

Editorial comment on “Phenotyping of immediate-type food allergies based on 10 years of research: A latent class analysis”



Kyohei Takahashi

Phenotyping allergic manifestations using data-driven approaches have gained traction over the last decade. These methods have revealed that the heterogeneity in the presentation and clinical course of common allergic conditions such as atopic dermatitis and asthma can be in part explained when considering them as multiphenotypic conditions.¹⁻³ Differential risk factors have been identified which predispose individuals to different phenotypes, suggesting that the underlying mechanism driving different phenotypes to differ.²⁻⁶ Phenotyping allergic diseases, where individual risk factors and potentially pathophysiology are identified, represents an important contribution to the field because it can inform prevention, management options, and prognosis. Food allergy is an early manifestation of allergic diseases but is variable in its presentation including triggers, reaction severity, and natural history. Phenotyping food allergy can incorporate this variability; however, few studies have examined phenotypes of food allergy in childhood. The Australian HealthNuts cohort identified 5 phenotypes of allergic disease in infancy using data on food sensitization, challenge-confirmed food allergy, eczema, and wheeze. These were no allergic disease (70%), non-food-sensitized eczema (16%), single egg allergy (9%), multiple food allergies (predominantly peanut) (3%), and multiple food allergies (predominantly egg) (2%). Shared and differential risk factors for all allergic phenotypes were identified, suggesting differential drivers of early allergic disease.⁴

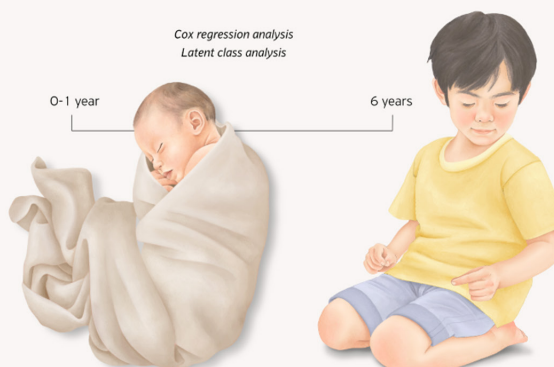
Phenotyping of immediate-type food allergies based on 10 years of research: A latent class analysis

Longitudinal study performed in the Department of Pediatrics, Sagami National Hospital.



7 classes of prognosis for food allergy

Sensitization only (28.4%)
[LARGEST] Transient egg allergy alone (19.6%)
 Milk ± transient egg allergy (17.5%)
 Prolonged egg allergy (13.1%)
 Wheat ± transient milk allergy (7.8%)
 Persistent egg and milk allergy (7.2%)
[SEVERE] Multiple food allergy (6.5%)



Cox regression analysis
 Latent class analysis

Sensitization only patients (n = 276)

Immediate-type food allergy patients (n = 915)

Tolerance at age 6:

eggs: 609 (51%)	74%
milk: 443 (37%)	69%
wheat: 235 (20%)	75%
multiple food allergies: 302 (25%)	



In this issue of *Pediatric Allergy and Immunology*, Takahashi et al present the first report of longitudinal phenotypes of food allergies.⁷ This study aimed to classify and characterize the long-term prognosis of the three most common immediate-type food allergies in Japan, hen's egg, cow's milk, and wheat. Using data from hospital records, children who presented to Sagamihara National Hospital for the assessment of food allergy prior to 12 months of age were included in the study. Food allergy was defined on the basis of a convincing history of immediate reaction to food and confirmation of sensitization, or oral food challenge. Resolution of food allergy was recorded when the child was able to eat and tolerate the food without reaction up to the age of 6 years. Latent class analysis was used to identify phenotypes of tolerance patterns among children with food allergy diagnosed before 12 months of age, using data on tolerance to egg, milk, and wheat at 6 monthly intervals ($n = 915$). Tolerance to food by 6 years of age was achieved in 74% allergic to eggs, 69% allergic to milk, and 75% allergic to wheat.

An additional 276 children with asymptomatic sensitization only were included for the latent class analysis, which revealed 7 phenotypes. The *sensitization only* (28.4%) class comprised children who were sensitized to food but able to tolerate them. *Transient egg allergy alone* (19.6%) comprised children who outgrew egg allergy by 3 years of age, and they were less likely to have atopic dermatitis. *Milk $\pm$ transient egg allergy* (17.5%) included children with milk allergy, about half of whom acquired tolerance by 4 years and a quarter also had transient egg allergies. The *prolonged egg allergy* phenotypes (13.1%) included children with egg allergy, and around half were persistently allergic at age 6 years. They also had higher egg white and ovomucoid-sIgE levels, and a higher prevalence of atopic dermatitis. Children in the *wheat $\pm$ transient milk allergy* (7.8%) class had wheat allergy and around a quarter had transient milk allergies. The *persistent egg and milk allergy* phenotype (7.2%) comprised children with persistent egg and milk allergies, and they tended to have higher egg white and milk-sIgE levels. Finally, the *multiple food allergy* phenotype (6.5%) included children who were allergic to eggs, milk, and wheat, and these allergies were likely to persist.

The authors developed a simulation software to predict the prognosis of food allergy using parameters from Cox regression models of predictors of food allergy persistence. This approach of developing tools to predict the natural course of food allergy will be useful for informing clinical management and identifying children who are less likely to naturally outgrow food allergy and would benefit from interventions. Such tools require validation in other settings because food allergy triggers and prevalence is known to differ by geographic region; whether the natural history differs by region is less clear. The implementation code used to create this software is open source and will allow other researchers to create their own versions using data from their settings.

CONFLICT OF INTEREST

No conflict of interest.

PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1111/pai.13875>.

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