Secular Trends and Rural–Urban Differences in Diagnostic Prevalence of Hay Fever: A Claims-Based Study in Germany

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Purpose: We aimed to examine possible variations in diagnostic prevalence of hay fever between urban and rural regions as well as in age-specific temporal developments.

Patients and Methods: We used nationwide outpatient claims data from the years 2010 to 2019. The data contain information for all individuals with statutory health insurance (SHI) in Germany who were treated at least once in respective years (n = 71,410,121 in 2019). Individuals with a confirmed diagnosis of hay fever were defined as prevalent cases. We examined the association between the degree of urbanization and age- and sex-standardized prevalence of hay fever. We used the age- and sex-structure of SHI insurees in the year 2010 as a reference population for direct standardization.

Results: The standardized prevalence of hay fever increased from 6.2% in 2010 to 7.2% in 2019, corresponding to a relative increase of 16%. However, we observed a clear decrease in prevalence among children, with the strongest relative reduction in young children (0–2 years: −53%). The standardized prevalence in the total population in 2019 was lowest in rural areas with a low population density (6.6%) and highest in big urban municipalities (7.8%). In stark contrast, prevalence in 0–14-year-olds was lowest in big urban municipalities (4.3%).

Conclusion: We observed a decrease in the prevalence of hay fever in children and increase in the older age groups. A clear urban–rural association observed over years may be explained by environmental factors. Deviations from this general regional pattern in children of the age group 0–14 years may be explained by differing age-specific risk factors of hay fever.

Keywords: diagnostic prevalence, hay fever, urban–rural differences, statutory health insurance, temporal trends, Germany

Introduction

According to estimations, about 30 million individuals in Germany suffer from allergic diseases. One of the most common allergic diseases in all age groups is hay fever (pollinosis). The Health Surveys of the Robert Koch Institute report nationwide representative data on the frequency of allergic diseases including hay fever. The lifetime prevalence of hay fever among children and adolescents was 10.7% [95% confidence interval (CI): 10.2–11.3%] in the baseline KiGGS study (“German Health Interview and Examination Survey for Children and Adolescents”) from the years 2003 to 2006. In the following two survey waves, an increase was seen in the years 2009–2011 up to a lifetime prevalence of 12.6% [95% CI: 11.8–13.5%] and a later decrease in the years 2014–2017 to 11.0% [95% CI: 10.3–11.8%].

Several interview and examination studies were conducted in adults that provide representative prevalence data on allergic diseases, including the GEDA study (“German Health Update study”) and the DEGS study (“Study on the Health of Adults in Germany”). In the GEDA study (2014–2015), 28.1% [95% CI: 27.3–29.0%] of the participants reported at least one allergic disease in the last 2 months. A somewhat higher prevalence of at least one allergic disease (34.7%
[95% CI: 33.4–36.0%]) was observed in the recent GEDA study (2019–2020). However, these studies did not differentiate across various allergic diseases such as hay fever.

The lifetime prevalence of hay fever in adults was investigated in the DEGS study, showing a prevalence of 14.8% [95% CI: 13.9–15.8%] in the years 2008–2011. Hereby, differences between rural and urban regions were found for allergic diseases in general. The lifetime prevalence of at least one allergic disease was significantly increased among individuals living in big cities (≥100,000 inhabitants) with 33.2% [95% CI: 30.9–35.6%] compared to those living in towns with 5000 to <20,000 inhabitants: 26.5% [95% CI: 23.9–29.3%]. However, no clear urban–rural gradient was found, as the prevalence in rural municipalities (<5000 inhabitants: 28.7% [95% CI: 25.4–32.2%]) was higher compared to towns with 5000 to <20,000 inhabitants. Also, the difference between big cities and rural areas was not statistically significant. An assessment of regional differences in the prevalence of hay fever was not part of the DEGS study. In a recent study from South Germany, Tizek et al examined the rural–urban differences across various allergic diseases, including hay fever. Participants from rural (6.1%) and suburban areas (8.3%) were less likely to report hay fever than those living in urban areas (18.4%). This association pattern remained even after controlling for further variables such as sex, age and occupation.

