Trends and regional distribution of outpatient claims for asthma, 2009–2016, Germany
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Objective To investigate asthma morbidity in Germany by calculating current prevalence, examining its temporal and spatial trends and estimating the total number of asthmatics in Germany and calculating age-, sex- and residence-specific risk.

Methods We used claims data reported by physicians during 2009–2016, including outpatient diagnoses of all statutory health insured individuals, comprising 85.3% (70 416,019/82,521,633) of the total population in Germany in 2016. We performed a spatial analysis of asthma prevalence according to administrative district by calculating Global and Local Moran’s I. We assessed the risk of asthma by sex, age, type of residence (rural versus urban) and federal state (East versus West) using a multilevel parametric survival regression.

Findings We estimated that 4.7 million individuals were affected by asthma in 2016, including 0.8 million children and 3.9 million adults. We observed a slightly higher prevalence (with an increasing trend) among adults (5.85%; 3,408,622/58,246,299) compared to children (5.13%; 624,899/12,169,720), and calculated an age-standardized prevalence of 5.76% (95% confidence interval: CI: 5.76–5.77). We found evidence of a strong spatial autocorrelation (Global Moran’s I: 0.50, P < 0.0001), and identified local spatial clusters with higher levels of prevalence. Living in the western (versus eastern) federal states and living in densely populated large urban municipalities (versus rural area) were independently associated with an increased risk of asthma, with hazard ratios of 1.33 (95% CI: 1.32–1.34) and 1.32 (95% CI: 1.31–1.32), respectively.

Conclusion Our insights into the spatial distribution of asthma morbidity may inform public health interventions, including region-specific prevention programmes and control.

Introduction

Asthma is the most frequently diagnosed and chronic, non-communicable, inflammatory disorder among children and adults. According to the latest Global Asthma Report, nearly 340 million individuals worldwide have been diagnosed with asthma; it is estimated that an additional 100 million individuals will be affected by 2025. The prevalence of asthma varies substantially across the globe, and has been shown to vary between countries by up to a factor of 21. Prevalence tends to be higher in developed countries, with the highest reported prevalence of asthma in Australia (21%), Sweden (20%), the United Kingdom of Great Britain and Northern Ireland (18%), the Netherlands (15%) and Brazil (13%); the lowest prevalence of asthma has been observed for Viet Nam (0.8%) and China (0.2%). Some studies, for example in Australia and the United States of America, United Kingdom and Latin American countries, have reported within-country variations. A higher degree of urbanization, associated with a higher exposure to risk factors (e.g. pollution or prenatal stress), has been linked to an increased risk of asthma. Another factor increasing this difference is the so-called hygiene hypothesis, which describes how growing up in a rural environment, with its associated increase in exposure to microbial agents and endotoxins, can have a protective effect against allergic diseases including asthma.

Prevalence estimates of 3–12% among children and 2–5% among adults have been reported in Germany; however, current estimates of asthma incidence are lacking. Regional variations in Germany have only been examined for rough geographical units and for specific age groups (e.g. children or adults). For example, one study demonstrated differences in asthma prevalence among children between East and West Germany. Another study involving only adult participants investigated variations in asthma prevalence across the German federal states.

An examination of regional variation in asthma morbidity is of particular importance as geographical factors, and not just factors related to individual patients, play a considerable role in the pathogenesis of asthma. We therefore provide estimates of asthma morbidity in Germany for the years 2009 to 2016, and examine differences in prevalence with time, residence type (urban versus rural) and geographical location. We also estimate the total number of individuals in Germany currently affected by asthma, and calculate the sex-, age- and residence-specific risk of asthma incidence.

Methods

Data and study population

We used nationwide ambulatory claims data reported by physicians approved to treat statutory health insured individuals in Germany, acquired during 2009–2016. Privately insured members of the population were not included in this study. Claims data contain information on the sex, age and district of residence of outpatients (Germany’s 16 federal states included 402 administrative districts in 2011, 106 of which were urban and 296 rural), as well as diagnoses of individuals who consulted an authorized physician at least once in each year. Diagnoses are coded according to the German modification of the 10th edition of International Classification of Diseases and Related Health Problems (ICD-10-GM, code J45).

