

# BMJ Open Regional variations and prevalence of psoriasis in Germany from 2010 to 2017: a cross-sectional, spatio-epidemiological study on ambulatory claims data

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## ABSTRACT

**Objectives** Global prevalence rates of psoriasis differ significantly, with lowest rates in the equator region and increasing tendencies towards the north but also differences within-country. Information on regional variations in Germany is missing. This study aims to analyse the change of psoriasis prevalence in Germany over time and to detect regional variations.

**Design** Cross sectional, spatio-epidemiological study on regional psoriasis prevalence in Germany.

**Setting** Claims data study based on nationwide outpatient billing data on county level.

**Methods** Analyses based on outpatient billing data for 2010–2017 derived from all people insured in statutory health insurances (about 72.8 million). We performed descriptive spatio-temporal analyses of prevalence rates using probability mapping and statistical smoothing methods, identified spatial clusters and examined a north-south gradient using spatial statistics.

**Results** The prevalence increased from 147.4 per 10000 in 2010 to 173.5 in 2017. In 2017, counties' prevalence rates ranged between 93.8 and 340.9. Decreased rates occurred mainly in southern counties, increased rates in northern and eastern counties. Clusters of low rates occur in southern and south-western Germany, clusters of high rates in the north and north-east. The correlation between counties' latitudes and their prevalence rates was high with Pearson's  $r=0.65$  ( $p<0.05$ ).

**Conclusion** Increased prevalence of psoriasis over time and marked regional variations in Germany were observed which need further investigation.

## INTRODUCTION

Psoriasis is a very common chronic inflammatory skin disease with high impact on patients' health and quality of life.<sup>1</sup> The disease typically involves thick pruritic plaques and can affect nails and joints.<sup>1</sup> Psoriasis often occurs with other serious comorbidities, such as depression, diabetes or hypertension.<sup>1</sup> Severe psoriasis is associated with higher mortality.<sup>2</sup> Some countries show increasing prevalence rates of psoriasis over the last decade,<sup>3</sup> which is assumed to be a worldwide phenomenon. However, those prevalence estimates differ

## Strengths and limitations of this study

- This study is based on a unique data set, which covers all statutory health insured people which are approximately 90% of the German population.
- Multidisciplinary methods from the fields of epidemiology, geography and spatial statistics were used to answer the research questions about the regional variation of psoriasis prevalence in Germany.
- The use of outpatient billing data, which are not 'epidemiological prevalences', is limiting.
- Counties as a spatial level are not small enough to make further detailed statements on regional variation.

widely regionally, with national rates of 0.51%–11.43% in adults and 0%–2.1% in children.<sup>4–6</sup> On the one hand, those geographical variations may be explained by different case definitions in prevalence studies. On the other hand, they can be attributed to different ethnicities, environmental factors and demographic characteristic.<sup>3–5 7 8</sup> Lacking data on the prevalence of psoriasis in many countries impede conclusions about regional differences.<sup>4</sup> However, some studies suspect a latitudinal trend, with a positive correlation between prevalence and distance from the equator.<sup>5 6 9</sup> Variations not only occur across countries but are also observed within one country, when applying a consistent case definition.<sup>8 10</sup> Springate *et al* detected a regional trend in the UK: Both the prevalence and incidence of psoriasis were following a latitudinal trend, with increasing cases northwards. In order to plan the best possible care for psoriasis and to distribute resources efficiently, it is important to provide politicians and decision-makers with precise and up-to-date data on the prevalence and distribution of psoriasis. Here, methods of spatial epidemiology and geographical information can give important information.<sup>11 12</sup> For



Germany, there have not been such analyses conducted to date despite population-based epidemiological studies being indispensable.

Therefore, this study aims to (1) analyse the change in the regional prevalence of psoriasis in Germany over time and (2) detect regional variations in the prevalence of psoriasis in Germany.

