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Article type : Letter to the Editor

"Childhood Allergy and tolerance: bioMarkers and Predictors (CHAMP) and quality of life".

Associate Editor: Professor Philippe Eigenmann

To the Editor

Allergic diseases, including atopic dermatitis (AD), food allergy (FA), asthma and allergic rhinitis/rhinoconjunctivitis (AR) are the most prevalent chronic childhood diseases affecting one in four children in the Western world (1). This global health problem imposes a significant burden on patient's quality of life (2), family, health care and society. The current state of knowledge assumes that complex interactions between genetic and environmental factors influence a child's immune maturation prior to the development of allergic diseases (3). To date, no reliable predictions of allergy development exists. Current scores, including clinical features and laboratory data, have only reached limited specificity and/or sensitivity (4).

In 2017, the German Federal Ministry for Education and Research funded a framework program for health research in children and adolescents: "Healthy for life", with CHAMP (Childhood Allergy and tolerance: bioMarkers and Predictors) being one of its projects. CHAMP is a novel

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/PAI.13652](#)

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multicentre German allergy consortium, which investigates the critical needs of children with allergic diseases, namely prediction of allergic diseases and improvement of health-related quality of life (HrQoL).

The CHAMP consortium includes eight subprojects (SP1-8, Tab.S1), investigating determinants of different allergic diseases from birth to adolescence. As demanded by organisations like EAACI (5), the aim is to improve diagnostics by identifying clinically relevant biomarkers predicting allergy onset, progression, remission and severity.

Within CHAMP an online survey was conducted, questioning families with allergic children about their needs and expectations towards health care and their professionals (SurveyMonkey, Supplement). Members of the German Allergy and Asthma Foundation (DAAB) were contacted via E-mail, if they had children with allergic diseases (1275 invitations). Moreover, an advertisement was published on Facebook (FB), targeting participants with children with an interest in keywords like allergy, nuts, mites, cough, sneeze.

851 families answered the online survey conducted by DAAB via email or Facebook link. 786 families (555 DAAB-members), with n=1037 children included after plausibility checks. Compared to DAAB-members, non-DAAB-members were younger, their children had less allergies, particularly less hay fever and had also younger children with less allergies (Tab.S2/S3). Members and non-member were pooled for further analysis.

The most prevalent allergic disease of children was FA (74.6%), followed by AD (58.3%), AR (50.7%), and asthma (38.5%)(Tab.1). On average, the children had 2.2 out of 4 allergic diseases. Details regarding sex can be found in Tab S4.

82% of participants expressed interest in the prediction of the course of a current allergic (Fig.1A), even when special blood values are required. The interest for prediction of additional allergic disease development was equally high. Of most interest was FA, closely followed by asthma: 42% wanted to know it anyway and only 8% never (Fig.1B). When asked how satisfied people were with the current therapy of their children, over 70% were satisfied or very satisfied, while less than 10% were not satisfied at all (Fig.S1A). If a deterioration of a current allergic disease was suspected, there was a high willingness to act: 50.1% would move for better outcome, 58.7% would visit a doctor earlier and 84.2% would attend a specialist clinician (Fig.S1B). When asked about the importance of distinct research priorities and fields of action (Fig.1C), doctor's training was ranked as most important (86.9%), allergy prevention as second (73.8%), followed by research into care (65.9%), new drug therapy (63.6%) and a better understanding of allergy in general (65.5%).

The DAAB survey illustrated that families affected by allergies are highly interested in the prediction of allergies and disease development. Satisfaction with current allergy therapy varied,

confirming the results of other studies (5–7) and supporting an additional major interest for affected families in the identification of novel medication and prevention of allergies.

We developed the CHAMP research projects covering all major allergic diseases and all age groups addressing some of these critical patient needs. Three SPs (SP3,5,6) aim at prediction of asthma by identifying novel biomarkers and predictors for onset, severity or remission. In infancy and early childhood, AD and FA are common, often resolving completely within one year (8). Investigating natural or induced tolerance development is central for FA and asthma remission (SP4/6). Recent studies have shown that epigenetic targets (e.g. FOXP3-demethylation) are critical for early life and childhood immune regulation (9) and together with genetic polymorphisms and environmental factors can determine allergy development (10). Therefore, planned omics analysis from cord or peripheral blood comprise genome-wide association studies (GWAS, GSA-chip), genome-wide methylation (EPIC-chip, Illumina), whole genome expression (RNASeq) and gene expression panels. For patients with asthma, throat swabs were taken, while for FA or AD stool samples and/or skin swabs were collected. Bed dust will be obtained and analysed within SP4 in regards to tolerance development in FA. All samples were prepared and analysed following common standard operating procedures (SOPs), which were established in a collaborative process, enabling us to analyse and compare results. As recent data also suggest, that changes in the microbiome are involved in allergy development (11), microbiome analysis (16S rRNA-gene sequencing) within all cohorts (SP7) were added.

Overarching is a study on affected children and their families (SP2) and a translational murine project, assessing pathomechanisms in different allergy models (SP8).

For the analysis of prediction of allergy development a number of pre-existing cohorts were included and new patient cohorts were established. Clinical and epidemiological questionnaires were used to collect information on health conditions, emphasizing on respiratory and atopic symptoms, sociodemographic and environmental exposures. Five different phenotypes (asthma, severe asthma, AD, FA and AR) were defined.

