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Hamburg University of Applied Sciences

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Comorbid skin diseases in psoriasis – results of nationwide occupational skin screenings

- master thesis -

In collaboration with the Institute for Health Services Research in Dermatology and Nursing

University Medical Center Hamburg-Eppendorf (UKE)

IVDP
Institute for Health Services Research in Dermatology and Nursing

First examiner: Prof. Dr. med. Ralf Reintjes (HAW Hamburg)

Second examiner: Prof. Dr. med. Matthias Augustin (UKE, Hamburg)

Submitted by: Nicole Zander, matriculation number: 2013497

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Table of Contents

List of tables

List of figures

Abbreviations

95% CI	95% Confidence Interval
ANOVA	Analysis of Variance
BMI	Body Mass Index
IVDP	Institute for Health Services Research in Dermatology and Nursing
NRS	Numerical rating scale
OR	Odds Ratio
PASI	Psoriasis Area and Severity Index
QoL	Quality of Life
RKI	Robert Koch-Institut
SF-36	Short Form 36
SPSS	Statistical Package for Social Sciences
UKE	University Medical Center Hamburg-Eppendorf
VEGF	Vascular endothelial growth factor
WHO	World Health Organization

Abstract

Background: Psoriasis is a skin disease with high relevance for public health that causes burden both for the patients and the society. While general comorbidities of psoriasis are known quite well, the field of comorbid skin diseases is only fragmentarily explored with partly opposing results.

Objective: To further investigate the complex field of psoriasis and associated skin diseases by identifying skin comorbidity patterns and defining patient groups with special needs in an extensive cohort of employees in Germany.

Methods: Multivariate analysis of data deriving from occupational skin cancer screenings was conducted. From 2001 to 2014 German workers between 16 and 70 years from different branches underwent single whole-body screenings provided by trained dermatologists on the occasion of screening for skin cancer as offered by the companies. All clinical dermatological findings were recorded electronically using a standardized data entry mask. Need for treatment was determined on the basis of the dermatologist's assessment. Next to descriptive analyses correlations were examined by cross tabulations, t-test analyses and analyses of variance.

Results: Data from 138,930 persons (56.5% male, mean age 43.2) were evaluated. Psoriasis prevalence was 2.0%. Compared to participants without psoriasis, increased prevalences of further skin diseases were found for teleangiectasia (12.1%), onychomycosis (8.6%), folliculitis (6.4%), tinea pedis (6.2%), and rosacea (3.8%). Psoriatic patients had significantly higher BMI. Cardiovascular remedies and steroids were used more frequently by psoriasis patients. An increased need for treatment among psoriatic patients was found for onychomycosis (4.5%), tinea pedis (3.5%), dysplastic nevi (6.0%), actinic keratosis (1.4%), and basal cell carcinoma (1.1%).

Conclusion: People with psoriasis are at special risk to suffer from comorbid diseases. In the dermatological context, particular attention should be paid on fungal diseases.

1. Introduction

To illustrate the relevance of this work, background information will be provided. For that purpose the current state of literature concerning basic facts on psoriasis and the association with comorbidity, body mass index (BMI), and pharmaceutical treatment will be presented. Based on that, the research objective will be drawn.

1.1 Psoriasis in clinical aspects, epidemiology and current health care situation in Germany

Psoriasis is one of the most prevalent immune-mediated disorders in Germany, affecting about 2.5% of the general population [1]. It is a recurrent skin disease that does not only manifest in scaling skin lesions, but is rather a systemic disorder with a multifactorial etiology based on a genetic predisposition and triggered by internal and external factors [2]. Psoriasis is chronic in 90% of the cases [3]. Due to the visible nature of lesions and associated complaints, patients are facing striking impairment in quality of life (QoL) [4]. The concept of QoL is a patient-reported measure that reflects how individuals experience their health status including physical and emotional well-being as well as satisfaction with social functioning [5, 6]. Many psoriatic patients report physical discomfort, limitations in their daily activities and social contacts, impaired social functioning, and a negative body and self-image [7]. Furthermore, psoriasis can have a negative impact on work and profession. Studies have shown that the ability to work can be reduced and that there is a negative correlation between psoriasis severity with employment and income levels [8–11]. In addition, substantial direct costs, work limitations and productivity loss cause a significant societal burden [12–15].

Due to the complexity of psoriasis as a systemic disease, the treatment often requires the involvement of various providers of care. In Germany, the treatment of psoriasis has been standardised by recommendations given in an evidence-based (S3) guideline that was published in 2006 and reviewed in 2011 [2]. Nevertheless, nationwide studies on the quality of care have shown that a significant proportion of patients with psoriasis is not treated according to these guidelines [16] and that there are great regional variations in the quality of care [17]. Consequently, many patients claim to be dissatisfied with the treatment of their disease [18, 19].

One common symptom of psoriasis with a strong impact on the patient's QoL is pruritus [20]. It describes an unpleasant skin condition that causes the desire to scratch the skin in order to get relief [21]. Referring to the International Forum for the Study of Itch, chronic pruritus can be defined as itching for at least 6 weeks causing highly impaired QoL and night sleep [22]. Almost 90% of psoriatic patients reported pruritus in a study conducted by Reich et al. in 2010. Compared to patients who did not experience itching, they had a significantly impaired QoL ($p=0.02$). Furthermore, severity of pruritus was associated with feelings of stigmatisation, stress, and depressive symptoms. [23] In a study by Globe et al., the majority of psoriasis patients reported that pruritus is the most important, severe, and troublesome symptom, affecting daily activities like concentration, attendance at work, and sleep [24].

1.2 Comorbidities in psoriasis

Knowing common comorbidities of diseases is important in order to have the possibility to prevent them or at least to detect them early. This and appropriate treatment are essential for avoiding progression to more advanced stages and more severe negative impact on the course of disease and patient's QoL. In the particular case of psoriasis, studies have shown that those patients with a comorbid disease show worse QoL scores, especially in the physical component of the SF-36, a questionnaire to assess health-related QoL [25]. By identification of skin comorbidity patterns, patient groups with special needs in psoriatic care can be defined, which is a requirement for targeted, adequate, and economical health care.

A growing amount of literature recognises psoriasis as a systemic inflammatory disease which is consequently associated with several comorbidities [26–28]. About 19% of psoriasis patients suffer from psoriatic arthritis [29]. Other common comorbidities are cardiovascular diseases, metabolic syndrome, which includes arterial hypertension, obesity, and abnormalities in lipid and glucose metabolism, often resulting in diabetes, and chronic autoimmune diseases [27, 30]. Psychosocial stigmatisation and resulting depression can also be viewed as comorbid diseases intensifying the patient's burden [31].

While the above mentioned comorbidities and their implications on the treatment of psoriasis have been constantly discussed in the past years, there is little data on how psoriasis is associated with other dermatological diseases. Current literature has reported associations between psoriasis and certain skin diseases but often these results are inconsistent. One example is tinea pedis, the most common superficial fungal infection [32]. Literature findings range from a lower prevalence of tinea in psoriasis [33], over no difference compared to the general population [34], to increased prevalences [35]. Lately, Leibovici et al. reported a tinea pedis prevalence of 13.8% among psoriatic patients, which was significantly higher than in healthy control subjects (p=0.043) [36].

Another skin disease that could occur in concordance with psoriasis is onychomycosis, the most common nail disease [37]. In psoriasis, nail involvement is present in 15 to 79% of the cases with a lifetime incidence of 80-90% [38]. The psoriatic nail symptoms are morphologically similar to those of onychomycosis and therefore a distinction is often difficult. Possibly due to this similarity, studies examined in a systematic review by Klaassen et al. appear to be very heterogeneous with onychomycosis prevalence in psoriasis ranging from 4.6 to 63.1%. Nevertheless, a distinction and awareness of the coexistence of these diseases would be important in terms of contraindicated treatment regimens: While nail psoriasis is mostly treated with immunosuppressive pharmaceuticals like steroids or biologics, these drugs could exacerbate mycotic nail infections like onychomycosis [39].

Both onychomycosis and tinea pedis are common fungal infections and are known to frequently occur together in one patient [40]. Szepietowski et al. found a coexistence of tinea pedis and toenail onychomycosis in 33.8% of the cases [41].

Similar varying results are reported for vitiligo. As vitiligo is an autoimmune condition as well, associations with psoriasis appear to be very likely. In a retrospective study conducted by Sheth et al., psoriasis was the second most common comorbidity of vitiligo with a prevalence of 7.6% [42]. Zhu et al. examined genetic similarities between these two skin conditions and found that psoriasis and vitiligo share common genetic variants [43]. Sawchuk et al. concluded in a review

that appearing coexistences of psoriasis and vitiligo are most likely due to chance [44].

Poljacki et al. examined the association of psoriasis with other autoimmune skin disorders and found lichen ruber planus to occur most frequently (0.3% of psoriasis cases) followed by alopecia and vitiligo (0.2% each). None of these correlations appeared to be significant [45].

As shown above, current literature is rather inconsistent in terms of associations of psoriasis with other skin diseases. Consequently, further research is needed in that field.

1.3 BMI in dermatology

Body weight is a remarkable factor in dermatology. Obesity can result in changes in skin barrier function and collagen structure and can affect wound healing, microcirculation, and subcutaneous fat [46]. As a consequence, obesity is associated with a wide spectrum of dermatological diseases [47, 48]. As an example, Khalil et al. concluded that obese men differ significantly from non-obese in terms of intertrigo and folliculitis [49] and Alan et al. showed a positive correlation between BMI and the severity of acne [50].

The BMI is the most common measure to assess overweight and obesity. Although frequently discussed and questioned, it still functions as a reliable indicator for health-affecting body composition [51]. Khalil et al. assigned the BMI to be a significant determinant for skin diseases with a parallel association of the frequency of skin diseases and the degree of obesity. Obesity measured by the BMI reflects the abnormal metabolism, often resulting in insulin resistance, which is strongly associated with the development of skin diseases [49]. Engin et al. again underline the importance of the BMI especially in psoriasis as other parameters like fat-free mass, muscle mass, total body water, or bone mass are not directly connected to obesity and metabolism and therefore cannot function as relevant determinants of dermatological risk [52].

Many studies proved the increased prevalence of obesity among people with psoriasis [53–55]. Herron et al. for example found that 34% of psoriasis patients

are affected by obesity, compared to 18% in the general population [55]. This association can be explained by the relationship between the immune system, adipokines, and metabolism. The increased amount of fat tissue causes a lower degree of proinflammatory status [56, 57]. Inflammatory cells stimulate the production of vascular endothelial growth factor (VEGF) which can, at increased levels and in combination with inflammation, not only result in psoriasis but as well causes more severe courses of disease [58]. Accordingly, numerous studies found a positive correlation between the BMI and the severity of psoriasis as measured by the Psoriasis Area and Severity Index (PASI) [54, 59]. Hamminga et al. suggest that obesity and psoriasis might even share a common etiological mechanism [57]. Nevertheless, the causality and whether psoriasis and obesity are connected reciprocally or unidirectional still remain unclear [54, 60].

1.4 Pharmaceutical treatment of psoriasis

As psoriasis is a systemic disease with many associated comorbidities, patients are often on multi-drug regimens [61]. 23.3% of psoriasis patients use more than three systemic medications, and of these 11.2% use even more than ten [62].

According to the S3 guideline, mild psoriasis can be predominantly treated with topical agents while moderate to severe psoriasis requires systemic treatment [2]. In Germany, common pharmaceuticals used for the treatment of psoriasis include methotrexate, fumaric acid esters, cyclosporine, and acitretin [2]. The most frequently prescribed systemic agents, although not recommended in the guideline, are corticosteroids [63]. The use of biologics and lately biosimilars in moderate to severe cases of psoriasis is a rather new and promising treatment approach. Biologic agents address immune pathways that lead to psoriasis [64] and because this specificity, adverse drug reactions are limited [65].

Next to the drugs that are used directly for the treatment of psoriasis, psoriatic patients can be assumed to also have an increased intake of pharmaceuticals that are supposed to treat the comorbidities such as cardiovascular diseases, metabolic syndrome, and depression. In some cases these agents are suspected to be reciprocally related to the development of psoriasis. Beta-blockers, lithium, synthetic antimalarials, nonsteroidal anti-inflammatory drugs, and tetracyclines

appear to have a strong causal relationship to psoriasis [66]. Beta-blockers are commonly used as treatment for cardiovascular diseases such as hypertension which is associated with psoriasis [53]. In contrast to other literature, in their case control study Brauchli et al. did not find evidence that the use of anti-hypertensives is associated with an increased risk of developing psoriasis [67]. Lithium is widely used as an antipsychotic. 3.4 to 45% of patients treated with lithium develop a dermatological disease, mainly psoriasis or acne [68]. However, these reactions are often rather a psoriasisform dermatitis than a true psoriasis [69]. In their case-control analysis, Brauchli et al. found that the use of lithium increases the risk of developing psoriasis and is therefore one of the drugs most commonly associated with triggering or inducing psoriasis [70]. Nevertheless, the causal association should be treated carefully. For example, stress is a known risk factor for psoriasis. Therefore it is possible that rather a stressful psychiatric crisis has induced the occurrence of psoriasis than lithium treatment [69]. Tetracyclines are one of the antibiotics often used in psoriasis but their influence on the course of psoriasis remains controversial [71]. Tsankov et al. for example found that 4.11% of psoriatic patients had an exacerbation of their disease after tetracycline treatment [72].

The state of knowledge concerning the association between psoriasis and drugs is not fully clear. While there are studies that report correlations, others do not. For example Xhaja et al. did an epidemiological study on trigger factors in psoriasis and found no significant difference between people who received certain drugs and those who did not [73]. Generally, most of the drugs seem to exacerbate psoriasis rather than inducing it [69]. Nevertheless, the analysis of commonly used drugs in psoriasis can contribute to examining possible influences: for example, the intake frequency of certain drugs can give a hint on the presence of comorbidities such as hypertension, psychiatric conditions, or diabetes.

1.5 Objective

Data presented above indicate that psoriasis is a disease with high relevance for public health, causing burden both for the patients and the society. The BMI is known to be associated with dermatological conditions in general and especially to have an influence on psoriasis. Knowing comorbidities is essential for proposing adequate treatment and for avoiding more severe negative impact on the patient's QoL. Up to now however, the field of skin-related comorbidities is only fragmentarily explored with partly opposing results.

Therefore, the objective of the present work is to further investigate the complex field of psoriasis and associated skin diseases by identifying skin comorbidity patterns and defining patient groups with special needs in a large cohort of employees in Germany.

This objective is to be investigated by answering the following research questions:

1. Do people with psoriasis show a stronger association with other skin diseases compared to people without psoriasis?
2. Pruritus:
    a. Do people with psoriasis suffer significantly more often from pruritus?
    b. Does psoriasis have an influence on the pruritus severity degree?
    c. How does the degree of severity differ between different skin diseases?
3. Is obesity more prevalent among people with psoriasis?
4. Do people with psoriasis have a higher BMI than
    a. people without psoriasis?
    b. people who suffer from other inflammatory skin diseases?
5. Is the use of pharmaceuticals for widespread diseases like e.g. high blood pressure associated with psoriasis?
6. Which percentage of people with psoriasis exhibit at least one dermatological condition which requires treatment or follow-up?
7. Does the proportion of skin diseases with need for further treatment vary according to the presence or absence of psoriasis?

2. Methods

To answer the research questions, secondary data was analysed, meaning that data was not collected directly for this purpose. Consequently, a sample size and power calculation was not applied. The long-term standardised assessment is expected to provide an extensive data set that is suitable to allow expedient analysis. Nevertheless, the validity of data will be tested in the course of the statistical procedures.

2.1 Study design and participants

The present analysis was designed as an observational study. Data were derived from systematic documentation of dermatological whole-body screenings conducted from 2001 to 2014 in adult workers in Germany. Within this timeframe, several screenings were conducted assessing data at one particular point of time. Accordingly, data collection was cross-sectional. In 2009 and 2010 there was no data assessment. The screenings were initiated by Heigel GmbH, a company that works in the field of secondary prevention of dermatological, phlebological, and cardiovascular diseases throughout Germany since 1989. Dermatologists provided whole-body screening examinations for skin cancer and standardised interviews. These screenings were done on a voluntary basis during the regular working hours. The mean duration of an examination was approximately 15 minutes.

The participating companies mostly belonged to producing branches as well as service and marketing organisations. Examples are car industry, chemical industry, banks, insurance companies, printing houses, or energy companies. They varied in size from 150 to 65,000 employees. The smaller ones were mainly branches of banks or postal services and the bigger ones predominantly automobile factories. All employees, regardless of age, sex, or societal status, were invited to participate.

The methodology and validity of these procedures have been proven in previous studies that used data of these occupational screenings for different objectives [74, 75].

All data that has been transmitted to the analysing institute IVDP has been anonymised for scientific purposes so that the researchers are not able to draw conclusions on certain persons. Data retention and data protection in the institute is done after ISO 9001:2000. Since the conducted study is non interventional, no ethics committee vote is needed.

2.2 Outcomes

For every participant, age, gender, melanocytic and epithelial tumours were documented. Further parameters collected were historical information on skin cancer, UV exposure, atopic diseases, and allergies. Skin type, inflammatory, viral, fungal, and bacterial skin diseases, non-malignant non-inflammatory skin changes, cysts and subcutaneous skin changes, suspected malignant skin changes and their preliminary stages, and vessel changes of the skin were directly diagnosed by the dermatologist. In case of abnormal findings, the patients got explanatory letters and were advised to consult a dermatologist. All findings were recorded in a standardised computer-based report form.