## METHODS

### Data set and data preparation

Nationwide ambulatory claims data on statutory health insured people were provided by the National Association of Statutory Health Insurance Physicians (German: Kassenärztliche Bundesvereinigung, KBV). In Germany, approximately 90% of the population (~70 000 000 people) is covered by statutory health insurance,<sup>13</sup> and therefore, represented in this data set. The remaining 10% are privately insured people. The provided data set comprises information on billed diagnoses (primarily by dermatologists and general practitioners in the ambulatory sector) according to International Classification of Diseases (ICD)-10 for psoriasis (L40.0–L40.9), from 2010 to 2017 at county level (Nomenclature des unités territoriales statistiques, NUTS 3). We excluded L40.5 (psoriasis arthritis) in the analysis because it is a comorbidity of psoriasis. To avoid overestimation of prevalence due to misdiagnosis, we defined cases as at least two billed confirmed diagnoses of psoriasis in different quarters within the year (M2Q definition). We included individuals whose sex and year of birth could be clearly determined and who were not older than 110 years. The regional classification of patients is according to the place of residence of the patients in the respective period on county level as of 2011 with 402 counties. All statistical and spatial analyses were performed with ArcGIS V.10.3.1 (ESRI, Redlands, California, USA), QGIS V.3.10 A Coruna (QGIS Development Team) and R Studio V.3.6.1 (RStudio, PBC, Boston, Mississippi, USA).

### Descriptive and temporal trend analyses

Age-standardised and sex-standardised prevalence rates per 10 000 for all years between 2010 and 2017 were calculated. For data protection reasons, the standardisation was carried out by the KBV using an internal method. Both the prevalence calculation and the weight for standardisation based on the distribution of the statutory health insured population who had received at least one medical treatment in the respective year and met our inclusion criteria. We calculated the mean of prevalence rates on county level (N=402 counties) with SD, minimum, maximum and the median for each year. Expected values were calculated for each county. A county's expected value represents the prevalence rate that we would expect in accordance with the age and sex composition of the respective county, considering the nationwide prevalence rate for that respective year. In order to identify regional variations for each year of the prevalence of psoriasis, we

computed both the extremal quotient (EQ) and the Gini coefficient with associated Lorenz curve for prevalence rates on county level. The EQ is a less precise measurement instrument than the Gini, but the EQ is more suitable for comparison. The EQ is obtained by dividing the maximum identified value in a region, here county, by the minimum value and thus expresses the level of regional differences.<sup>14</sup> To exclude outliers, we calculated the EQ for values between the 1st percentile and the 99th percentile. The Gini coefficient was initially developed to evaluate economic inequalities<sup>15</sup> but can also be used in epidemiology to express regional differences in health and healthcare.<sup>16–18</sup> The associated Lorenz curve graphically describes to which extent the observed distribution deviates from equality. The Gini coefficient ranges from 0 (complete equality) to 1 (complete inequality) and corresponds to the area between the line of equality and the observed Lorenz curve.

For the illustration of the temporal trend of the prevalence rates, we compared the mean prevalence rates of each year and calculated the differences in prevalence rates between 2010 and 2017 for each county. Here, positive values represent an increase and negative values a decrease over time.

### Spatial trend analyses, cluster and outlier analyses

We carried out all analyses for the year 2017. To identify spatial trends in the prevalence of psoriasis, we applied the probability mapping method and a spatial statistical smoothing method.<sup>19</sup> These methodologies are used complementary to offer a higher validity of the analyses. Both demonstrate a certain kind of relative risk for each county. The probability map illustrates whether the observed value in a region deviates significantly from the mean of all values ( $p < 0.05$ ) and if so, in which direction.<sup>20 21</sup> For spatial smoothing, we applied an explorative Bayesian procedure with 1000 sequential Monte Carlo iterations. This model takes values of neighbouring counties with a binary adjacency matrix into account, based on the assumption that they have similar characteristics. Smoothed values indicate ratios, with 1 representing the expected value of a county. Counties with values below 1 have lower prevalence rates and vice versa.<sup>19 22 23</sup> In addition, we examined the relationship between the prevalence rates (standardised and fitted) and the latitude (Universal Transverse Mercator coordinate system; 1 northing equals 1 m). For this, correlations of counties' latitude (measured at the centroids of counties) with prevalence rates were calculated using Pearson's  $r$  coefficient. Furthermore, we computed linear regressions with the latitude as independent variable and prevalence rates as dependent variables.

