Incidence of pemphigoid diseases in Northern Germany in 2016 – first data from the Schleswig-Holstein Registry of Autoimmune Bullous Diseases

N. van Beek,1 A. Weidinger,2 S.W. Schneider,3 A. Kleinheinz,4 R. Gläser,2 M.M. Holtsche,1 A. von Georg,1 C.M. Hammers,1,5 F. Hübner,1 A.-L. Lima,1 D. Gola,6 C.D. Sadik,1 D. Zillikens,1 A. Katalinic,7 E. Schmidt,1,5 I.R. König6,*

1Department of Dermatology, Allergology, and Venereology, University of Lübeck, Lübeck, Germany
2Department of Dermatology, Venereology, and Allergology, University Hospital Schleswig-Holstein, Kiel, Germany
3Department of Dermatology and Venerology, University Hospital Hamburg-Eppendorf, Hamburg, Germany
4Department of Dermatology, Elbe Medical Center, Buxtehude, Germany
5Lübeck Institute of Experimental Dermatology (LIED), University of Lübeck, Lübeck, Germany
6Institute of Medical Biometry and Statistics, University of Lübeck, Lübeck, Germany
7Institute of Social Medicine and Epidemiology, University of Lübeck, Lübeck, Germany
*Correspondence: I.R. König. E-mail: Inke.Koenig@uni-luebeck.de

Abstract
Background Autoimmune bullous diseases (AIBD) are rare disorders characterized by autoantibody formation against components of adhesion molecules; in pemphigoid diseases (PD), these are proteins of hemidesmosomes and basement membrane, important for cell-matrix adhesion in skin and/or mucous membranes. Incidences of these diseases vary considerably between different populations.

Objectives To establish a registry prospectively recruiting all AIBD patients in a geographically well-defined region in Northern Germany (Schleswig-Holstein).

Methods Only patients with verified disease (by clinical presentation, histology, direct and/or indirect immunofluorescence and/or ELISA) living in Schleswig-Holstein were included. Incidences of PD were estimated based on the total number of inhabitants in Schleswig-Holstein, stratified by birth year and sex.

Results Of 67 patients with PD [35 male, 32 female, mean age 75 (standard deviation 14.3 years)], 83% were patients with bullous pemphigoid [n = 56, 28 male, 28 female, mean age 78 (SD 9.9)]. The resulting crude incidences were 23.4 patients/million/year for all pemphigoid patients, 19.6 patients/million/year for bullous pemphigoid (age-standardized 16.9 patients/million/year) with a strong increase in bullous pemphigoid patients in the age group of 85–90 years with 262 patients/million/year. Incidences for bullous pemphigoid were higher in urban compared to rural areas. Other PD (mucous membrane pemphigoid, linear IgA disease, anti-p200 pemphigoid) were less frequent with crude incidences of 2.1, 1.0 and 0.7 patients/million/year, respectively.

Conclusions This study prospectively analyses the incidence of PD in a carefully defined geographical area. The highest incidence among PD patients was found for bullous pemphigoid. The incidence of bullous pemphigoid is considerably increased compared to previous reports and reveals regional differences. Further studies are needed in order to clarify these findings.

Received: 19 June 2020; Accepted: 10 December 2020

Conflicts of interest
The authors declare they have no conflict of interest with respect to this research study and paper.

Funding source
This registry was supported by the DFG through the Clinical Research Unit 303 Pemphigoid diseases (BE58661/1-1 and 1-2, KO2250/5-1 and 5-2). Structural support was obtained by the Excellence Cluster 2167 Precision Medicine in Chronic Inflammation.
Introduction
The group of autoimmune bullous diseases (AIBD) is formed by a number of diverse rare disorders all characterized by autoantibodies directed against structural components of the skin and mucous membranes. They can be categorized according to the molecules targeted by their specific autoantibodies: (i) in pemphigus, the intra-epidermal adhesion molecules of desmosomes are targeted while (ii) in pemphigoid diseases (PD), autoantibodies against proteins in the basement membrane zone and hemidesmosomes are characteristic. (iii) A third category can be defined by autoantibodies targeting the epidermal and/or tissue transglutaminases as seen in dermatitis herpetiformis.1–5

