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## SUPPORTING INFORMATION

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# Social media to monitor prevalent diseases: Hay fever and Twitter activity in Germany

To the Editor,

Allergic rhinitis (AR), also known as hay fever, is the most common allergic disease worldwide, affecting up to 30% of the global population.[1] The analysis of publicly available, population-based data can be beneficial for novel insights and monitoring of the disease burden in populations.[2] One source for these data is social media, which are gaining increased interest in medicine and public health. Twitter is among the most popular social media sites in Germany, with a market share of about 20%.[3] Tweet counts were shown to correlate with local pollen counts in some countries.[4] The aim of our study was to provide insight into the German AR landscape on Twitter and to identify influential regional climate factors for the future development of tailored awareness and prevention campaigns.

A total of 43,965 tweets in German language containing the keyword "*heuschnupfen*" (hay fever) from 2018 to 2021 were found by querying the Twitter Academic API using the query string "*heuschnupfen lang:de*." The keyword is searched against the tokenized tweet body (i.e., split by punctuation or spaces) and includes hashtags. The year range was chosen based on the available pollen data in Bavaria, which were kindly provided by the Center Allergy and Environment (ZAUM) and used as proxies for pollen counts in Germany. The tweets originated from the German-speaking countries such as Germany, Austria, and Switzerland; however,

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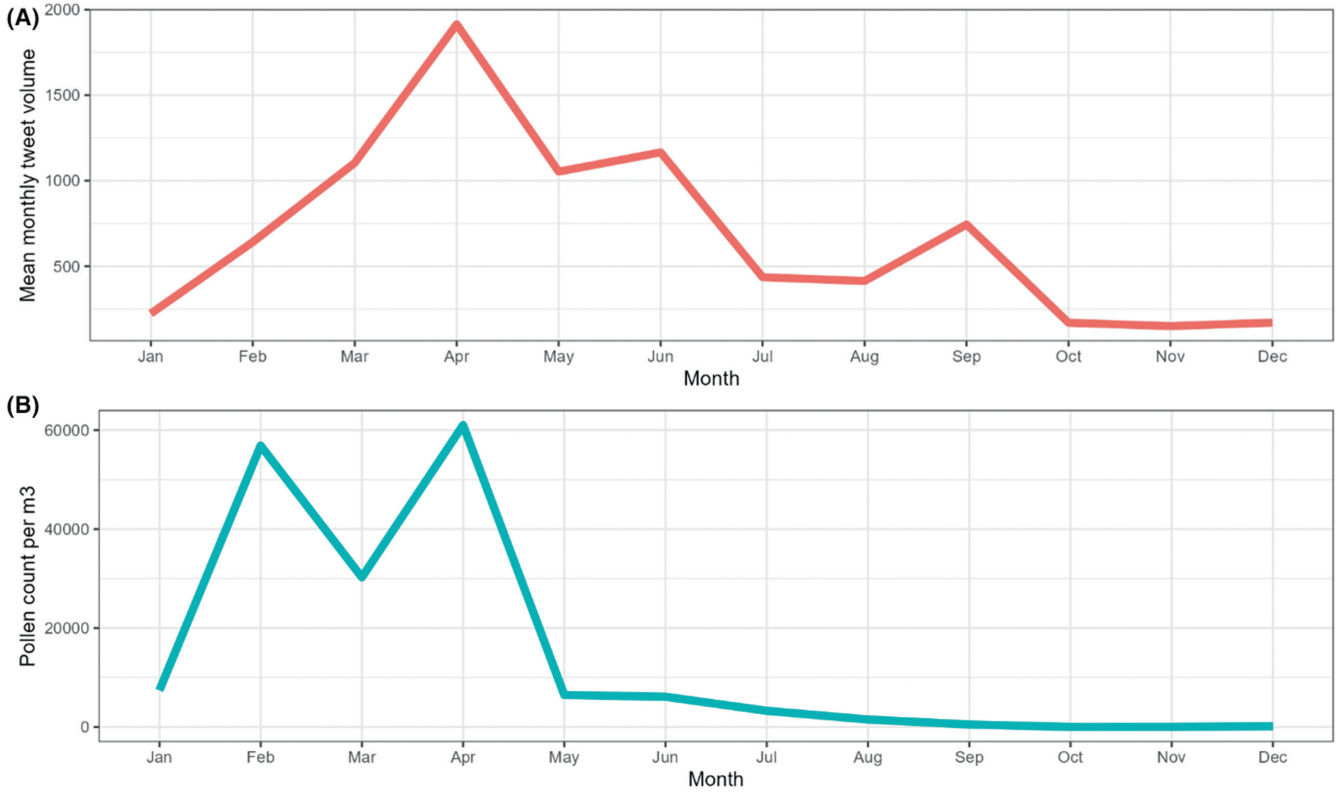