Little is known about regional, especially small-area variations of allergic diseases in Germany. In an earlier study, we have reported a noticeable variation in the prevalence of asthma on district level. Furthermore, local spatial clusters were present with an increased prevalence in Lower Saxony, North Rhine-Westphalia, Schleswig-Holstein and Thuringia. The risk of developing asthma was also higher in urban as compared to rural regions. Urban–rural differences of allergic diseases have also been reported in international studies. However, no small-area investigations on hay fever in Germany are available so far.

We aimed to examine possible variations in diagnostic prevalence of hay fever between urban and rural regions as well as in age-specific temporal developments.

Material and Methods

Data and Study Population

This study is based on nationwide pseudonymized outpatient claims data encompassing all German statutory health insurances (SHI) according to §295 of the Social Code Book V (SGB V) in the years 2010 to 2019. In brief, about 87% of the total population in Germany were insured statutorily in 2019. About 178,000 SHI-authorized physicians in Germany provided medical care in 2019. They are represented by the 17 regional Associations of Statutory Health Insurance Physicians (ASHIP), through which they submit their claims for provided medical services to the patients’ health insurance fund. The database is a comprehensive collection of administrative outpatient data of all SHI insurees who received outpatient medical services during the study period. Besides demographic characteristics such as age, sex and place of residence, the data include, amongst others, information on provided medical services and diagnoses as well as physician-related characteristics such as specialist group and practice location.

Case Ascertainment

SHI-authorized physicians code diagnoses according to the German Modification of the 10th edition of the International Classification of Diseases and related Health Problems (ICD-10-GM). In addition, they use diagnostic modifiers such as “confirmed diagnosis”, “suspected diagnosis” or “cured diagnosis” to increase diagnostic certainty. Hay fever was defined by the ICD-10 codes “J30.1” (allergic rhinitis due to pollen), “J30.2” (other seasonal allergic rhinitis), or “J30.4” (allergic rhinitis, unspecified) additionally coded as “confirmed” in at least one quarter of the year. The three codes J30.1, J30.2, and J30.4 showed mostly concurrent seasonality, while J30.3 (“other allergic rhinitis”) differed considerably and therefore was not used to code hay fever (Supplementary Figure 1).

Regional Differences

Regional differences in the diagnostic prevalence on ASHIP and district level were examined using the age- and sex-standardized prevalence. In addition, differences in the standardized prevalence of hay fever were examined between
eastern and western Germany. We used the age- and sex-structure of SHI insurees in the year 2010 as a reference population for direct standardization. The degree of urbanization was adopted from the Federal Institute for Research on Building, Urban Affairs and Spatial Development (BBSR), which classifies districts into four groups based on their settlement structure. This classification comprises rural areas with a low population density, rural areas with population concentrations, urban districts, and big urban municipalities.

**Statistical Analysis**

The annual diagnostic prevalence was calculated as the proportion of patients with the above-mentioned diagnosis codes among all insurees who received outpatient services in the respective year. This analysis was done by sex, age as well as on district level (402 districts, administrative territorial status in 2011 corresponding to the level 3 of the Nomenclature of Territorial Units for Statistics [ie NUTS 3]). The age segment of 0–14 years was divided into four groups (0–2, 3–6, 7–10 and 11–14 years) and the age segment of ≥15 years into 5-year age groups. In addition, the total prevalence was age- and sex-standardized and the prevalence by sex was age-standardized. A potential relationship between the degree of urbanization and the age- and sex-standardized prevalence was assessed on the district level by Kruskal–Wallis test.

**Results**

**Temporal Trends in Diagnostic Prevalence**

Overall, 5,043,224 patients (of whom 439,279 [8.7%] were children and adolescents) received a confirmed diagnosis of hay fever in the year 2019, corresponding to a crude diagnostic prevalence of 7.1% in the population of all SHI insurees. Both, the crude as well as the age- and sex-standardized prevalence increased over the study period of 10 years (Table 1 and Figure 1). The latter increased from 6.2% in 2010 to 7.2% in 2019 (+16%) (Figure 1). A stepwise increment over time was observed for both males and females (Table 1). In 2019, females showed a 7% higher prevalence than males (females 7.4% vs males 7.0%; Figure 1). Of the 5,043,224 patients with at least one diagnosis of hay fever in the year 2019, 34% were diagnosed in only one, 19% in two, 17% in three and 30% in all four quarters.