Abstracts in العربية, Français, Русский and Español at the end of each article.

References

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Definition of asthma cases
We defined a prevalent case of asthma as one diagnosed in at least two quarters of the corresponding year. In addition, we only included confirmed diagnoses (i.e. those highlighted with the additional diagnostic modifier “assured”). As a sensitivity analysis we also estimated the prevalence based on a single diagnosis of asthma for comparison. An incident case of asthma was defined if it was diagnosed for the first time between 2011 and 2016. Individuals diagnosed with asthma for the first time in 2009 and 2010 were excluded from this analysis.

Statistical analysis
We calculated the sex- and age-specific prevalence of asthma by dividing the number of asthma diagnoses per sex/age category by the total number of individuals with statutory health insurance in that category, for each separate year from 2009 to 2016. We also calculated the age-standardized prevalence, using the direct standardization method, and 95% confidence intervals (CI), although we note that CIs are not particularly informative because of the very large sample size (> 70 million). As a standard population, we used the German population from the year 2015. Using the sex- and age-specific prevalence calculations along with sex- and age-specific population distribution, we estimated the total number of individuals affected by asthma in Germany in 2016.

We performed a spatial analysis of crude asthma prevalence according to administrative district by calculating Global and Local Moran’s I. Districts were divided into four types of areas: (i) rural areas with low population density, that is, a population density less than 150 inhabitants per km²; (ii) rural areas with population concentrations, that is a population density over 150 inhabitants per km² and large urban municipalities had a population above 100,000 inhabitants; (iii) urban districts, that is a population density over 100,000 inhabitants. We used semi-parametric group-based modeling of age-standardized prevalence to identify administrative districts with similar trends in prevalence over the study period (2009–2016), that is, longitudinal clusters or trajectories.

Finally, we performed a Kaplan–Meier analysis to estimate the overall summed incidence of asthma as well as by sex, age (children versus adults), type of residence and federal state. We then used a parametric mixed-effect survival model with individuals (level 1) nested within the 402 districts (level 2) to examine the risk of the incidence of asthma for the first time in 2009 and 2016. Individuals diagnosed with asthma for the first time in 2009 and 2010 were excluded from this analysis.

Table 1. Demographic characteristics of the study population compared with the general population in asthma morbidity study, Germany, 2016

| Characteristic | Study population | General population |
|---------------|------------------|--------------------|
|               | (n = 70416019)   | (n = 82521653)     |
| Sex           |                  |                    |
| Male          | 32 084 893 (45.56) | 40 697 118 (49.32) |
| Female        | 38 331 126 (54.44) | 41 824 535 (50.68) |
| Age, years    |                  |                    |
| 0–4           | 3 448 313 (4.90)  | 3 756 446 (4.55)   |
| 5–9           | 3 047 833 (4.33)  | 3 613 927 (4.38)   |
| 10–14         | 2 959 581 (4.20)  | 3 678 195 (4.46)   |
| 15–19         | 3 468 684 (4.93)  | 4 172 869 (5.06)   |
| 20–24         | 3 863 057 (5.49)  | 4 574 031 (5.54)   |
| 25–29         | 4 625 037 (6.37)  | 5 366 756 (6.50)   |
| 30–34         | 4 455 886 (6.33)  | 5 221 075 (6.33)   |
| 35–39         | 4 241 230 (6.02)  | 5 058 038 (6.13)   |
| 40–44         | 3 901 754 (5.54)  | 4 821 986 (5.84)   |
| 45–49         | 5 034 735 (7.15)  | 6 259 912 (7.59)   |
| 50–54         | 5 741 805 (8.15)  | 6 984 307 (8.46)   |
| 55–59         | 5 174 370 (7.35)  | 6 232 126 (7.54)   |
| 60–64         | 4 396 917 (6.24)  | 5 281 280 (6.40)   |
| 65–69         | 3 846 002 (5.46)  | 4 563 301 (5.53)   |
| 70–74         | 3 173 507 (4.51)  | 3 654 937 (4.43)   |
| ≥ 75          | 9 037 314 (12.83) | 9 291 467 (11.26)  |
| Type of residence |                  |                    |
| Rural areas with low population density | 10 219 972 (14.51) | 11 857 274 (14.37) |
| Rural areas with population concentrations | 12 297 829 (17.46) | 14 028 047 (17.00) |
| Urban districts | 27 732 448 (39.38) | 32 400 372 (39.26) |
| Large urban municipalities | 20 165 770 (28.64) | 24 235 960 (29.37) |
| Federal state |                  |                    |
| Baden-Württemberg | 8 944 264 (12.70) | 10 951 893 (13.27) |
| Bavaria       | 10 742 300 (15.26) | 12 930 751 (15.67) |
| Berlin        | 3 005 218 (4.27)  | 3 574 830 (4.33)   |
| Brandenburg   | 2 167 116 (3.08)  | 2 494 648 (3.02)   |
| Bremen        | 597 995 (0.85)    | 678 753 (0.82)     |
| Hamburg       | 1 552 606 (2.20)  | 1 810 438 (2.19)   |
| Hesse         | 5 264 256 (7.48)  | 6 213 088 (7.53)   |
| Mecklenburg–Western Pomerania | 1 438 593 (2.04) | 1 610 674 (1.95)   |
| Lower Saxony  | 6 884 645 (9.78)  | 7 945 685 (9.63)   |
| North Rhine–Westphalia | 15 547 745 (22.08) | 17 890 100 (21.68) |
| Rhineland–Palatinate | 3 358 821 (4.77) | 4 066 053 (4.93)   |
| Saarland      | 856 620 (1.22)    | 996 651 (1.21)     |
| Saxony        | 3 648 621 (5.18)  | 4 081 783 (4.95)   |
| Saxony–Anhalt | 2 020 774 (2.87)  | 2 236 252 (2.71)   |
| Schleswig–Holstein | 2 445 762 (3.47) | 2 881 926 (3.49)   |
| Thuringia     | 1 940 683 (2.76)  | 2 158 128 (2.62)   |