To test for autocorrelation, global Moran's  $I$  with inversed distances of counties was utilised. The global Moran's  $I$  with associated  $p$  value and  $z$ -score expresses an aggregate value for all counties and ranges from  $-1$  to  $1$ . If the  $p$  value is significant, autocorrelation is present.<sup>24</sup>

**Table 1** Mean standardised prevalence of psoriasis on county level per 10 000 statutory health insured people

	2010	2011	2012	2013	2014	2015	2016	2017	Change 2010–2017
Mean	147.4	152.8	157.0	160.7	165.8	168.6	171.9	173.5	+26.1
Median	145.6	149.8	152.4	155.5	161.2	162.7	166.6	168.2	+24.3
SD	32.82	31.63	33.19	34.37	35.30	36.39	36.56	37.06	15.0
Min	71.3	84.3	87.3	92.2	93.9	95.3	99.9	93.8	-11.1
Max	281.8	291.4	299.7	308.3	319.3	330.1	339.6	340.9	+107.1
EQ	2.48	2.56	2.56	2.44	2.52	2.55	2.53	2.48	-
GC	0.125	0.115	0.117	0.119	0.118	0.120	0.118	0.118	-

EQ, extremal quotient; GC, Gini coefficient.

The cluster and outlier analyses include Anselin local Moran's I. It is a relative measure, expresses values for each individual county and indicates whether it is part of a cluster or an outlier. Given a significant p value, a positive value for I indicates similar values for neighbours, that is, a cluster. High-high clusters are an accumulation of high values, low-low clusters of low values. A negative value for I indicates an outlier. High-low outliers have high values, surrounded by low values, low-high outliers vice versa.<sup>25</sup>

### Patient and public involvement

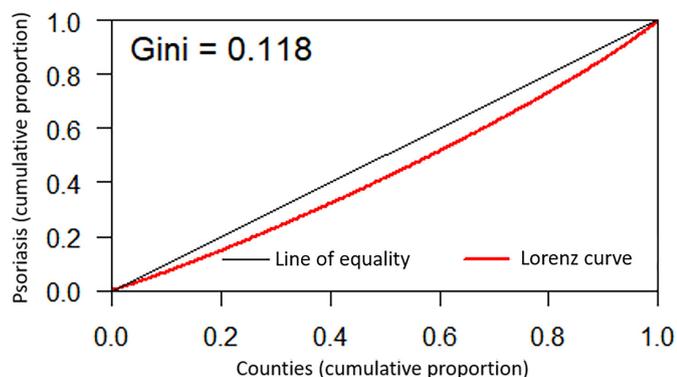
Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

## RESULTS

### Descriptive and temporal trend analyses

With the M2Q case definition, the total number of psoriasis cases was N=1 220 188 in 2017 with slightly more women (51.7%) affected. The mean standardised prevalence rate in German counties increased from 147.4 per 10 000 in 2010 to 173.5 in 2017 (table 1). The EQ remained similar for all years, highest in 2011 with 2.56 and lowest in 2013 with 2.44. The Gini coefficient was highest in 2010 with 0.125 and lowest in 2011 with 0.115. Figure 1 presents the Lorenz curve of 2017 and its deviation from the line of equality.

Mean prevalence rates for Germany increased each year consistently with an increase of about 3–5 per 10 000



**Figure 1** Lorenz curve and Gini coefficient for psoriasis prevalence rates on county level in Germany (2017).

(figure 2A). On county level, most counties had increasing prevalence rates between 2010 and 2017. The increases were particularly strong in the eastern regions and some northern counties of Germany. Only few decreasing prevalence rates were observed, most of them in western Germany (figure 2B).

