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 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).

Whithin CHAMP an online survey was conducted, aiming at needs and expectations of families with allergic children 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 were 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.S1/S2). 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 S3.

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 resulting in identification of novel medication and prevention of allergies being of major interest for affected families.

To address these critical patient needs, we developed the CHAMP research projects covering all major allergic diseases and all age groups. The CHAMP consortium includes eight subprojects (Tab.2), investigating determinants of different allergic diseases from birth to adolescence. As demanded by organisations like EAACI (7), the aim is to improve diagnostics by identifying clinically relevant biomarkers predicting allergy onset, progression, remission and severity.

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 HRQoL of 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-existiing 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°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.

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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 diseas **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

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