The following inclusion criteria apply for all cohorts: informed consent of parents or caretakers, age 6 months to 18 years, active/ passive understanding of German. Children were excluded from study visits and biomaterials in the case of fever ($>38.5^{\circ}\text{C}$). Healthy controls (hc) were defined as children without a doctor's diagnosis or parent reported doctor's diagnosis of any allergic disease out of FA, asthma, AD and AR and otherwise healthy. All studies were approved by local ethics committees. CHAMP is registered under <http://www.drks.de/DRKS00015204>.

The variety of cohorts, resulting in different levels of phenotype definition (specialist diagnosis, doctor's diagnosis, parent reported doctor's diagnosis) presents one of the major challenges within CHAMP. To address the resulting heterogeneity of phenotypes, a common database was

established, where relevant variables regarding allergic diseases and potential confounders were generated. The HRQoL survey (12) in SP2 applied in most subprojects contained a core questionnaire with detailed information on childhood allergic diseases, disease specific symptoms, medication, further supporting the comparison of phenotypes. The variety also represents a major strength of CHAMP, as the various study populations cover the whole pediatric age range and all common allergic diseases at different stages of manifestation.

The results from the CHAMP project will add novel insight to the puzzle of early onset, natural tolerance and remission of different allergic diseases. Laying the ground for the development of preventive strategies and novel therapeutic options, this will clearly make an impact on the HRQoL of allergic patients and their families.

Acknowledgements

We would like to thank all participating families. Special thanks to all staff for technical support and study physicians for patient recruitment and blood sample collection.

Keywords

Allergy, Biomarker, Childhood, Cohorts, Health-Related Quality of Life, Prediction, Survey

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Figure legend

Fig. 1: Results from the DAAB survey (participants n=786): Interest of families with allergic children in the prediction of A) course of current allergic disease or developing a further allergic disease (left) and if the answer is yes/not sure, which allergic disease are you interested in (right); B) What probability of your child to develop an additional allergic disease do you count as reliable; C) How important do you consider certain fields of action and research in health? AD-atopic dermatitis, AR-allergic rhinoconjunctovitis, FA-food allergy

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Conflict of Interest

BS report grants from DFG, grants from EU, advisory board/consulting fees outside the submitted work (Sanofi, GSK, Novartis).

EvM reports personal fees from Pharmaventures, from OM Pharma S. A., from Springer-Verlag GmbH, from Elsevier GmbH and Elsevier Ltd., from Peptinnovate Ltd., from Turun Yliopisto, from Tampereen Yliopisto, from Helsingin Yliopisto, from European Respiratory Society, from Deutsche Pharmazeutische Gesellschaft e. V., from Massachusetts Medical Society, from Chinese University of Hongkong, from European Commission, from Böhringer Ingelheim International GmbH, from Universiteit Utrecht, Faculteit Diergeneeskunde, from Universität Salzburg, from Georg Thieme Verlag, from Japanese Society of Pediatric Allergy and Clinical Immunology (JSPACI), outside the submitted work; In addition, Dr. von Mutius has a patent LU101064 - Barn dust extract for the prevention and treatment of diseases pending, a patent EP2361632: Specific environmental bacteria for the protection from and/or the treatment of allergic, chronic inflammatory and/or autoimmune disorders with royalties paid to ProtectImmun GmbH, a patent Publication number EP 1411977: Composition containing bacterial antigens used for the prophylaxis and the treatment of allergic diseases. licensed to ProtectImmun GmbH, a patent Publication number EP1637147: Stable dust extract for allergy protection licensed to ProtectImmun GmbH, and a patent Publication number EP 1964570: Pharmaceutical compound to protect against allergies and inflammatory diseases licensed to ProtectImmun GmbH.

EH has consulted for AllergoPharma, ALK, Boehringer Ingelheim, Bencard, GlaxoSmithKline, HAL Allergy, Novartis, Nutricia, and Teva and has received research support from the German National Ministry of Education and Research (BMBF) and the German Research Society (DFG). He is president of the German Asthma Net (GAN e.V.) and vice president of the German Allergy Society (DGAKI).

KB reports advisory board/consulting fees from Aimmune Therapeutics, Bencard, Danone/Nutricia, DBV, Hycor, Infectopharm, Mabyon, Meda Pharma/Mylan, Nestle, Novartis; speakers bureau for Aimmune Therapeutics, Danone/Nutricia, Di-Text, Hammer und Rall Media, Infectopharm, Meda Pharma/Mylan, Med Update, Nestle, Novartis, ThermoFisher; and research grants from Aimmune, ALK, Danone/Nutricia, DBV Technologies, Good Mills, Hipp, Hycor, Infectopharm, ThermoFisher, VDI outside the submitted work. WG and SK are members of the EuroQoL Group Association.

AB, CS, DW, GH, IG, JDW, JEK, JK, KU, KZ, MD, MK, PK, SdS, SSCH, have nothing to disclose.