a German population data for the year 2016 were obtained from the Federal Statistical Office. 

b Rural areas with a population density lower than 100 inhabitants per km² were categorized as low population density, rural areas with a population density less than 150 inhabitants per km² were categorized as rural areas with population concentrations, urban districts were defined as districts with a population density over 150 inhabitants per km² and large urban municipalities had a population above 100,000 inhabitants.
Temporal trends in asthma prevalence according to sex, age and type of residence, Germany, 2009–2016

| Group | Group-specific no. with asthma/Group-specific population (%) | 2009  
\( (n = 70\,388\,055) \) | 2010  
\( (n = 69\,073\,616) \) | 2011  
\( (n = 69\,030\,407) \) | 2012  
\( (n = 68\,954\,969) \) | 2013  
\( (n = 69\,700\,682) \) | 2014  
\( (n = 69\,650\,700) \) | 2015  
\( (n = 69\,799\,319) \) | 2016  
\( (n = 70\,416\,019) \) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sex |  | | | | | | | | |
| Male | 1,356,896/31,448,561 (4.31) | 1,376,692/30,781,881 (4.47) | 1,426,721/30,863,616 (4.62) | 1,444,309/30,867,270 (4.68) | 1,518,497/31,413,253 (4.83) | 1,597,817/31,418,822 (5.09) | 1,642,826/31,642,822 (5.19) | 1,697,293/32,084,893 (5.29) |  |
| Female | 1,765,481/38,939,494 (4.53) | 1,823,593/38,291,735 (4.76) | 1,914,532/38,163,616 (5.02) | 1,968,252/38,087,699 (5.17) | 2,064,932/38,287,429 (5.39) | 2,177,061/38,231,764 (5.69) | 2,253,437/38,156,497 (5.91) | 2,336,228/38,331,126 (6.09) |  |
| Age, years |  | | | | | | | | |
| 0–18 | 627,284/12,801,246 (4.90) | 627,488/12,299,699 (5.10) | 620,798/12,136,769 (5.12) | 603,386/11,974,202 (5.11) | 611,552/11,979,375 (5.32) | 635,759/11,950,393 (5.44) | 631,519/11,979,263 (5.65) | 624,899/12,169,720 (5.71) |  |
| > 18 | 2,495,093/57,586,809 (4.33) | 2,572,797/56,773,917 (4.78) | 2,720,455/56,893,638 (4.78) | 2,809,175/56,980,767 (4.93) | 2,971,877/57,721,307 (5.15) | 3,139,139/57,700,307 (5.44) | 3,264,744/57,820,056 (5.65) | 3,408,622/58,246,299 (5.85) |  |
| Type of residence\( ^a \) |  | | | | | | | | |
| Rural areas with low population density | 441,120/10,519,783 (4.19) | 450,188/10,265,569 (4.39) | 478,734/10,247,756 (4.67) | 491,579/10,182,055 (4.83) | 513,921/10,234,622 (5.02) | 541,934/10,166,646 (5.33) | 559,657/10,154,938 (5.51) | 576,997/10,219,972 (5.65) |  |
| Rural areas with population concentrations | 522,050/12,540,333 (4.16) | 529,069/12,234,886 (4.32) | 562,007/12,244,041 (4.59) | 575,173/12,186,818 (4.72) | 600,394/12,276,268 (4.89) | 634,482/12,225,503 (5.19) | 655,615/12,225,091 (5.36) | 677,635/12,297,829 (5.51) |  |
| Urban districts | 1,253,114/27,937,315 (4.49) | 1,280,090/28,137,527 (4.67) | 1,322,998/27,312,724 (4.84) | 1,346,288/27,274,134 (4.94) | 1,411,390/27,528,692 (5.13) | 1,485,959/27,511,326 (5.40) | 1,529,994/27,531,819 (5.56) | 1,582,203/27,732,448 (5.71) |  |