**Differences in Prevalence by Sex and Age**

Comparing the age- and sex-specific prevalence between the years 2010 and 2019, a considerable decrease can be observed over time among children (Figure 2). The difference between 2010 and 2019 was most pronounced in the age group of 0–2 years for both sexes. Here, a prevalence reduction of 53% from 1.0% to 0.49% was seen in girls, and from 1.1% to 0.53% in boys. In the age group 3–6 years the decline was 37% in girls (prevalence 2010: 2.6% and 2019: 1.7%) and 32% in boys (2010: 4.2% and 2019: 2.8%). A less pronounced decline was observed in the age group 7–10 years; 16% in girls (2010: 5.6% and 2019: 4.7%) and 13% in boys (2010: 8.7% and 2019: 7.6%, Figure 2). The prevalence of hay fever among males increased with age and peaked in the age group 11–14 years in both years (prevalence 2010: 11.0% and 2019: 10.8%). In contrast to men, a two-peaked distribution was found in women in the beginning as well as at the end of the study period. The first peak was observed in the age group 15–19 years in all study years. The second peak had its highest value of 8.7% in 2010 in the age group of 35–39 years and shifted to the age group 45–49 years in 2019 (10.0%). This trend resulted from an increasing prevalence over time in the entire age segment of ≥25 years in both sexes. The strongest absolute increase in hay fever prevalence during the study period was observed in men in the age group 50–54 years with 2.6 percentage points (2010: 5.2% and 2019: 7.8%) and in women with 2.5 percentage points in the age group 70–74 years (2010: 4.0% and 2019: 6.6%), which corresponds to relative increases of 50% and 63%, respectively (Figure 2).

**Urban–Rural Differences**

Figure 2A shows the district-specific age- and sex-standardized prevalence of hay fever by district type in the year 2019. Diagnostic prevalence was higher in urban compared to rural areas (p<0.0001, df=3, n=402, Kruskal–Wallis test). The age- and sex-standardized prevalence increased with the degree of urbanization (Figure 3A). In the year 2019, the standardized prevalence was lowest in rural areas with a low population density (6.6%), followed by rural areas with population concentrations (6.9%), urban districts (7.3%) and big urban municipalities (7.8%). This pattern was observed in all reported
### Table 1: Annual Nationwide Administrative Prevalence of Hay Fever, Overall and by Sex in the Years 2010 to 2019

<table>
<thead>
<tr>
<th>Years</th>
<th>Overall</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Population, N</td>
<td>Patients, n</td>
<td>Prevalence, % (95% CI)</td>
</tr>
<tr>
<td>2012</td>
<td>68,959,472</td>
<td>4,259,735</td>
<td>6.18 (6.17, 6.18)</td>
</tr>
<tr>
<td>2013</td>
<td>69,699,277</td>
<td>4,536,457</td>
<td>6.51 (6.50, 6.51)</td>
</tr>
<tr>
<td>2015</td>
<td>69,777,509</td>
<td>4,760,917</td>
<td>6.82 (6.82, 6.83)</td>
</tr>
<tr>
<td>2017</td>
<td>71,006,438</td>
<td>4,785,443</td>
<td>6.74 (6.73, 6.75)</td>
</tr>
<tr>
<td>2018</td>
<td>72,057,156</td>
<td>4,990,445</td>
<td>6.93 (6.92, 6.93)</td>
</tr>
<tr>
<td>2019</td>
<td>71,410,121</td>
<td>5,043,224</td>
<td>7.06 (7.06, 7.07)</td>
</tr>
</tbody>
</table>

**Note:** Source: Nationwide outpatient claims data encompassing all German statutory health insurances according to §295 SGB V.