Next to the previously mentioned core variables that were assessed in every screening with secondary data character, there were some years with additional conditions in focus. These additional topics can be classified as primary data as they were commissioned for certain research objectives. From 2006 to 2008, the intake of the most common pharmaceuticals was assessed. These were cardiovascular remedies, oral contraceptives, thyroid drugs, lipid reducers, antiallergics, analgesics, antacids, steroids, antipsychiatric drugs, and antibiotics. In 2008, the presence and characteristics of pruritus and intensity (scored on a numerical rating scale [NRS] from 0 for lowest to 10 for highest intensity) was documented. In 2011, the focus was hyperhidrosis and from 2012 to 2014, occupational dermatoses were assessed additionally. Another screening in 2012 explored allergies more deeply including associated medication use and hyposensitisation therapy. In total, there is one master data set containing all core variables assessed from 2001 to 2014. Additional screenings where data on pharmaceuticals, pruritus and BMI were assessed were merged to separate data

sets. Table 1 shows an overview of the used data sets of the present thesis. (See appendix 2 for the whole variable list.)

Table 1: Data sets used for analysis

data set	years of data collection	n
master data set	2001-2014	138,930
pharmaceuticals	2006-2008	42,215
pruritus	2008	11,732
BMI	2012-2014	18,725

As body composition parameters, weight and height were assessed. The BMI was calculated (weight [kg]/(height [m]^2)) and the resulting values were categorized into groups according to the classification used by the World Health Organization (WHO): < 18.5 underweight, 18.5-24.99 normal range, ≥ 25 overweight, ≥ 30 obesity [76].

During the screenings, the dermatologists used computer-based entry masks for the data assessment (see appendix 1). Information got automatically transferred into excel files which were sent to the analysing institute separately for each screening period. The single screenings were merged to one data set containing all core variables. Additionally smaller data subsets were created to examine the more specialised topics like pruritus, pharmaceuticals or BMI.

2.3 Definition of the need for treatment

Besides the presence of a clinical finding it was also recorded whether it requires treatment or follow-up. This was done regardless whether the patient was already attending dermatologic therapy. The dermatologist determined need for care after recording historical information and the clinical examination. During the years of data collection, the coding of the need for treatment changed. While in the first three years there was a distinction between “treatment needed” and “treatment urgently needed”, this differentiation was eliminated in the following screenings in order to avoid variances due to the subjectivity of the rating of how urgently a treatment is needed. To make the whole data set comparable, the two categories “treatment needed” and “treatment urgently needed” were summarised where

necessary and a dichotomous variable on the presence of the need for treatment was created for each disease assessed.

2.4 Statistical analyses

All data analyses were performed using SPSS (Statistical Package for Social Sciences) version 22. Inclusion criterion was age between 16 and 70 years at the time of examination. This was done in order to obtain a data set representing adult workers in Germany. All missing values were interpreted as absence of the certain disease or “not applicable” for example in the case of solarium use or drug intake.

Data was collected on a voluntary basis. Thus a selection bias cannot be ruled out completely, which could, for example, lead to an over- or underrepresentation of certain age groups due to diverse attitudes towards skin cancer screenings or age specific health concerns. In order to control for this possible bias, data were standardised on the basis of the age distribution of the general German working population. For that purpose, the age distribution in the present data set was compared to data of the whole working population and a weighting factor for each age group was calculated. All following calculations of rates and correlations were weighted by this factor.

For all analyses the significance level was set to 5%.

Prevalences were calculated for the whole study population and stratified by gender. Age was categorized into decades beginning at 30 years. Participants between 16 and 30 years were summarised into one group as they represent only a small subgroup.

Before conducting correlation analyses, data were checked for plausibility. For that purpose, prevalences of the relevant diseases were calculated and then compared to literature findings on the emergence of these diseases. Additionally, the age and BMI distribution in the data set were compared to the overall German population. This allows to rate the representative status of the data set for Germany.

The data set consists of several single sets that can be combined and then analysed as a whole due to the consistency of the assessed variables.

Nevertheless, variations over time are possible. In order to control for that and to be able to make statements on the time trends, each data set was analysed separately with regard to psoriasis prevalence, age, and BMI.

Correlations were examined by cross tabulations and evaluated by the chi square test. Additionally, odds ratios (OR) and their 95% confidence intervals (95% CI) were calculated. In the screening process, the single diseases were assessed on a 4-point scale (detected, treatment needed, treatment needed urgently, under treatment). These variables were transformed into dichotomous variables representing the presence of the disease whereas a missing was rated as absence. These dichotomous variables were then analysed for associations. Because of the reported association of the fungal diseases tinea pedis and onychomycosis [40], these two conditions were additionally summarised into a new variable, expressing the presence of tinea pedis and/or onychomycosis.

T-test analyses were used to test whether there are differences between participants with and without psoriasis with regard to continuous variables such as pruritus severity, BMI, and number of findings with need for treatment. The pruritus severity degree was assessed only for those who stated to be bothered by itching from a moderate to high degree. For the t-test analysis of the need for care, a new variable expressing the number of findings that need follow-up was calculated. For this purpose, all findings were summed up except for psoriasis in order to specifically count the additional burden.

One way analyses of variance (ANOVA) were conducted for pruritus severity degree and BMI as dependent variables. As independent variable, the exclusively present inflammatory disease was used. This variable counts how many participants can be allocated exclusively to one certain inflammatory disease, meaning participants with more than one inflammatory disease were not considered. Consequently only the influence of that certain disease and no possible accumulated effects of various inflammatory diseases were measured.

3. Results

Firstly, the participant characteristics will be portrayed including age and BMI distribution as well as psoriasis prevalence and the emergence of pruritus. Afterwards, results of the multivariate analyses, conducted to answer the research questions, will be shown.

3.1 Participant characteristics

In total, 139,207 persons were examined. 277 did not meet the inclusion criterion of age 16-70 and therefore were excluded from analysis. The remaining data set that was used for statistical analyses consisted of n=138,930 participants. 56.5% of them were male and 43.5% female. The mean age was 43.2 (± 10.9) (44.1 for male and 42.0 for female) with a range from 16 to 70 years. Age group distribution is shown in figure 1.

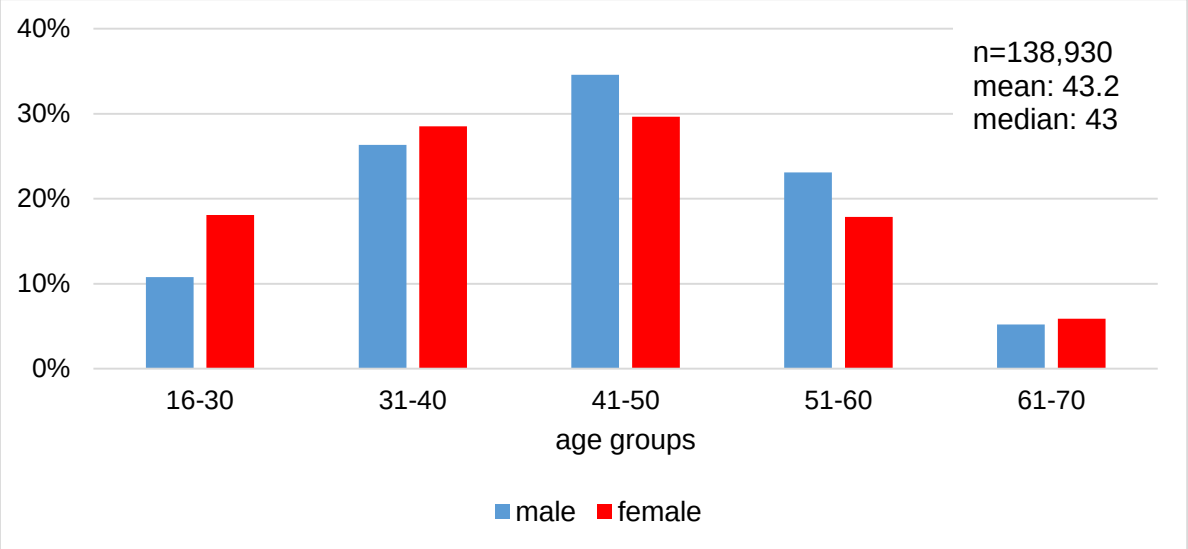

Figure 1: Age distribution in the master data set, n=138,930

Over the years of data collection, the mean age had a range of 4.2 years and was lowest in 2001 (39.8 years) and highest in 2007 (44.1 years). There was no observable trend over the timeframe of data collection (see appendix 3.2).

On average, 11,578 participants were examined per year (see appendix 3.3). The number of participants was lowest in 2001 with 739 participants and highest in 2007 (16,258 participants).

The data subset that contains information on the BMI includes n=18,725 employees. The mean BMI was 25.3 kg/m² (± 4.1). The BMI can be allocated to the categories given by the WHO as shown in figure 2.

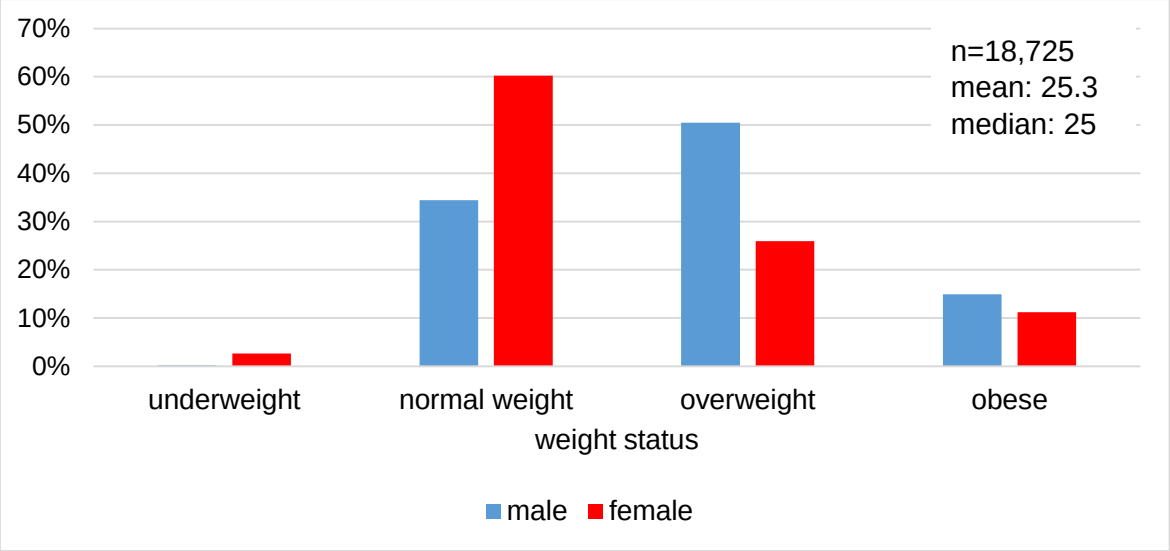

Figure 2: BMI distribution in the master data set, n=18,725

45.4% of the participants reported normal weight, obesity prevalence was 13.3%.

At least one dermatological finding requiring treatment was found in 26,983 (19.4%) participants. The proportion of patients with need for care increased continuously with increasing age, from 15.5% among the youngest to 25.6% of the people between 61 and 70 years.

The screenings that were done since 2012 collected information on the field of work. The participants were allocated to the categories office work, metal processing, chemical profession/laboratory, storage area and other professions. Figure 3 shows the distribution of the different branches. Almost 80% of the participants were doing office work.

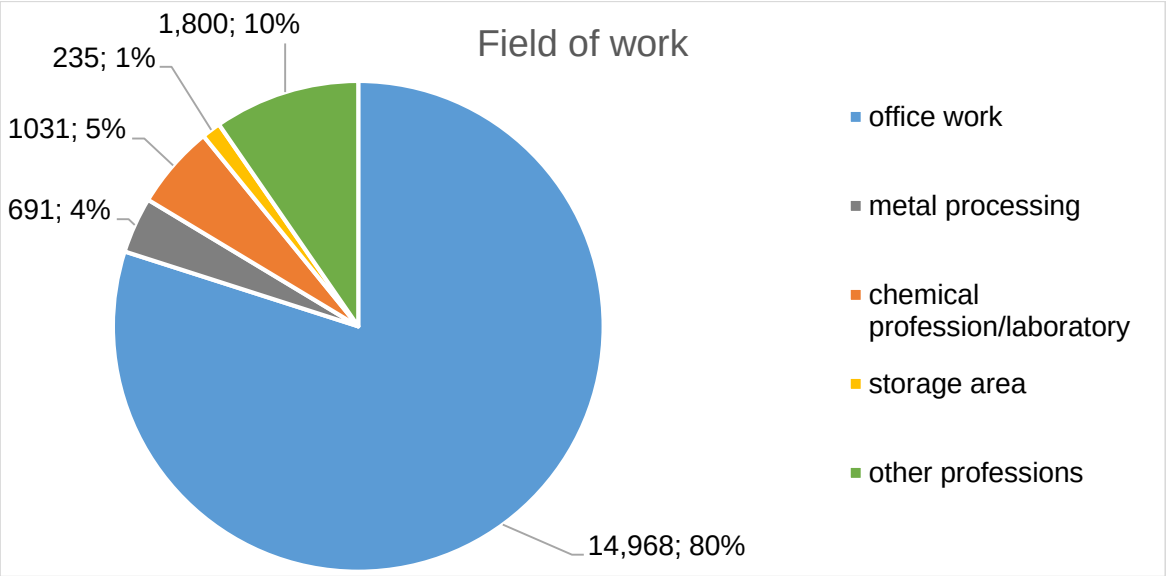

Figure 3: Distribution of the field of work, n=18,725

3.2 Plausibility Checks

To check whether the data set is representative for the German working population, the age distribution of the data set and the population of Germany were compared. The same was done with the BMI. While the BMI was quite similar in both populations except for the age group over 60, there is greater variance in age composition with employees from 30 to 50 years of age being somewhat more represented in the data set. Figures 4 and 5 show these comparisons.

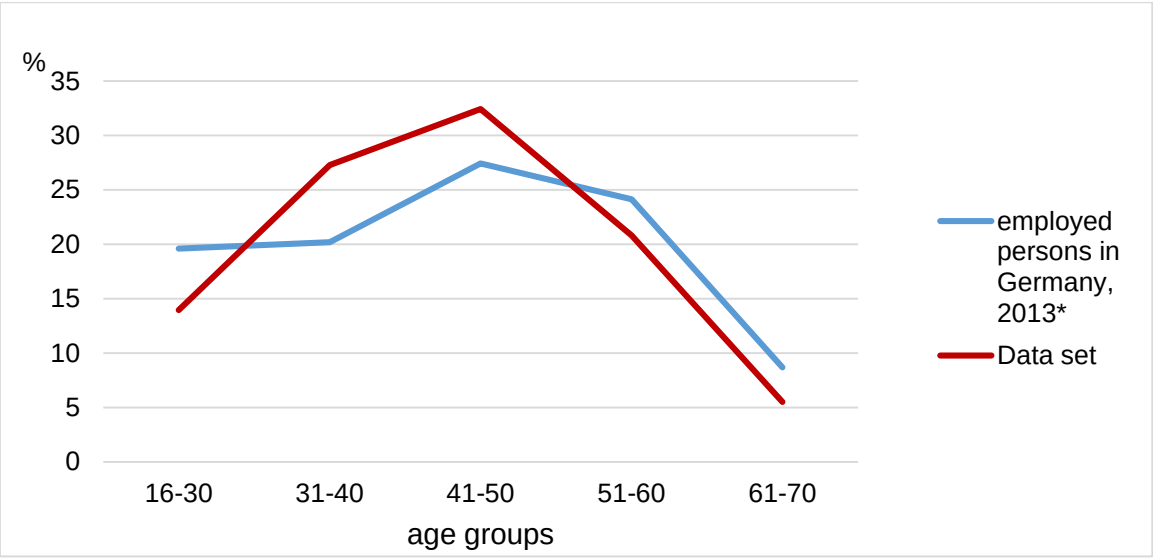

*Figure 4: Comparison of the distribution of age groups amongst employed persons, *Mikrozensus 2013[77]*

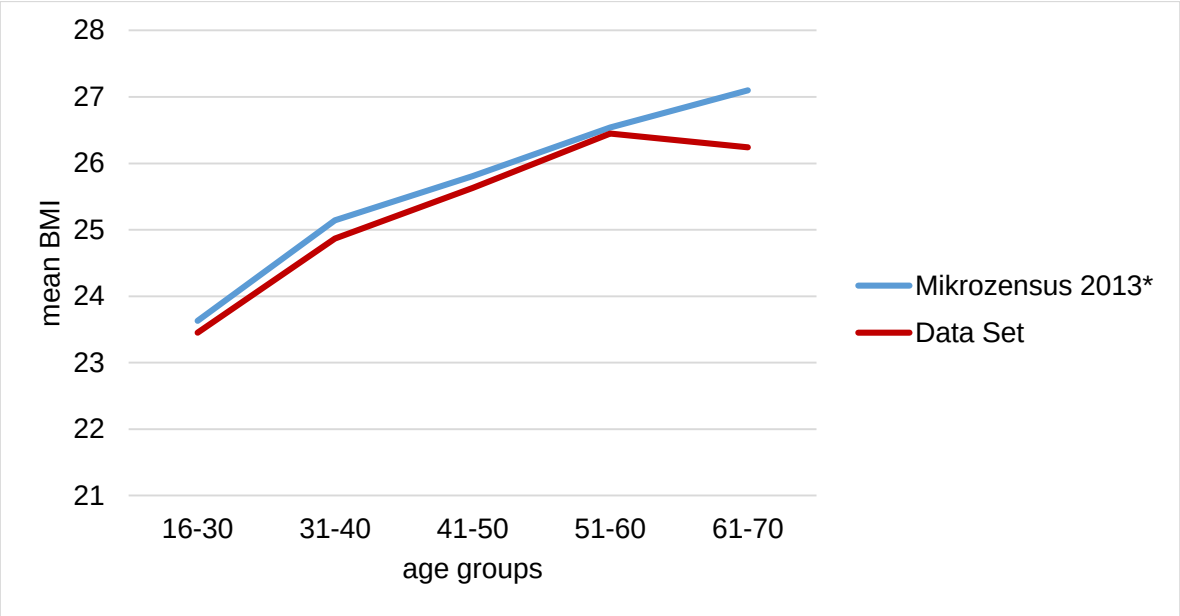

*Figure 5: Comparison of the BMI of participants included in analysis and whole Germany, *Mikrozensus 2013[77]*

3.3 Prevalence

Psoriasis

Out of the 138,930 participants, 2,781 had psoriasis, resulting in a prevalence of 2%. Male participants (2.2%) were affected more often than female (1.7%). Age standardisation on the basis of all employed persons in Germany had no influence on the prevalence of psoriasis. Stratification for age showed that psoriasis was found more often in the higher age groups, except for the oldest age group where a slight decrease of prevalence could be observed. Through the years of screening, the prevalence ranged from 1.8% in 2013 to 2.4% in 2001. The differences did not show any trends or regularities (see appendix 3.1).