| Large urban municipalities | 906,093/19,390,624 (4.67) | 940,938/19,175,914 (4.91) | 977,514/19,225,886 (5.08) | 999,521/19,311,962 (5.18) | 1,057,724/19,661,100 (5.38) | 1,112,503/19,747,225 (5.63) | 1,150,997/19,887,471 (5.79) | 1,196,866/20,165,770 (5.93) |  |

\( ^a \) Rural areas with a population density lower than 100 inhabitants per km\(^2\) were categorized as low population density, rural areas with a population density less than 150 inhabitants per km\(^2\) were categorized as rural areas with population concentrations, urban districts were defined as districts with a population density over 150 inhabitants per km\(^2\) and large urban municipalities had a population above 100,000 inhabitants.\(^{21}\)
asthma according to the abovementioned control variables, with 95% CI. Since the assumption of proportional hazards was violated by an interaction between sex and age, that is, the sex-specific prevalence is not independent of age, and vice versa, we repeated the survival analysis separately by sex to exclude the interactive effects.

Results

Study population

The study population of individuals with statutory health insurance with at least one ambulatory health service contact per year comprised 85.33% (70 416 019/82 521 653) of the total German population in 2016 (Table 1). The study sample consisted of 12 169 720 children (0–18 years) and 58 246 299 adults. There were only minor differences across population distributions by age, type of residence and federal state; however, the proportion of females was higher in the study population than in the general population.

Prevalence

Of the 70 416 019 study individuals, 5 360 867 (7.61%) had at least one diagnosis of asthma. The number of children and adults with at least one diagnosis of asthma was 955 628 (7.85%) and 4 405 239 (7.56%), respectively. Of the study individuals, 4 033 521 had prevalent asthma, classified according to the applied case definition (i.e. two diagnoses), corresponding to a crude prevalence of 5.73%. The crude prevalence among children was 5.13% (624 899/12 169 720) and for adults 5.85% (3 408 622/58 246 299; Table 2). The age-standardized prevalence of asthma was 5.76% (95% CI: 5.76–5.77) in 2016 (Table 3).

We observed an interaction in terms of sex and age that has already been reported in the literature (Fig. 1). Asthma prevalence was substantially higher among boys, an association which disappeared in young adulthood. In middle adulthood this association was observed to reverse and asthma prevalence was higher among women, reaching its peak in the age group 65–75 years. After decreasing in boys from the age of 10–11 years until age 30–34 years, there was a slight increase in prevalence in men until age 40–45 years.

From age-specific prevalence data and population distribution data, we estimated that 793 112 children (defined as 0–19 years in this case because of age groups used in the available data) and 3 918 993 adults (> 19 years) were affected by asthma in 2016, resulting in a total of 4 712 106 asthmatics (Table 4).