**Abbreviation:** CI, confidence interval.
years (Figure 3B). In the year 2010, the standardized prevalence was 26% higher in big urban municipalities with 6.8% compared to rural areas with a low population density with a prevalence of 5.4% – rural areas with population concentrations and urban districts were in between with 5.8% and 6.4%, respectively (Figure 3B). However, rural areas with a low population density and rural areas with population concentrations showed stronger increases of +22% and +20% during the study period, respectively, while the increase was less pronounced in urban districts with +14% and big urban municipalities with +16%. Accordingly, variations in the prevalence across the four district types decreased slightly over the study period.
Figure 3  Age- and sex-standardized diagnostic prevalence of hay fever in districts by district type in 2019 (A), its development over time (2010–2019) by district type (B) and age-specific prevalence by district type in 2019 with prevalence ratios as the quotient of the prevalence in big urban municipalities and in rural areas with a low population density (C).

Notes: The classification of districts into four district types was adopted from the Federal Institute for Research on Building, Urban Affairs and Spatial Development (BBSR). In (A) and (B), age- and sex-standardized prevalence was used. The population of all SHIs in Germany was used as a standard reference for direct standardization. Source: Nationwide outpatient claims data encompassing all German statutory health insurances according to §295 SGB V.
In the year 2019, a growth in standardized prevalence of hay fever by degree of urbanization was found for most of the age groups under investigation (Figure 3C). An exception were, however, children in the age group 0–14 years: In strong contrast to the overall population they showed the lowest values in big urban municipalities (4.3%), followed by urban districts (4.5%). The highest value for this age group was seen in rural areas with population concentrations (4.6%), with only slight differences to rural areas with a low population density (4.6%, Figure 3C). The distribution in all higher age groups was characterized by a prevalence rising with the degree of urbanization. At this, the relative difference between rural areas with a low population density and big urban municipalities grew with advancing age (Figure 3C). While the prevalence ratio was 1.08 [95% CI: 1.07–1.09] in those aged 25–34 years, it increased continuously by age up to 1.84 [95% CI 1.79–1.89] in those aged >84 years, thereby corresponding to a 84% higher prevalence in big urban municipalities than in rural areas with a low population density (Figure 3C).

Regional Differences
The age- and sex-standardized prevalence in 2019 was 7.3% in western and 7.2% in eastern Germany (without Berlin; prevalence in Berlin: 7.5%). The ratio of the standardized prevalence in western compared to eastern Germany amounted to 1.04 in 2010 and showed a declining trend over the study period (Supplementary Figure 2). This effect disappeared in 2019 (prevalence ratio = 1.00).

Across ASHIP regions in 2019, the by far highest age- and sex-standardized prevalence was observed in Hamburg (8.3%) followed by North Rhine (7.9%), Saxony (7.9%) and Hesse (7.7%, Figure 4A). Baden-Württemberg (6.4%) and Schleswig-Holstein (6.7%, Figure 4A) showed the lowest values.

Figure 4 Age- and sex-standardized diagnostic prevalence of hay fever in ASHIP regions (A) and by district (B) in 2019.
Notes: Five classes with equal intervals were created. Source: Nationwide outpatient claims data encompassing all German statutory health insurances according to §295 SGB V. ASHIP, regional Associations of Statutory Health Insurance Physicians. In total, there are 17 ASHIPs in Germany, of which 15 corresponding to 15 German federal states and two ASHIPs existing in the federal state of North Rhine-Westphalia. 402 districts according to the administrative structure of 31.12.2011. The population of all SHIs in Germany was used as a reference population for direct standardization.
On district level, the age- and sex-standardized prevalence of hay fever varied by a factor of 2 in 2019 between 4.3% (district of Tuttlingen, Baden-Württemberg) and 9.6% (district of Fürth, Bavaria) (Figure 4B). High prevalence with values over ≥8.5% was identified in some districts in Bavaria (n=7), Lower Saxon (n=5), North Rhine (n=5), Rhineland-Palatinate (n=4), Westphalia-Lippe (n=2), Saxony (n=2) and Thuringia (n=1) (Figure 4B).

Discussion
The present study investigated the prevalence of diagnosed hay fever in SHI insurees over time and by age and urbanization degree of the place of residence. Overall and for adults, an increase in the prevalence of hay fever was observed during the 10-year study period. An exception was the entire pediatric age segment that showed a decrease in the diagnostic prevalence of hay fever between 2010 and 2019. Here, a distinct prevalence reduction of 53% was seen in toddlers. In the overall population of all SHI insurees who used outpatient medical services, a clear and timewise stable urban–rural difference in prevalence was revealed. However, a prevalence below average was observed among children and adolescents living in big urban municipalities and urban districts.