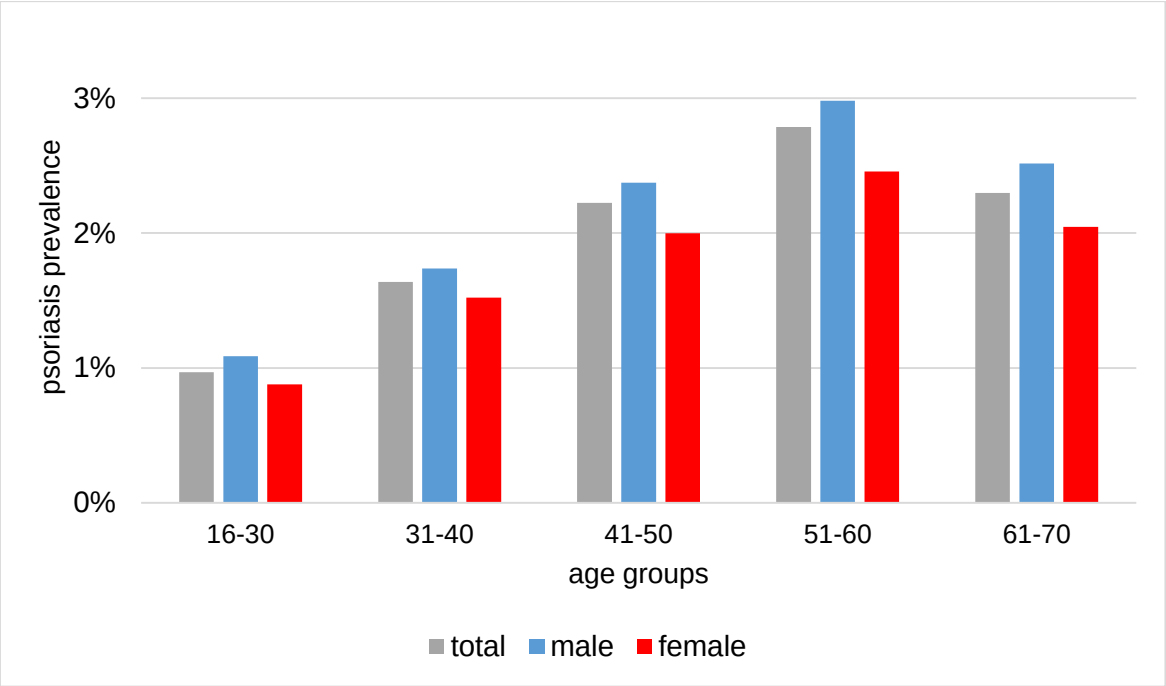

Figure 6: People with psoriasis by age and sex, n=138,930

The skin type had no significant influence on the occurrence of psoriasis. The prevalence was between 1.7 and 2.1%.

The lowest psoriasis prevalence (1.8%) was measured in employees doing office work and metal processing, followed by 1.9% in chemical professions/laboratory, and 2.1% in storage area workers. These differences were not significant.

Pruritus

The data set containing information on pruritus comprises 11,732 participants (51.8% male and 48.2% female). The mean age was 44.1 (± 12.3). Data collection was done in 2008. 1,961 participants claimed that they experienced pruritus within the past 6 weeks, resulting in a point prevalence of 16.7%. Among those, the itching was mentioned to be occasionally present in 74.0%, frequently in 18.8% and constantly present in 7.2%. Women were slightly more affected than men with a prevalence of 17.5% compared to 16.0%. Chi square test showed that this difference was significant with p=0.031. Information on the severity was present for those 696 participants who stated to be bothered by itching to a moderate or high degree. Measured on a NRS ranging from 0 (lowest intensity) to 10 (highest

intensity) the mean degree of severity was 5.4 (± 2.3). It was slightly higher in women (5.7) than in men (5.1).

Figure 7 shows the presence of pruritus in the different exclusively present inflammatory skin diseases.

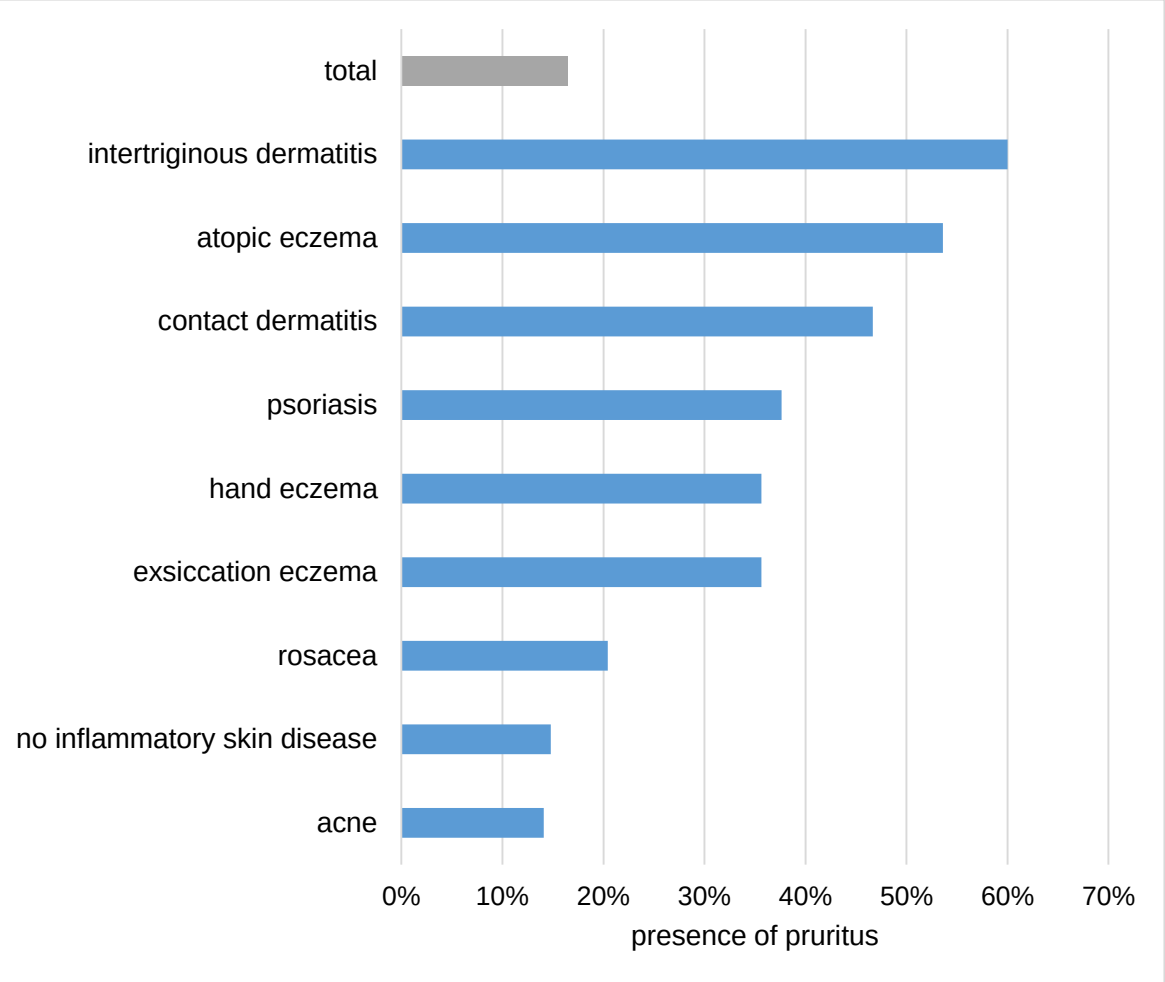

Figure 7: Pruritus in inflammatory diseases, n=11,617

3.4 Multivariate data analyses

In this section the correlation of psoriasis with different parameters is analysed. The association of psoriasis with other skin diseases is examined in order to answer research question number 1. Research question number 2 is faced by analysing the emergence of pruritus among psoriatic patients and people suffering from further inflammatory skin diseases. The role of the BMI is examined in accordance with research questions 3 and 4. Question number 5 concerning the use of pharmaceuticals follows and eventually the association of psoriasis and the

presence of further conditions with need for treatment is dealt with to meet research questions 6 and 7.

3.4.1 Psoriasis and other skin diseases

Both for men and women onychomycosis was the most frequent skin-related comorbidity of psoriasis (11.0% for men, 4.7% for women) followed by folliculitis (8.3% for men, 3.4% for women). In both cases men were significantly more affected than women. The third most common comorbidity in men was tinea pedis (8.2%) and rosacea in women (3.6%). 35.1% of tinea pedis patients additionally suffered from onychomycosis. The association was significant with p≤0.001 and OR=9.5 (95% CI 9.0-10.0).

The most common inflammatory skin-related comorbidity was rosacea with a prevalence of 3.8%. Table 2 shows the prevalence of the examined diseases among psoriasis patients and the significance of the sex differences calculated by the chi square test.

Table 2: Prevalence of skin diseases among psoriatic patients, significance of gender differences

	prevalence among patients with psoriasis			**difference between men and women asymptotic significance (2-sided)**
	total (n=2,781)	**male (n=1,728)**	**female (n=1,053)**	
inflammatory skin diseases				
rosacea	3.8%	3.9%	3.6%	0.721
acne	2.0%	2.2%	1.7%	0.374
atopic eczema	0.9%	1.0%	0.8%	0.454
intertriginous dermatitis	0.9%	0.4%	1.8%	≤0.001
exsiccation dermatosis	0.9%	1.2%	0.4%	0.032
hand eczema	0.5%	0.6%	0.4%	0.472
contact dermatitis	0.1%	0.1%	0.3%	0.126
viral diseases of the skin				
verruca vulgaris (feet)	2.2%	2.1%	2.4%	0.249
verruca vulgaris (hands)	0.7%	0.8%	0.5%	0.346
fungal diseases of the skin				
tinea pedis and/or onychomycosis	12.8%	16.7%	6.6%	≤0.001

	prevalence among patients with psoriasis			difference between men and women asymptotic significance (2-sided)
	total (n=2,781)	male (n=1,728)	female (n=1,053)	
onychomycosis	8.6%	11.0%	4.7%	≤0.001
tinea pedis	6.2%	8.2%	2.9%	≤0.001
pityriasis versicolor	0.5%	0.4%	0.6%	0.537
tinea corporis	0.5%	0.6%	0.4%	0.471
bacterial diseases of the skin				
folliculitis	6.4%	8.3%	3.4%	≤0.001
pyoderma	0.4%	0.5%	0.1%	0.069

Haemangioma and solar (senil) lentigines were the most frequent skin changes both in men and women with psoriasis. Spider veins are significantly more common among women and were the third frequent skin changes among them, while in men fibromas ranked third. Table 3 shows the emergence of all assessed skin changes in men and women and the significance of the sex differences calculated by the chi square test.

Table 3: Prevalence of skin changes among psoriatic patients, significance of gender differences

	prevalence among patients with psoriasis			difference between men and women asymptotic significance (2-sided)
	total (n=2,781)	male (n=1,728)	female (n=1,053)	
non-malignant non-inflammatory skin changes				
solar (senil) lentigines	42.3%	39.9%	46.4%	≤0.001
fibromas	30.4%	29.6%	31.7%	0.239
seborrhoic keratosis	27.4%	25.6%	30.4%	0.007
ephelides	17.3%	16.2%	19.0%	0.058
histiocytoma	16.7%	15.6%	18.6%	0.037
café au lait spots	5.2%	4.9%	5.8%	0.286
vitiligo	0.5%	0.5%	0.7%	0.481
cysts and subcutaneous skin changes				
lipoma	1.3%	1.7%	0.8%	0.040
suspected malignant skin changes and their preliminary stages				
total	10.9%	11.3%	10.2%	0.356
dysplastic nevi	7.0%	6.5%	7.8%	0.211

	prevalence among patients with psoriasis			difference between men and women asymptotic significance (2-sided)
	total (n=2,781)	male (n=1,728)	female (n=1,053)	
actinic keratosis	2.8%	3.9%	1.0%	≤0.001
basal cell carcinoma	1.1%	1.0%	1.2%	0.638
Bowen's disease	0.1%	0.1%	0.2%	0.617
squamous cell carcinoma	0.1%	0.1%	0.1%	0.723
malignant melanoma	0.1%	0.1%	0.1%	0.871
vessel changes of the skin				
haemangioma	44.9%	46.5%	42.4%	0.032
spider veins	20.7%	12.8%	33.6%	≤0.001
teleangiectasia	12.1%	10.8%	14.2%	0.006
naevus flammeus	5.9%	4.9%	7.7%	0.002

Table 4 shows the prevalences of the listed skin diseases among patients with and without psoriasis. Only those diseases are shown where significant associations with psoriasis were detected.

Among the inflammatory skin diseases, significant associations with psoriasis could be detected with varying direction of association. Acne prevalence was significantly lower in people with psoriasis compared to those without psoriasis. Rosacea was more frequent among people suffering from psoriasis. These findings were significant both for men and women. Stratification for sex showed also an additional significant association for intertriginous dermatitis. Women with psoriasis were more than twice as often affected than women without psoriasis.

Regarding fungal diseases, participants with psoriasis showed higher prevalences of onychomycosis and tinea pedis whereas pityriasis versicolor was significantly more frequent among people without psoriasis. These differences were significant for both sexes combined as well as for men alone.

Folliculitis was more prevalent among people without psoriasis. This difference was not significant for women alone.

Among non-malignant non-inflammatory skin changes, there were significant associations with psoriasis for café au lait spots and ephelides. In both cases the prevalence was lower for people with psoriasis compared to those without. The

association of café au lait spots was only significant for female participants. Furthermore, additional significant associations with psoriasis among the females were found for fibromas, seborrhoic keratosis, and solar (senile) lentigines.

Taking all suspected malignant skin changes together, the frequency was significantly lower in men with psoriasis than among those without. Dysplastic nevi were significantly more common among people without psoriasis than among psoriatic participants. Again this association was not significant for women alone.

Table 4: Prevalences of skin diseases among patients with and without psoriasis, red: higher prevalence for people with psoriasis, green: higher prevalence for people without psoriasis

	prevalence with psoriasis (n=2,781)			prevalence without psoriasis (n=136,149)			asymptotic significance (2 sided)			OR (95% CI)		
	total	male	female	total	male	female	total	male	female	total	male	female
inflammatory skin diseases												
acne	2.0%	2.2%	1.7%	3.6%	3.6%	3.5%	≤0.001	≤0.001	0.002	0.6 (0.4-0.7)	0.6 (0.4-0.8)	0.5 (0.3-0.8)
atopic eczema	0.9%	1.0%	0.8%	1.4%	1.3%	1.5%	0.037	0.28	0.055	0.7 (0.5-0.9)	0.8 (0.5-1.2)	0.5 (0.3-1.0)
intertriginous dermatitis	0.9%	0.4%	1.8%	0.7%	0.7%	0.7%	0.097	0.164	≤0.001	1.4 (0.9-2.1)	0.6 (0.3-1.2)	2.8 (1.7-4.4)
rosacea	3.8%	3.9%	3.6%	2.2%	2.3%	2.0%	≤0.001	0.000	≤0.001	1.8 (1.4-2.1)	1.7 (1.3-2.2)	1.8 (1.3-2.5)
fungal skin diseases												
onychomycosis	8.6%	11.0%	4.7%	6.8%	9.2%	3.9%	≤0.001	0.01	0.181	1.3 (1.1-1.5)	1.2 (1.0-1.4)	1.2 (1.1-1.5)
pityriasis versicolor	0.5%	0.4%	0.6%	1.0%	1.2%	0.8%	0.004	0.003	0.437	0.5 (0.3-0.8)	0.3 (0.2-0.7)	0.7 (0.3-1.6)
tinea pedis	6.2%	8.2%	2.9%	4.9%	7.0%	2.2%	≤0.001	0.053	0.122	1.3 (1.1-1.5)	1.2 (0.9-1.4)	1.3 (0.9-1.9)
tinea pedis and/or onychomycosis	12.8%	16.7%	6.6%	10.0%	13.6%	5.4%	≤0.001	≤0.001	0.108	1.3 (1.2-1.5)	1.3 (1.1-1.4)	1.2 (0.9-1.6)
bacterial diseases of the skin												
folliculitis	6.4%	8.3%	3.4%	7.4%	9.8%	4.5%	0.046	0.035	0.104	0,9 (0,7-0,9)	0,8 (0,7-0,9)	0,8 (0,5-1,1)
non-malignant non-inflammatory skin changes												
café au lait spots	5.2%	4.9%	5.8%	6.7%	5.6%	8.2%	0.002	0.195	0.005	0.8 (0.6-0.9)	0.9 (0.7-1.1)	0.7 (0.5-0.9)
ephelides	17.3%	16.2%	19.0%	21.6%	19.5%	24.3%	≤0.001	≤0.001	≤0.001	0.8 (0.7-	0.8 (0.7-	0.7 (0.6-

										0.8)	0.9)	0.9)
fibromas	30.4%	29.6%	31.7%	29.6%	31.0%	27.9%	0.391	0.218	0.007	1.0 (0.9-1.1)	0.9 (0.8-1.0)	1.2 (1.0-1.4)
seborrhoic keratosis	27.4%	25.6%	30.4%	25.2%	25.4%	25.0%	0.007	0.806	≤0.001	1.1 (1.0-1.2)	1.0 (0.9-1.1)	1.3 (1.1-1.5)
solar (senil) lentigines	42.3%	39.9	46.4%	39.8%	39.4%	40.4%	0.008	0.711	≤0.001	1.1 (1.0-1.2)	1.0 (0.9-1.1)	1.3 (1.1-1.4)
suspected malignant skin changes												
dysplastic nevi	7.0%	6.5%	7.8%	8.1%	8.7%	7.4%	0.032	0.002	0.66	0.9 (0.7-0.9)	0.7 (0.6-0.9)	1.1 (0.9-1.3)
total	10.9%	11.3%	10.2%	11.6%	13.3%	9.4%	0.249	0.016	0.418	0.9 (0.8-1.1)	0.8 (0.7-0.9)	1.1 (0.9-1.3)
vessel changes of the skin												
teleangiectasia	12.1%	10.8%	14. 2%	8.9%	8.0%	10.0%	≤0.001	≤0.001	≤0.001	1.4 (1.3-1.6)	1.4 (1.2-1.6)	1.5 (1.3-1.8)
spider veins	20.7%	12.8%	33.6%	20.3%	12.8%	29.6%	0.589	0.970	0.005	1.0 (0.9-1.1)	1.0 (0.9-1.2)	1.2 (0.9-1.1)

Teleangiectasia was the only vessel change of the skin where a significant association with psoriasis could be detected for both sexes. It was more frequent among people with psoriasis than those without. Female participants with psoriasis were significantly more often affected by spider veins than those without psoriasis.