The incidences of AIBD are different depending on the disease entity but also vary considerably based on geographical regions and ethnicities.6–8 In Central Europe and North America, bullous pemphigoid forms the most frequent AIBD with reported incidences ranging from 13 to 42 patients/million inhabitants/year.6,8–11 Bullous pemphigoid is mostly characterized by autoantibodies against the hemidesmosomal proteins BP180 and BP230. Intriguingly, its incidence rises with age; particularly, when only elderly individuals above the age of 70 are studied, the incidence shows an increase to 150–190 patients/million inhabitants/year.6,8–13 Lower incidences have been reported in Romania, Poland and Kuwait with 2.5–4.5 cases/million/year.14–16 Reports on prevalence range from 120 to 259 patients/million inhabitants in Germany and Denmark.17,18 Given the ageing societies in Western countries and increasing life expectancies, both incidence and prevalence of bullous pemphigoid are likely to rise even more in the coming years. However, epidemiologic analyses on PD are still scarce.

Pemphigoid diseases other than bullous pemphigoid are less frequent. These include mucous membrane pemphigoid, anti-p200 pemphigoid, pemphigoid gestationis, linear IgA disease and epidermolysis bullosa acquisita.1,19–22 Incidences of mucous membrane pemphigoid were estimated as 0.9–2.0 patients/million inhabitants/year in Germany and the UK and a prevalence of 24 patients/million inhabitants in Germany.6,8,17,23,24 The incidence and prevalence of pemphigoid gestationis have been reported as 0.8–2.0 patients/million inhabitants/year in Kuwait and Central Europe and 13.6 patients/million female inhabitants in Germany, respectively.5,8,11,13,16,23 Incidences for epidermolysis bullosa acquisita and linear IgA disease have been shown to range from 0.08–0.5 to 0.2–1.0 cases/million inhabitants/year, respectively, while no incidence has so far been stated for anti-p200 pemphigoid, as an ICD10 code is lacking and only approximately 100 cases have been reported in the literature.6,16,25–27

Despite an increasing number of prospective studies on the epidemiology of PD mainly at referral centres, more epidemiological data are still based on retrospective analyses with most data available on bullous pemphigoid (reviewed in Ref. 28,29).

Here we report population-based data on PD from a prospective registry in the state of Schleswig-Holstein, Germany, which allows a comprehensive epidemiological analysis of these diseases due to its unique geographical setting.

Methods
Registry design
This registry comprises all patients with newly diagnosed AIBD in the state of Schleswig-Holstein, Germany. Geographically, Schleswig-Holstein is unique within Germany given a national border to Denmark in the north and natural borders to the North and the Baltic Sea in the west and the east, respectively. Overall, this state has ~2.9 million inhabitants, of whom ~825,000 (~28%) are older than 60 years.

Patients were included prospectively starting from October 2015.

To achieve a most complete recruitment of all newly diagnosed AIBD patients living in the state of Schleswig-Holstein and to further ensure a high public awareness of the registry among physicians and patients, the measures taken are outlined in Table 1.

Table 1 Measures to increase recruitment in the Schleswig Holstein Registry for autoimmune bullous diseases