Temporal Changes in Prevalence of Hay Fever
In the course of the 10-year study period, the annual prevalence of diagnosed hay fever among SHI insurees increased gradually about 16%. The absolute number of patients in outpatient treatment for hay fever grew by 800,000 up to about 5 million between the years 2010 and 2019. Although the findings of our study are not directly comparable with findings from population-based studies of the RKI mainly due to methodological differences in assessing the outcome variable, we observed several similarities. In accordance with results from the DEGS1 study, we found a higher prevalence among women than men in adult age, resulting in a moderately higher prevalence in female insurees over the entire age spectrum. Also, in line with the KiGGS study, a reversed pattern of the sex-specific values was found in children and adolescents, which was characterized by a higher prevalence in boys than in girls. This age- and sex-interaction has also been reported for asthma and could be explained by sex-specific physiological differences.

The age-specific analysis of changes in the prevalence over time showed opposing development in children aged 0–10 years in comparison to the age segment of 25 years and older. In adult age, comparable age group-specific values were found for the relative increase in both sexes. The most pronounced rise was present in the age segment of 80 years and older. The observed pattern of an increase over all adult age groups may also reflect changing patterns of usage of service by those affected. Current numbers from representative studies on the development of the self-reported hay fever prevalence in adults that could be used for further classification of the observed trends are not available for Germany. Comparisons of results from previous surveys based on self-report on diagnosed hay fever show an unchanged 12-month prevalence between 1998 and the study period 2008–2011.

While adults in nearly all age groups showed increasing numbers, the prevalence decreased considerably in children aged 0–10 years with 25% in boys and 30% in girls. Here, toddlers aged 0–2 years showed the highest reduction over both sexes. Also, a comparison between the first (2009–2012) and the second (2014–2017) wave of the KiGGS study suggests a decline of hay fever in young children aged 0–6 years, but not in those aged 7–10 years. According to this, the 12-month prevalence in the age group 0–2 years was 3.4% [95% CI: 2.3–4.9%] in the first wave and 2.8% [95% CI: 1.7–4.4%] in the second wave. The corresponding values in 3–6-year-old children were 5.7% [95% CI: 4.6–7.1%] and 3.3% [95% CI: 2.6–4.3%], respectively. Applying a simplified comparison of confidence intervals in both study waves, reductions were statistically significant only in the age group 3–6 years. As opposed to KiGGS, the present study reveals a substantially declining prevalence trend in the entire pediatric age spectrum, even in the age group of 7–10 years with moderate decreases of 13% (boys) and 16% (girls). This resulted in about 60,000 fewer children aged 6–10 years being affected by diagnosed hay fever in 2019 compared to 2010, despite a higher overall number of children in the SHI in 2019. Owing to comparably moderate relative decreases (girls: −5.0%, boys: −2.5%) in the, however, especially affected age group of 11–14 years, this number accumulated to 88,000 children and adolescents affected in the age spectrum of 0–14 years.
Regional Variations

Regional variations in the distribution of hay fever were examined at different geographical scales, including east-west, rural–urban differences, differences across ASHIP regions and at district level. Numbers for the year 2019 showed an only slightly lower standardized prevalence in eastern compared to western Germany. This unexpected observation points out that the low frequency of atopic diseases in eastern Germany, which was seen after the reunification of eastern and western Germany,² at least for hay fever does not exist anymore. An alignment between eastern and western Germany could already be shown in the frequency of atopies in children and adolescents based on results from KiGGS for the study period of 2003 to 2006,¹⁷ that showed a west-east gradient in the early years after the reunification of Germany.¹⁸ Our results indicate an advancing alignment of the hay fever prevalence between eastern and western Germany in SHI insurees in the study period.

