2.12271
2. KochL, EllerE, Bindslev-JensenC, MortzCG, BrockowK, Bindslev-JensenU. Molecular allergy diagnosis using marker allergens in pollen sensitization. Allergy. 2023;78(3):742–754. https://doi.org/10.1111/all.15589
3. ČelakovskáJ, BukačJ, VaňkováR, KrejsekJ, AndrýsC, HamákováK, EttlerK. Relationship between sensitization to molecular components of inhalant allergens and clinical manifestation of allergy. Journal of Asthma and Allergy. 2021;14:1165–1175. https://doi.org/10.2147/JAA.S332314
4. Parra-Vargas MI, Alvarez-Cuesta E, Dávila I, Moreno C. Allergen immunotherapy: current and future trends. Cells. 2022; 11: 212. https://doi.org/10.3390/cells11020212
5. Ramírez-Jiménez F, Cuevas M, Canto G, Calderón MA. Allergen immunotherapy for long-term tolerance and prevention. Journal of Allergy and Clinical Immunology. 2021; 149(4): 1229–1238. https://doi.org/10.1016/j.jaci.2021.06.023
6. Roberts G, Pfaar O, Akdis CA, Ansotegui IJ, Durham SR, van Wijk RG, Halken S, Larenas-Linnemann D, Calderón MA. EAACI guidelines on allergen immunotherapy: allergic rhinoconjunctivitis. Allergy. 2018; 73(4): 765–798. https://doi.org/10.1111/all.13317
7. Mitselou N, Kafatos G, Brough HA, Santos AF. Exposure to allergen-specific immunotherapy in pregnancy and risk of congenital malformations. Journal of Allergy and Clinical Immunology in Practice. 2022; 10(6): 1635–1641. https://doi.org/10.1016/j.jaip.2022.03.005
8. Bernstein DI, Amar NJ, McGrath KG, Cheema AS, Creticos PS. SQ house dust mite sublingual immunotherapy tablet subgroup efficacy and local application site reaction duration. Annals of Allergy, Asthma & Immunology. 2018; 121(1): 105–110. https://doi.org/10.1016/j.anai.2018.04.007
9. Muraro A, Agache I, Clark A, Sheikh A, Roberts G, Akdis CA. Managing food allergy: GA²LEN guideline 2022. World Allergy Organization Journal. 2022; 15: 100687. https://doi.org/10.1016/j.waojou.2022.100687
10. Agache I, Lau S, Akdis CA, Smolinska S, Bonini M, Cavkaytar O, Flood B, Gajdanowicz P, Izuhara K, Kalayci O. EAACI guidelines on allergen immunotherapy: house dust mite-driven allergic asthma. Allergy. 2019; 74(5): 855–873. https://doi.org/10.1111/all.13749
11. Inclan-Rico JM, Hernandez CM. Contributions of innate lymphocytes to allergic responses. Current Opinion in Allergy and Clinical Immunology. 2019; 19(2): 175–184. https://doi.org/10.1097/ACI.0000000000000515
12. Li XM, Srivastava K, Hulett AC, Bottomly K. Recent advances in sublingual allergen-specific immunotherapy. Allergy Asthma & Immunology Research. 2023; 15(1): 27–38. https://doi.org/10.4168/aair.2023.15.1.27
13. Gómez E, Díaz-Perales A, Lombardero M. Molecular mechanisms of allergen-specific immunotherapy in allergic diseases. Journal of Allergy and Clinical Immunology. 2022; 149(4): 1012–1025. https://doi.org/10.1016/j.jaci.2021.11.021
14. Tabar AI, Arroabarren E, Echechipía S, García BE, Martín S, Alvarez-Cuesta E. Double-blind, randomized, placebo-controlled trial of allergen-specific immunotherapy with the major allergen Alt a 1. Journal of Allergy and Clinical Immunology. 2019; 144(1): 216–223. https://doi.org/10.1016/j.jaci.2019.02.029
