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Abstract

Background: Psychosocial factors are supposed to play a central role in the development of allergic diseases. Associations with seasonal and perennial forms of allergies have not been investigated, yet. **Objectives:** The aim of the study was to investigate the associations of psychosocial factors (social status, depression, generalized anxiety, psychosocial stress, Type-D personality) with seasonal, perennial, and other forms of allergies in adults. **Method:** The

analysis of self-reported data of the KORA FF4 study was performed with SAS 9.4. The sample consisted of 1,782 study participants in the study region of Augsburg (39–88 years, 61 years, 51.1% female). Descriptive bivariate statistics and multinomial logistic regression models were performed. Age, sex, family predisposition, and smoking status were considered possible confounders. Moreover, several sensitivity analyses were carried out to check whether missing values distorted the results. **Results:** A positive association between generalized anxiety and seasonal allergies was found in the multivariate model. Depression was positively, and anxiety negatively, associated with perennial allergies. No association between the analyzed psychosocial factors and other forms of allergies could be found. **Conclusion:** The results support the relevance of psychosocial factors in association with allergies. Looking at the psychosocial factors, a separate consideration of seasonal and perennial allergies seems reasonable. Further longitudinal studies should investigate the direction of the associations, the underlying mechanisms, and other psychosocial factors, such as coping mechanisms, in confirmed allergies.

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Introduction

Most allergy patients report more severe symptoms under psychosocial stress or they remember life events as trigger factors for allergy pathogenesis. Nevertheless, allergy researchers often focus on biological and physical influencing factors. It is assumed that allergies can be explained by a biopsychosocial disease model [1]. Therefore, psychosocial factors should be investigated as well.

A bidirectional relationship between psychosocial factors and allergic or atopic diseases was found in many studies [2]. This means that there are associations in both directions, but molecular pathways and underlying mechanisms are still unclear. Allergies, for example, are one of the few diseases that occur more often in high socioeconomic status groups (reversed social gradient) [3]. Explanations for the phenomenon are as multiple as diverse. One reason for this fact might be a protective effect of a larger number of siblings and early childhood infections, which is found to be more common in lower socioeconomic status groups [4]. Depression and anxiety also seem to be associated with allergies [5]. Mental stress, especially chronic stress, is associated with allergic reactions [6], which can be explained by interactions between the nervous system, the endocrine system, and the immune system [7]. The possibility to treat allergic symptoms through psychosocial interventions (e.g., self-hypnosis or stress management) [8–10] points to the importance of psychoneuroimmunologic interactions in allergies.

Most studies conclude that personality types are not linked to specific diseases. Nevertheless, personality patterns might be associated with the perception of diseases, coping mechanisms, and therefore with disease persistence. A personality pattern, which gained attention in the field of cardiovascular diseases, is the Type-D personality [11]. The Type-D concept embraces negative affectivity and social inhibition. It is a depression-related concept,

but it still represents another dimension of distress than depression [12]. Promising results have shown that symptom control and quality of life in asthma patients are associated with Type-D, although it was not distinguished between allergic and non-allergic asthma [13]. It is not investigated yet whether seasonal or perennial allergies are associated with this personality pattern.

On the basis of the high and increasing prevalence of allergic diseases [14, 15] (at the moment 28.1% in adults in Germany [16]), there is a public health relevance to further investigate the associations between psychosocial factors and allergies. The investigation of associations between psychosocial factors and allergies as well as the finding of underlying molecular mechanisms with potential therapy options might not only help to improve the quality of life of the respective patients. It might also help to reduce the economic costs arising from health care costs, a lower performance at work, or absence from work due to allergies [17–19].

Most current studies about allergies and psychosocial factors refer to atopic diseases like allergic rhinitis, asthma, and atopic dermatitis. Other aspects of allergies are often disregarded. A division into seasonal and perennial allergies is reasonable to allow for a more detailed analysis.

We could not classify according to ARIA guidelines into intermittent (“symptoms are present <4 days a week or for <4 weeks” [20]) and persistent (“symptoms are present at least 4 days a week and for at least 4 weeks” [20]) allergies because we did not have any information on symptom duration and severity. Therefore, we differentiated between those, who have only seasonal symptoms, that is, seasonal allergies only (tree or grass pollen), those who have symptoms throughout the whole year, that is, perennial allergies (house dust mite and animal hair; including those with additional seasonal allergies), and those who have other non-respiratory allergies (food, medicaments, insect sting; including those with additional seasonal, or perennial allergies).

The aim of the study was to investigate the associations of psychosocial factors (social status, depression, generalized anxiety, psychosocial stress, Type-D personality) with seasonal, perennial, and other allergies in adults.

Materials and Methods

Study Design

Data of the second follow-up period of the KORA baseline study S4 (KORA FF4) were used for the analysis. The population-based KORA S4 survey was carried out in the region of Augsburg and refers to a cohort aged between 25 and 74 at baseline [21]. By now, there are 2 follow-up studies, which took place after 7 and 14 years respectively.