Furthermore, over the study period, a distinct urban–rural association was found for the one-year prevalence in the total SHI population but not in children and adolescents. Overall, the risk of a diagnosed hay fever gradually rose with the degree of urbanization of the place of residence and in 2019 was about 20% higher in big urban municipalities compared to rural areas with a low population density. A lower hay fever prevalence in rural than in urban areas could also be observed in the large majority of international publications on this topic.¹⁹,²⁰ As an explanation for this association, an increased air pollution in urban areas as well as a protective effect of a higher exposure to microorganisms in rural areas have, among other things, been considered.²⁰ According to the hygiene hypothesis, an increased exposure to a high diversity of microorganisms in early life goes along with a decreased occurrence of atopic diseases, including hay fever and asthma.²¹ This explanatory approach has first been developed based on an observed inverse association between family size and the occurrence of atopic diseases.²² Later studies have repeatedly shown that growing up on farms with livestock farming was related to a lower burden of atopic diseases, presumably due to the more intense exposure to a higher microbiotic diversity.²³,²⁴ In the present study, however, no information was available neither on the degree of urbanization of the place of residence in early life nor on the family size or other potentially relevant individual risk factors. Furthermore, whilst seen in the total SHI population, the urban–rural difference could not be observed in children and adolescents. In clear contrast to the urban–rural association in adults, a lower morbidity was seen for the age spectrum of 0–25 years in districts with the two highest degrees of urbanization. In combination with the decreasing prevalence in children compared to adults, these age-specific regional variations may indicate an age-dependency with regard to differently dominating risk factors for hay fever.

Here, for the first time, it could be shown that the urban–rural association of the hay fever prevalence among adults in Germany increased with age and peaked with an increase by the factor of nearly 2 around the age of 85 years.

Strengths and Limitations

Administrative outpatient data show the relevance of hay fever in outpatient care and, due to their actuality and their relatively inexpensive availability, represent an important complement to representative population-based surveys from national health reporting. In contrast to studies with primary data collection, the reliability of the results is not impacted by the participants’ willingness to participate. However, the assessment of morbidity using administrative data depends on the use of outpatient services by the insurees. Patients who were not in contact with a physician cannot be identified as such in our data. However, about 95% of the insurees contact physicians annually.

Yet, investigating the morbidity of atopic diseases in the population comes with specific methodological challenges. As per national and international guidelines, the diagnosis of allergic rhinitis, including hay fever, should be based on both, symptoms and in vivo and/or in vitro detection of allergen-specific IgE. In the present study we only used the ICD-10 codes to identify patients with hay fever. It is unknown whether the diagnoses were based on objectively measured laboratory parameters or symptoms only. Thus, the validity of case ascertainment may be limited. However, this limitation may also apply to population-based primary studies that mainly use self-reported information of the participants on medically diagnosed hay fever which also may be prone to recall bias.²
For the ASHIP region Baden-Württemberg, an underestimation of the hay fever prevalence cannot be excluded due to a comparably large care rate by GP-centered health care, as these data are not available in our datasets. The same applies for the ASHIP region Bavaria, even though to a smaller extent.

Conclusions
A growing prevalence of diagnosed hay fever among SHI insurees in Germany over the study period of ten years indicates increasing use of medical services. Welcome noticeable decreases in the prevalence in the pediatric age groups stand in opposition to the development of hay fever prevalence in adults. A clear urban–rural association observed consistently over the study period likely underlines a substantial relevance of environmental factors in the context of the urbanization degree of the place of residence. Contrasting trends of prevalence and clear differences in regional variations between children and adults suggest age-dependent dissimilarities in dominating risk factors for the occurrence of hay fever.

Abbreviations
ASHIP, Association of Statutory Health Insurance Physicians; BBSR, Federal Institute for Research on Building, Urban Affairs and Spatial Development; CI, confidence intervals; DEGS, Study on the Health of Adults in Germany; GEDA, German Health Update study; ICD-10-GM, German Modification of the 10th edition of the International Classification of Diseases and related Health Problems; KiGGS, German Health Interview and Examination Survey for Children and Adolescents; NUTS, Nomenclature of Territorial Units for Statistics; SCB, Social Code Book; SHI, Statutory Health Insurance.

Ethics Approval
The use of claims data for scientific research is regulated by the Social Code Book (SGB V) in Germany. An ethical approval and informed consent are not required as this study used routinely collected anonymized data. The research was conducted in accordance with the Helsinki Declaration (in its current revised form: 64th WMA General Assembly, Fortaleza, Brazil, October 2013).

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