For viral and bacterial diseases as well as cysts, no significant differences in the prevalence between people with and without psoriasis could be detected.

3.4.2 Psoriasis and pruritus

A significant association with p≤0.001 was found between psoriasis and pruritus. Among participants with psoriasis, pruritus was present in 39.1% in the past six weeks whereas it was only 16.2% in people without psoriasis. The odds for suffering from pruritus was OR=3.3 (95% CI 2.6-4.3) for psoriasis patients. Figure 8 shows this distribution for the different age groups.

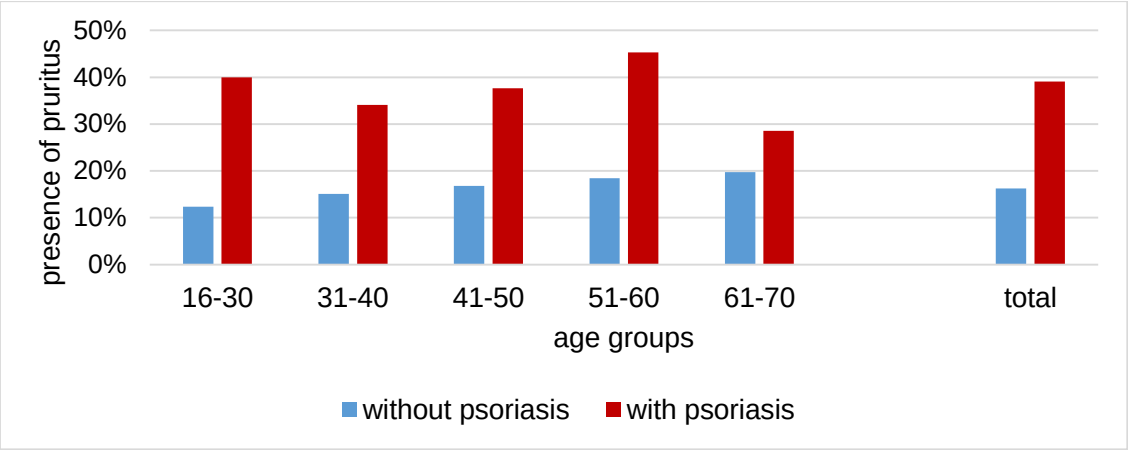

Figure 8: Pruritus within the last six weeks by age for patients with and without psoriasis, n=11,730

The mean pruritus severity degree was 5.4 (± 2.3) among people without psoriasis and 5.9 (± 2.0) among people with psoriasis. T-test analysis showed that this difference was not significant.

The average degree of pruritus severity for different inflammatory skin diseases is shown in table 5. Intertriginous dermatitis and contact dermatitis were summarised due to small group size (3 cases each).

Table 5: Average degree of pruritus of inflammatory skin diseases

exclusively present inflammatory disease	n	mean pruritus severity degree	standard deviation	standard error	95%-confidence interval of means		min	max
					lower limit	upper limit		
no inflammatory skin disease	502	5.2	2.4	0.1	5.1	5.5	0	10
acne	20	4.7	1.5	0.3	4.0	5.4	2	9
atopic eczema	49	6.0	2.5	0.4	5.3	6.8	1	10
exsiccation eczema	32	5.1	1.8	0.3	4.4	5.7	2	9
hand eczema	23	6.2	2.1	0.4	5.3	7.1	3	10
intertriginous dermatitis or contact dermatitis	6	5.8	2.3	0.9	3.4	8.2	2	8
psoriasis	36	5.5	2.0	0.3	4.9	6.2	1	9
rosacea	24	5.5	2.5	0.5	4.4	6.5	1	10
total	693	5.4	2.3	0.1	5.2	5.5	0	10

Levene's test was significant with p=0.009, indicating the requirement of homogeneity of variances is not given. Accordingly, the robust Welch test for the analysis of means was used. The test showed that the groups did not differ significantly with F(7/53.903)=1.7 and p=0.123.

3.4.3 BMI in psoriasis

Obesity (BMI≥30) had a prevalence of 21.2% among the people with psoriasis and 13.1% among those without. This difference was significant for both sexes with p≤0.001. The odds for being obese was 1.8 times higher for people with psoriasis than for people without (OR=1.8; 95% CI 1.4-2.3). Stratification for age groups showed that within the single age groups there were no significant associations of psoriasis and obesity, except for the highest age group (61-70 years). The percentage of people with obesity was generally higher in men than in women.

Time trend analysis of the BMI indicated that the mean BMI increased over time. Analyses of variance with the BMI as dependent variable and the year of data collection as independent factor showed that the differences between the groups were significant with F(2/18723)=37.2 and p≤0.001. Scheffé's post hoc test identified significant differences between every year of data collection. Table 6 shows these results.

Table 6: BMI development over time

	year of data collection		
	2012 (n=1,209)	**2013 (n=9,495)**	**2014 (n=8,021)**
mean BMI	24.7	25.2	25.6
± standard deviation	±4.0	4.1	4.0

The mean BMI among people without psoriasis was 25.3kg/m² (± 4.1) while it was 26.5kg/m² (± 4.5) for psoriasis patients. T-test analysis showed that this difference was significant with p≤0.001. Table 7 shows mean BMI values in different inflammatory diseases.

Table 7: Average BMI in inflammatory skin diseases

exclusively present inflammatory skin disease	n	mean BMI	standard deviation	standard error	95%-confidence interval of means		min	max
					lower limit	upper limit		
no inflammatory skin disease	16,657	25.2	4.0	0.03	25.2	25.3	14	67
acne	403	24.3	3.9	0.2	23.9	24.7	17	49
atopic eczema	290	25.2	3.9	0.2	24.7	25.7	17	46
exsiccation eczema	63	27.7	5.4	0.7	26.4	29.1	20	48
hand eczema	101	25.9	3.2	0.3	25.3	26.5	19	35
intertriginous dermatitis	422	25.5	4.1	0.2	25.1	25.9	17	40
contact dermatitis	21	28.2	5.8	1.3	25.6	30.9	20	45
psoriasis	329	26.5	4.4	0.2	26.0	26.9	18	46
rosacea	321	27.0	4.9	0.3	26.5	27.6	18	49
total	18,606	25.3	4.1	0.1	25.2	25.3	14	67

Levene's test of homogeneity of variances was significant with $p \leq 0.001$, therefore the robust Welch test for the analysis of means was used. BMI means differed significantly ($F(8/295.045)=14.1$; $p \leq 0.001$). Post-hoc Scheffé test showed that this effect was due to a difference between psoriasis and the groups no inflammatory skin disease and acne. Further significant differences between groups are shown in table 8.

Table 8: Significant results of Scheffé multiple comparisons of means, dependent variable: BMI

diseases		**mean difference**	**significance**
no inflammatory skin disease	acne	0.96	0.005
no inflammatory skin disease	exsiccation eczema	2.49	0.003
no inflammatory skin disease	psoriasis	1.21	≤0.001
no inflammatory skin disease	rosacea	1.78	≤0.001
acne	exsiccation eczema	3.45	≤0.001
acne	intertriginous dermatitis	1.19	0.023
acne	contact dermatitis	3.94	0.017
acne	psoriasis	2.16	≤0.001
acne	rosacea	2.74	≤0.001
atopic eczema	exsiccation eczema	2.55	0.009
atopic eczema	rosacea	1.83	≤0.001
exsiccation eczema	intertriginous dermatitis	2.26	0.031
intertriginous dermatitis	rosacea	1.55	≤0.001

3.4.4 Pharmaceutical treatment

The data set containing variables on the use of common pharmaceuticals consists of 42,215 participants. Mean age was 44.0 (±12.4). 53.2% were male and 46.8% female. The prevalence of psoriasis in this data subset was 2.0%.

Cardiovascular drugs were the most commonly used pharmaceuticals, followed by oral contraceptives and thyroid drugs. Figure 9 shows the intake of all assessed drugs, divided by sex.

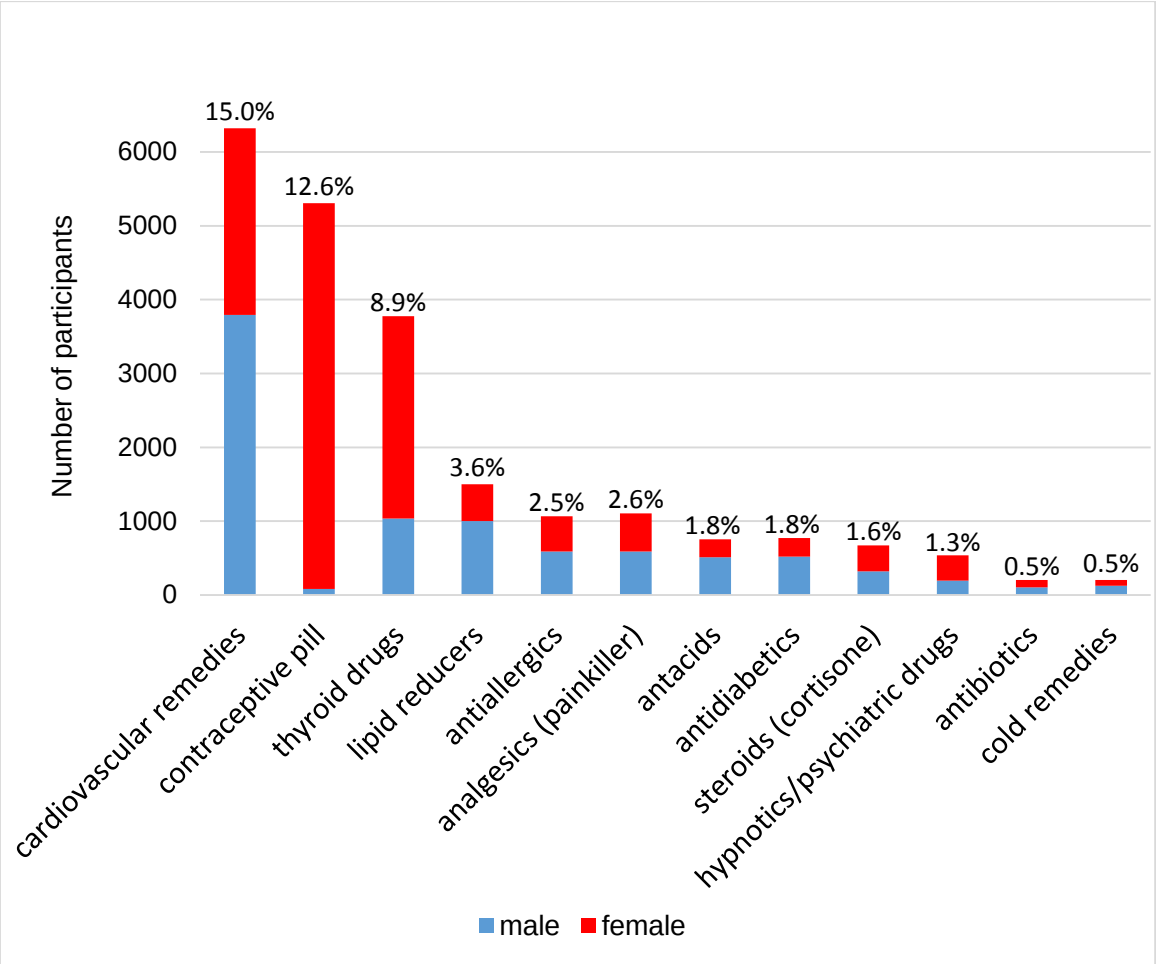

Figure 9: Use of common pharmaceuticals in absolute numbers and percentage by sex, n=42,215

Comparison of the usage frequency by people with and without psoriasis shows that most of the pharmaceuticals are more commonly used among people affected by psoriasis. Significantly higher intake by both sexes was found for cardiovascular remedies and steroids. While 19.5% of the participants with psoriasis were currently using cardiovascular drugs, only 14.9% of people that did not suffer from psoriasis were using them. Chi square test showed that this difference is significant with $p \leq 0.001$. 3.4% of people with psoriasis used steroids compared to 1.4% of people without psoriasis, this difference was significant with $p \leq 0.001$. Further significant differences were found for the male participants regarding analgesics use with 4.8% compared to 2.6% ($p=0.002$), and hypnotics/psychiatric drugs with 2.0% compared to 0.8% ($p=0.006$). Among women with psoriasis, intake of oral contraceptives was significantly ($p \leq 0.001$)

lower than among those without psoriasis (20.8% compared to 26.5%). Figure 10 shows the comparison of the use of pharmaceuticals among people with and without psoriasis.

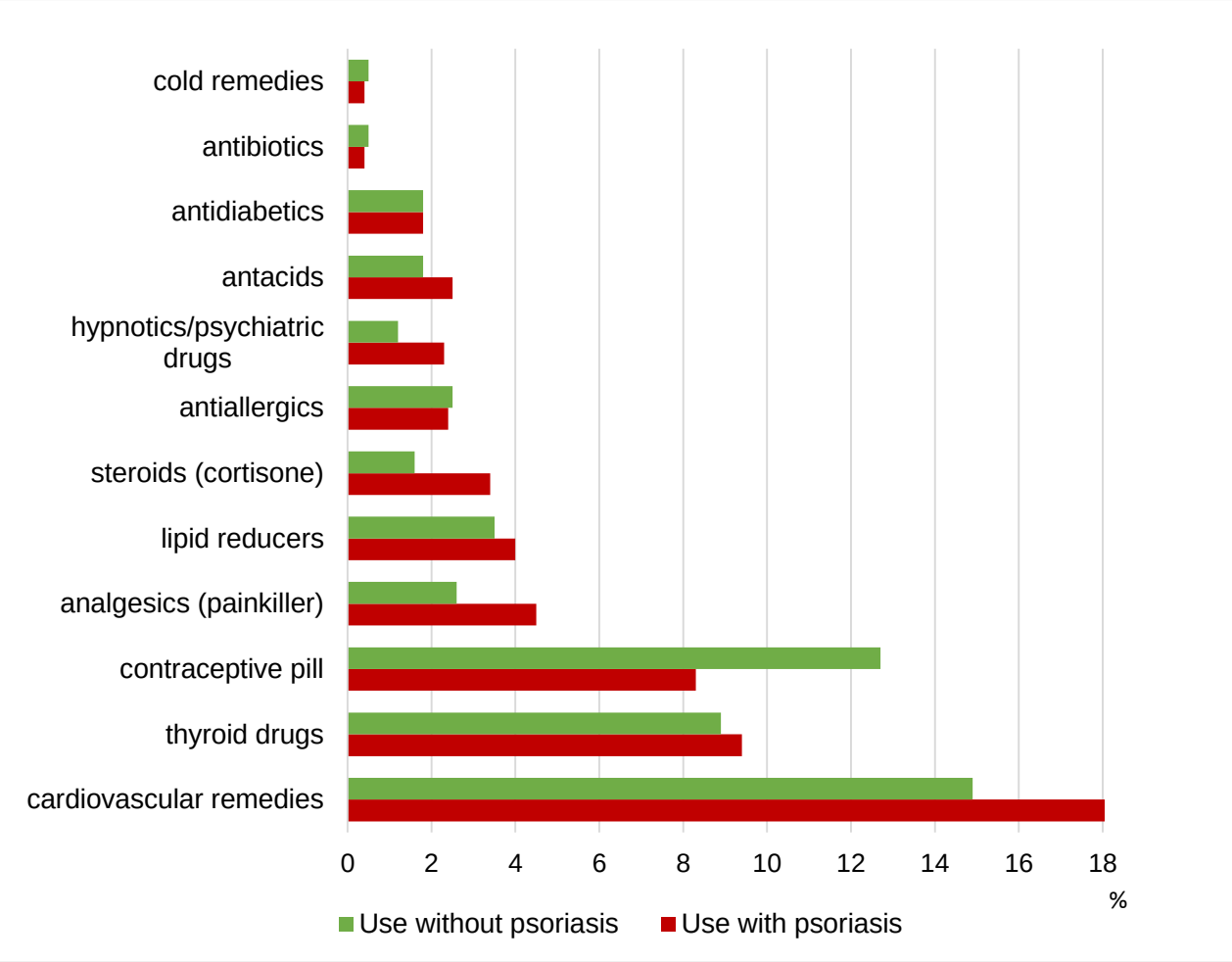

Figure 10: Use of common pharmaceuticals among people with and without psoriasis, n=42,215

3.4.5 Need for treatment

There was no significant difference with regard to the constructed variable “need for treatment of at least one dermatological condition” comparing people with and without psoriasis. Among the participants without psoriasis 19.1% had a finding that needed follow-up which is slightly more than among people with psoriasis (18.8%). T-test analysis of the number of findings that need further treatment besides psoriasis comparing people with and without psoriasis showed that these groups do not differ. In both groups people had on average 0.23 additional findings with need for treatment.