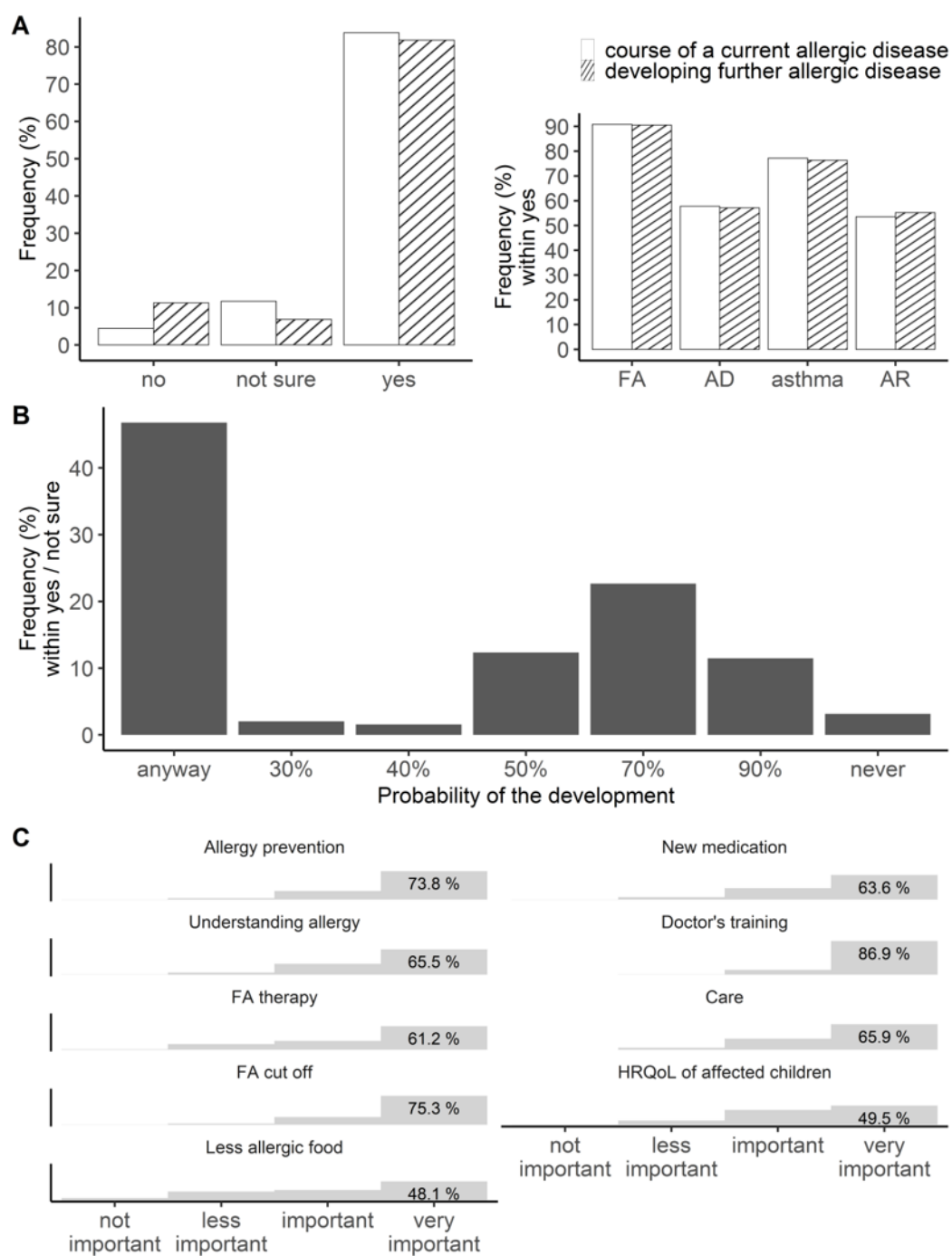
Financial support

This work was supported by a framework program for health research in children and adolescents funded by the German Federal Ministry for Education and Research: “Healthy for life” BMBF 01GL1742A-F (all), Else-Kröner-Fresenius Stiftung (AB, BS); Hauner Verein (KaZ, BS); DFG SCHA-997/8-1 (BS, MS), 01GL1742F (GH); EXC2155 “Resist” ID39087428 (GH); Titus Else-Kröner-Fresenius Stiftung (GH).

Tab. 1: Characteristics on DAAB survey participants (A) and their children (B) with respect to their allergic disease: p-values derived from Chi-Square-test