A sub-sample of participants who took part in the Environmental Medicine Survey, which was sent to all participants of the second follow-up study KORA FF4, was analyzed as these participants provided data about their allergy status (Fig. 1).

The investigations were carried out in accordance with the Declaration of Helsinki, including the written informed consent of all participants. All study methods were approved by the Ethics Committee of the Bavarian Chamber of Physicians, Munich (FF4: EC No. 06068).

Analyzed Variables

Data about depression, generalized anxiety, personality type, smoking, as well as sociodemographic and socioeconomic variables were derived from the KORA FF4 study. Data about allergies and psychosocial stress were derived from the Environmental Medicine Survey.

Allergies

Only self-reported type-1 allergies were taken into account. The study differentiated between people without any allergy, people with seasonal allergies only (tree or grass pollen), perennial allergies (house dust mite and animal hair; including those with additional seasonal allergies) and other allergies (food, medicaments, insect sting; including those with additional

seasonal or perennial allergies). The information about the allergy status was gained by asking the study participants about their allergies and several answers were possible by choosing their respective allergies in the survey.

Psychosocial Factors

The social status of the participants was operationalized with the index of Helmert and Shea [22], which is based on income, education, and occupation. It ranges from 1 to 27 and was subdivided into lower social class (<10), middle social class (>9 and <19) and upper social class (>18). Depression was measured with the Brief Patient Health Questionnaire-9 [23]. The instrument consists of 9 items and is based on the DSM-IV criteria for major depression. The score ranges from 0 to 27. While 0 means “no depression,” anything between 1 and 27 means minimal, mild, moderate, or severe “depression” [23]. As there were only a few cases with depression, we did not differentiate between minimal, mild, moderate, and severe forms of depression. Anxiety was captured with the Generalized Anxiety Disorder Scale-7 [24], which consists of 7 items and is based on the DSM-IV criteria for generalized anxiety. The score ranges from 0 to 21 and was subdivided into “minimal and mild” (0–9) or “moderate and severe” (10–21) anxiety symptoms. The Type-D personality was measured with the Type-D Scale-14 [25]. The instrument consists of 14 questions on social inhibition and negative affectivity and can identify the Type-D pattern. Mental stress burden was assessed with a single-item-dichotomized measure. Study participants were asked for their risk factors and one of them was “too much stress and/or rush”; they could answer with “yes,” “no” or “unknown.” The answer “unknown” was treated like a missing value.

Confounders

Age (at date July 1, 2014), sex, smoking status, and a family predisposition for atopic diseases (allergic asthma, hay fever, atopic dermatitis, or food allergy in parents) were considered possible confounders.

Statistics

The software SAS 9.4 was used to analyze the data. A bivariate analysis (ORs, chi-square tests, asymptotic U tests according to Mann-Whitney-Wilcoxon and Kruskall-Wallis tests) as well as a multivariate analysis (multinomial logistic regression) to check for confounders were performed. In the multivariate model, allergy was defined as a dependent variable and the psychosocial factors as well as the confounders were defined as independent variables. Cases with missing values were excluded, first. In the sensitivity analysis, missing values were replaced by extremes. All results were considered significant if the *p* value did not exceed 0.05. No correction of alpha was done.

Results

Univariate Statistics

Men and women were distributed nearly equally (51.1% female) within the selected sample. Age ranged from 39 to 88 years with the mean set at 61 years. About two-thirds of the participants could be classified as middle socioeconomic class (58.0%), more than one out of 4 could be classified as upper class (26.8%), and about one sixth was considered lower class (15.2%). Most participants were non-smokers or previous smokers (86.4%) and did not have a family predisposition for atopic diseases (92.9%). Overall, the prevalence of self-reported allergies was 27.4%. The prevalence of seasonal and perennial allergies was 7.7% and 6.1%, respectively, and 13.6% in the case of participants who reported other types of allergies. Depressive disorder or generalized anxiety was found in 3.9% and 4.0% of the participants respectively. About one third of the sample claimed to have a mental stress burden (32.8%). About one out of 6 participants could be classified as Type-D (16.9%; Table 1).

Bivariate Statistics

Among the allergic subjects there were more women, young people, people with family predisposition and non-smokers. Tendencies (i.e., associations that were not statistically significant but still of importance) showed that depressive disorder was more common in allergic subjects. Study participants with allergies reported psychosocial stress more often than participants without allergies did. The Type-D personality pattern was more likely to be found in participants with perennial allergies compared to people with other forms of allergy or without any allergy. There was no difference in the social status of people without or with allergies (Table 2).

Missing values were more frequent in non-allergic subjects. The age-stratified analysis of missing values showed no association between the allergy type and the missing values. Subjects of 70 years and older were more likely not to have answered the questions on psychosocial factors (Fisher's exact test: $p < 0.0001$).