**FIGURE 1** Mean monthly hay fever–related tweet volume (Germany) and pollen count (Bavaria) over 4 years. Part (A) shows post counts of German language hay fever–related tweets aggregated by month from 2018 to 2021. Part (B) shows total pollen counts in Bavaria aggregated by month from 2018 to 2021.

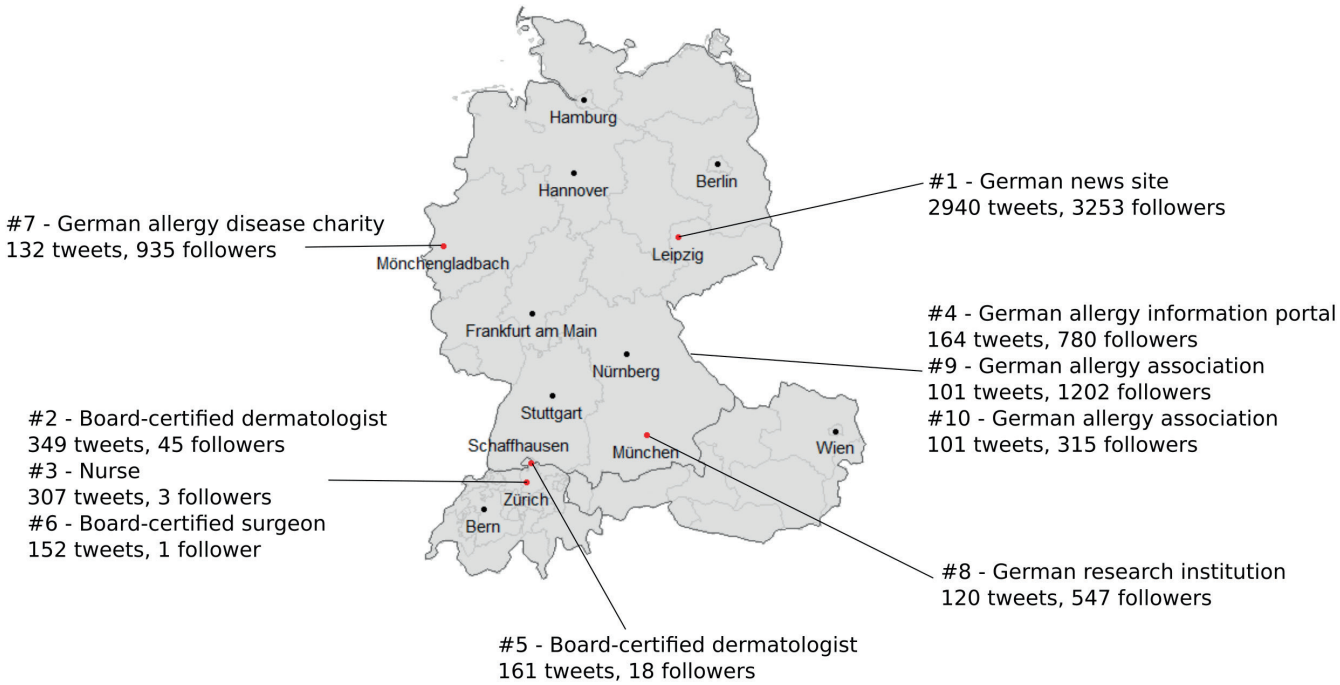


**FIGURE 2** Top 10 accounts according to number of posts. This map of Germany, Switzerland, and Austria shows the location and details of the top 10 posting accounts from 2018 to 2021. The accounts are ranked by total tweet volume.