### Spatial trend analyses, cluster and outlier analyses

The probability map shows significantly higher rates in counties in northern and eastern Germany and significantly lower rates in southern Germany, especially in counties of Bavaria and Baden-Württemberg (figure 3A). Counties in central Germany have smoothed prevalence values ranging around 1, indicating that they are similar to their expected value (figure 3B). Northern counties show increased values, especially in the north-east of Germany. Lower values can be found in the south, in Baden-Württemberg and parts of Bavaria and Rhineland-Palatinate.

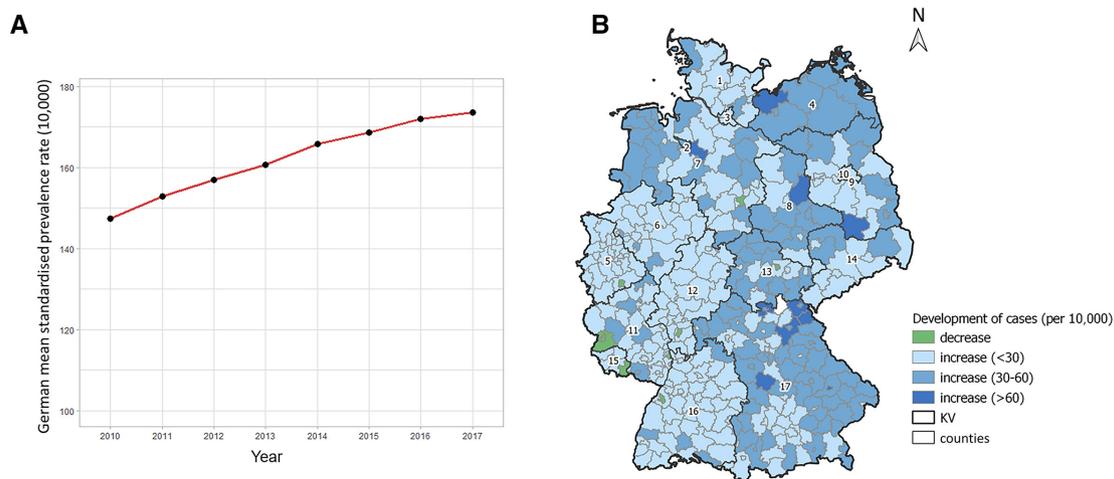
The correlation between the latitude of counties and prevalence rates were high, indicating significantly higher prevalence rates in northern counties (figure 4). The fitted values increased by about 24 per 10 000 every 100 km further north, with Pearson's  $r=0.72$  (95% CI 0.57 to 0.76;  $p<0.05$ ). The standardised values increased by about 30 per 10 000 every 100 km further north, with Pearson's  $r=0.65$  (95% CI 0.58 to 0.70;  $p<0.05$ ).

The global Moran's I value for prevalence rates of 2017 was 0.47 with a z-score of 15.8 and a p value of  $<0.001$ , indicating that autocorrelation is present. The cluster and outlier analyses showed low-low clusters in the regions of Baden-Württemberg, as well as parts of Bavaria, and Rhineland-Palatinate. High-high clusters appear in eastern Germany, as well as parts of Schleswig-Holstein and Lower Saxony. Two high-low outlier regions can be detected in Rhineland-Palatinate, in western Germany. Low-high outliers appear in Berlin and the region of Halle (Saale) in eastern Germany (figure 5).