There were higher odds for seasonal allergies in younger participants, people with a family predisposition, people with generalized anxiety and in participants reporting high mental stress levels. Higher odds for perennial allergies could be found in younger participants, people with a family predisposition and in participants reporting a mental stress burden. Furthermore, there were higher odds for other types of allergy in women, younger participants, people with a family predisposition, and in participants reporting generalized anxiety or mental stress burden (Table 3).

Anxious people as well as participants with mental stress burden were generally younger than subjects without the respective psychosocial burden (U test: $p = 0.02$ and <0.0001 respectively).

Multivariate Statistics

After fitting the model, psychosocial stress was not associated with seasonal, perennial, or other allergies, which is different from the results of the bivariate statistics. The association between family predisposition and allergies got weaker in terms of decreasing ORs. The odds

for depression increased in people with perennial allergies. Other ORs (sex, age, smoking status, Type-D, social class and any allergy, depression and seasonal /other allergy, anxiety and seasonal allergy) were found to be at a level that is similar to the level of bivariate statistics as shown in Table 3 and Figure 2. The associations of age and generalized anxiety with other allergies lost significance. The association of any allergy with smoking status and the association between anxiety and perennial allergies reached significance.

Sensitivity Analysis

As cases with missing values were excluded in the first model, the influence of the missing values on the odds ratios was investigated by coding these values either as an existing psychosocial burden or as a non-existing psychosocial burden. Nearly all odds ratios remained at the same level. Therefore, we concluded that the missing values had no influence on the odds ratios (online suppl. Table 1–3; for all online suppl. material, see www.karger.com/doi/10.1159/000499042).

Discussion

In this paper, we show associations between psychosocial factors and allergy. Notably, participants with seasonal or perennial allergies differed in their influencing psychosocial factors. In the KORA FF4 survey of 1,782 middle-aged subjects, it could be shown that generalized anxiety was positively associated with seasonal allergies, depression was positively and anxiety negatively associated with perennial allergies, and none of the analyzed psychosocial factor was associated with other allergy types.

Besides the psychosocial factors, family predisposition was associated with all allergy categories. Lower age was associated with an increased prevalence of seasonal or perennial allergies and non-smoking with a higher prevalence of any allergy. Female sex was found to be

associated with a higher prevalence of other allergies. The sensitivity analysis showed that missing values – although being extensive – did not distort the odds ratios.

Generalized Anxiety

Although the literature suggests an association between anxiety and allergies, surprisingly only seasonal allergies were positively and significantly associated with generalized anxiety in this sample. Perennial allergies were even negatively associated with anxiety. However, the existing studies either focused on asthma, allergic rhinitis, atopic dermatitis, or food allergy [5, 26–29] or investigated other forms of anxiety as, for example, panic disorder [30]. It should be further explored why the positive association was found only in seasonal allergies. It might be that people with perennial allergies adopted other coping strategies or resilience factors.

Depression

An association between depression and perennial allergies could be found. Trikojat et al. [31] talk about an "allergic mood," as they found associations between low mood and inflammatory, endocrine, and allergic markers in patients with acute seasonal allergic rhinitis during pollen season. A population-based study reported an increase of 59% in the probability for depression in allergic subjects [32]. In contrast, another study showed that depression is not more frequent in allergic subjects, but allergies are more frequent in depressive subjects compared to healthy controls [33]. It could be assumed that depression might be a potential risk factor for allergies or that allergies might increase the vulnerability to depression. The cross-sectional design does not allow any assumptions on the direction or causality of the associations. As the directions of the associations are unknown and as there are psychobiological mechanisms, which can explain the association in both directions, these results deserve subsequent prospective studies. As Type-D did not turn out to be significantly

associated with any allergy, it seems that personality does not have an effect on the prevalence of seasonal or perennial allergies.

Psychosocial Stress

Psychosocial stress was associated with allergies in several studies. Pathways, which may explain the association have widely been explored [7], for example through the hypothalamus-pituitary-adrenal-axis [34]. Therefore, the non-existence of a significant association between stress and allergies after fitting the model has not been anticipated. Age could be identified as a relevant confounder. On average, the participants who reported psychosocial stress were about 10 years younger compared to the ones without high stress levels. This can be potentially explained by retirement. As the age of the sample ranges from 39 to 88, the older participants are in retirement. Retirement might also be associated with less psychosocial stress because retired people are relieved from work-related strain [35]. Another possible explanation is that stress coping skills increase with the age [36]. Moreover, it might represent a generational divide as younger adults rather report mental health issues than older adults, for example, because some older adults have a negative stereotype about mental illness [37] or they do not perceive their problems severe enough to report [38]. At the same time, younger study participants were reporting allergies more often. At first sight there seemed to be an association between stress and allergy, which disappeared after adjusting the model for age. Possibly stress does not have an influence on the fact that somebody has an allergy, but on the fact how severe and how often somebody experiences symptoms [6].