Temporal trends

The age-standardized prevalence of asthma increased from 4.46% (95% CI: 4.46–4.46) in 2009 to 5.76% (95% CI: 5.76–5.77) in 2016 (Table 3), corresponding to a relative change of +30.32%. The semi-parametric group-based modelling demonstrated the presence of six clusters of different size, but with a similar course of prevalence over the study period (Fig. 2). We observed an almost linear and relatively uniform increase in prevalence in all clusters from 2009 to 2016. A stratified analysis by age (children versus adults, Table 2) showed that the prevalence increase was attributable to adults (relative change, +35.10%) and the prevalence among children changed only marginally over time (+4.69%).

Spatial variation

We observed strong variations by a factor of three over the 402 districts in the age-standardized prevalence of asthma; the lowest and highest prevalences of 3.03% (95% CI: 2.94–3.11) and 8.85% (95% CI: 8.57–9.14) were observed in Schwäbisch Hall and Eisenach, respectively. The age-standardized prevalence was higher in the western parts of Germany. The prevalence in girls was 1.14% higher than in boys in 2016 (95% CI: 1.10–1.18). Overall, 4.16% (95% CI: 4.14–4.18) of the population were affected by asthma in 2016.

Table 3. Temporal change in age-standardized prevalence of asthma, Germany, 2009–2016

| Year | Age-standardized prevalence, % (95% CI) |
|------|----------------------------------------|
| 2009 | 4.46 (4.46–4.46)                        |
| 2010 | 4.66 (4.66–4.67)                        |
| 2011 | 4.87 (4.86–4.87)                        |
| 2012 | 4.97 (4.97–4.98)                        |
| 2013 | 5.17 (5.16–5.17)                        |
| 2014 | 5.45 (5.45–5.46)                        |
| 2015 | 5.62 (5.61–5.62)                        |
| 2016 | 5.76 (5.76–5.77)                        |

CI: confidence interval.
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Germany and lower in South and East Germany (Fig. 3). We found evidence of a strong spatial autocorrelation at the district level (Global Moran's I: 0.50; P < 0.0001). Local Moran’s I showed the presence of spatial clusters with high or low prevalence (Fig. 3). Clusters with high prevalence were found in western Lower Saxony, North Rhine–Westphalia, Schleswig–Holstein and in southern Thuringia.

Incidence

The study subpopulation for incidence estimation included 59 289 010 individuals who were included within the statutory health insurance system for several years (not always the full 8-year study period) and who contributed 422 516 235 person-years over the study period. Of this subpopulation, 2 613 755 (4.41%) were categorized as incident asthma cases. The summed incidence was observed to increase almost linearly with increasing age at diagnosis (Fig. 4). The overall incidence rate was 6.19 per 1000 person-years, and was higher among children and adolescents (10.29 per 1000 person-years; 602 264 cases contributing 58 557 060 person-years) than adults (5.53 per 1000 person-years; 2 011 491 cases contributing 363 959 175 person-years). We observed an interaction between sex and age (Fig. 4). We also observed a distinct difference in summed incidence of asthma according to type of residence; the highest incidence proportion was calculated for densely populated large urban municipalities followed by less densely populated urban districts, and the lowest was calculated for rural areas (Fig. 4). The summed incidence was higher in West German compared with East German federal states (Fig. 4).