(A) Characteristics on Participant / Parent					
Number of allergies	none (N=355)	single (N=190)	multiple (N=241)	Total (N=786)	p value
Sex					0.09
Female	341 (96.1%)	175 (92.1%)	223 (92.5%)	739 (94.0%)	
Male	14 (3.9%)	15 (7.9%)	18 (7.5%)	47 (6.0%)	
Age					0.336
20-29	15 (4.2%)	9 (4.7%)	11 (4.6%)	35 (4.5%)	
30-39	194 (54.6%)	99 (52.1%)	112 (46.5%)	405 (51.5%)	
40-49	133 (37.5%)	73 (38.4%)	100 (41.5%)	306 (38.9%)	
50-59	13 (3.7%)	8 (4.2%)	15 (6.2%)	36 (4.6%)	
Over 60	0 (0.0%)	1 (0.5%)	3 (1.2%)	4 (0.5%)	
Allergic diseases of participant					
FA		20 (10.5%)	146 (60.6%)	166 (21.1%)	
AD		34 (17.9%)	123 (51.0%)	157 (20.0%)	
Asthma		13 (6.8%)	135 (56.0%)	148 (18.8%)	
AR		123 (64.7%)	216 (89.6%)	339 (43.1%)	
Participant's family					
Having a child with FA	324 (91.3%)	169 (88.9%)	199 (82.6%)	692 (88.0%)	0.005
Having a child with AD	212 (59.7%)	127 (66.8%)	168 (69.7%)	507 (64.5%)	0.032
Having a child with asthma	123 (34.6%)	80 (42.1%)	131 (54.4%)	334 (42.5%)	< 0.001
Having a child with AR	156 (43.9%)	111 (58.4%)	158 (65.6%)	425 (54.1%)	< 0.001
(B) Characteristics on participant's children with allergies					
Number of allergies	single one (N=310)	multiple (N=727)	Total (N=1037)	p value	
Sex				0.004	
Female	144 (46.5%)	268 (36.9%)	412 (39.7%)		
Male	166 (53.5%)	459 (63.1%)	625 (60.3%)		
Age				0.006	
First year of life	14 (4.5%)	15 (2.1%)	29 (2.8%)		

1-3 years		81 (26.1%)	133 (18.3%)	214 (20.6%)	
4-6 years		74 (23.9%)	192 (26.4%)	266 (25.7%)	
7-12 years		97 (31.3%)	286 (39.3%)	383 (36.9%)	
13-18 years		35 (11.3%)	74 (10.2%)	109 (10.5%)	
Over 18 years		9 (2.9%)	27 (3.7%)	36 (3.5%)	
Children's allergic diseases					
FA		149 (48.1%)	625 (86.0%)	774 (74.6%)	< 0.001
AD		77 (24.8%)	528 (72.6%)	605 (58.3%)	< 0.001
Asthma		26 (8.4%)	373 (51.3%)	399 (38.5%)	< 0.001
AR		58 (18.7%)	468 (64.4%)	526 (50.7%)	< 0.001



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Supplement

DAAB Survey

Q1: If your pediatrician could predict how the allergic disease(s) of your child may develop by e.g., using a special blood value, would you like to know? Example: Your child developed atopic dermatitis with 3 months and food allergy with 7 months of age. Would you like to know whether and with which probability your child will develop asthma at school age?

- I. Yes
- II. No
- III. I don't know

Q2: If you answer yes to Q1, for which allergic disease would you like to know this prediction?

- I. Atopic dermatitis
- II. Food allergy
- III. Asthma
- IV. Hay fever
- V. Venom allergy
- VI. Drug allergy

Q3: If your pediatrician could predict a probability for your child to develop an additional allergic disease: from which percentage on would you like to know the prognosis?

- I. Anyway
- II. 30%
- III. 40%
- IV. 50%
- V. 70%
- VI. 90%
- VII. Never

Q4: Would you like to know, how a current allergic disease of your child would develop? Example: Your child has had asthma since toddler age. Would you like to know, whether that asthma will be lifelong?

- I. Yes
- II. No
- III. I don't know

Q5: If answer yes to Q4, for which allergic disease would you like to know this assessment?

- I. Atopic dermatitis
- II. Food allergy
- III. Asthma
- IV. Hay fever
- V. Venom allergy
- VI. Drug allergy

Q6: If your pediatrician would assume a less favorable course of disease (e.g., becoming more severe or developing additional allergic diseases), what would be your consequences? (Multiple answers possible)

- I. If getting worse, I would go earlier to a doctor.
- II. I would consult a specialist for the treatment of this allergic disease.
- III. I would move for better medical care (specialist nearby).
- IV. I would move for a better course of disease, e.g. moving away from a busy street, moving out of a house with mold.
- V. I would try alternative healing methods in addition to academic medicine.
- VI. I would not change anything.
- VII. Other (please add):

Q7: How important do you consider the following research topics and field of action? Please give an assessment.

- a. Development of new therapies for better tolerance of food allergens, to increase the amount of an allergen that can be tolerated (threshold)
 - I. Very important
 - II. Important
 - III. Less important
 - IV. Not important
- b. Development of new therapies to enable digesting a normal portion of a specific allergen, e.g. for milk, a glass of milk.
 - I. Very important
 - II. Important
 - III. Less important
 - IV. Not important
- c. Research into current medical care and treatment of patients with allergic diseases to reveal gaps
 - I. Very important
 - II. Important
 - III. Less important
 - IV. Not important
- d. Better education of medical doctors specializing in allergies
 - I. Very important
 - II. Important
 - III. Less important
 - IV. Not important
- e. Development of novel drugs to treat allergic symptoms, e.g. for hay fever or asthma more effectively
 - I. Very important
 - II. Important
 - III. Less important
 - IV. Not important
- f. Research on the interplay of different allergic diseases
 - I. Very important
 - II. Important
 - III. Less important

- IV. Not important
- g. Research on affected children about their coping strategies
 - I. Very important
 - II. Important
 - III. Less important
 - IV. Not important
- h. Research on allergy prevention to develop strategies to prevent the development of allergic diseases
 - I. Very important
 - II. Important
 - III. Less important
 - IV. Not important

Q8: How satisfied are you with the current therapy of your child, recommended by your doctor?