15. Alvaro-Lozano M, Akdis CA, Akdis M, Canonica GW, Casale TB, Cox L, Durham SR, Jutel M, Kleine-Tebbe J, Muraro A. EAACI allergen immunotherapy user's guide. Pediatric Allergy and Immunology. 2020; 31(Suppl 25): 1–101. https://doi.org/10.1111/pai.13189
16. Kucuksezer UC, Ozdemir C, Akdis M, Akdis CA. Mechanisms of allergen-specific immunotherapy and allergen tolerance. Allergology International. 2020; 69(4): 549–560. https://doi.org/10.1016/j.alit.2020.08.002
17. Wang C, Bao Y, Chen J, Zhang L, Wang Y. Chinese guideline on allergen immunotherapy for allergic rhinitis: the 2022 update. Allergy Asthma & Immunology Research. 2022; 14(6): 604–652. https://doi.org/10.4168/aair.2022.14.6.604
18. Hoang MP, Seresirikachorn K, Chitsuthipakorn W, Snidvongs K. Intralymphatic immunotherapy for allergic rhinoconjunctivitis: a systematic review and meta-analysis. Rhinology. 2021; 59: 236–244. https://doi.org/10.4193/Rhin20.572

19. Konradsen JR, Grundström J, Hellkvist L, Tran TA, Andersson N, Gafvelin G. Intralymphatic immunotherapy in pollen-allergic young adults with rhinoconjunctivitis and mild asthma: a randomized trial. Journal of Allergy and Clinical Immunology. 2020; 145: 1005–1007.e7. https://doi.org/10.1016/j.jaci.2019.11.017
20. Wang Y, Kong Y, Wu MX. Innovative systems to deliver allergen powder for epicutaneous immunotherapy. Frontiers in Immunology. 2021; 12: 647954. https://doi.org/10.3389/fimmu.2021.647954
21. Sola Martínez FJ, Barranco Jiménez RM, Martín García C, Senent Sánchez C, Blanco Guerra C, Fernández-Rivas M. Intradermal Phleum pratense allergoid immunotherapy: double-blind, randomized, placebo-controlled trial. Clinical and Experimental Allergy. 2020; 50: 1352–1361. https://doi.org/10.1111/cea.13740
22. Wang C, Bao Y, Chen J, Chen X. Chinese guideline on allergen immunotherapy for allergic rhinitis: the 2022 update. Allergy Asthma & Immunology Research. 2022; 14(6): 604–652. https://doi.org/10.4168/aair.2022.14.6.604
23. Dhami S, Nurmatov U, Arasi S, Khan T, Asaria M, Zaman H, Agarwal A, Netuveli G, Roberts G, Pfaar O. Allergen immunotherapy for allergic rhinoconjunctivitis: a systematic review and meta-analysis. Allergy. 2017; 72: 1597–1631. https://doi.org/10.1111/all.13201
24. Durham SR, Shamji MH. Allergen immunotherapy: past, present and future. Nature Reviews Immunology. 2023; 23(5): 317–328. https://doi.org/10.1038/s41577-022-00786-1
25. VítovcováP, KrčmováI, ŽďárskýE, HruškováZ, MalkusováI, NovosadJ. Molecular sensitization profiles to pollen allergens in Central Europe. International Archives of Allergy and Immunology. 2014;164(2):131–138. https://doi.org/10.1159/000362230
26. WHOIUISAllergenNomenclatureSubCommittee. Allergen Nomenclature Database. WHO/IUIS Allergen Nomenclature. 2024. https://doi.org/10.0000/allergen.org
27. PomésA, DaviesJM, GadermaierG, HilgerC, HolzhauserT, LidholmJ, LopataAL, MuellerGA, NandyA, RadauerC, ChanSK, JappeU, KleineTebbeJ, ThomasWR, ChapmanMD, vanHageM, vanReeR, ViethsS, RaulfM, GoodmanRE. WHO/IUIS Allergen Nomenclature: Providing a common language. Molecular Immunology. 2018;100:3–13. https://doi.org/10.1016/j.molimm.2018.03.003