## DISCUSSION

### Regional variations of psoriasis prevalence

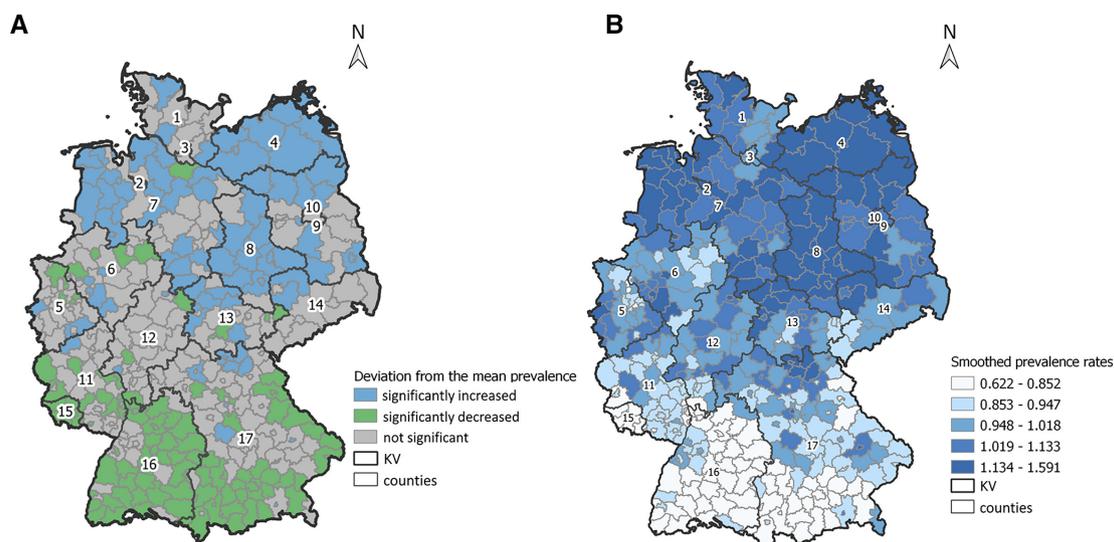
The analyses show that there are regional variations of psoriasis prevalence in Germany, independently



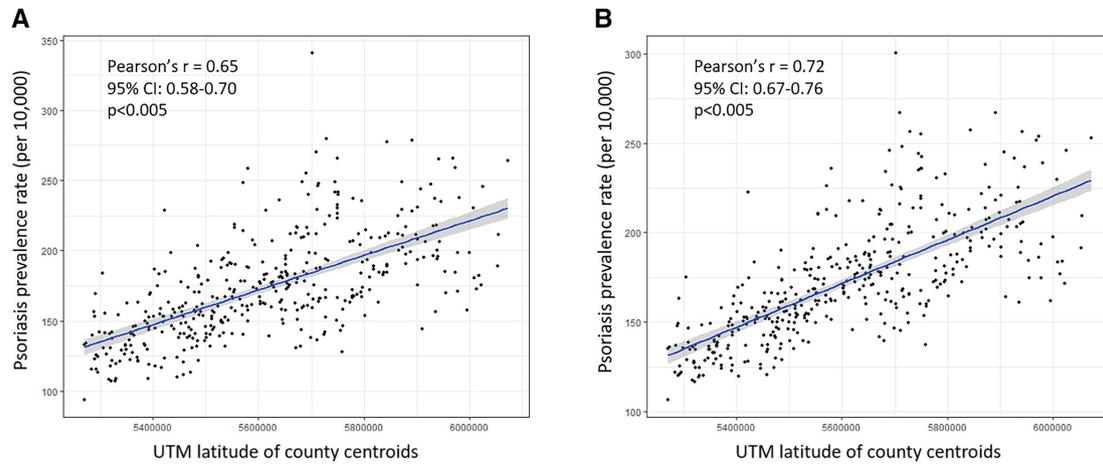
**Figure 2** Development of standardised prevalence rates (per 10 000) from 2010 to 2017 in Germany: (A) German mean prevalence rate; (B) prevalence rates on county level in Germany. 1 Schleswig-Holstein; 2 Bremen; 3 Hamburg; 4 Mecklenburg-Western Pomerania; 5 North Rhine; 6 Westphalia-Lippe; 7 Lower Saxony; 8 Saxony-Anhalt; 9 Brandenburg; 10 Berlin; 11 Rhineland-Palatinate; 12 Hesse; 13 Thuringia; 14 Saxony; 15 Saarland; 16 Baden-Württemberg; 17 Bavaria. KV, regions of the association of statutory health insurance physicians.