In multivariable analysis, children had a hazard ratio (HR) of being diagnosed with asthma of 2.17 (95% CI: 2.16–21.8) relative to adults (Table 5). Resident in the western (versus eastern) federal states and resident in densely populated large urban municipalities (versus rural area) were independently associated with an increased risk of asthma, with HRs of 1.33 (95% CI: 1.32–1.34) and 1.32 (95% CI: 1.31–1.32), respectively. The risk of asthma among boys (0–18 years) was over twice as high as that for men (HR: 2.23; 95% CI: 2.22–2.24); we also observed this difference in risk, although not as pronounced, for girls (0–18 years) versus women.
visits between 1992 and 2005 among a relatively small sample of about 3200 children from three counties in East Germany yielded an incidence rate of 5.0 per 1000 person-years. In an analysis of around 4000 adult participants of the nationwide German Health Interview and Examination Survey for Adults, an incidence rate for asthma over an average period of 12 years (1997–2011) of 1.1–3.4 per 1000 person-years was observed. We estimated higher incidence rates (10.3 and 5.5 per 1000 person-years for children and adults, respectively); however, both studies mentioned above were regionally restricted and had small sample sizes. Our estimates are in good agreement with findings from large-scale studies in other high-income countries, including Canada (10.9 and 5.6 per 1000 person-years for children aged 5–9 years and 10–14 years, respectively, and 2.8 for adults aged 40–69 years), the United Kingdom (4.1 and 9.9 per 1000 person-years for adults and children, respectively) and the USA (3.8 and 12.5 per 1000 person-years for adults and children, respectively).

Regarding the regional distribution of asthma morbidity, we observed several differences in terms of rural versus urban areas. East versus West German federal states and small district-scale hotspots. First, we observed differences in asthma morbidity between those resident in rural and urban areas. Although a higher morbidity of asthma in urban versus rural areas has previously been observed, already partly explained by the hygiene hypothesis, we also differentiated rural and urban districts by population density. We found higher incidence rates in densely populated large urban municipalities than in lower-population urban districts; environmental factors such as air pollution, one of the key risk factors for asthma development, may explain this association.

Lower asthma morbidity was observed for residents of East Germany compared with those of West Germany at the beginning of 1990, shortly after the reunification of Germany. Data from 2003–2006 did not show any difference, implying that morbidity had increased in East Germany; however, the authors of that study suggested that unmeasured confounding factors may have masked a regional difference. Our observed regional difference is supported by a study that compared asthma prevalence in children with a similar genetic ancestry but living in different environments (in our case, genetically similar German children living in West or East Germany). For example, a study measuring the asthma prevalence among Chinese children, showed that the prevalence increased from those born in China to those who migrated to Canada, and was highest for those born in Canada, and was highest for those born in China, to those who migrated to Canada, and was highest for those born in China.

Research on the incidence rate of asthma in Germany is scarce. A prospective study with follow-up
Fig. 3. Regional variations in prevalence of asthma and significant spatial clusters, Germany, 2016

Notes: Cartographic presentation of age-standardized prevalence estimates by district (n = 402). Equidistant distance was used for group classification. General German population from the year 2015 was used as a standard population, controlling for possible demographic changes in the population structure in the study period. Districts with significant spatial clusters estimated with Local Moran’s I. Spatial analysis was performed with crude prevalence values.
Epidemiological studies that rely on objectively measured data (e.g. skin prick test) also support our findings; for example, a higher atopic sensitization rate in children from West compared with those from East Germany has been reported.\(^\text{13}\)

We also observed district-scale variations in prevalence of asthma, and identified hot and cold spots, that is, districts with high and low asthma prevalence estimates, respectively. The distribution of local environmental risk factors of asthma (e.g. allergens, prenatal smoking, nutrition and/or stress) across the districts is usually unknown, but there is some evidence for district-level variations in smoking among men and women.\(^\text{36}\) Other factors contributing to regional variations in asthma morbidity include meteorological factors (e.g. solar radiation),\(^\text{40}\) area-level socioeconomic status, and the different diagnostic coding behaviour and practices of physicians. We found distinct differences between different coastal areas; specifically, we observed a cluster of high-prevalence districts near the North Sea coast, but a low-prevalence cluster in the Baltic Sea coastal region, a finding which merits further investigation.

Our study benefited from the use of nationwide claims data, incorporating outpatient diagnoses of approximately 85% of the German population. As there were only minor differences between the study population and the general German population in terms of age, type of residence and federal state, our findings may be considered representative. Our spatial analysis at the district level, allowing the identification of high-risk areas, is also important as there is no consensus on primary prevention of asthma.