Socioeconomic Status

Although literature assumes a reversed social gradient in allergies, no association between the socioeconomic status and the allergies of a participant could be found within this study. The reason might be a social change. Although there are still differences between social classes, the overall level of prosperity in the Augsburg region has increased (“trickle-down

effect" [39]). This effect has potentially led to the loss of protective living conditions in former lower social classes. The proportion of families with a higher number of children, for example, has decreased not only in high, but especially in low socioeconomic status groups [40]. Moreover, the increased awareness of allergies has possibly led to more allergy diagnoses. This includes groups of people who have a lower grade of education or pertain to lower socioeconomic status groups [41]. As many studies on allergies refer to children, it might also be that the social status of the parents and not of the allergic subjects themselves affects the prevalence of allergies. Another possible explanation is that an association could not be seen due to rather low diversity in the socioeconomic factors as most participants were classified as middle or upper class in the study population (Table 1). This might be the result of an upper class bias (online suppl. Table 4).

Strengths and Limitations

One of the strengths of the study was the consideration of the separation between seasonal and perennial allergies. This aspect of allergies is often neglected in existing research. Results show that this distinction is sensible when it comes to psychosocial factors. Another strength is the use of validated questionnaires for depression, generalized anxiety, and Type-D personality. Furthermore, the results are plausible. The strength of the association between anxiety and seasonal allergies is similar to the one between family predisposition and allergies. Family predisposition is the only variable which is consistent, strong, and dose-dependent associated with allergies [42].

This study has some limitations. First, self-reported data was used without biomaterials (e.g., IgE) to validate the allergy status and no validated questionnaire was used to measure psychosocial stress. This could have led to biased results because persons with a psychosocial burden might report allergies in a different way than persons without psychosocial burden. On the other hand, the overall self-reported prevalence of allergies fits to the results in other German-wide studies [43]. Second, there was a reasonable number of missing values – but a

sensitivity analysis was performed to demonstrate that the missing values did not distort the results. Third, there was only a small number of participants with anxiety or depression within the selected dataset, which could have led to wide confidence intervals and insignificant results. Moreover, the age of the participants started at 39 years, while allergies and mental health issues seem to occur more often in younger adults [43, 44]. This might also affect the effect size of the odds ratios and the significance levels. Finally, the design of the study itself was a limitation because data collection took place at 2 different time points. The extension to environmental medicine was carried out 1 year after the original KORA FF4. This might limit the validity of the results. As the analyzed variables (allergies, mental disorders, personality, social class, and psychosocial stress burden) usually do not change within 1 year, we decided to tolerate this bias in order to analyze the respective variables. Additionally it was not accounted for multiple testing because this exploratory study aimed to generate hypothesis rather than testing them.

Conclusion

The results confirm the relevance of psychosocial factors in association with allergies. We found differences in the psychosocial factors between seasonal and perennial allergies in the dataset. Longitudinal studies are needed to determine the direction of the associations and additional research is needed to understand the underlying mechanisms of the associations. The measurement of allergies should not only include self-reported data but also skin prick tests or IgE. Other psychosocial factors, such as risk perception, resilience, or coping strategies, should be investigated as well.

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Statement of Ethics

The investigations were carried out in accordance with the Declaration of Helsinki, including the written informed consent of all participants. All study methods were approved by the ethics committee of the Bavarian Chamber of Physicians, Munich (FF4: EC No. 06068).

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

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Author Contributions

K.H., G.H. and C.T.-H. were responsible for the conception of the study. L.K., B.L., A.P., L.S., H.J., K.-H.L. and C.T.-H. collected data. K.H. analyzed the data and drafted the manuscript. G.H., L.S., K.-H.L., B.L., J.R., and C.T.-H. critically revised the article. All authors approved of the version to be published.

References

1 Gieler U, Niemeier V, Kupfer J. Allergie und Psychosomatik. In: Biedermann T, Heppt W, Renz H, Röcken M, editors. Allergologie. Berlin, Heidelberg: Springer-Verlag; 2016. pp. 453–62.

2 Chida Y, Hamer M, Steptoe A. A bidirectional relationship between psychosocial factors and atopic disorders: a systematic review and meta-analysis. Psychosom Med. 2008 Jan;70(1):102–16.

3 Mercer MJ, Joubert G, Ehrlich RI, Nelson H, Poyser MA, Puterman A, et al. Socioeconomic status and prevalence of allergic rhinitis and atopic eczema symptoms in young adolescents. Pediatr Allergy Immunol. 2004 Jun;15(3):234–41.

4 von Mutius E, Martinez FD, Fritzsch C, Nicolai T, Reitmeir P, Thiemann HH. Skin test reactivity and number of siblings. BMJ. 1994 Mar;308(6930):692–5.

5 Sansone RA, Sansone LA. Allergic rhinitis: relationships with anxiety and mood syndromes. Innov Clin Neurosci. 2011 Jul;8(7):12–7.

6 Patterson AM, Yildiz VO, Klatt MD, Malarkey WB. Perceived stress predicts allergy flares. Ann Allergy Asthma Immunol. 2014 Apr;112(4):317–21.