| Recruitment measures | Public awareness measures |
|----------------------|---------------------------|
| • All AIBD patients from both Departments of Dermatology from the University Hospital Schleswig-Holstein in Lübeck and Kiel (UKSH) are recruited | • Public appearance by information in printed media (Schleswig-Holsteinisches Ärzteblatt September 2016) |
| • The neighbouring dermatology departments south of Schleswig–Holstein in Buxtehude and at the University of Hamburg were affiliated to the project to recruit their newly diagnosed AIBD patients from the state of Schleswig–Holstein | • Development of a website of the Schleswig-Holstein registry of AIBD patients (www.sh-register-pemphigoid-pemphigoid.de) to inform both patients and physicians about study centres, structure and contact as well as information on individual AIBDs and patient consent forms and datasheet can be downloaded |
| • Yearly information of dermatologists in Schleswig-Holstein about the registry and approach to include their patients directly or refer their patients to one of the 2 university departments | • The registry webpage is linked with the webpage of the German AIBD patient support group, Pemphigus und Pemphigoid Selbsthilfegruppe e.V. (www.pemphigus-pemphigoid-selfshhilfe.de), to further increase visibility among patients, relatives and physicians |
| • The routine laboratory for AIBD of the department of dermatology in Lübeck sent information about the registry with every newly diagnosed AIBD sample possibly living in Schleswig–Holstein | |
Inclusion and exclusion criteria
Eligible for the registry are all patients at any age with a home address at the time of diagnosis located in the state of Schleswig-Holstein, Germany, and with newly diagnosed AIBD. Patients have to fulfil the criteria of the German guideline for diagnosis of bullous pemphigoid. In case of PD other than bullous pemphigoid, patients are included if they fulfil the diagnostic criteria previously described. Briefly, patients with matching clinical presentation and with IgG/IgA deposits in indirect and/or IgG/IgA/C3 deposits in direct immunofluorescence microscopy and/or ELISA/immunoblotting matching the respective disease are considered.

Patients were excluded if the diagnosis could not be confirmed by these criteria or the home address at the time of diagnosis was not confirmed to be in the state of Schleswig-Holstein.

For this report, only PD patients diagnosed from January 1st to December 31st 2016 were evaluated.

Recruitment
Patients considered eligible for the registry by assessment of inclusion and exclusion criteria in the participating centres are recruited after having received oral and written information about the registry and providing written informed consent. Here, patients consented to registration only, to recording of additional data using a standardized datasheet, to use of biomaterial, and/or to being contacted for additional information.

Patients who fulfil the diagnostic criteria but could not be reached or opt out of providing more detailed information (see above) are also considered. Patients recruited from primary care dermatologists are asked by them for consent to transfer their contact data to the participating centres prior to any communication between these centres and the patients. The registry is part of a clinical research unit (CRU303 PD, funded by the DFG, https://gepris.dfg.de/gepris/projekt/269234613) and PD patients participate in the CRU according to the patients’ consent. This study was conducted following the declaration of Helsinki and was approved by the local ethics committee of the University of Lübeck (approval no 15-051 and 18-046) and all participating centres.

Data collection
Data was retrieved from the datasheets containing a previously designed comprehensive set of clinical, immunopathological and laboratory data and in case of a patient seen at the dermatology departments in Lübeck or Kiel, additional data from the patients’ medical records. Additionally, a yearly check of death statistics was performed to assess mortality.

Briefly, the datasheet collects information on the first appearance of skin/mucous membrane lesions, date of diagnosis, country of origin of the patient and his/her first and second degree relatives, any family member with autoimmunity, the number of lesions at diagnosis and the immunopathological data (results of direct and indirect immunofluorescence microscopy as well as ELISA/immunoblotting results on circulating autoantibodies), concomitant illnesses and their duration, malignancies and medication both specific for the PD and for concomitant illnesses, including duration of intake.

Statistical analysis
Incidence was estimated based on the total number of inhabitants in Schleswig-Holstein, stratified by birth year and sex, according to the Statistikamt Nord. Age-standardized incidences were estimated based on the EU-27 + EFTA standard population (https://ec.europa.eu/eurostat/) using the R package epitools. Furthermore, the incidence of bullous pemphigoid was estimated separately for inhabitants of cities with more than 100 000, 50 000–100 000 inhabitants, and <50 000 inhabitants, respectively.

Relative survival was estimated based on the background mortality according to the mortality tables of the Federal Statistical Office Germany (www.destatis.de) using the R package periodR with a cohort approach.

Results
Descriptive analysis
Sixty-seven patients with a newly diagnosed PD were identified in 2016, including 35 males and 32 females. Out of these 67, 56 patients suffered from bullous pemphigoid (28 females and 28 males), six from mucous membrane pemphigoid (two males, four females), three male patients from linear IgA disease, two male patients from anti-p200 pemphigoid, while no patient with epidermolysis bullosa acquista or gestational pemphigoid was identified. The mean age at diagnosis was 75 years (SD 14.3 years, range 5–93) for all PD patients. In bullous pemphigoid patients, the mean age was slightly higher (78 years, SD 9.9 years, range 50–93), but considerably higher compared to the remaining group of PD with a mean age of 65 years (SD 24.1 years, range 5–89).