- a. Hay fever
 - I. Not applicable
 - II. Very satisfied
 - III. Satisfied
 - IV. Less satisfied
 - V. Not satisfied
- b. Asthma
 - I. Not applicable
 - II. Very satisfied
 - III. Satisfied
 - IV. Less satisfied
 - V. Not satisfied
- c. Atopic dermatitis
 - I. Not applicable
 - II. Very satisfied
 - III. Satisfied
 - IV. Less satisfied
 - V. Not satisfied
- d. Food allergy
 - I. Not applicable
 - II. Very satisfied
 - III. Satisfied
 - IV. Less satisfied
 - V. Not satisfied

Q9: What gender are you?

- a. Female
- b. Male

Q10: How old are you?

- a. 20-29
- b. 30-39
- c. 40-49

- d. 50-59
- e. above 60

Q11: Do you have an allergic disease yourself (Multiple answers possible)?

- a. No
- b. Asthma
- c. Atopic dermatitis
- d. Hay fever
- e. Food allergy

Q12: How old is your child/ are your children (please only answer for children with allergic diseases/ asthma)

- a. Child 1
 - i. Baby
 - ii. 1-3 years
 - iii. 4-6 years
 - iv. 7-12 years
 - v. 13-18 years
 - vi. over 18 years
- b. Child 2
 - I. Baby
 - II. 1-3 years
 - III. 4-6 years
 - IV. 7-12 years
 - V. 13-18 years
 - VI. over 18 years
- c. Child 3
 - I. Baby
 - II. 1-3 years
 - III. 4-6 years
 - IV. 7-12 years
 - V. 13-18 years
 - VI. over 18 years

Q13: What gender is your child/ are your children? (Please only answer for children with allergic diseases/ asthma)

- a. Child 1
 - I. Female
 - II. Male
- b. Child 2
 - I. Female
 - II. Male
- c. Child 3
 - I. Female
 - II. Male

Q14: Which allergic disease has your child/have your children?

- a. Child 1

- I. Hay fever
 - II. Atopic dermatitis
 - III. Asthma
 - IV. Food allergy
- b. Child 2
- I. Hay fever
 - II. Atopic dermatitis
 - III. Asthma
 - IV. Food allergy
- c. Child 3
- I. Hay fever
 - II. Atopic dermatitis
 - III. Asthma
 - IV. Food allergy

Q15: Are you or your family a member of the DAAB?

- a. Yes
- b. No

Table S1: The CHAMP study group: Project partners and description

Partners and subproject	Aim	Epidemiological or clinical cohorts	Phenotypes /questionnaire	Bio samples and analyses	Current status
SP2: W. Greiner/ S. Kreimeier, Bielefeld – Health-related quality of life (HRQoL) in children and adolescents with allergic diseases and quality of life (QoL) of their parents	Explore the influence of different allergic diseases on HRQoL of young patients and QoL of their parents	Joint effort. recruitment is ongoing from cohorts, outpatient-clinics (SP3-SP6, planned N=1800) and supported by the DAAB	Generic and disease-specific HRQoL questionnaires for different age groups of patients, QoL questionnaire for parents including questions on allergic diseases, socio-demographic, environmental information. Baseline assessment plus a one- and two-year follow-up	Comparison of patients' HRQoL, parents' QoL data between different allergic patient groups and subgroups (e.g. age groups, gender)	Baseline data are analyzed. In the first phase of SP2, an adaption of a disease-specific HRQoL questionnaire for children suffering from AA and AR for the German context was established
SP3: B. Schaub, Munich – Coordination and Early priming of allergic disease: development of a novel molecular allergy risk score	Define subgroups of children at risk to develop allergic diseases	Two cord blood studies: PAULINA/PAULCHE N, n=283 and PASTURE/EFRAIM, n=1133 Cross sectional asthma study, n=335	Doctor's diagnosis of asthma Parent's reported diagnosis of asthma, AD, FA, AR and detailed sociodemo-graphic data, health and environmental information from questionnaires on all cohorts	Genome-wide analysis for DNA, Epigenome and RNA Protein expression Cellular characterization Stool samples/ Skin swabs (microbiome composition) Allergic sensitization	Differences between healthy and allergic children by a combination of genome-wide genetics, epigenetic variability and gene expression in two birth cohorts are assessed.
SP4: K. Beyer, Berlin - Natural resolution factors in tolerance development of food allergy	Identify „resolution factors“ involved in natural and therapeutically induced tolerance development in already established food allergy	Peanut Oral Immunotherapy (OIT =SOTI) n= 42 (total 63) Eczema & Food Allergy (EFA) n= 172 (total 550)	FA: Study physician diagnosed IgE-mediated food allergy using allergen-specific IgE measurement and oral food challenges AD: Study physician diagnosed eczema based on the modified criteria of Hanifin and Rajka, Questionnaires: socio-demographic data and health information	EDTA blood for DNA, RNA Cells for chip-cytometry and cytokine determination in cell culture supernatants Serum/plasma/saliva for immunoglobulin and chemokine determination Stool samples/ Skin swabs (microbiome composition) House and bed dust for determination of food allergens	192 patients are already enrolled for “induced tolerance development” in peanut allergic versus “natural tolerance development” in peanut- and/or hen's- egg-allergic, while analyses of bio samples and clinical data will take place in parallel to ongoing enrolment.