7 Montoro J, Mullol J, Jáuregui I, Dávila I, Ferrer M, Bartra J, et al. Stress and allergy. J Investig Allergol Clin Immunol. 2009;19 Suppl 1:40–7.

8 Langewitz W, Izakovic J, Wyler J, Schindler C, Kiss A, Bircher AJ. Effect of self-hypnosis on hay fever symptoms - a randomised controlled intervention study. Psychother Psychosom. 2005;74(3):165–72.

9 Miller GE, Cohen S. Psychological interventions and the immune system: a meta-analytic review and critique. Health Psychol. 2001 Jan;20(1):47–63.

10 Chida Y, Steptoe A, Hirakawa N, Sudo N, Kubo C. The effects of psychological intervention on atopic dermatitis. A systematic review and meta-analysis. Int Arch Allergy Immunol. 2007;144(1):1–9.

11 Denollet J, Sys SU, Stroobant N, Rombouts H, Gillebert TC, Brutsaert DL. Personality as independent predictor of long-term mortality in patients with coronary heart disease. Lancet. 1996 Feb;347(8999):417–21.

12 Denollet J, de Jonge P, Kuyper A, Schene AH, van Melle JP, Ormel J, et al. Depression and Type D personality represent different forms of distress in the Myocardial INfarction and Depression - Intervention Trial (MIND-IT). Psychol Med. 2009 May;39(5):749–56.

13 Kim SR, Kim HK, Kang JH, Jeong SH, Kim HY, Kim SR, et al. Does type D personality affect symptom control and quality of life in asthma patients? J Clin Nurs. 2015 Mar;24(5-6):739–48.

14 Ring J, Akdis C, Behrendt H, Lauener RP, Schäppi G, Akdis M, et al. Davos declaration: allergy as a global problem. Allergy. 2012 Feb;67(2):141–3.

15 Ring J, Akdis C, Lauener R, Schäppi G, Traidl-Hoffmann C, Akdis M, et al. Global Allergy Forum and Second Davos Declaration 2013 Allergy: barriers to cure—challenges and actions to be taken. Allergy. 2014 Aug;69(8):978–82.

16 Schmitz R, Kuhnert R, Thamm M. 12-Monats-Prävalenz von Allergien in Deutschland. Journal of Health Monitoring. 2017;2(1):77–82.

17 Böcking C, Renz H, Pfefferle PI. [Prevalence and socio-economic relevance of allergies in Germany]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2012 Mar;55(3):303–7.

18 Traidl-Hoffmann C. [Allergy - an environmental disease]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2017 Jun;60(6):584–91.

19 Campbell AP, Hoehle LP, Phillips KM, Caradonna DS, Gray ST, Sedaghat AR. Depressed mood is associated with loss of productivity in allergic rhinitis. Allergy. 2018 May;73(5):1141–4.

20 Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB, et al.; Global Allergy and Asthma European Network; Grading of Recommendations

Assessment, Development and Evaluation Working Group. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. J Allergy Clin Immunol. 2010 Sep;126(3):466–76.

21 Holle R, Happich M, Löwel H, Wichmann HE; MONICA/KORA Study Group. KORA–a research platform for population based health research. Gesundheitswesen. 2005 Aug;67 Suppl 1):S19–25.

22 Helmert U, Shea S. Social inequalities and health status in western Germany. Public Health. 1994 Sep;108(5):341–56.

23 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001 Sep;16(9):606–13.

24 Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006 May;166(10):1092–7.

25 Denollet J. DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. Psychosom Med. 2005 Jan-Feb;67(1):89–97.

26 Lu Y, Mak KK, van Bever HP, Ng TP, Mak A, Ho RC. Prevalence of anxiety and depressive symptoms in adolescents with asthma: a meta-analysis and meta-regression. Pediatr Allergy Immunol. 2012 Dec;23(8):707–15.

27 Dieris-Hirche J, Gieler U, Kupfer JP, Milch WE. Suizidgedanken, Angst und Depression bei erwachsenen Neurodermitikern. Hautarzt. 2009 Aug;60(8):641–6.

28 Thyssen JP, Hamann CR, Linneberg A, Dantoft TM, Skov L, Gislason GH, et al. Atopic dermatitis is associated with anxiety, depression, and suicidal ideation, but not with psychiatric hospitalization or suicide. Allergy. 2018 Jan;73(1):214–20.

29 Ferro MA, Van Lieshout RJ, Ohayon J, Scott JG. Emotional and behavioral problems in adolescents and young adults with food allergy. Allergy. 2016 Apr;71(4):532–40.

30 Schmidt-Traub S, Bamler KJ. The psychoimmunological association of panic disorder and allergic reaction. Br J Clin Psychol. 1997 Feb;36(Pt 1):51–62.