Of the bullous pemphigoid patients who gave additional information on our datasheet, 32 out of 35 (91%) were of German decent, and 25 gave information about their first degree relatives out of which one (4%) reported to have first degree relatives with an autoimmune disease.

Incidence
The crude incidence for all PD was 23.4 patients/million/year. As expected, with 56 patients, bullous pemphigoid was the most frequent PD accounting for a crude incidence of 19.6 patients/million/year, almost equally distributed between male (20 patients/million/year) and female (19 patients/million/year) patients, with a mean age slightly higher in male patients (mean 78.4, SD 8.5 vs. mean 77.8, SD 11.1 years). The age-standardized incidence for bullous pemphigoid using a European standard population was 16.9 patients/million/year.
Our data for bullous pemphigoid show the expected peak in the higher age groups of 65 years and older accounting for 85% of all bullous pemphigoid patients with the highest numbers at the age of 85–90 years and an incidence raised up to 262 patients/million/year in this age group (Fig. 1).

The crude incidences for other PD were considerably lower with an incidence of 2.1 patients/million/year in mucous membrane pemphigoid which was almost double in females (2.7 patients/million/year) compared to males (1.4 patients/million/year). Incidences for linear IgA disease and anti-p200 pemphigoid were 1.0 patients/million/year and 0.7 patients/million/year, respectively, and in this cohort, only males were affected.

Furthermore, we saw an increased incidence of bullous pemphigoid in cities with more than 100 000 inhabitants (32 patients/million/year) compared to smaller cities (21 patients/million/year) and rural areas (16 patients/million/year) (Table 2).

Relative survival
In 33 bullous pemphigoid patients, information about survival until 12/2018 was available. In these, the relative 1- and 2-year-survival was 98.7 (SE = 4.4) and 97.4 (SE = 6.3), respectively, showing a small excess risk. For the other diagnostic groups, sample sizes were too small to estimate relative survival. Notably, both patients with anti-p200 pemphigoid died within 1 year.

Discussion
Epidemiological studies of PD, although scarce, have shown a great variation of incidences within this group of diseases with regard to disease entity, ethnicities and geographical region studied.6–8,34

In the present study, the incidence of bullous pemphigoid with 19.6 (16.9 age-standardized) cases per million inhabitants per year shows a rise compared to the previously described incidences in Southern Germany with 6.6 cases/million/year 1989–1994 and 13.4 cases/million/year in 2001–2002.6,27 The currently found incidence is in line with recent numbers of 21.7 (crude, 2000–2005) and 18.8 (age-standardized, 2010–2015) cases/million/year reported in distinct regions in France.11,34

Explanations for the rise in incidence have been seen in better diagnostic tools as well as recently described clinical variants and the ageing Western societies. The latter is taken into account by the age-standardized incidence of bullous pemphigoid (16.9 cases/million/year) which is only slightly lower than the crude incidence, and in between an age-standardized incidence reported from a Finish retrospective cohort with 14 per 1 million person-years (95% CI 12–17; 1985–2009) and the age-standardized incidence of 18.8 cases/million/year reported in a recent prospective French study.34 Furthermore, increased incidence in neurological diseases and a more frequent use of certain drugs such as loop diuretics and gliptins (described as risk factors for the development of bullous pemphigoid) as well as improved awareness and diagnostic tools for the condition contributed to the observed increase.

Table 2 Incidence stratified by number of inhabitants

| City size | Total inhabitants | BP patients | BP incidence |
|-----------|------------------|-------------|--------------|
| <50 000 inh. | 2154304 | 35 | 16.25 |
| 50 000–100 000 inh. | 241851 | 5 | 20.67 |
| >100 000 inh. | 462559 | 15 | 32.43 |

City size based on number of inhabitants; total number of inhabitants in Schleswig-Holstein, number of bullous pemphigoid (BP) patients and BP incidence (crude) per million inhabitants. Cities with >100 000 inhabitants are Kiel and Lübeck; cities with 50 000–100 000 inhabitants are Flensburg, Neumünster and Norderstedt.
pemphigoid) have been reported as reasons for the rising incidence of bullous pemphigoid.\(^\text{11,29,35,36}\)