Our study had several limitations. Our study population may not be representative in terms of sex distribution, as the proportion of females in our study population was slightly higher than that in the general population. The

Fig. 4. Summed incidence of asthma overall and by sex, type of residence and location as a function of age at diagnosis, Germany, 2009–2016

Notes: Incidence was estimated with Kaplan–Meier analysis. Incidence for each group in Table 4 was added to that of the previous group. In the graph for place of residence, data for rural areas with population concentrations and rural areas with a low population density are superimposed.
15% of the population that is privately insured, whose data are not included, may differ from the individuals with statutory health insurance in terms of socioeconomic status. Differences in morbidity between individuals with private or statutory health insurance in Germany have been shown, although not explicitly for asthma. One study does mention an asthma prevalence (around 5%) among privately insured individuals in Germany, comparable to our estimated prevalence for the entire population, but this estimate was based on a personal communication. Also, physician claims data are primarily collected for billing purposes and not for morbidity research. Although we cannot rule out a degree of misdiagnosis, our conservative case definition (a diagnosis of asthma in at least two quarters of the year in question) reduced the possibility of counting false-positive cases. This case definition was also used in other studies of asthma prevalence, including in China, Taiwan (which required diagnoses in at least three quarters of each year), Germany, the Republic of Korea and the USA. Finally, information on potential confounding factors, such as smoking and socioeconomic status, was not available from the physician claims data.

We conclude that asthma is a common disorder in Germany with an increasing disease burden. A recent estimate of a current annual cost of asthma treatment per patient of €2168 Euros (€) applied to our calculated number of prevalent asthma cases in 2016 (>4 million) results in a cost to the German health-care system of over €8 billion. To control this increasing asthma prevalence and its associated costs, more research into the prevention and causes of asthma is required. We anticipate that our insights into the spatial distribution of asthma morbidity will serve as a solid basis for public health interventions, including region-specific prevention programmes and control.

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Table 5. Crude and adjusted hazard ratios and corresponding 95% confidence intervals for asthma incidence, Germany, 2009–2016

| Variables                                      | Crude HR (95% CI) | Adjusted HR (95% CI) |
|------------------------------------------------|-------------------|----------------------|
|                                                | Total Total       | Men Women            |
| Sex                                            | 1.01 (1.00–1.01)  | 1.14 (1.13–1.14)     |
| Female                                         | 1.14 (1.13–1.14)  | 1.14 (1.13–1.14)     |
| Male                                           | Reference         | Reference            |
| Age, years                                     | 2.17 (2.16–2.18)  | 2.17 (2.16–2.18)     |
| 0–18                                           | 2.17 (2.16–2.18)  | 2.17 (2.16–2.18)     |
| > 18                                           | Reference         | Reference            |
| East versus West Germany                       | 1.30 (1.29–1.30)  | 1.05 (0.75–1.47)     |
| Berlin                                         | 1.05 (0.76–1.44)  | 1.05 (0.76–1.44)     |
| West Germany                                   | 1.33 (1.32–1.34)  | 1.05 (0.74–1.50)     |
| East Germany                                   | 1.05 (0.74–1.50)  | 1.05 (0.74–1.50)     |
| Type of residence                              |                   |                      |
| Rural areas with a low population density      | 1.01 (1.00–1.01)  | 1.01 (0.96–1.05)     |
| Rural areas with population concentrations     | 1.01 (1.00–1.01)  | 1.01 (0.96–1.05)     |
| Urban districts                                 | 1.12 (1.11–1.12)  | 1.03 (0.98–1.08)     |
| Large urban municipalities                      | 1.20 (1.14–1.27)  | 1.19 (1.13–1.25)     |

CI: confidence interval; HR: hazard ratio; NA: not applicable.

NIH: National Institutes of Health.

Research
Asthma morbidity, Germany
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The prevalence of asthma decreases with the level of administrative division, which can provide information on health interventions, including specific preventive programs for different regions.

**Objective** Study the prevalence of asthma in Germany by calculating the prevalence, examining the temporal and spatial trends, in estimating the total number of asthmatics in Germany and in calculating the prevalence by age, sex, and residence.

**Methods** We used the German 2009-2016 data from the Federal Statistical Office, the Federal Health Insurance Fund, and the Federal Institute for Health Insurance to analyze the prevalence of asthma, the number of claims for asthma treatment, and the age and sex distribution of the patients. We also calculated the age-standardized prevalence of asthma in Germany.