of age and sex distribution of the population. The EQ and the Gini coefficient do not reveal enormous overall inequality between counties, but along a north-south gradient inequality becomes visible. The finding of higher prevalence rates in the north is in line with results from the study of Springate *et al*, who also showed higher prevalence rates of psoriasis in the northern part of the UK compared with the south, finding a correlation of prevalence rate and latitudes.<sup>8</sup> Unfortunately, other national studies on regional variations are scarce. However, our results support the worldwide observation of Parisi *et al* of a dependency between distance of equator and psoriasis prevalence, with less occurrence

near the equator.<sup>5</sup> Jacobson *et al*, too, found a weak association between latitude and psoriasis prevalence and suspected ultraviolet radiation (UV) to play a role.<sup>9</sup> This could also apply to Germany, as UV levels differ within regions. Aside from this environmental factor, sociodemographic structures of the regions may be important as well. A study from Sweden found that the level of deprivation in counties could affect the presence of psoriasis.<sup>26</sup> Especially in the region of north-eastern Germany, several deprived areas exist. For other chronic diseases, such as diabetes or obesity, it has been shown that prevalence rates are higher here<sup>27 28</sup> and that the overall morbidity is worse.<sup>29</sup>



**Figure 3** Spatial trends for psoriasis prevalence rates in 2017: (A) German counties with a significant increase or decrease compared with the mean standardised prevalence rate in 2017; (B) smoothed prevalence values for German counties in accordance with Bayes. 1 Schleswig-Holstein; 2 Bremen; 3 Hamburg; 4 Mecklenburg-Western Pomerania; 5 North Rhine; 6 Westphalia-Lippe; 7 Lower Saxony; 8 Saxony-Anhalt; 9 Brandenburg; 10 Berlin; 11 Rhineland-Palatinate; 12 Hesse; 13 Thuringia; 14 Saxony; 15 Saarland; 16 Baden-Württemberg; 17 Bavaria. KV, regions of the association of statutory health insurance physicians.



**Figure 4** Pearson's correlations of 2017 psoriasis prevalence rates with counties' centroid Universal Transverse Mercator coordinate system (UTM) latitude in Germany: (A) standardised psoriasis prevalence rates (per 10 000); (B) fitted psoriasis prevalence rates (per 10,000).