However, for single conditions significant differences in need for further treatment were found between participants with and without psoriasis (see table 9). There were significantly more cases of intertriginous dermatitis, rosacea, tinea pedis, and spider veins that needed to be cared for among psoriatic patients than among participants without psoriasis. The significant difference for rosacea was only present among women. In contrast, the need for treatment of acne and pityriasis versicolor was higher among people without psoriasis.

Table 9: Dermatological conditions with need for further treatment by sex, red: higher proportion among people with psoriasis, green: higher proportion among people without psoriasis

	need for treatment with psoriasis (n=2,781)			need for treatment without psoriasis (n=136,149)			asymptotic significance (2-sided)			OR (95% CI)		
	total	male	fe-male	total	male	fe-male	total	male	fe-male	total	male	fe-male
inflammatory skin disease												
acne	0.4%	0.3%	0.6%	0.8%	0.8%	0.7%	0.021	0.014	0.539	0.5 (0.3-0.9)	0.3 (0.1-0.8)	0.8 (0.3-1.7)
intertriginous dermatitis	0.4%	0.0%	1.0%	0.1%	0.1%	0.1%	≤0.001	0.118	≤0.001	3.0 (1.7-5.2)	-	9.1 (4.8-17.2)
rosacea	0.5%	0.3%	0.9%	0.4%	0.4%	0.4%	0.314	0.646	0.026	1.3 (0.8-2.2)	0.8 (0.4-1.9)	2.1 (1.1-4.1)
fungal diseases of the skin												
tinea pedis	3.5%	4.6%	1.6%	2.6%	3.8%	1.0%	0.003	0.071	0.074	1.4 (1.1-1.7)	1.2 (0.9-1.5)	1.6 (0.9-2.5)
pityriasis versicolor	0.2%	0.2%	0.3%	0.5%	0.6%	0.4%	0.033	0.023	0.602	0.4 (0.2-0.9)	0.3 (0.1-0.9)	0.7 (0.2-2.3)
tinea pedis and/or onychomycosis	6.9%	9.1%	3.4%	5.4%	7.6%	2.6%	≤0.001	0.021	0.105	1.3 (1.1-1.5)	1.2 (1.0-1.4)	1.3 (0.9-1.8)
vein status												
spider veins	0.2%	0.2%	0.1%	0.1%	0.1%	0.2%	0.345	0.02	0.546	1.5 (0.6-3.7)	3.1 (1.1-8.7)	0.6 (0.1-4.0)
suspected malignant skin changes and their preliminary stages												
dysplastic nevi	6.0%	5.7%	6.5%	7.1%	7.7%	6.4%	0.026	0.002	0.906	0.8 (0.7-0.9)	0.7 (0.6-0.9)	1.0 (0.8-1.3)

Among psoriatic patients the proportion of people in need of further treatment was ≥1% for onychomycosis, tinea pedis, actinic keratosis, basal cell carcinoma and dysplastic nevi (see table 10). For onychomycosis, tinea pedis, and actinic

keratosis men exhibited a need for further treatment significantly more often than women.

Table 10: Dermatological conditions with need for further treatment among psoriatic patients

	total (n=2,781)	male (n=1,728)	female (n=1,053)	asymptotic significance (2-sided)
fungal diseases of the skin				
tinea pedis and/or onychomycosis	6.9%	9.1%	3.4%	≤0.001
onychomycosis	4.5%	5.8%	2.2%	≤0.001
tinea pedis	3.5%	4.6%	1.6%	≤0.001
suspected malignant skin changes and their preliminary stages				
actinic keratosis	1.4%	1.7%	0.8%	0.031
basal cell carcinoma	1.1%	1.0%	1.2%	0.638
dysplastic nevi	6.0%	5.7%	6.5%	0.434

4. Discussion

Methods applied in the present work are discussed below. Considering strength and limitations, implications for the results are illustrated. Subsequently, the results are interpreted and discussed in comparison with results reported by recent studies.

4.1 Methods

The present data analysis is based on an occupational screening. These types of screenings have a high relevance for research because the extensive number of cases allows analysing also rare diseases. Furthermore data are gathered population based. In contrast to selected populations of patients, occupational screenings reach a broad mass of people and they represent the German working population well. Nevertheless it has to be pointed out that this examination only represents a limited part of the population and is prone to the healthy worker effect. This effect is a type of selection bias reflecting the better health status of

workers relative to the general population. This bias has two reasons. Firstly, only those persons get hired that were initially healthy enough, known as the healthy hire effect. The second cause is the healthy worker survivor effect, meaning that less-healthy workers are taking more time off work, retiring earlier and accumulating less occupational exposure. [78] That means only those people are included that are healthy enough to work and therefore multimorbidity does not appear in respective cohorts. Furthermore, the screenings were done on a voluntary basis. This could lead to different effects. Either only those people who are interested in their health and are therefore following a healthy lifestyle take part in the examinations which would lead to a “healthier” study population. The other consequence could be that people with serious dermatological conditions are already under constant treatment and therefore do not feel the need of an additional occupational screening. As a result, people with already diagnosed chronic dermatological diseases might be underrepresented in this study population. This is especially relevant for psoriasis patients as their treatment requires frequent consultations. In summary, the present data set merely represents the amount of working people and not the whole German population. Additionally, due to the described selection bias, this subpopulation might appear healthier than it really is.

The core variables analysed were derived from secondary data collection. This means that the screenings were not initiated for the purpose of answering the present research questions. The collected information can be used for answering them but the questionnaires were not designed for this purpose and potentially interesting parameters were not assessed. In the case of psoriasis, information on the degree of severity, measured for example by the PASI (Psoriasis Area and Severity Index), would have allowed to do more extensive analyses and to draw more distinct conclusions. On the other hand, the screening focussing on pruritus was conducted as primary data collection. Therefore, more specialised parameters like feeling bothered, localisation, or degree of severity could be assessed.

Data was assessed over a period of 14 years. This long time of data collection bears advantages but also some disadvantages. A disadvantage might be that external conditions influencing the results might change, such as an outbreak of a certain disease. This type of limitation is not relevant in this field of research since

psoriasis is not that prone to external variations like for example influenza. Other changes might occur in the health care system like new treatment options or new screening or prevention methods. In the case of psoriasis the market introduction of biologicals in 2004 lead to a revolution in the treatment [79] because they are highly effective in reducing the PASI with limited adverse reactions [65]. Such variations over time can be controlled for by not only analysing the data set as a whole but also by calculating prevalences for single years of data collection.

An advantage of long-term data collection is the possibility to reach a large amount of people and to identify trends over time. Additionally, each screening period functions like a pilot test for the next round. This way the screening can be improved over time. This was done in case of the need for treatment assessment, where the subjective rating of urgency was eliminated after the first screenings.

The data was collected at one time point. That allows statements on associations of different variables but not on chronological structure or causality. More specifically, it is possible to conclude whether the intake of a certain drug is associated with a disease, but no conclusions on causality can be drawn.

The question might occur whether the examination time of 15 minutes is sufficient to reliably diagnose various skin diseases. However, in the case of psoriasis the skin lesions appear to be very characteristic [80], so a dermatologist should be able to at least recognize the presence of the disease. Further examinations on severity that lead to decisions on further treatment are not meant to be done in an occupational screening.

Data collection has been done through a time period of 14 years. In this time no screening was done twice in the same company. Hence there should be no participant that has been examined and included more than once. However, there is still the possibility that someone changed the company and therefore it cannot be fully excluded that some people might have attended the screening twice.

All data sets have been standardised for age. This was conducted on the basis of the age distribution of employed persons in Germany as reported by the German Federal Statistical Office [77]. This was done in order to avoid a selection bias resulting from certain age groups being more willing to participate in skin cancer screenings. Furthermore, this procedure increases the comparability of not only

the analysed data and the German population but also among the four used data sets. Nevertheless it has to be kept in mind that standardisation was done on the basis of employed persons in Germany and accordingly, conclusions on the working population can be drawn but one has to be careful when transferring them on the whole German population.

Every missing value in the data set has been set to 0 and is therefore included in the analysis. This could lead to an underestimation of the true prevalence because it is assumed that the disease is not present when no data entry has been done. Hence there is the possibility that the participant has a certain condition although the physician did not tick the box. However, in most of the cases it can be assumed that if the dermatologist detects a disease it gets noted and therefore a missing specification is suggestive of absence.

4.2 Results

In the following, the results of the data analysis will be discussed. Firstly, the checks for plausibility will be interpreted in terms of representative status of the data. Afterwards, findings of the sections comorbid skin diseases, BMI, pharmaceuticals, and need for treatment will be discussed and compared with the current literature status.

4.2.1 Plausibility

The checks for plausibility indicate that the present data set is mostly representative for the German working population in terms of age, BMI, and psoriasis prevalence. Figure 4 shows that the age groups in the present data set and in the Mikrozensus study by the German Federal Statistical Office [77] are mostly represented to similar proportions. Statutory health insurances start promoting the statutory skin cancer screening at the age of 35. This may be an explanation why the age groups 31-40 years and 41-50 years are overrepresented in the current data set. In this study, only those people can be reached who are willing to participate in the skin cancer screening while the data on the employed

persons in Germany in 2013 of the German Federal Statistical Office [77] includes the overall working population.

In the comparison of BMI distribution the healthy worker effect becomes visible. The healthy worker effect often leads to an underestimation of prevalences [78]. In terms of BMI, the present data set is rather similar to the overall German population up to the age of 60 years while the gap widens among the elderly. This is due to the fact that the Mikrozensus data on BMI include all German habitants while in this study only the working population is represented. People with higher weight and BMI tend to retire earlier and accordingly, the mean BMI of the working population is lower especially in the older age groups.

4.2.2 Psoriasis

The prevalence of psoriasis in Germany is reported to be 2.5% [1]. The prevalence of 2% found in this study is in the same order of magnitude. Additionally, the increasing prevalence with higher age and men being affected more frequently than women corresponds to current knowledge [1]. Again the healthy worker effect explains the superior state of health of the working population over overall Germany especially in the higher age groups. Psoriasis was least frequent in chemical or laboratory professions. This might be surprising at first as these professions are expected to be associated with skin diseases. However, it can be assumed that those who suffer from a serious skin disease like psoriasis already had to opt out of chemical professions or intentionally chose a job in another sector.

Time trend analyses of age and psoriasis prevalence showed no noticeable pattern. This leads to the assumption that there were no external confounders like changes in conditions that could have influenced the results over time. The previously mentioned market introduction of biologicals and their remarkable impact on psoriasis treatment has no effect on the prevalence but might influence the degree of severity. As the PASI was not assessed in this study, this hypothesis cannot be confirmed.

Among the inflammatory diseases, psoriasis is the one where pruritus occurs the fourth most common. As expected, people with psoriasis differed significantly ($p \leq 0.001$) in experiencing pruritus from those without psoriasis. For psoriatic patients the odds for suffering from pruritus was 3.3. Surprisingly, the mean degree of pruritus severity did neither differ for people with and without psoriasis nor among the other inflammatory diseases. This can be assumed to be due to the fact that the degree of severity was only assessed for those who reported to be bothered by pruritus in a moderate or high degree. Consequently, the selection of participants for that comparison is biased as completely healthy individuals are not included in the analysis. Accordingly, the data is not appropriate to compare the degree of severity of psoriatic patients with healthy participants.

4.2.3 Psoriasis and other skin diseases

The most frequent skin-related comorbidity of psoriasis was onychomycosis. This corresponds to the range of prevalence from 4.6 to 63.1% as reported in the systematic review by Klaassen et al. [39]. However, the similarity of the symptoms of onychomycosis and nail psoriasis should be considered at this point. It has to be taken in mind that screening examinations usually lead to clinical diagnoses, which are not confirmed by laboratory test. Thus, in cases of similar clinical appearances, misclassification cannot be ruled out completely.

Folliculitis was the second most frequent comorbidity of psoriasis. The difference of emergence among people with and without psoriasis was significant with people without psoriasis being affected more often. Accordingly, folliculitis seems to be rather common in general but is not specifically related to psoriasis. This thesis is supported by published studies where no evidence for a direct association of psoriasis and folliculitis could be found. Yet there are studies that report connections due to pharmaceutical treatment. Both psoriasis and folliculitis were found to be cutaneous side effects of the treatment with lithium [68, 81]. Lithium is used in antipsychotics and could therefore be associated with psoriasis-related treatment of depressive symptoms. Kragballe et al. found folliculitis to be an adverse drug reaction on topical corticosteroid use, which is common in the treatment of psoriasis [63].

Rosacea was the most common inflammatory skin-related comorbidity of psoriasis. The difference between patients with and without psoriasis was highly significant ($p \leq 0.001$), indicating that the emergence of psoriasis and rosacea might be somehow connected. Analysis of BMI also gives hints on similarities. Patients with both diseases had an increased BMI (psoriasis: 26.5, rosacea: 27.0) and the mean BMI of both psoriasis and rosacea differed significantly from those participants that had no inflammatory skin disease. In the literature, no known associations between psoriasis and rosacea could be found. Yazici et al. found that there were already two cases reported where rosacea was induced by etanercept, one of the biologics commonly used to treat psoriasis [2]. This could be a hint on a further adverse drug reaction resulting from psoriasis therapy.

Regarding the association of psoriasis with tinea pedis, the current study corresponds to findings by Alteras et al. [35] and Leibovici et al. [36] in terms of tinea being more prevalent among psoriatic patients. However, the prevalence among patients with psoriasis was much lower in the present data set (5.9%) than in the study by Leibovici (13.8%). The healthy worker effect could be an explanation as it can be assumed that mainly the less severe cases of psoriasis were included in the current study. This can result in lower rates of comorbidity.

Literature already suggests the coexistence of tinea pedis and onychomycosis [40, 41, 82]. The current analysis supports this thesis with 35.1% of tinea pedis patients additionally suffering from onychomycosis. Taken together, tinea pedis and onychomycosis are the most common skin-related comorbidities of psoriasis.

In contrast to other studies [42, 43], no significant association was found between psoriasis and vitiligo which supports the thesis by Sawchuk et al. [44] that reported coexistence of psoriasis and vitiligo is most likely due to chance. Poljacki et al. found vitiligo to be present among psoriatic patients to a similar extent (0.2%) as in the current analysis (0.5%) but also did not detect this prevalence to be significantly increased compared to people without psoriasis.

The data analysis clearly indicates gender-specific differences in the emergence of fungal and bacterial diseases of the skin. Especially onychomycosis, tinea pedis and folliculitis are significantly more frequent among men than women. This corresponds to published literature for example by Pierard reporting that both tinea

pedis and onychomycosis are more common in men [82] or to the study by Pichardo-Geisinger et al. who found higher prevalence of tinea pedis in men than in women [83]. On the other hand, non-malignant non-inflammatory skin changes and vessel changes of the skin appear to be more common among females.

Suspected malignant skin changes were significantly more common among people without psoriasis. An explanation for this finding could be that psoriasis patients are most likely under constant dermatological treatment. Possible malignant skin changes could be observed and clarified during these regular consultations. Patients without psoriasis can be assumed to not consult a dermatologist that often and therefore conspicuous skin changes might remain undiscovered.

Generally it has to be noted that the nature of detected associations remains unclear. The occurrence of two diseases in one patient could be the matter of poor coexistence, shared genetic mutations, or further external factors like certain risk exposure. As noted before, some diseases can also evolve as adverse drug reactions of psoriasis treatment.

4.2.4 BMI in psoriasis

Even in the rather short time frame of three years of data collection where BMI was assessed, the overall development of increasing BMI, as reported by the German Federal Statistical Office [84], is visible. People with psoriasis were significantly more often obese than people without. This finding was already reported in multiple other studies before [53–55]. Analysis of variance of the mean BMI in inflammatory diseases revealed significant differences of people without any inflammatory disease towards those suffering from acne, exsiccation eczema, psoriasis, or rosacea. While people with acne had a lower BMI, the other three where associated with an increased BMI. These results support the observation that overweight is associated with inflammation [56]. Lower BMI in acne is opposing to Alan et al. who reported a positive correlation between BMI and acne [50]. This variance could be due to different study populations as the mentioned study only included female participants.

4.2.5 Pharmaceutical treatment

The frequency of pharmaceutical usage allows conclusions on morbidity within a population. In a report on the application of drugs among adults in Germany [85] the Robert Koch-Institut (RKI) reported that cardiovascular remedies were the most frequent medication. Lipid reducers, thyroid drugs, and hormone preparations like oral contraceptives were used next most frequently, the latter ones markedly more often among females. In the present data analysis a similar distribution was observed. For obvious reasons oral contraceptives were expected to be consumed mainly by women. Thyroid diseases are also known to affect women five times more than men [86].