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our analysis focused on Germany because it is the most populous country of the three by a large degree. Manual content analysis of 500 random tweets revealed that 392 tweets (78.4%) were presumably from allergic individuals. When aggregating AR-related tweet counts by month, the data showed a seasonal pattern, with peaks in the European spring months (March–May; Figure 1B). This pattern was consistent across all analyzed years (Figure S1). The mean AR-related tweet count over the 4 years rose from 223 per month in January to a peak of 1914 per month in April. The number of tweets per month correlated moderately with local total pollen counts and strongly with local birch pollen counts (Figure 2 and Table S1; for total pollen $r = .59$, $p = .046$; for birch pollen $r = .7$, $p = .011$). The number of tweets did not correlate with temperature and precipitation in Germany (data not shown). Previous studies found positive correlations between AR symptom severity with local temperatures and precipitation.[5] Our data set unfortunately does not provide any more insight into this relationship, likely because it is too small to accurately reflect this complex relationship.

The 10 accounts with the highest tweet volume included news sites, healthcare professionals, disease advocacies, and research institutions (Figure 2). These accounts published only a small fraction of the total number of tweets (between 101 [0.2%] and 2940 [6.7%] tweets per account during the analyzed period; percentage of total analyzed tweets), suggesting a diversified landscape of AR-related tweets with lack of central authority.

The data are limited by the fact that social media data are subject to selection bias. For example, the Internet is primarily used by younger individuals for health-related information in Germany.[6] In addition, tweet counts were only correlated to Bavarian pollen counts. However, since Bavaria is the biggest federal state by area and extends to about half of Germany's overall longitude and one third of Germany's latitude, this limitation is weakened to a certain degree. Indeed, the mean peak date in the years 2020–2022 for birch pollen between Munich in the south and Berlin in the north differed by only 1 day (n.s., data not shown). We assimilated monthly Twitter data and think that the differences in pollen season within Germany are much less than this resolution. Our analysis did not include other keywords beyond "hay fever," which excludes AR-related posts with, perhaps, more unspecific keywords such as symptoms.

In summary, our study highlights the relevance of social media for prevalent diseases like AR. Pollen count and, thus, disease burden correlated well with post volume. Tweet volume for hay fever can, therefore, be used to estimate disease burden. Furthermore, the study offers an overview of the relatively fragmented landscape of AR-related content in German language on Twitter. Social media platforms like Twitter have the possibility for not only monitoring public disease burden but also improving awareness about common diseases like AR and minimizing misinformation.

## AUTHOR CONTRIBUTIONS

S. S.—conceptualization, methodology, formal analysis, data curation, visualization, writing—original draft; H. W.—methodology, investigation, writing—review and editing; J. B.—supervision, resources, validation, writing—review and editing; T. B.—supervision, writing—review and editing; A. Z.—supervision, writing—review and editing.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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# JPH203, a LAT1 inhibitor, alleviates steroid-resistant murine airway inflammation mediated by Th17 cells

To the Editor,

Owing to the establishment of a steroid-based therapeutic strategy, bronchial asthma is becoming increasingly manageable. However, severe asthma that is refractory to steroid treatment remains a concern. Th17 cells have been implicated in steroid-resistant asthma, through the investigation of human pathology and animal models.[1] We have demonstrated that JPH203 (also known as Nanvuranlat), an inhibitor of L-type amino acid transporter 1 (LAT1), inhibits IL-17 production by human T cells as well as allergic inflammatory responses elicited in a Th2 cell-dominant mouse model, by interfering with the incorporation of large neutral amino acids.[2,3] Here, we investigated the potential of JPH203 to control steroid-resistant asthma using a murine Th17-dependent airway inflammation model.