31 Trikojat K, Luksch H, Rösen-Wolff A, Plessow F, Schmitt J, Buske-Kirschbaum A. “Allergic mood” - Depressive and anxiety symptoms in patients with seasonal allergic rhinitis (SAR) and their association to inflammatory, endocrine, and allergic markers. Brain Behav Immun. 2017 Oct;65:202–9.

32 Sanna L, Stuart AL, Pasco JA, Jacka FN, Berk M, Maes M, et al. Atopic disorders and depression: findings from a large, population-based study. J Affect Disord. 2014 Feb;155:261–5.

33 Bell IR, Jasnoski ML, Kagan J, King DS. Depression and allergies: survey of a nonclinical population. Psychother Psychosom. 1991;55(1):24–31.

34 Hashimoto M, Sato EF, Hiramoto K, Kasahara E, Inoue M. Role of the hypothalamo-pituitary-adrenal axis in the modulation of pollinosis induced by pollen antigens. Allergol Int. 2010 Jun;59(2):201–6.

35 Eibich P. Understanding the effect of retirement on health: mechanisms and heterogeneity. J Health Econ. 2015 Sep;43:1–12.

36 Schilling OK, Diehl M. Reactivity to stressor pile-up in adulthood: effects on daily negative and positive affect. Psychol Aging. 2014 Mar;29(1):72–83.

37 Segal DL, Coolidge FL, Mincic MS, O’Riley A. Beliefs about mental illness and willingness to seek help: a cross-sectional study. Aging Ment Health. 2005 Jul;9(4):363–7.

38 Robb C, Haley WE, Becker MA, Polivka LA, Chwa HJ. Attitudes towards mental health care in younger and older adults: similarities and differences. Aging Ment Health. 2003 Mar;7(2):142–52.

39 Beck U. Erstausg. 1st ed. Frankfurt am Main: Suhrkamp; 1986.[Risk society: Towards a new modernity].

40 Statistisches Bundesamt (Destatis). Kinderlosigkeit, Geburten und Familien. Ergebnisse des Mikrozensus 2016. 2017.

41 Hermann-Kunz E. Häufigkeit allergischer Krankheiten in Ost- und Westdeutschland. Gesundheitswesen. 1999 Dec;61(Spec No):S100–5.

42 von Mutius E. Epidemiologie allergischer Erkrankungen. In: Heppt W, Renz H, Röcken M, editors. Allergologie. Berlin, Heidelberg: Springer Verlag; 1998. pp. 1–12.

43 Langen U, Schmitz R, Steppuhn H. [Prevalence of allergic diseases in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1)]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2013 May;56(5-6):698–706.

44 Busch MA, Maske UE, Ryl L, Schlack R, Hapke U. [Prevalence of depressive symptoms and diagnosed depression among adults in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1)]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2013 May;56(5-6):733–9.

Appendix after References (Editorial Comments)

Legend(s)

Fig. 1. Participant flow: From the baseline study KORA S4 to the Environmental Medicine Survey. The participant flow from KORA S4 to the extension of KORA FF4 to environmental medicine is shown in Figure 1 (from top to bottom). Between the baseline study KORA S4 and the second follow-up study KORA FF4 the first follow-up study (F4) took place between 2006 and 2008. KORA F4 is not shown in the participant flow. The KORA FF4 study took place from June 2013 to September 2014. The Environmental Medicine Survey was conducted with a self-report questionnaire, which was sent by post to all study participants of KORA FF4 and filled in between March and August 2015. For the statistical analysis only participants of the Environmental Medicine Survey were taken into account.

Fig. 2. Raw and adjusted ORs for seasonal, perennial, and other forms of allergies (multinomial logistic regression models). The forest plots show ORs as small boxes and CIs as horizontal lines. Raw ORs are grey and adjusted ORs are black. Adjusted ORs derive from a multinomial logistic regression model. In this model, the allergy status was defined as a dependent variable and psychosocial factors as well as covariates were defined as independent variables (sex, age, family predisposition, smoking status, social class, depression, generalized anxiety, stress, Type-D personality). Missing values were excluded.

Table(s)

Footnote(s)

Table 1. Description of the study population

Variables	*n* (*n* = 1,782)	% Mean ± SD
Gender		
Male	872	48.9
Female	910	51.1
Age, years	1,782	61.0±12.1
Age groups		
39–50	431	24.2
51–60	446	25.0
61–70	451	25.3
≥71	454	25.5
Family predisposition		
No	1,655	92.9
Yes	127	7.1
Smoking status		
Non-smoker	1,539	86.4
Smoker	243	13.6
Depression		
No	1,712	96.1
Yes	69	3.9
Generalized anxiety		
Minimal and mild	1,364	76.5
Moderate and severe	72	4.0
Mental stress burden		
No	755	42.4
Yes	585	32.8
Type-D personality		
No	1,141	64.0
Yes	301	16.9
Social class index[a]	1,782	15.1±5.0
Social classes		
Lower class	271	15.2
Middle class	1,033	58.0
Upper class	478	26.8
Allergy status		
No allergies	1,293	72.6
Seasonal allergies only	137	7.7
Perennial allergies (± seasonal)	109	6.1
Other allergies (± seasonal or perennial)	243	13.6

[a] After Helmert and Shea (Scale from 1 to 27).