When analysing associations of psoriasis with pharmaceuticals, the relevant drugs can be allocated to three groups. The first group are those which are used directly for the treatment of psoriasis. Among those assessed in this screening, steroids including cortisone, which is used to treat inflammation, belong to this category [63]. The second group are those pharmaceuticals that are used for the treatment of comorbidities associated with psoriasis. Cardiovascular remedies, antidiabetics and lipid reducers to treat the metabolic syndrome, and psychiatric drugs belong to that field, and an increased intake of those drugs indicates the presence of respective comorbidities. Antacids, antiallergics, oral contraceptives, and thyroid drugs are not known to be associated with psoriasis or its comorbidities.

Following this classification it can be assumed that having psoriasis is associated with the intake of steroids. The present analysis confirms this assumption: the intake of steroids was more than twice as high among people with psoriasis (3.4% compared to 1.4%).

In terms of pharmaceuticals that are used for the treatment of comorbidities, the significantly higher intake of cardiovascular remedies confirms cardiovascular diseases being common comorbidities of psoriasis [30]. Furthermore, the significantly higher use of psychiatric drugs among male participants with psoriasis verifies that, at least in men, psychiatric conditions are associated with psoriasis [31]. Analgesics were also significantly more often consumed by men suffering from psoriasis. This indicates that psoriasis and its comorbidities lead to increased

experiences of pain. Although not significant, the higher use of lipid reducers and antidiabetics supports the observation of the metabolic syndrome as a comorbidity of psoriasis.

In contrast to Tsankov et al. who stated that antibiotics appear to have a strong causal relationship with psoriasis [66], no significant association could be found in this data set. Antibiotics were even used more frequently by people without psoriasis. However, these findings are not contradictory: while the study by Tsankov assumes antibiotics to trigger or induce psoriasis, the present study merely excludes associated use of antibiotics among people who are already diagnosed with psoriasis. This does not reject the possibility that antibiotics may have induced the development of psoriasis at some time.

Oral contraceptives were used significantly more often by women without psoriasis. An explanation might be that the prevalence of psoriasis increases with higher age while the percentage of affected women of childbearing age, and consequently those who would take oral contraceptives, decreases. Furthermore, people with psoriasis often already are on multi-drug regimen [61] which might keep women from adding more medication.

4.2.6 Need for treatment

A disease that was rated as needed to be cared for can be assumed to be undiagnosed or at least not treated properly. This can lead to avoidable exacerbation and impairment in patient's QoL. Patients with psoriasis exhibited increased need for further treatment of the fungal diseases onychomycosis and tinea pedis as well as actinic keratosis, basal cell carcinoma and dysplastic nevi. Again the gender-specific difference in the emergence of fungal diseases gets visible with men exhibiting a need for treatment of onychomycosis and tinea pedis twice as frequently as women.

In general, people with psoriasis did not differ from those without psoriasis in terms of need for treatment. Nevertheless, the amount of people with a needed care for intertriginous dermatitis, rosacea, tinea pedis, and spider veins was significantly higher among participants with psoriasis. All four of these conditions were

identified before to be more common among psoriatic patients. The need for care of these diseases indicates a lack of awareness of them being psoriasis comorbidities. Sufficient awareness would allow earlier diagnosis and more targeted treatment. On the other hand, despite being more common among patients with psoriasis, onychomycosis does not require more treatment when comparing people with and without psoriasis. Still, it is the condition with the highest frequency of a need for treatment. Therefore it can be assumed that onychomycosis is an often unappreciated disease regardless whether participants have psoriasis or not.

The lower need for treatment of acne, pityriasis versicolor, and dysplastic nevi is concordant with these diseases being less frequent among psoriatic patients. Additionally these skin conditions, especially acne, are more obvious and are therefore very likely to be diagnosed in the course of one of the various psoriasis-related visits at the dermatologist.

5. Conclusion

The present data analysis of nationwide occupational skin cancer screenings allows conclusions on comorbid skin diseases in psoriasis and can consequently contribute to more targeted, adequate, and economical health care. However, when interpreting findings it has to be noted that conclusions are only valid for the working population and not for whole Germany. Furthermore, cross-sectional data was used, therefore conclusions on causality are not proved and can only be speculated.

Participants with psoriasis presented with higher rates of comorbidity for certain skin diseases, especially fungal diseases (onychomycosis 8.6%, tinea pedis 6.2%) compared to people without psoriasis. Other significantly increased prevalences compared to participants without psoriasis were found for teleangiectasia (12.1% vs. 8.9%) and rosacea (3.8% vs. 2.2%). Significantly higher prevalences only among women were found for solar lentigines (46.4% vs. 40.4%), spider veins (33.6% vs. 29.6%), fibromas (31.7% vs. 27.9%), seborrhoic keratosis (30.4% vs. 25%), and intertriginous dermatitis (1.8% vs. 0.7%).

People with psoriasis suffered significantly more often from pruritus (39.1% vs. 16.2%). The presence of psoriasis did not have an influence on the degree of pruritus, at least not among those who suffered from itching in a moderate to high degree. In that group of participants the degree of pruritus severity did not differ between various inflammatory skin diseases.

Obesity was more prevalent among people with psoriasis (21.2% vs. 13.1%). Concordantly, mean BMI was significantly higher in participants with psoriasis than those without (26.5kg/m² vs. 25.3kg/m²). Differences in mean BMI were found between different inflammatory skin diseases, and people with psoriasis differed significantly from those with acne and no inflammatory skin disease.

The use of pharmaceuticals for common diseases was increased among psoriatic patients. Participants with psoriasis had a significantly higher use of steroids, which are used to treat their disease, and cardiovascular remedies, used to treat comorbid cardiovascular conditions. Among men, higher intake of medication treating psychiatric conditions and pain were found. Although not significant, the use of lipid reducers and antidiabetic remedies, indicating treatment of the metabolic syndrome, was also increased among participants with psoriasis.

19.1% of psoriatic patients exhibited at least one dermatological finding requiring treatment or follow-up. This percentage is only slightly higher than for people without psoriasis (18.8%). Among psoriasis patients, the most common skin diseases with need for care were onychomycosis (4.5%) and tinea pedis (3.5%) as well as dysplastic nevi (6.0%), actinic keratosis (1.4%), and basal cell carcinoma (1.1%). A significantly higher percentage of occurrence in psoriatic participants compared to people without psoriasis was found only for tinea pedis.

In conclusion, all research questions could be answered by the present analysis. People with psoriasis represent a group of patients with special needs, not only concerning the treatment of disease-specific symptoms and common comorbidities like psoriatic arthritis, cardiovascular and autoimmune diseases, metabolic syndrome, and depression, but they are also prone to a series of comorbid skin diseases, especially fungal diseases. This finding needs to be considered in the treatment of psoriatic patients, both for primary prevention through awareness of special risks in order to prevent the occurrence of further

diseases, as well as secondary and tertiary prevention, to reduce progression and impact of the diseases. In this context, contraindicated treatment regimens for psoriasis and concurrent fungal diseases need to be considered.

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7. Declaration of independent work

I hereby declare that I wrote this thesis without any assistance and used only the aids listed. Any material taken from other works, either as a quote or idea have been indicated under “References”.

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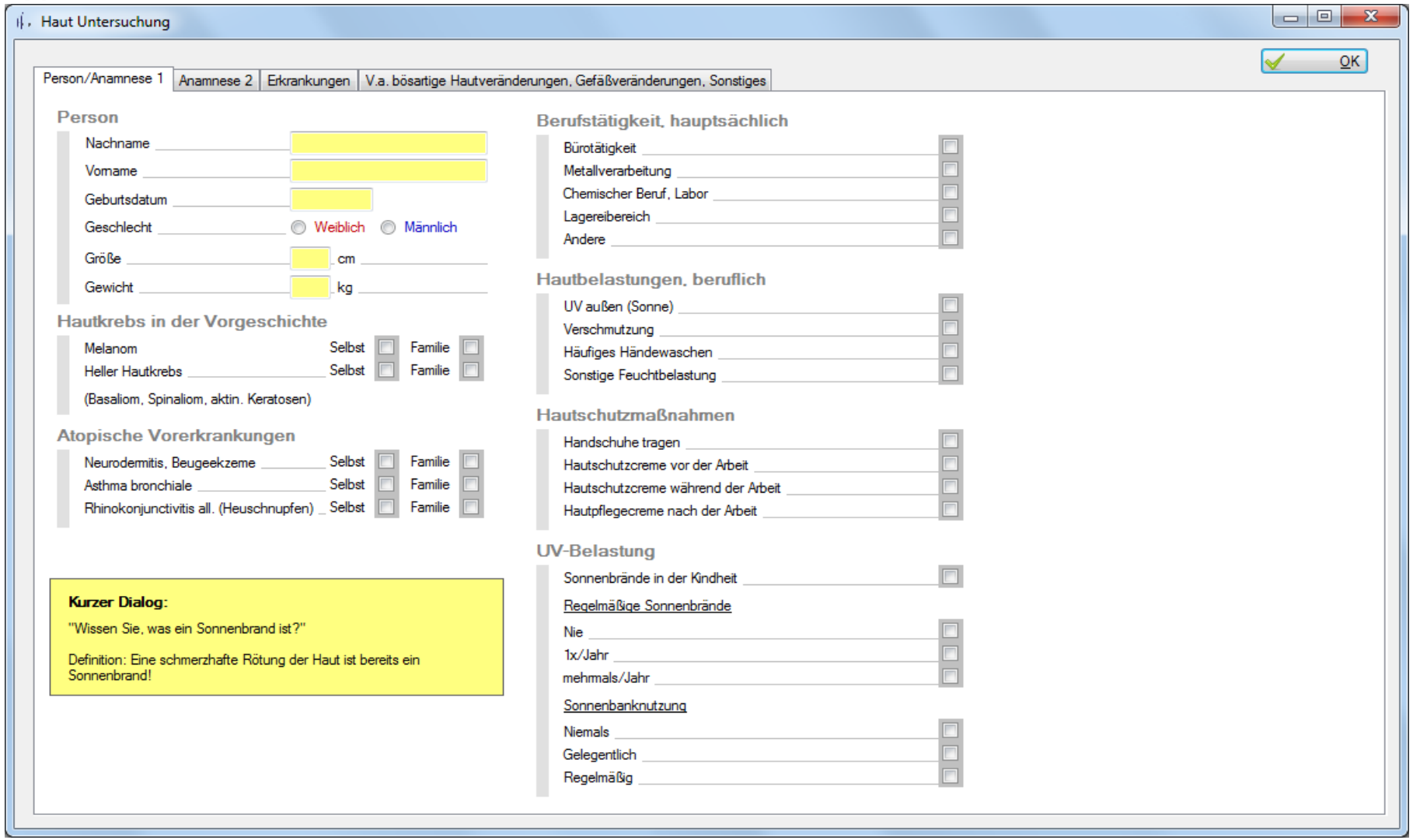
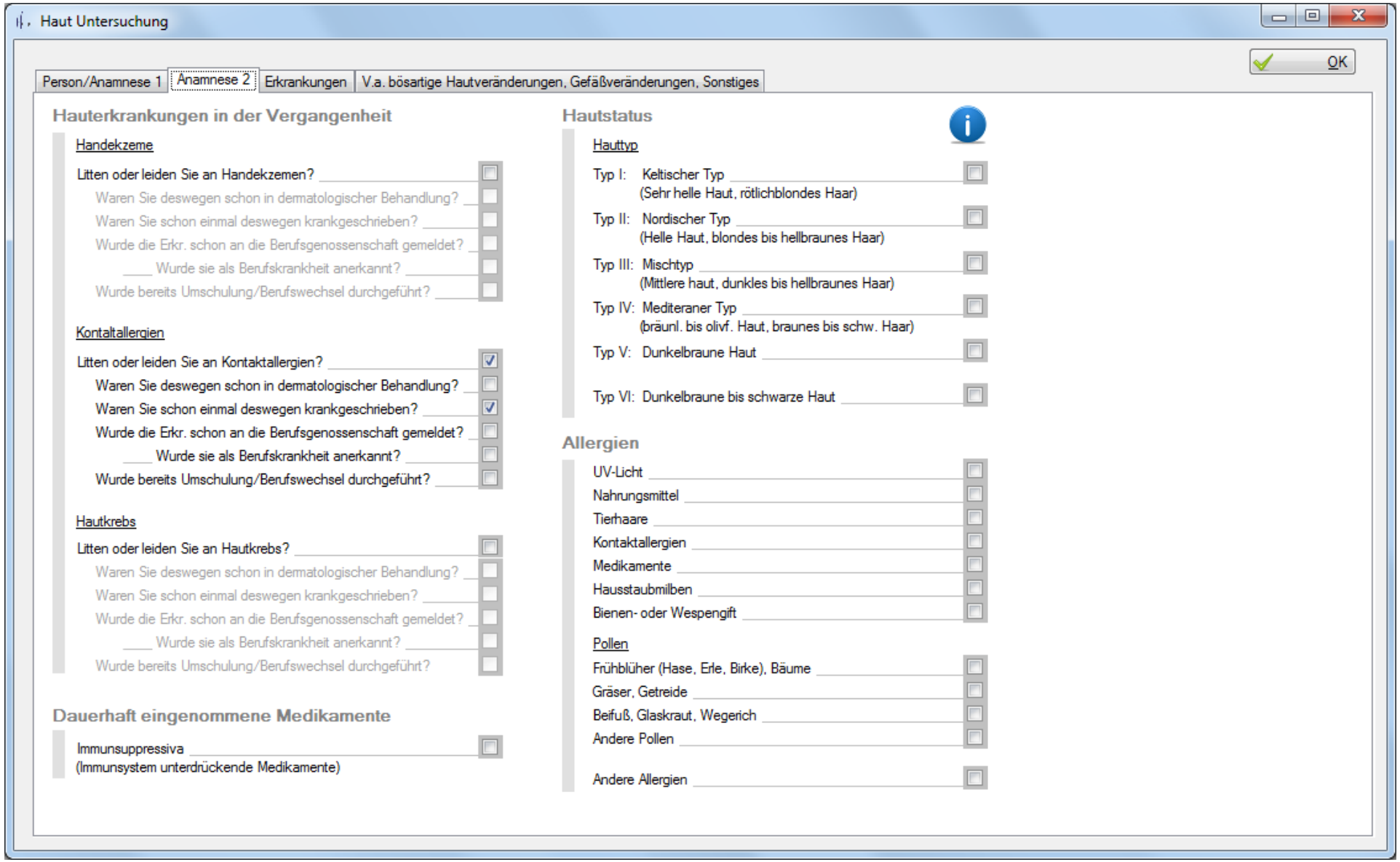
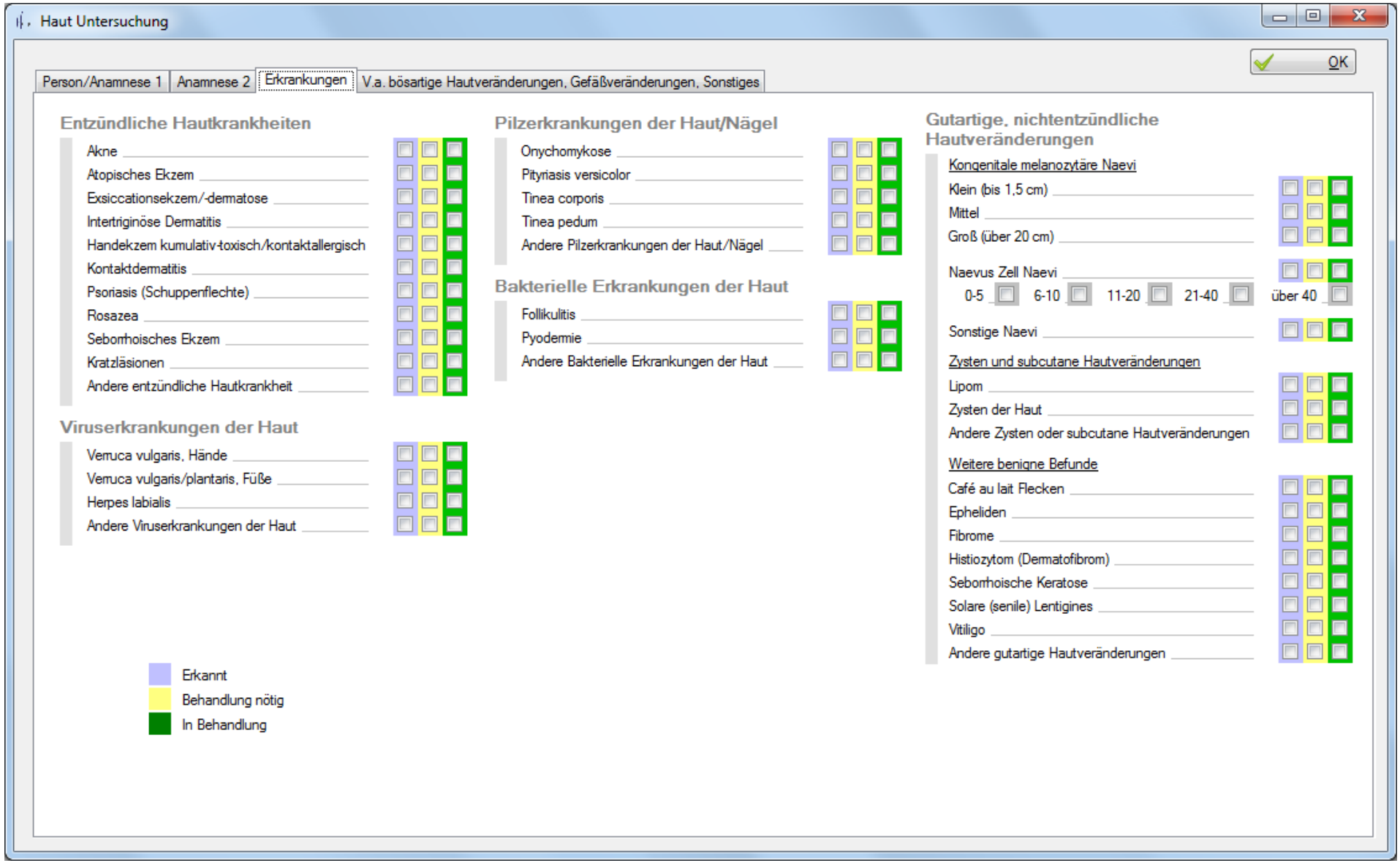
(Nicole Zander)