SP5: E. Hamelmann, Bielefeld - Severity and co-morbidities of allergic diseases	Identify the mechanisms leading to progression of allergic diseases to more severe allergic subtypes	German Asthma Net (GAN) with ongoing and additional recruitment of severe asthmatics from SP3 and SP6), n= 24 (planned 60) NIKI, n= 138	Doctor's diagnosis Clinical information (E-data base)	DNA for genetics and epigenetics, whole blood for RNA sequencing, faeces and nasopharyngeal swabs for microbiota Metabolic diagnostic (ADMA/ NO-Parameter), Cytokine, IgE	Patients and data of the German Asthma Network (GAN) register are utilized. Within the NIKI-Cohort, children with asthma and comorbidities such as obesity and attention deficit hyperactivity disorder are compared regarding underlying mechanisms
SP6: M. Kabesch, Regensburg - Systematic detection of mechanisms & markers for allergy remission in children & adolescents	Identify and characterize the mechanisms of asthma and allergy remission either spontaneously or after immunotherapy in late childhood and adolescence	Children with atopic diseases from the KUNO Kids health study (n=3600) Replication populations: Follow-MAGICS (n=577) and SOLAR (n=480)	Doctor's diagnosis Detailed disease data and health status information from questionnaires	Genetics: GWAS Epigenetics: Infinium Human Methylation EPIC BeadChip Transcriptomics: RNA seq Microbiome:16S Pyrosequencing analysis Metabolomics: MaxP Quant 500 Kit (BIOCRATES Life Sciences).	Collecting samples of children and adolescents with atopic asthma, AR and/ or AD to acquire a comprehensive picture of biological processes from before and 6 months after start of remission.
SP7: E. von Mutius/ M. Depner, Munich - Analysis and integration of microbiome data from allergy cohorts	Understand the role of the microbiome in the context of progression or remission of allergic diseases	This study is a cooperated effort. Participants will be recruited from specific cohorts out of SP3-SP6.	Diagnosis as described in the respective cohorts, questionnaire data and/or measured parameters e.g. tests for lung function or specific IgE for better comparison of phenotypes	Microbiome 16S rRNA from the respective sub-projects on different sites (throat for AA, skin for FA, and faeces for all)	Microbiome data from distinct allergy cohorts and different allergic diseases (SP7) sites are characterized with respect to main bacteria species and diversity.
SP8: G. Hansen, Hannover - Perinatal priming of tolerance and allergy	Assess underlying mechanisms of allergy development with focus on early tolerance induction	Not applicable Findings from the cohorts are tested in the models and vice versa.	Murine models of Allergic Asthma, Food allergy, and Atopic Dermatitis; Influence of microbial stimulation; Influence of the inflammasome NLRP3; Strains: C57BL/6J and B6.129S6-Nlrp3tm1Bhk/J mice	Allergic sensitization and tolerization models (Ovalbumin) with lung function, gene expression, protein expression, histology, flow cytometry and cellular characterization	Results revealed hitherto unknown regulatory mechanisms for NLRP3 in maternal tolerance induction and protection from allergic diseases, involving both the innate and adaptive immune system.

DAAB – Patient Involvement: allergic diseases from a patient point of view	Develop and carry out a survey to allergic children and their parents with emphasis on the personal needs and requirements of the families	N = 599 DAAB members N = 251 DAAB non-members	Socio-demographic data, information about different allergic diseases from questionnaires	Comparison between members and non-members	See this publication for results
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Tab S2: Characteristics for participants (parents) of the DAAB survey: DAAB members compared to non-members, p-values derived from Chi-square-test

* Allergic diseases (all, AR, FA, AD, Asthma) were listed from the parents.

Details	DAAB member (N=599)	DAAB Non-member (N=252)	Total (N=851)	p-value
Contact				< 0.001
Email to members	474 (79.1%)	0 (0.0%)	474 (55.7%)	
Facebook link	125 (20.9%)	252 (100.0%)	377 (44.3%)	
Sex				0.008
Female	550 (91.8%)	244 (96.8%)	794 (93.3%)	
Male	49 (8.2%)	8 (3.2%)	57 (6.7%)	
Age				< 0.001
20-29	8 (1.3%)	27 (10.7%)	35 (4.1%)	
30-39	280 (46.7%)	161 (63.9%)	441 (51.8%)	
40-49	271 (45.2%)	60 (23.8%)	331 (38.9%)	
50-59	35 (5.8%)	4 (1.6%)	39 (4.6%)	
over 60	5 (0.8%)	0 (0.0%)	5 (0.6%)	
Allergic disease *				0.070
No	259 (43.2%)	126 (50.0%)	385 (45.2%)	
Yes	340 (56.8%)	126 (50.0%)	466 (54.8%)	
AR*				0.006
No	321 (53.6%)	161 (63.9%)	482 (56.6%)	
Yes	278 (46.4%)	91 (36.1%)	369 (43.4%)	
FA*				0.148
No	463 (77.3%)	206 (81.7%)	669 (78.6%)	
Yes	136 (22.7%)	46 (18.3%)	182 (21.4%)	
AD*				0.999
No	473 (79.0%)	199 (79.0%)	672 (79.0%)	
Yes	126 (21.0%)	53 (21.0%)	179 (21.0%)	
Asthma*				0.809
No	483 (80.6%)	205 (81.3%)	688 (80.8%)	
Yes	116 (19.4%)	47 (18.7%)	163 (19.2%)	