Table 2. Differences between non-allergic subjects, seasonal allergies, perennial allergies and other forms of allergy in sociodemographic, socioeconomic, and psychosocial factors

	No allergies (*n* = 1,293), *n* (%)	Seasonal allergies only (*n* = 137), *n* (%)	Perennial allergies (± seasonal) (*n* = 109), *n* (%)	Other allergies (± seasonal or perennial) (*n* = 243), *n* (%)	Signifi-cance *p* value[a]
Gender					
Male	673 (52.1)	67 (48.9)	49 (45.0)	83 (34.2)	<0.0001
Female	620 (48.0)	70 (51.1)	60 (55.1)	160 (65.8)	
Age, years, mean ± SD	62.4±11.9	55.5±11.1	54.8±10.9	59.0±11.8	<0.0001
Age groups					
39–50	258 (20.0)	55 (40.2)	48 (44.0)	70 (28.8)	<0.0001
51–60	305 (23.6)	38 (27.4)	35 (32.1)	68 (28.0)	
61–70	351 (27.2)	28 (20.4)	13 (11.9)	59 (24.3)	
≥71	379 (29.3)	16 (11.7)	13 (11.9)	46 (18.9)	
Family predisposition					
No	1,240 (95.9)	119 (86.9)	89 (81.7)	207 (85.2)	<0.0001
Yes	53 (4.1)	18 (13.1)	20 (18.4)	36 (14.8)	
Smoking status					
Non-smoker	1,098 (84.9)	122 (89.1)	99 (90.8)	220 (90.5)	0.04
Smoker	195 (15.1)	15 (11.0)	10 (9.2)	23 (9.5)	
Depression					
No	1,247 (96.4)	131 (95.6)	102 (93.6)	232 (95.5)	0.4
Yes	45 (3.5)	6 (4.4)	7 (6.4)	11 (4.5)	
Generalized anxiety					
Minimal and mild	971 (75.1)	112 (81.8)	96 (88.1)	185 (76.2)	0.02
Moderate and severe	42 (3.3)	11 (8.0)	3 (2.8)	16 (6.6)	
Mental stress burden					
No	569 (44.0)	58 (42.3)	41 (37.6)	87 (35.8)	<0.0001
Yes	368 (28.5)	59 (43.1)	49 (45.0)	109 (44.9)	
Type-D personality					
No	806 (62.3)	99 (72.3)	73 (67.0)	163 (67.1)	0.4
Yes	211 (16.3)	22 (16.1)	27 (24.8)	41 (16.9)	
Social class index[a], mean ± SD	15.0±5.1	15.7±5.0	15.7±5.0	15.4±4.9	0.2
Social classes					
Lower class	207 (16.0)	14 (10.2)	17 (15.6)	33 (13.6)	0.4
Middle class	749 (57.9)	86 (62.8)	56 (51.4)	142 (58.4)	
Upper class	337 (26.1)	37 (27.0)	36 (33.0)	68 (28.0)	

[a] Results of chi-square tests for nominal and ordinal measurement scales or Kruskall-Wallis tests for not normally distributed variables with interval measurement scales (age and social class index, Kolmogorov-Smirnov test: $p < 0.01$ respectively).

[b] After Helmert and Shea (Scale from 1 to 27).

Table 3. Raw and adjusted Odds Ratios of the associations between allergies and sociodemographic, socioeconomic, and psychosocial factors (multinomial logistic regression models)