However, the study design of these previous reports has been rather variable with most data retrieved from retrospective cohorts as well as prospective single centre studies and referral centre-based approaches which may contribute to the heterogeneity of the incidences reported.\(^\text{11,34,37,38}\) On the one hand, single centre studies might have underestimated the incidence as some bullous pemphigoid patients from the periphery most likely have been treated in neighbouring dermatology departments. On the other hand, retrospective registries may overestimate or underestimate the incidence as diagnosis often cannot be re-evaluated and may not have been confirmed. For example, retrospective analysis of coding-based diagnoses depending on the stringency of in- and exclusion criteria may or may not include coding for similar diseases (as in ICD-10-based coding ‘other pemphigoid’ or ‘pemphigoid, not classified’ in the group of bullous pemphigoid patients).\(^\text{8,37–39}\) Therefore, the Schleswig-Holstein registry for AIBD aims at complete inclusion of all cases in this specific state which is extraordinarily suited for a registry. It is surrounded by the Baltic Sea in the east, the Northern Sea in the west and the national border to Denmark in the north, thus having only a southern border where patients might seek treatment outside this state.

Since two major dermatology departments outside the southern border of Schleswig-Holstein, i.e. the departments at the General Hospital of Buxtehude and at the University Hospital of Hamburg participated in the study, only the individual patient diagnosed on clinical criteria alone may have failed to be included in the registry. In line with our approach, a recent French registry study highlighted the importance of structured prospective registries for epidemiological research.\(^\text{34}\)

In agreement with previous data, in bullous pemphigoid, we see a mean age of 78 years, a rise in incidence along with age and an equal gender distribution, although some authors described men to be more prone to the disease.\(^\text{12}\) Reported data about mortality and survival of bullous pemphigoid patients are quite heterogeneous. In our study, we found an only slightly lower relative survival in bullous pemphigoid patients, compared to a standard population. Other authors have found 1-year mortality rates of 24.1% in Israeli bullous pemphigoid patients, a 6–7 times increased 1-year mortality in a Danish cohort, and overall survival was reported 91% after 1 year in a US cohort.\(^\text{37,40,41}\) Data from a French study showed a standardized mortality ratio of 6.6.\(^\text{11}\) These varying results might be due to different calculation methods and/or regional differences.

Interestingly, contradicting to a previous report from Poland, our data suggest a rise in incidence of bullous pemphigoid from rural areas towards urban areas despite slightly lower mean age and lower percentage of citizens above 65 years in urban areas (21.1% in larger cities, 22.3% in smaller cities and 23.8% in rural areas).\(^\text{33,42}\) This might be due to several bias factors: (i) both university hospitals of Schleswig-Holstein are in the two largest cities of the state more likely to diagnose and recruit these patients, and (ii) nursing homes probably are more likely located in cities rather than the rural areas. However, further studies are needed in order to confirm and further explain these findings.

The incidence of 2.1 patients/million inhabitants/year for mucous membrane pemphigoid and 1.0 patients/million inhabitants/year for linear IgA disease detected in this study was in line with the upper limit of reported incidences from 0.9–2.0 to 0.2–1.0 patients/million inhabitants/year, respectively.\(^\text{6,13,16,26}\) In addition, an incidence of 0.7 patients/million inhabitants/year for p200 pemphigoid was found in our cohort which is higher than reported estimates expecting an incidence similar to epidermolysis bullosa acquisita as incidence reports are not available due to the rarity of the disease.\(^\text{31,43}\)

Our data serve as a first outline for future evaluations on population-based associations derived from the registry and will provide deeper insight into epidemiology of PD in Schleswig-Holstein with its data becoming stronger with the growing numbers of patients and the number of years of recording.

**Acknowledgement**

We are indebted to Anette Baratay and all dermatologists who included patients in the registry and to Sarah Gaugel for handling of bio samples as well as Kerstin Saalmüller and Frank Sandig for data management. Open Access funding enabled and organized by Projekt DEAL.