Tab S3: Characteristics for children of DAAB members versus non-members, participating in the DAAB survey: p-values derived from Chi-square-test

	Children of DAAB members (N=751)	Children of non-members no (N=286)	Total (N=1037)	p-value
Sex				0.846
Female	297 (39.5%)	115 (40.2%)	412 (39.7%)	
Male	454 (60.5%)	171 (59.8%)	625 (60.3%)	
Age				< 0.001
First year of life	8 (1.1%)	21 (7.3%)	29 (2.8%)	
1-3 years	123 (16.4%)	91 (31.8%)	214 (20.6%)	
4-6 years	191 (25.4%)	75 (26.2%)	266 (25.7%)	
7-12 years	309 (41.1%)	74 (25.9%)	383 (36.9%)	
13-18 years	94 (12.5%)	15 (5.2%)	109 (10.5%)	
Over 18 years	26 (3.5%)	10 (3.5%)	36 (3.5%)	
FA				0.694
No	188 (25.0%)	75 (26.2%)	263 (25.4%)	
Yes	563 (75.0%)	211 (73.8%)	774 (74.6%)	
AD				0.197
No	322 (42.9%)	110 (38.5%)	432 (41.7%)	
Yes	429 (57.1%)	176 (61.5%)	605 (58.3%)	
asthma				0.115
No	451 (60.1%)	187 (65.4%)	638 (61.5%)	
Yes	300 (39.9%)	99 (34.6%)	399 (38.5%)	
AR				< 0.001
No	340 (45.3%)	171 (59.8%)	511 (49.3%)	
Yes	411 (54.7%)	115 (40.2%)	526 (50.7%)	
Number of allergic diseases (out of the 4 above)				0.013
1	220 (29.3%)	90 (31.5%)	310 (29.9%)	
2	229 (30.5%)	111 (38.8%)	340 (32.8%)	
3	183 (24.4%)	51 (17.8%)	234 (22.6%)	
4	119 (15.8%)	34 (11.9%)	153 (14.8%)	

Tab S4 Characteristics for children of families participating in the DAAB survey, female versus male: p-values derived from Chi-square-test

Sex	Female (N=412)	Male (N=625)	Total (N=1037)	p-value
Age				0.009
First year of life	15 (3.6%)	14 (2.2%)	29 (2.8%)	
1-3 years	72 (17.5%)	142 (22.7%)	214 (20.6%)	
4-6 years	107 (26.0%)	159 (25.4%)	266 (25.7%)	
7-12 years	147 (35.7%)	236 (37.8%)	383 (36.9%)	
13-18 years	59 (14.3%)	50 (8.0%)	109 (10.5%)	
Over 18 years	12 (2.9%)	24 (3.8%)	36 (3.5%)	
FA				0.011
No	122 (29.6%)	141 (22.6%)	263 (25.4%)	
Yes	290 (70.4%)	484 (77.4%)	774 (74.6%)	
AD				0.412
No	178 (43.2%)	254 (40.6%)	432 (41.7%)	
Yes	234 (56.8%)	371 (59.4%)	605 (58.3%)	
asthma				0.043
No	269 (65.3%)	369 (59.0%)	638 (61.5%)	
Yes	143 (34.7%)	256 (41.0%)	399 (38.5%)	
AR				0.002
No	228 (55.3%)	283 (45.3%)	511 (49.3%)	
Yes	184 (44.7%)	342 (54.7%)	526 (50.7%)	
Number of allergic diseases (out of the 4 above)				< 0.001
1	144 (35.0%)	166 (26.6%)	310 (29.9%)	
2	146 (35.4%)	194 (31.0%)	340 (32.8%)	
3	73 (17.7%)	161 (25.8%)	234 (22.6%)	
4	49 (11.9%)	104 (16.6%)	153 (14.8%)	

Fig. S1: Interest and needs of families with allergic children from the DAAB survey (n=786)

Fig. S1A: Satisfaction of families with allergic children with their child's current therapy recommended by their paediatrician depending on the allergic disease of the child