	Seasonal allergies		Perennial allergies (± seasonal)		Other allergies (± seasonal or perennial)	
	raw OR (95% CI)	adjusted OR[a] (95% CI)	raw OR (95% CI)	adjusted OR[a] (95% CI)	raw OR (95% CI)	adjusted OR[a] (95% CI)
Gender						
Male	1.0	1.0	1.0	1.0	1.0	1.0
Female	1.1 (0.8–1.6)	0.9 (0.6–1.4)	1.3 (0.9–2.0)	1.2 (0.7–1.9)	2.1 (1.6–2.8)***	1.9 (1.3–2.8)**
Age groups						
39–50	1.0	1.0	1.0	1.0	1.0	1.0
51–60	0.6 (0.4–0.9)*	0.7 (0.4–1.2)	0.6 (0.4–1.0)*	0.6 (0.4–1.1)	0.8 (0.6–1.2)	1.0 (0.7–1.5)
61–70	0.4 (0.2–0.6)***	0.5 (0.3–1.0)*	0.2 (0.1–0.4)***	0.2 (0.1–0.3)***	0.6 (0.4–0.9)*	0.8 (0.5–1.3)
≥71	0.2 (0.1–0.4)***	0.2 (0.1–0.8)*	0.2 (0.1–0.3)***	0.2 (0.04–0.7)**	0.4 (0.3–0.7)***	0.4 (0.1–1.1)
Family predisposition						
No	1.0	1.0	1.0	1.0	1.0	1.0
Yes	3.5 (2.0–6.2)***	2.4 (1.2–4.5)**	5.3 (3.0–9.2)***	2.9 (1.5–5.8)**	4.1 (2.6–6.4)***	3.2 (1.9–5.4)***
Smoking status						
Non-smoker	1.0	1.0	1.0	1.0	1.0	1.0
Smoker	0.7 (0.4–1.2)	0.5 (0.3–1.0)*	0.6 (0.3–1.1)	0.3 (0.1–0.7)**	0.6 (0.4–0.9)	0.6 (0.4–1.0)*
Depression						
No	1.0	1.0	1.0	1.0	1.0	1.0
Yes	1.3 (0.5–3.0)	0.9 (0.3–3.2)	1.9 (0.8–4.3)	7.6 (2.1–27.9)**	1.3 (0.7–2.6)	0.9 (0.3–2.7)
Generalized Anxiety						
Minimal and mild	1.0	1.0	1.0	1.0	1.0	1.0
Moderate and severe	2.3 (1.1–4.5)*	2.7 (1.0–7.1)*	0.7 (0.2–2.4)	0.1 (0.02–0.7)*	2.0 (1.1–3.6)*	1.9 (0.8–4.3)
Mental stress burden						
No	1.0	1.0	1.0	1.0	1.0	1.0
Yes	1.6 (1.1–2.3)*	1.1 (0.7–1.7)	1.8 (1.2–2.9)**	1.0 (0.6–1.6)	1.9 (1.4–2.6)***	1.4 (0.9–2.0)
Type-D personality						
No	1.0	1.0	1.0	1.0	1.0	1.0
Yes	0.8 (0.5–1.4)	0.7 (0.4–1.3)	1.4 (0.9–2.3)	1.6 (0.9–2.7)	1.0 (0.7–1.4)	1.0 (0.7–1.6)
Social classes						
Lower class	1.0	1.0	1.0	1.0	1.0	1.0
Middle class	1.7 (0.9–3.0)	1.1 (0.5–2.2)	0.9 (0.5–1.6)	0.5 (0.3–1.1)	1.2 (0.8–1.8)	1.2 (0.6–2.3)
Upper class	1.6 (0.9–3.1)	0.9 (0.4–1.9)	1.3 (0.7–2.4)	0.8 (0.4–1.8)	1.3 (0.8–2.0)	1.4 (0.7–2.7)

[a] The allergy status was defined as dependent variable, all psychosocial factors and all covariates were defined as independent variables in the model (sex, age, family predisposition, smoking status, social class, depression, generalized anxiety, stress, Type-D). Missing values were excluded (*n* = 992).

* The association is significant on the level <0.05.

** The association is significant on the level <0.01.

*** The association is significant on the level <0.0001.

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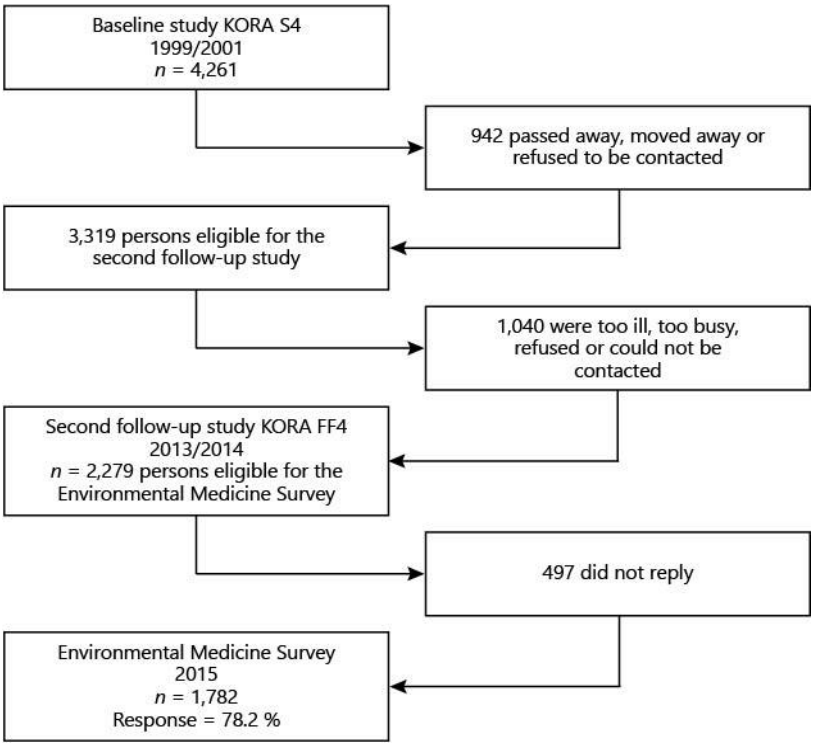

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