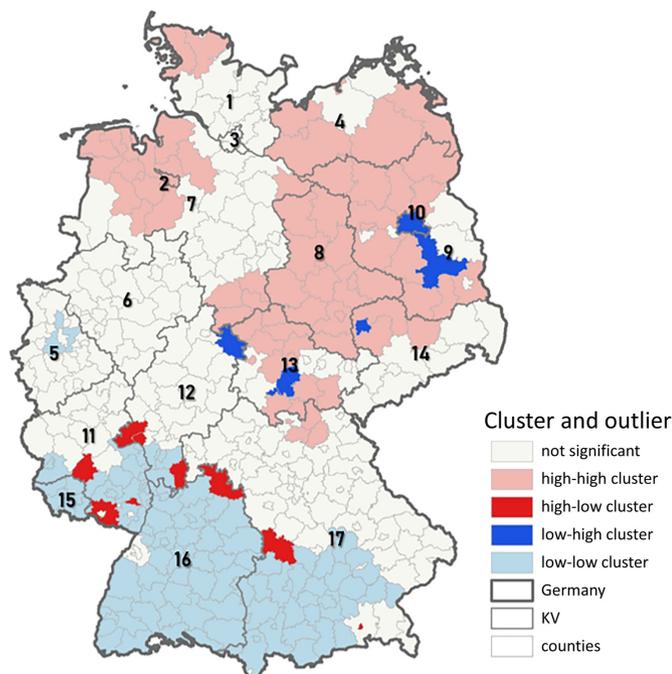
### Increasing prevalence of psoriasis

We found that psoriasis prevalence rates are increasing in Germany as in several other countries.<sup>1 3</sup> However, to investigate reasons for the increase, incidence data for Germany are lacking. Reasons for the prevalence increase could either be an increasing incidence rate or a decreasing mortality rate of psoriasis patients from their comorbidities. Higher billing rates of physicians for psoriasis are also discussed in literature.<sup>30</sup> With our case

definition of at least two billed diagnoses of psoriasis per year, we aimed to avoid an overestimation of those billed diagnoses. The study from the UK suggests that incidence rates seem to be stable and people tend to live longer with the disease.<sup>8</sup> But regardless of the reason, it is important that decision makers are aware of the increase and can adapt if necessary.

### Strengths and limitations

This study contributes to psoriasis research with a unique database that largely represents the German population over an 8-year period. In addition, it is the first study known to us that examines regional variations of psoriasis in Germany and among few internationally. We applied various statistical and geographical methods thoroughly to examine the regional patterns from different perspectives. Though, some limitations need to be addressed. For data protection reasons, the standardisation was carried out by the data provider using an internal method. In addition, we did not have access to the raw data for the same reasons, so the best possible approach to calculate the national prevalence rates was to calculate a nationwide average. Unfortunately, this fact can make comparisons with other international studies more difficult. We have no access to incidence rates and cannot fully explain why the prevalence is rising. In comparison to other prevalence studies in Germany, this study detected lower prevalence rates of 1.47%–1.74%, possibly due to our stricter case definition.<sup>30–35</sup> This definition possibly excluded mild cases, but also allowed us to better align different coding patterns in the regions. In addition, we rely on billing data and cannot validate this data. The level of counties in Germany has the disadvantage that the size and composition of the population can be very heterogeneous. In rare diseases, cases in small counties can therefore generate outliers and hamper interpretation. Yet for psoriasis we had enough cases per county and the use of standardised rates as well as the smoothing process prevented the overestimation of outliers. However, when



**Figure 5** Spatial clusters and outliers for standardised psoriasis prevalence rates in Germany on county level. 1 Schleswig-Holstein; 2 Bremen; 3 Hamburg; 4 Mecklenburg-Western Pomerania; 5 North Rhine; 6 Westphalia-Lippe; 7 Lower Saxony; 8 Saxony-Anhalt; 9 Brandenburg; 10 Berlin; 11 Rhineland-Palatinate; 12 Hesse; 13 Thuringia; 14 Saxony; 15 Saarland; 16 Baden-Württemberg; 17 Bavaria. KV, regions of the association of statutory health insurance physicians.

interpreting the results, the ecological fallacy must be taken into account. The results generated here are based on aggregated data and cannot directly be related to the individual.

## CONCLUSION

The results show increasing prevalences of psoriasis in Germany. However, significant differences in standardised prevalence rates across the country exist with high rates in northern and eastern Germany. With regard to the care of psoriasis, reasons for the variations still need to be determined in detail. Since psoriasis is often accompanied by severe comorbidities, it is for instance important to investigate whether their prevalence rates are also increasing and vary regionally. This could indicate a greater need for treatment.

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**Contributors** The contributors VA and JA had full access to all data in this study and take responsibility for the integrity and accuracy of the data analysis. They were also responsible for the study concept and design. VA, SW, MA, NM and JA were involved in the interpretation and preparation of the manuscript as well as the critical review. VA and JA revised the content of the manuscript. VA, JA and SW were involved in the statistical analysis. JA and MA were responsible for administrative, technical or material support. JA is responsible for the overall content.

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**Data availability statement** Data are available on reasonable request. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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