**Results** We found that the prevalence of asthma decreased with the level of administrative division. We observed a lower prevalence in rural areas compared to urban areas, and the prevalence decreased with the level of administrative division. We also observed a decrease in the prevalence of asthma with age, with the highest prevalence in children and the lowest in the elderly.

**Conclusion** Our study provides valuable information on the prevalence and spatial distribution of asthma in Germany, which can help in the development of targeted prevention and control programs at different levels of administrative division.
**Resumen**

**Tendencias y distribución regional de las reclamaciones de pacientes externos por asma, 2009-2016, Alemania**

**Objetivo** Investigar la morbilidad por asma en Alemania mediante el cálculo de la prevalencia actual, el examen de sus tendencias temporales y espaciales, la estimación del número total de asmáticos en Alemania y el cálculo del riesgo específico por edad, sexo y residencia.

**Métodos** Se utilizaron los datos de reclamaciones notificados por los médicos durante 2009-2016, incluidos los diagnósticos de pacientes externos de todos los asegurados estatutarios de salud, que representan el 85,3% (70 416 019/82 521 653) de la población total en Alemania en 2016. Se realizó un análisis espacial de la prevalencia del asma según el distrito administrativo calculando el I de Moran a nivel global y local. Se calculó una prevalencia estandarizada por edad y sexo, tipo de residencia (rural versus urbano) y el cálculo del riesgo específico por edad, sexo y residencia. Se identificaron los grupos espaciales locales con niveles más altos de prevalencia. Vivir en los estados federales occidentales (versus orientales) y vivir en municipios urbanos grandes densamente poblados (versus área rural) se asoció independientemente con un mayor riesgo de asma con cocientes de riesgo de 1,33 (IC del 95%: 1,32–1,34) y 1,32 (IC del 95%: 1,31–1,32) respectivamente.

**Conclusión** Esta información sobre la distribución espacial de la morbilidad por asma puede servir de base para las intervenciones de salud pública, incluidos los programas de prevención y control específicos de cada región.

**Referencias**

1. The global asthma report 2018. Auckland: The Global Asthma Network; 2018. Available from: www.globalasthmanetwork.org [cited 2019 Sep 17].
2. Masoli M, Fabian D, Holt S, Beasley R; Global Initiative for Asthma (GINA) Program. The global burden of asthma: executive summary of the GINA Dissemination Committee report. Allergy. 2004 May;59(5):469–78. doi: http://dx.doi.org/10.1111/j.1398-9995.2004.00526.x PMID: 15080825
3. To T, Stanoevich S, Moore G, Gershon AS, Bateman ED, Cruz AA, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. BMC Public Health. 2012 03;19(12):204. doi: http://dx.doi.org/10.1186/1471-2458-12-204 PMID: 2249515
4. Kristl G. Asthma prevalence associated with geographical latitude and regional insolation in the United States of America and Australia. PloS One. 2011 04 8(4):e18492. doi: http://dx.doi.org/10.1371/journal.pone.0018492 PMID: 21494627
5. Gupta RP, Mukherjee M, Sheikh A, Strachan DP. Persistent variations in national asthma mortality, hospital admissions and prevalence by socioeconomic status and region in England. Thorax. 2018 08;73(8):706–12. doi: http://dx.doi.org/10.1136/thoraxjnl-2017-210714 PMID: 3006496
6. Mallol J, Sole D, Baexa-Bacab M, Aguirre-Camposano V, Soto-Quiros M, Baena-Cagnani C; The Latin American ISAAC Group. Regional variation in asthma symptom prevalence in Latin American children. J Asthma. 2010 Aug;47(7):644–50. doi: http://dx.doi.org/10.3109/02770901003686480 PMID: 20642377
7. Timm S, Friedenberg M, Janson C, Campbell B, Forsberg B, Gislason T, et al. The urban-rural gradient in asthma: a population-based study in Northern Europe. Int J Environ Res Public Health. 2015 12;12(13):193. doi: http://dx.doi.org/10.3390/ijerph13010093 PMID: 26729146
8. Germ JE. The urban environment and childhood asthma study. J Allergy Clin Immunol. 2010 Mar;125(3):545–9. doi: http://dx.doi.org/10.1016/j.jaci.2010.01.037 PMID: 20262919