**References**

1. Schmidt E, Zillikens D. Pemphigoid diseases. *Lancet* 2013; **381**: 320–332.
2. Schmidt E, Zillikens D. Modern diagnosis of autoimmune blistering skin diseases. *Autoimmun Rev* 2010; **10**: 84–89.
3. Sardy M, Karpaticz S, Merkl B, Paulsson M, Smyth N. Epidermal transglutaminase (T(Gase 3) is the autoantigen of dermatitis herpetiformis. *J Exp Med* 2002; **195**: 747–757.
4. Kasperkiewicz M, Elsebrecht CT, Takahashi H et al. Pemphigus. *Nat Rev Dis Primers* 2017; **3**: 17026.
5. Schmidt E, Kasperkiewicz M, Joly P. Pemphigus. *Lancet* 2019; **394**: 882–894.
6. Bertram F, Brocker EB, Zillikens D, Schmidt E. Prospective analysis of the incidence of autoimmune bullous disorders in Lower Franconia, Germany. *J Disch Dermatol Ges* 2009; **7**: 434–440.
7. Kanwar AJ, De D. Pemphigus in India. *Indian J Dermatol Venerol Leprol* 2011; **77**: 439–449.
8. Langan SM, Smeeth L, Hubbard R, Fleming KM, Smith CJ, West J. Bullous pemphigoid and pemphigus vulgaris—incidence and mortality in the UK: population based cohort study. *BMJ* 2008; **337**: a180.
9. Marazza G, Pham HC, Scharer L et al. Incidence of bullous pemphigoid and pemphigus in Switzerland: a 2-year prospective study. *Br J Dermatol* 2009; **161**: 861–868.
10. Cozzani E, Parodi A, Rebora A et al. Bullous pemphigoid in Liguria: a 2-year survey. *J Eur Acad Dermatol Venereol* 2001; **15**: 317–319.
11. Joly P, Baricault S, Spara A et al. Incidence and mortality of bullous pemphigoid in France. *J Invest Dermatol* 2012; **132**: 1998–2004.
12. Jung M, Kippes W, Messer G, Zillikens D, Rzany B. Increased risk of bullous pemphigoid in male and very old patients: a population-based study on incidence. *J Am Acad Dermatol* 1999; **41**: 266–268.
13. Bernard P, Vaillant L, Labelle B et al. Incidence and distribution of subepidermal autoimmune bullous skin diseases in three French regions. *Bullous Diseases French Study Group. Arch Dermatol* 1995; **131**: 48–52.
serwin ab, bokiniec e, pisacik m, masny d, chodynicka b. epidemiological and clinical analysis of pemphigoid patients in northeastern poland in 2000–2005. med sci monit 2007; 13: cr360–4.

baican a, baican c, chiriac g et al. pemphigus vulgaris is the most common autoimmune bullous disease in northwestern romania. int j dermatol 2010; 49: 768–774.

nanda a, dvorak r, al-saeed k, al-sabah h, alsaleh qa. spectrum of autoimmune bullous diseases in kuwait. int j dermatol 2004; 43: 876–881.

hubner f, recke a, zillikens d, linder r, schmidt e. prevalence and age distribution of pemphigus and pemphigoid diseases in germany. j invest dermatol 2016; 136: 2493–2498.

eaton vv, pedersen mg, alladottir ho, gregory pe, rose nr, mortensen pb. the prevalence of 30 icd-10 autoimmune diseases in denmark. immunol res 2010; 47: 228–231.

hammers cm, stanley jr. mechanisms of disease: pemphigus and bullous pemphigoid. annu rev pathol 2016; 11: 175–197.

goletz s, zillikens d, schmidt e. structural proteins of the dermal-epidermal junction targeted by autoantibodies in pemphigoid diseases. exp dermatol 2017; 26: 1154–1162.

schmidt e, della torre r, borradori l. clinical features and practical diagnosis of bullous pemphigoid. dermatol clin 2011; 29: 427–438, viii–ix.

amber kt, murrell df, schmidt e, joly p, borradori l. autoimmune subepidermal bullous diseases of the skin and mucosa: clinical features, diagnosis, and management. clin rev allergy immunol 2018; 54: 26–51.