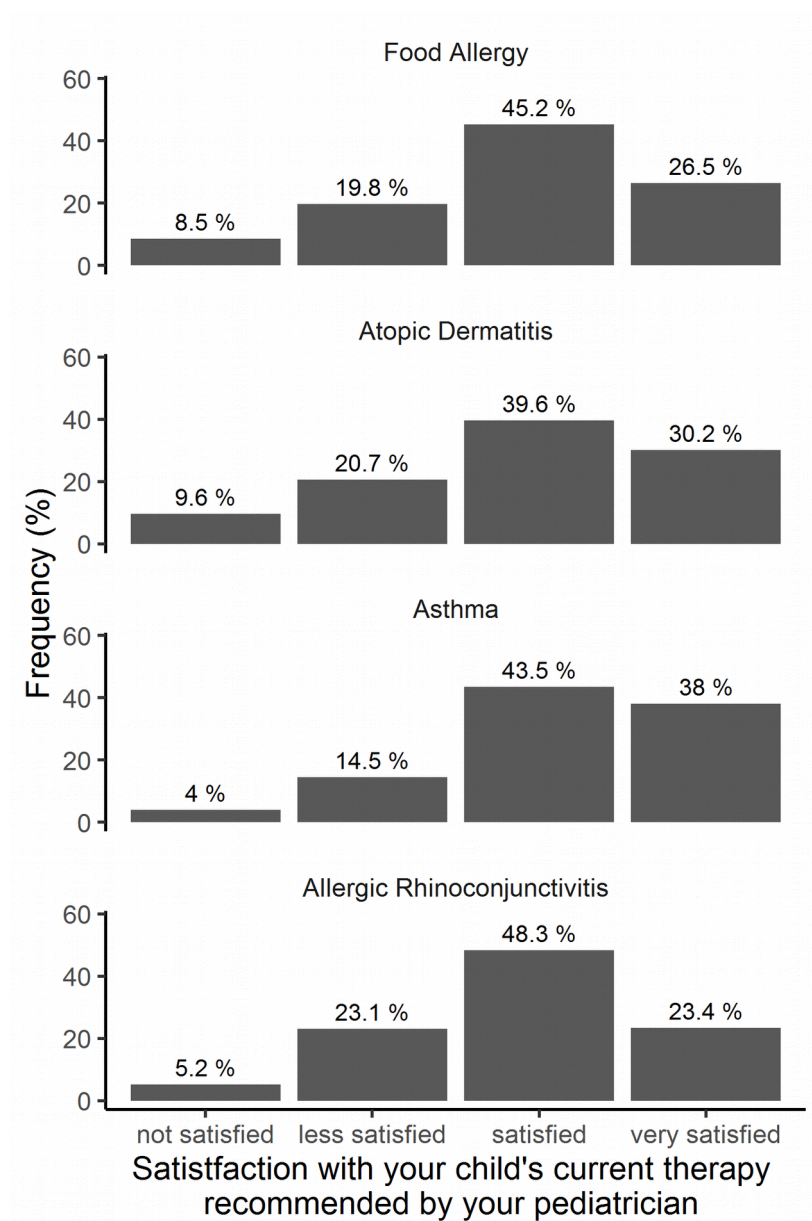


Fig. S1B: If your pediatrician expects worsening of your child's allergic disease, what would you be willing to do?

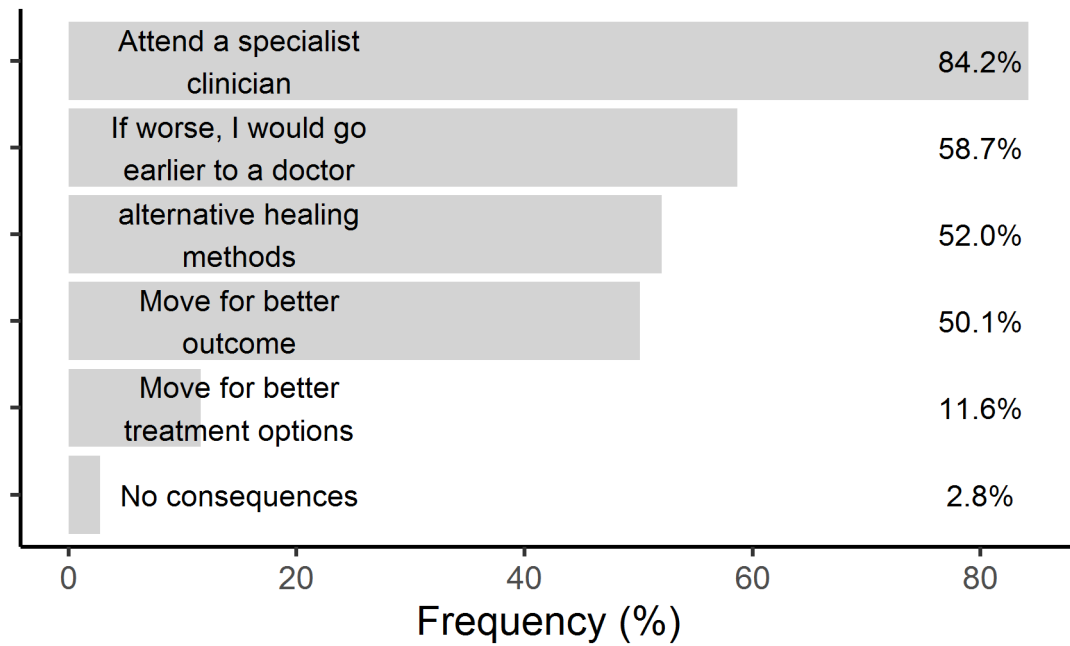


Fig. S2: CHAMP project: Analysing biomarkers and prediction of childhood allergy on several layers of onset, progression and remission of allergies from birth to adolescence