8. Appendix

Appendix 1: Screenshot of data entry mask




Haut Untersuchung
OK
Person/Anamnese 1
Anamnese 2
Erkrankungen
V.a. bösartige Hautveränderungen, Gefäßveränderungen, Sonstiges
Hauterkrankungen in der Vergangenheit
Handekzeme
Litten oder leiden Sie an Handekzemen?
Waren Sie deswegen schon in dermatologischer Behandlung?
Waren Sie schon einmal deswegen krankgeschrieben?
Wurde die Erkr. schon an die Berufsgenossenschaft gemeldet?
Wurde sie als Berufskrankheit anerkannt?
Wurde bereits Umschulung/Berufswechsel durchgeführt?
Kontaktallergien
Litten oder leiden Sie an Kontaktallergien?
Waren Sie deswegen schon in dermatologischer Behandlung?
Waren Sie schon einmal deswegen krankgeschrieben?
Wurde die Erkr. schon an die Berufsgenossenschaft gemeldet?
Wurde sie als Berufskrankheit anerkannt?
Wurde bereits Umschulung/Berufswechsel durchgeführt?
Hautkrebs
Litten oder leiden Sie an Hautkrebs?
Waren Sie deswegen schon in dermatologischer Behandlung?
Waren Sie schon einmal deswegen krankgeschrieben?
Wurde die Erkr. schon an die Berufsgenossenschaft gemeldet?
Wurde sie als Berufskrankheit anerkannt?
Wurde bereits Umschulung/Berufswechsel durchgeführt?
Dauerhaft eingenommene Medikamente
Immunsuppressiva
(Immunsystem unterdrückende Medikamente)
Hautstatus
Hauttyp
Typ I: Keltischer Typ
(Sehr helle Haut, rötlichblondes Haar)
Typ II: Nordischer Typ
(Helle Haut, blondes bis hellbraunes Haar)
Typ III: Mischtyp
(Mittlere haut, dunkles bis hellbraunes Haar)
Typ IV: Mediteraner Typ
(bräunl. bis olivf. Haut, braunes bis schw. Haar)
Typ V: Dunkelbraune Haut
Typ VI: Dunkelbraune bis schwarze Haut
Allergien
UV-Licht
Nahrungsmittel
Tierhaare
Kontaktallergien
Medikamente
Hausstaubmilben
Bienen- oder Wespengift
Pollen
Frühblüher (Hase, Erle, Birke), Bäume
Gräser, Getreide
Beifuß, Glaskraut, Wegerich
Andere Pollen
Andere Allergien


Haut Untersuchung
OK
Person/Anamnese 1
Anamnese 2
Erkrankungen
V.a. bösartige Hautveränderungen, Gefäßveränderungen, Sonstiges
Entzündliche Hautkrankheiten
Akne
Atopisches Ekzem
Exsiccationsekzem/-dermatose
Intertriginöse Dermatitis
Handekzem kumulativ-toxisch/kontaktallergisch
Kontaktdermatitis
Psoriasis (Schuppenflechte)
Rosazea
Seborrhoisches Ekzem
Kratzläsionen
Andere entzündliche Hautkrankheit
Viruserkrankungen der Haut
Verruca vulgaris, Hände
Verruca vulgaris/plantaris, Füße
Herpes labialis
Andere Viruserkrankungen der Haut
Pilzerkrankungen der Haut/Nägel
Onychomykose
Pityriasis versicolor
Tinea corporis
Tinea pedum
Andere Pilzerkrankungen der Haut/Nägel
Bakterielle Erkrankungen der Haut
Follikulitis
Pyodermie
Andere Bakterielle Erkrankungen der Haut
Gutartige, nichtentzündliche Hautveränderungen
Kongenitale melanozytäre Naevi
Klein (bis 1,5 cm)
Mittel
Groß (über 20 cm)
Naevus Zell Naevi
0-5
6-10
11-20
21-40
über 40
Sonstige Naevi
Zysten und subcutane Hautveränderungen
Lipom
Zysten der Haut
Andere Zysten oder subcutane Hautveränderungen
Weitere benigne Befunde
Café au lait Flecken
Epheliden
Fibrome
Histiozytom (Dermatofibrom)
Seborrhoische Keratose
Solare (senile) Lentigines
Vitiligo
Andere gutartige Hautveränderungen
Erkannt
Behandlung nötig
In Behandlung

Appendix 2: Variable list of all screenings

			screening period 1	screening period 2	screening period 3 (+focus on pruritus)	screening period 4	screening period 5	screening period 6	screening period 7	screening period 8	master data set (all screening periods)	BMI (screenings 6-8)	Pharmaceuticals (Screenings 2-3)
		year of data collection	2001-2005	2006-2007	2008	2011	2012 - 2013	2012	2013	2014	2002-2014	2012-2014	2006-2008
		number of items	98	117	118	135	113	121	123	123	74	121	106
	Items n=	Items											
	217												
		n (16-70)	48665	30483	11732	14161	15164	1270	9770	7685	138930	18725	42215
		age (mean)	43,23	43,68	43,70	42,16	43,53	41,25	42,24	42,90	43,19	42,44	44.04
demographic data	10												
		age	x	x	x	x	x	x	x	x	x	x	x
		date of data collection	x	x	x	x	x	x	x	x	x	x	x
		date of birth	x	x	x	x	x	x	x	x	x	x	x
		sex	x	x	x	x	x	x	x	x	x	x	
		height						x	x	x		x	
		weight						x	x	x		x	
		BMI						x	x	x		x	
		note					x	x	x	x		x	
		specialist					x	x	x	x		x	
		referral to specialist					x	x	x	x		x	
Skin cancer anamnesis	6												
		melanoma in the past	x	x	x	x	x	x	x	x	x	x	x
		melanoma in the	x	x	x	x							x

		family											
		basal cell carcinoma in the past		x	x	x		x	x	x		x	x
		basal cell carcinoma in the family		x	x	x							x
		actinic keratosis in the past		x	x	x							x
		actinic keratosis in the family		x	x	x							x
pigmented spots	2												
		pigmented spots changed in the past	x	x	x	x	x	x	x	x	x	x	x
		new pigmented sports in the past	x	x	x	x	x	x	x	x	x	x	x
UV exposure (sunburn)	7												
		had sunburns in the childhood	x	x	x	x	x	x	x	x	x	x	x
		never gets sunburns	x	x	x	x	x	x	x	x	x	x	x
		gets sunburn once a year	x	x	x	x	x	x	x	x	x	x	x
		gets sunburns several times a year	x	x	x	x	x	x	x	x	x	x	x
		no solarium use	x	x	x	x	x	x	x	x	x	x	x
		occasional solarium use	x	x	x	x	x	x	x	x	x	x	x
		regular solarium use	x	x	x	x	x	x	x	x	x	x	x
atopic pre-existing conditions	6												
		neurodermatitis,		x	x	x	x	x	x	x		x	x
		neurodermatitis in the family		x	x	x							x
		bronchial asthma	x	x	x	x	x	x	x	x	x	x	x

		bronchial asthma in the family		x	x	x							x
		rhinoconjunctivitis		x	x	x	x	x	x	x		x	x
		rhinoconjunctivitis in the family		x	x	x							x
allergies	8												
		UV light	x	x	x	x	x	x	x	x	x	x	x
		food	x	x	x	x	x	x	x	x	x	x	x
		pollen	x	x	x	x	x	x	x	x	x	x	x
		animal hair	x	x	x	x	x	x	x	x	x	x	x
		dust mites	x	x	x	x	x	x	x	x	x	x	x
		contact allergy	x	x	x	x	x	x	x	x	x	x	x
		pharmaceuticals	x	x	x	x	x	x	x	x	x	x	x
		other	x	x	x	x	x	x	x	x	x	x	x
currently used pharmaceuticals	17												
		analgesics (painkiller)	x	x	x	x							x
		antacids		x	x	x							x
		antiallergics		x	x	x							x
		antibiotics	x	x	x	x							x
		antidiabetics	x	x	x	x							x
		cold remedies		x	x	x							x
		cardiovascular remedies	x	x	x	x							x
		hormones (e.g. "the pill")	x	x									
		immunosuppressants						x	x	x		x	
		lipid reducers		x	x	x							x
		"the pill"		x	x	x							x
		psychiatric drugs	x	x									

		thyroid drugs		x	x	x							x
		hypnotics	x	x									
		hypnotics/psychiatric drugs		x	x	x							x
		steroids (cortisone)	x	x	x	x							x
		other	x	x	x	x							x
skin type: colour of skin and hair	6												
		type I: skin colur: very light to light, hair: reddish-blond	x	x	x	x	x	x	x	x	x	x	x
		type II: skin colour: light, hair: blonde to dark	x	x	x	x	x	x	x	x	x	x	x
		typ III: skin colour: dark, hair: dark-blonde to brown	x	x	x	x	x	x	x	x	x	x	x
		type IV: skin colour: brownish, hair: dark-brown to black	x	x	x	x	x	x	x	x	x	x	x
		type V: dark-brown skin				x	x	x	x	x		x	
		type VI: dark-brown to black skin				x	x	x	x			x	
inflammatory skin diseases	12												
		acne	x	x	x	x	x	x	x	x	x	x	x
		atopic eczema	x	x	x	x	x	x	x	x	x	x	x
		exsiccation eczema	x	x	x	x	x	x	x	x	x	x	x
		hand eczema	x	x	x	x	x	x	x	x	x	x	x
		intertriginous dermatitis	x	x	x	x	x	x	x	x	x	x	x
		scratching lesions			x	x	x	x	x	x		x	
		contact dermatitis	x	x	x	x	x	x	x	x	x	x	
		lichen ruber	x	x	x	x							x

		psoriasis	x	x	x	x	x	x	x	x	x	x	x
		rosacea	x	x	x	x	x	x	x	x	x	x	x
		seborrhoeic eczema	x	x	x	x	x	x	x	x		x	x
		others	x	x	x	x	x	x	x	x	x	x	x
viral diseases of the skin	8												
		Herpes genitalis	x										x
		Herpes labialis	x										
		herpes		x	x	x	x	x	x	x		x	
		condylmoas	x										
		Verruca vulgaris	x										
		verruca vulgaris/ hands	x	x	x	x	x	x	x	x	x	x	x
		verruca vulgaris/ feet	x	x	x	x	x	x	x	x	x	x	x
		other	x	x	x	x	x	x	x	x	x	x	x
fungal diseases of the skin	5												
		onychomycosis	x	x	x	x	x	x	x	x	x	x	x
		pityriasis versicolor	x	x	x	x	x	x	x	x	x	x	x
		tinea corporis	x	x	x	x	x	x	x	x	x	x	x
		tinea pedis	x	x	x	x	x	x	x	x	x	x	x
		others	x	x	x	x	x	x	x	x	x	x	x
bacterial diseases of the skin	3												
		folliculitis	x	x	x	x	x	x	x	x	x	x	x
		pyoderma	x	x	x	x	x	x	x	x	x	x	x
		others	x	x	x	x	x	x	x	x	x	x	x
non-malignant non-imflammatory skin changes	14												
		seborrhoic	x	x	x	x	x	x	x	x	x	x	x

		keratosis											
		vitiligo	x	x	x	x	x	x	x	x	x	x	x
		solar (senil) lentigines	x	x	x	x	x	x	x	x	x	x	x
		other nevi		x	x	x	x	x	x	x		x	x
		café au lait spots	x	x	x	x	x	x	x	x	x	x	x
		ephelides	x	x	x	x	x	x	x	x	x	x	x
		fibromas	x	x	x	x	x	x	x	x	x	x	x
		histiocytoma (dermatofibroma)	x	x	x	x	x	x	x	x	x	x	x
		hypertrophic sebaceous gland	x	x									
		lipoedema				x	x	x	x	x		x	
		lymphedema				x	x	x	x	x		x	
		others	x	x	x	x	x	x	x	x	x	x	x
		congenital melanocytic nevi: size	x	x	x	x	x	x	x	x	x	x	x
		melanocytic nevi: number	x	x	x	x	x	x	x	x	x	x	x
cysts and subcutaneous skin changes	7												
		melanocytic nevi: dermal nevi	x	x	x	x	x						x
		melanocytic nevi: Naevus Zell Naevus	x	x	x	x		x	x	x	x	x	x
		melanocytic nevi: papillomatous nevi	x	x	x								x
		lipoma	x	x	x	x	x	x	x	x	x	x	x
		others	x	x	x	x	x	x	x	x	x	x	x
		epidermal cyst	x	x									
		skin cysts		x	x	x	x	x	x	x		x	x

suspected malignant skin changes and their preliminary stages	11												
		Melanoma in situ	x										
		basal cell carcinoma	x	x	x	x	x	x	x	x	x	x	x
		actinic keratosis	x	x	x	x	x	x	x	x	x	x	x
		dysplastic nevi	x	x	x	x	x	x	x	x	x	x	x
		carcinoma	x	x									
		malignant melanoma, type	x	x	x	x	x	x	x	x	x	x	x
		Melanom	x	x			x						
		Bowen's disease	x	x	x	x	x	x	x	x	x	x	x
		squamous cell carcinoma	x	x	x	x	x	x	x	x	x	x	x
		premalignant lesions		x									
		others	x	x	x	x	x	x	x	x	x	x	x
regular control of nevi recommended	3												
		anamnestic noticeable finding	x	x	x	x	x	x	x	x	x	x	x
		noticeable nevi in colour, shape or size	x	x	x	x		x	x	x	x	x	x
		multiple nevi	x	x	x	x	x	x	x	x	x	x	x
vessel changes of the skin	3												
		teleangiectasia	x	x	x	x	x	x	x	x	x	x	x
		naevus flammeus	x	x	x	x	x	x	x	x	x	x	x
		haemangioma	x	x	x	x	x	x	x	x	x	x	x
vein status	6												

X

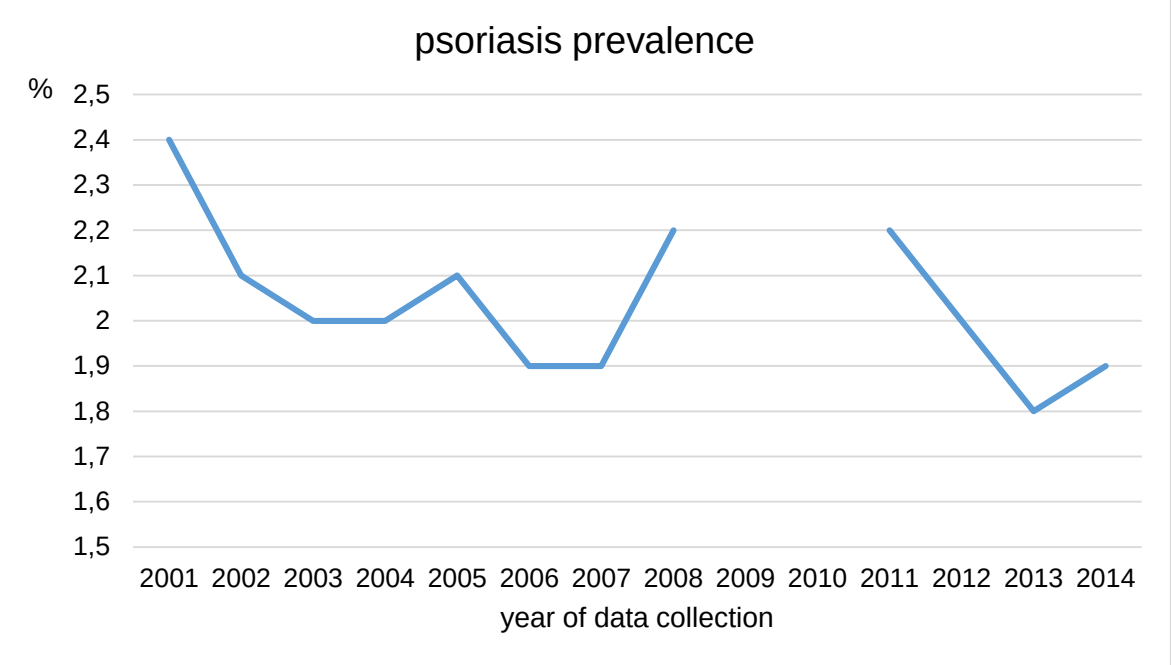
		varicosis, type	x										x
		spider veins	x	x	x	x	x	x	x	x	x	x	x
		ulcus cruris		x	x	x	x	x	x	x		x	x
		diabetic foot, without ulcus		x			x			x			
		diabetic foot, with ulcus		x	x	x							x
		other chronic wounds		x	x	x			x	x			x
medical consultation	1												
		medical consultation during the last months due to a skin disease, specialty		x	x								
pruritus	9												
		pruritus since			x								
		frequency in the last 6 weeks			x								
		disturbance			x								
		degree of severity			x								
		localisation			x								
		duration			x								
		medical consultation because of pruritus			x								
		cause			x								
		medication			x								
hyperhidrosis	24					x							
allergies and hyposensitisation	21						x						
occupation	5												
		office work						x	x	x		x	

		metal processing						x	x	x		x	
		laboratory						x	x	x		x	
		storage area						x	x	x		x	
		others						x	x	x		x	
occupational strains for the skin	4												
		UV (sun)						x	x	x		x	
		contamination						x	x	x		x	
		frequent hand-washing						x	x	x		x	
		other moisture exposure						x	x	x		x	
skin protection measures	4												
		wearing gloves						x	x	x		x	
		skin protection cream before work						x	x	x		x	
		skin protection cream during work						x	x	x		x	
		skin care cream after work						x	x	x		x	
skin diseases in the past	15												
		suffering from hand eczema						x	x	x		x	
		has been under dermatological treatment due to hand eczema						x	x	x		x	
		has been on sick leave due to hand eczema						x	x	x		x	
		hand eczema has been reported to professional association						x	x	x		x	