schmidt e, borradori l, joly p. epidemiology of autoimmune bullous diseases. in murrell df, ed. blistering diseases, 1st edn. springer, heidelberg, 2015: 251–264.

radford cf, razu s, williams gp, saw vp, dart jk. incidence, presenting features, and diagnosis of cicatrising conjunctivitis in the united kingdom. eye 2012; 26: 1199–1208.

milinkovic mv, jankovic s, medenica l et al. incidence of autoimmune bullous diseases in serbia: a 20-year retrospective study. j disch dermatol ges 2016; 14: 995–1005.

wong sn, chua sh. spectrum of subepidermal immunobullous disorders seen at the national skin centre, singapore: a 2-year review. br j dermatol 2002; 147: 476–480.

zillikens d, weyer s, roth a, weidenthaler-barth b, hashimoto t, brocker eb. incidence of autoimmune subepidermal blistering dermatoses in a region of central germany. arch dermatol 1995; 131: 957–958.

alpsoy e, akman-karakas a, uzun s. geographic variations in epidemiology of two autoimmune bullous diseases: pemphigus and bullous pemphigoid. arch dermatol res 2015; 307: 291–298.

kradin k. subepidermal autoimmune bullous diseases: overview, epidemiology, and associations. immunol res 2018; 66: 6–17.

schmidt e, goebeler m, hertl m et al. s2k guideline for the diagnosis of pemphigus vulgaris/foliaceus and bullous pemphigoid. j disch dermatol ges 2015; 13: 713–727.

goletz s, hashimoto t, zillikens d, schmidt e. anti-p200 pemphigoid. j am acad dermatol 2014; 71: 185–191.

prost-squarcioni c, caux f, schmidt e et al. international bullous diseases group - consensus on diagnostic criteria for epidermolysis bullosa acquisita. br j dermatol 2018; 179: 30–41.

rechts hsafrhu-hado. statistischer bericht, kennziffer: a 13 - j 15 sl. die bevölkerung in schleswig-holstein nach alter und geschlecht 2015 - endgültige ergebnisse - forschreibung auf basis des zensus 2011.

loget j, barbe c, duvert-lehembre s et al. the regibul register: a tool for monitoring the distribution and incidence of autoimmune bullous dermatoses in three french regions, 2010 to 2015. acta derm venerol 2018; 98: 380–381.

bastuji-garin s, joly p, lemodant p et al. risk factors for bullous pemphigoid in the elderly: a prospective case-control study. j invest dermatol 2011; 131: 637–643.

lloyd-lavery a, chi cc, wojnarowska f, taghipour k. the associations between bullous pemphigoid and drug use: a uk case-control study. jama dermatol 2013; 149: 58–62.

bech r, kibsgaard l, vestergaard c. comorbidities and treatment strategies in bullous pemphigoid: an appraisal of the existing literature. front med 2018; 5: 238.

kibsgaard l, bay b, deleuran m, vestergaard c. a retrospective consecutive case-series study on the effect of systemic treatment, length of admission time, and co-morbidities in 98 bullous pemphigoid patients admitted to a tertiary centre. acta derm venerol 2015; 95: 307–311.

forstki ak, jokelainen j, timonen m, tasanen k. increasing incidence of bullous pemphigoid in northern finland: a retrospective database study in oulu university hospital. br j dermatol 2014; 171: 1223–1226.

rozenblat m, halaj a, rozendalt t et al. mortality and risk factors among israeli bullous pemphigoid patients. arch dermatol res 2019; 311: 19–27.

brick ke, weaver ch, lohse cm et al. incidence of bullous pemphigoid and mortality of patients with bullous pemphigoid in olmsted county, minnesota, 1960 through 2009. j am acad dermatol 2014; 71: 92–99.

serwin ab, musialkowska e, pisacik m. incidence and mortality of bullous pemphigoid in north-east poland (podlaskie province), 1999–2012: a retrospective bicentric cohort study. int j dermatol 2014; 53: e432–437.

dainichi t, koga h, tsuji t et al. from anti-p200 pemphigoid to antilaminin gamma1 pemphigoid. j dermatol 2010; 37: 231–238.