As shown in Figure 1A, in vitro-differentiated ovalbumin (OVA)-specific Th17 cells were adoptively transplanted into BALB/c mice. These mice developed bronchial hyperresponsiveness (BHR) upon intratracheal OVA challenge (Figure 1B,C). JPH203 administration significantly suppressed BHR, whereas dexamethasone (Dex) did not show a significant improvement (Figure 1B,C). Inflammatory features accompanied by collagen deposition without mucus production observed in the lungs of allergen-challenged mice tended to be suppressed by JPH203 (Figure 1D). Bronchoalveolar lavage fluid (BALF) analysis revealed massive neutrophil infiltration into the lung in allergen-challenged mice and its significant alleviation by JPH203 but not by Dex (Figure 1E). JPH203 consistently reduced IL-17 production in the lungs evoked by an OVA challenge, whereas Dex had no significant effect (Figure 1F). JPH203 and Dex tended to, if any, but not significantly downregulate allergen-induced lung production of other Th17-related cytokines, IL-22 and CXCL1 (Figure S1). The number of allergen-specific T cells in the BALF was unaffected by OVA challenge or JPH203/Dex treatment (Figure S2A). The tendency toward Th17 cell infiltration upon OVA challenge was indicated in the lung tissue by detecting DO11.10 TCR; however, the response was not altered by JPH203 or Dex (Figure S3). Interestingly, allergen-induced accumulation of non-specific bystander $CD4^+$ T cells was significantly suppressed by JPH203 and Dex (Figure S2B). The lack of significant efficacy on allergen-induced BHR as well as inflammatory cell infiltration and IL-5 production in the lungs in an innate lymphoid cell 2-dominant steroid-resistant airway inflammation model (Figure S4), further revealed the specificity of JPH203. Overall, these findings indicate that JPH203 has the potential to mitigate Th17-mediated and steroid-resistant severe asthma.

We investigated the molecular events influenced by JPH203 in Th17 cells. Consistent with the in vivo effect, JPH203 inhibited IL-17 production more effectively than Dex in Th17 cells following TCR/co-stimulation (Figure 2A), whereas cell viability was unaffected by JPH203 (Figure S5). The recovery of the IL-17-reducing effect of JPH203 by excessive LAT1 substrate amino acids (Figure 2A), in agreement with the outstanding specificity for LAT1,[2] indicates that the effect of JPH203 arose from the amino acid deficiency. JPH203 decreased the phosphorylation of S6K (Figure 2B), a representative substrate of mechanistic target of rapamycin (mTOR), which functions as a sensor of amino acid sufficiency, whereas RORγt expression and STAT3 phosphorylation were unaffected (Figure S6). Furthermore, temsirolimus, an mTOR inhibitor, suppressed IL-17 production (Figure 2A), suggesting that the inhibitory effect of JPH203 on IL-17 production was at least partially mediated by mTOR inactivation. IL-22 was also produced by Th17 cells in vitro in response to TCR/co-stimulation (Figure S7). In contrast to the effect on IL-17, the suppressive effect of JPH203 on IL-22 was less than that of Dex (Figure S7). Together with the in vivo results, IL-22 did not appear to play a major role in the development of Th17 cell-mediated airway inflammation and its suppression by JPH203. To investigate the differences in the effects of JPH203 and Dex, the gene expression profiles of Th17 cells were examined using RNA sequencing (RNA-seq) (Figure S8). In addition to several common pathways (IL-17 signaling, antigen-processing and -presentation, inflammatory mediator regulation of transient receptor potential, and phagosome), several pathways were selectively suppressed by either JPH203 or Dex. Particularly,

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