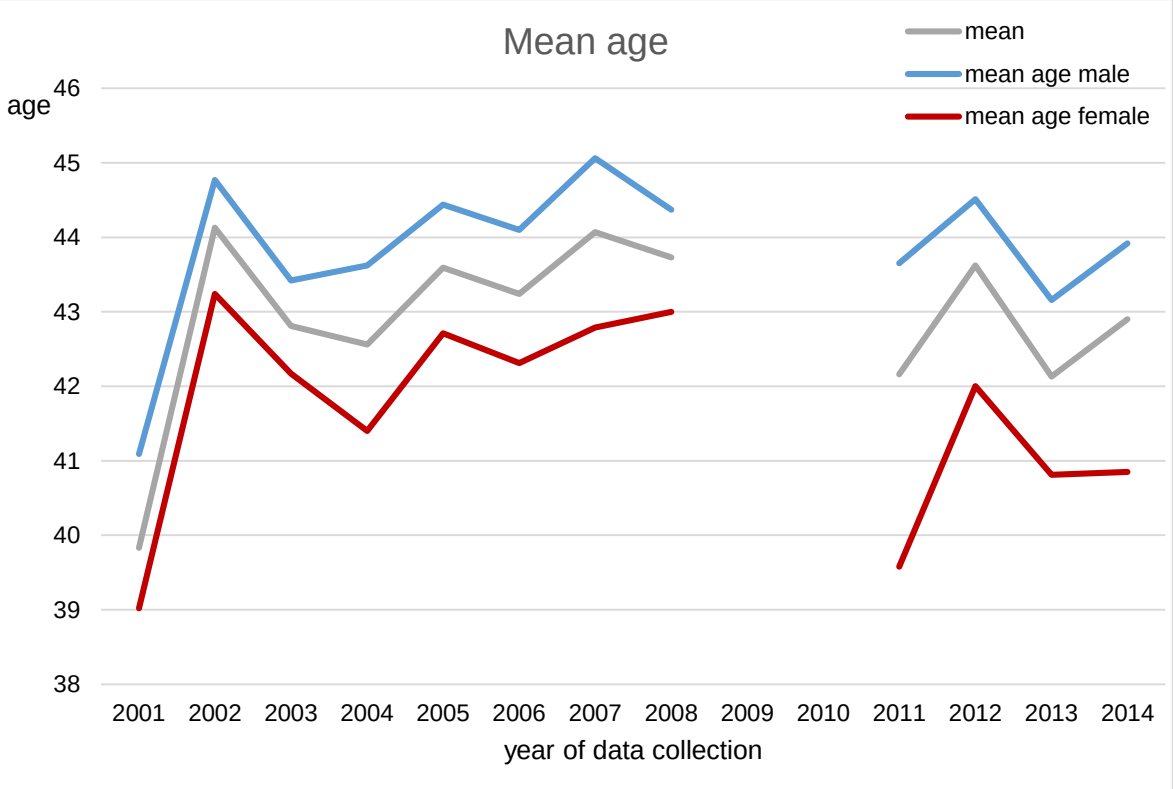
		hand eczema has been acknowledged as an occupational disease						x	x	x		x	
		retraining due to hand eczema						x	x	x		x	
		suffering from contact allergy						x	x	x		x	
		has been under dermatological treatment due to contact allergy						x	x	x		x	
		has been on sick leave due to contact allergy						x	x	x		x	
		contact allergy has been reported to professional association						x	x	x		x	
		contact allergy has been acknowledged as an occupational disease							x	x			
		retraining due to contact allergy						x	x	x		x	
		suffering from skin cancer						x	x	x		x	
		has been under dermatological treatment due to skin cancer						x	x	x		x	
		has been on sick leave due to skin cancer						x	x	x		x	

Appendix 3: Time trend analyses

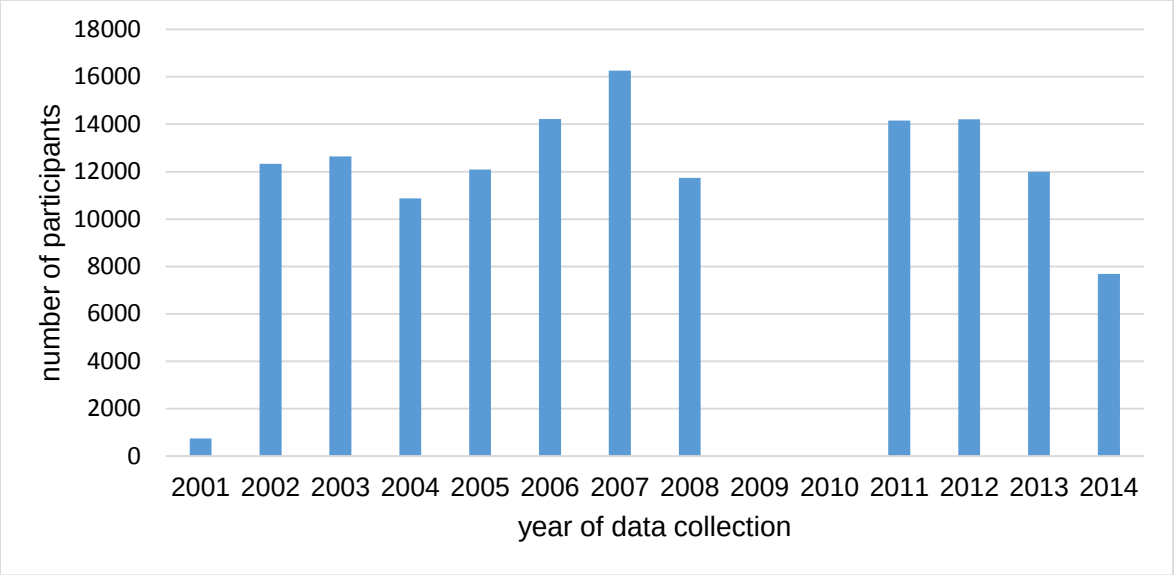
3.1 Psoriasis prevalence



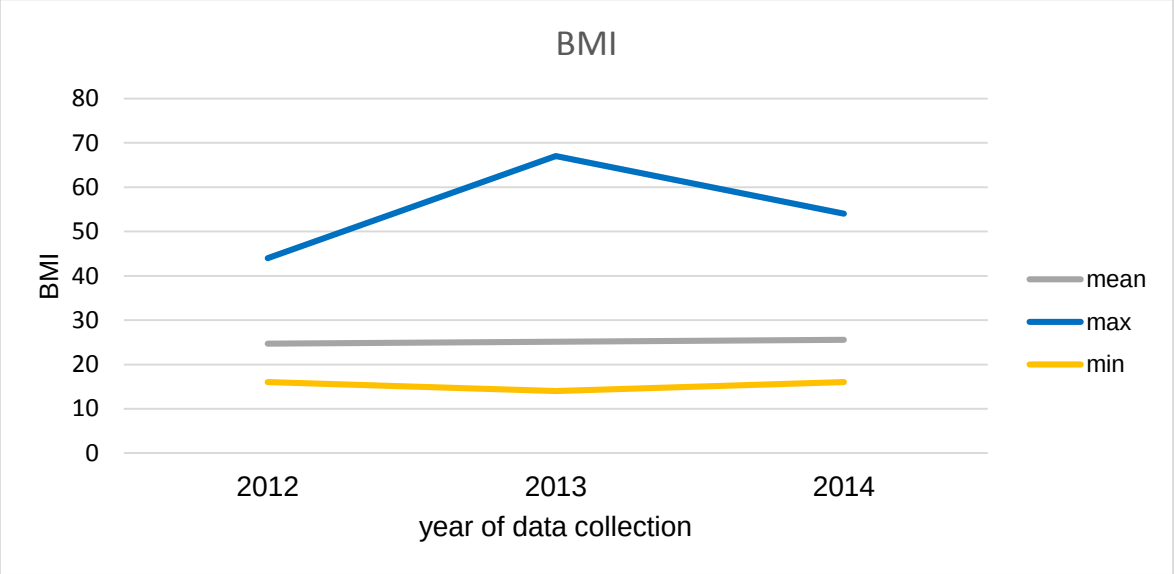
3.2 Age



3.3 Number of participants



3.4 BMI



Appendix 4: Skin diseases with and without psoriasis

	prevalence with psoriasis (n=2,781)			prevalence without psoriasis (n=136,149)			Asymptotic significance (2-sided)		
	total	male	female	total	male	female	total	male	female
Inflammatory skin diseases									
acne	2.0%	2.2%	1.7%	3.6%	3.6%	3.5%	≤0.001	≤0.001	0.002
atopic eczema	0.9%	1.0%	0.8%	1.4%	1.3%	1.5%	0.037	0.28	0.055
hand eczema	0.5%	0.6%	0.4%	0.8%	1.0%	0.6%	0.073	0.091	0.369
intertriginous dermatitis	0.9%	0.4%	1.8%	0.7%	0.7%	0.7%	0.097	0.164	≤0.001
contact dermatitis	0.1%	0.1%	0.3%	0.2%	0.2%	0.2%	0.317	0.135	0.790
rosacea	3.8%	3.9%	3.6%	2.2%	2.3%	2.0%	≤0.001	≤0.001	≤0.001
other	1.3%	1.2%	1.5%	1.6%	1.8%	1.4%	0.289	0.095	0.679
exsiccation eczema	0.9%	1.2%	0.4%	0.8%	0.9%	0.7%	0.705	0.294	0.273
viral diseases of the skin									
other	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.814	0.751	0.967
verruca plantaris	2.2%	2.2%	2.1%	2.4%	2.3%	2.5%	0.442	0.730	0.449
verruca palmaris	0.7%	0.7%	0.8%	0.5%	0.7%	0.3%	0.145	0.825	0.027
fungal diseases of the skin									
other	0.6%	0.5%	0.7%	0.2%	0.2%	0.1%	≤0.001	0.026	≤0.001
onychomycosis	8.6%	11.0%	4.7%	6.8%	9.2%	3.9%	≤0.001	0.01	0.181
pityriasis versicolor	0.5%	0.4%	0.6%	1.0%	1.2%	0.8%	0.004	0.003	0.437
tinea corporis	0.5%	0.6%	0.4%	0.4%	0.6%	0.2%	0.675	0.851	0.371
tinea pedis	6.2%	8.2%	2.9%	4.9%	7.0%	2.2%	≤0.001	0.053	0.122
bacterial diseases of the skin									
other	0.3%	0.4%	0.0%	0.2%	0.2%	0.1%	0.444	0.197	0.276
folliculitis	6.4%	8.3%	3.4%	7.4%	9.8%	4.5%	0.046	0.035	0.104
Pyodermie	0.4%	0.5%	0.1%	0.6%	0.7%	0.4%	0.131	0.305	0.131
non-malignant non inflammatory changes of the skin									
other	2.0%	1.8%	2.2%	2.1%	2.0%	2.2%	0.845	0.560	0.638
cafe au lait	5.2%	4.9%	5.8%	6.7%	5.6%	8.2%	0.002	0.195	0.005
ephelides	17.3%	16.2%	19.0%	21.6%	19.5%	24.3%	≤0.001	≤0.001	≤0.001
fibromas	30.4%	29.6%	31.7%	29.6%	31.0%	27.9%	0.391	0.218	0.007
histiocytoma (dermatofibroma)	16.7%	15.6%	18.6%	17.7%	16.8%	18.8%	0.199	0.178	0.910
seborrhoic keratosis	27.4%	25.6%	30.4%	25.2%	25.4%	25.0%	0.007	0.806	≤0.001
solar (senil) lentigines	42.3%	39.9%	46.4%	39.8%	39.4%	40.4%	0.008	0.711	≤0.001
vitiligo	0.5%	0.5%	0.7%	0.6%	0.7%	0.5%	0.598	0.256	0.543
nevi	87.9%	88.5%	86.9%	87.5%	87.7%	87.2%	0.506	0.292	0.737
cysts									
other	0.5%	0.5%	0.6%	0.4%	0.5%	0.3%	0.537	0.884	0.230

	prevalence with psoriasis (n=2,781)			prevalence without psoriasis (n=136,149)			Asymptotic significance (2-sided)		
	total	male	female	total	male	female	total	male	female
lipoma	1.3%	1.7%	0.8%	1.5%	2%	0.8%	0.595	0.386	0.886
suspected malignant skin changes									
other	0.0%	0.0%	0.1%	0.1%	0.1%	0.1%	0.225	0.129	0.954
basal cell carcinoma	1.1%	1.0%	1.2%	0.9%	1.1%	0.8%	0.375	0.835	0.087
dysplastic nevi	7.0%	6.5%	7.8%	8.1%	8.7%	7.4%	0.032	0.002	0.66
malignant melanoma, akrolentiginous	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.44	0.512	0.673
malignant melanoma, nodular	0.0%	0.0%	0.1%	0.0%	0.1%	0.0%	0.774	0.307	0.266
malignant melanoma, superficial spreading	0.1%	0.1%	0.0%	0.1%	0.2%	0.1%	0.335	0.527	0.332
Morbus Bowen	0.1%	0.1%	0.2%	0.1%	0.2%	0.1%	0.969	0.564	0.361
Plattenepithelkarzinom	0.1%	0.1%	0.1%	0.1%	0.1%	0.0%	0.638	0.823	0.163
Malignant Melanoma total	0.1%	0.1%	0.1%	0.2%	0.3%	0.1%	0.229	0.210	0.710
total	10.9%	11.3%	10.2%	11.6%	13.3%	9.4%	0.249	0.016	0.418
actinic keratosis	2.8%	3.9%	1.0%	2.5%	3.6%	1.1%	0.270	0.498	0.869
vessel changes of the skin									
Naevus flammeus	5.9%	4.9%	7.7%	5.7%	4.8%	6.8%	0.634	0.963	0.274
teleangiectasia	12.1%	10.8%	14.2%	8.9%	8.0%	10.0%	≤0.001	≤0.001	≤0.001
haemangioma	44.9%	46.5%	42.4%	43.2%	44.9%	41.0%	0.060	0.168	0.384
spider veins	20.7%	12.8%	33.6%	20.3%	12.8%	29.6%	0.589	0.970	0.005

Appendix 5: Need for treatment of skin diseases among psoriatic patients

	total (n=2,781)	male (n=1,728)	female (n=1,053)
bacterial diseases of the skin			
other	0.2%	0.3%	0.0%
folliculitis	0.4%	0.6%	0.0%
pyoderma	0.1%	0.1%	0.1%
inflammatory skin diseases			
acne	0.4%	0.3%	0.6%
other	0.5%	0.5%	0.6%
atopic eczema	0.4%	0.5%	0.2%
exsiccation eczema	0.3%	0.4%	0.1%
hand eczema	0.2%	0.2%	0.2%
intertriginous dermatitis	0.4%	0.0%	1.0%
contact dermatitis	0.0%	0.1%	0.0%
psoriasis	41.4%	42.5%	38.7%
rosacea	0.5%	0.3%	0.9%
vessel changes of the skin			
naevus flammeus	0.0%	0.0%	0.0%
teleangiectasia	0.0%	0.1%	0.0%
haemangioma	0.0%	0.0%	0.0%
vein status			
spider veins	0.2%	0.2%	0.1%
non-malignant non-inflammatory changes of the skin			
other	0.1%	0.1%	0.0%
café au lait spots	0.0%	0.0%	0.0%
ephelides	0.0%	0.0%	0.0%
fibromas	0.0%	0.0%	0.0%
histiocytoma (dermatofibroma)	0.0%	0.0%	0.0%
seborrhoic keratosis	0.1%	0.1%	0.1%
solar (senil) lentigines	0.0%	0.0%	0.0%
vitiligo	0.0%	0.1%	0.0%
cycts			
nevi	0.3%	0.3%	0.4%
other	0.0%	0.1%	0.0%
lipoma	0.1%	0.1%	0.0%
fungal diseases of the skin			
other	0.2%	0.1%	0.4%
onychomycosis	4.5%	5.8%	2.2%
pityriasis versicolor	0.2%	0.2%	0.3%
tinea corporis	0.3%	0.3%	0.2%

	total (n=2,781)	male (n=1,728)	female (n=1,053)
tinea pedis or onychmoycosis	6.9%	9.1%	3.4%
tinea pedum	3.5%	4.6%	1.6%
suspected malignant skin changes and their preliminary stages			
actinic keratosis	1.4%	1.7%	0.8%
other	0.0%	0.0%	0.1%
basal cell carcinoma	1.1%	1.0%	1.2%
dysplastic nevi	6.0%	5.7%	6.5%
morbus bowen	0.1%	0.1%	0.2%
squamous cell carcinoma	0.1%	0.1%	0.1%
viral diseases of the skin			
other	0.1%	0.1%	0.1%
verruca vulgaris/ feet	1.0%	1.2%	0.7%
verruca vulgaris/ hands	0.3%	0.3%	0.1%

Appendix 6: Syntax of data analysis

See attached CD