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INVESTIGATIVE REPORT

Incidence and Determinants of Chronic Pruritus: A Population-based Cohort Study

Uwe MATTERNE[1], Christian J. APFELBACHER[1,3], Lena VOGELGSANG[1], Adrian LOERBROKS[2] and Elke WEISSHAAR[1]
[1]Department of Clinical Social Medicine, Occupational and Environmental Dermatology, Health Services Research, University Hospital Heidelberg, [2]Mannheim Institute of Public Health, Social and Preventive Medicine, Mannheim Medical Faculty, University of Heidelberg, Heidelberg, and [3]Medical Sociology, Institute of Epidemiology and Preventive Medicine, University of Regensburg, Regensburg, Germany

Epidemiological data on chronic pruritus (>6 weeks) in the general population are sparse. We aimed to provide data on the incidence and prevalence of chronic pruritus, and identify its determinants based on cross-sectional and longitudinal analyses. A cohort of 1,190 participants from a cross-sectional baseline-study (response rate: 57.8%) was followed up after one year. The questionnaire assessed occurrence of chronic pruritus, medical, lifestyle and psychosocial variables. Incident chronic pruritus was defined as reported chronic pruritus at follow-up in those subjects free-of-the-symptom at baseline. Cross-sectional analyses of data from the follow-up assessments addressed potential associations of medical, lifestyle and psychosocial factors with prevalent chronic pruritus. Longitudinal analyses examined sociodemographic factors as potential predictors of incident chronic pruritus. The follow-up response rate was 83.1%. The mean age of subjects was 56 years, and 58% were female. The 12-month cumulative-incidence equalled 7.0% (95% confidence interval (95% CI) 5.2–9.2%. Lifetime prevalence was 25.5% (95% CI 21.8–27.8%). Incidence was significantly associated with age. Determinants of prevalent chronic pruritus in multivariable analyses were: liver disease, asthma, eczema and dry skin within the medical domain, an elevated body mass index within the lifestyle domain and higher anxiety scores within the psychosocial domain. Findings suggest a considerable 12-month incidence and lifetime prevalence and provide important directions for future research.
Key words: chronic pruritus; incidence; prevalence; longitudinal; predictors; determinants.

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Elke Weisshaar, University Hospital Heidelberg, Clinical Social Medicine, Occupational and Environmental Dermatology & Health Services Research, Thibautstrasse 3, DE-69115 Heidelberg, Germany. E-mail:elke.weisshaar@med.uni-heidelberg.de

Chronic pruritus strongly impairs affected individuals' quality of life (QoL) (1). Research suggests that its impact is similar to that of chronic pain (2). Recent surveys indicate the point-prevalence of chronic pruritus (defined as lasting >6 weeks (3)) to be around 13.5% in the general adult population (4) and 16.8% in employees (5). The 12-month prevalence in the general population was estimated at 16.4% (4). While these surveys suggest the burden of the symptom to be substantially higher than previously believed, little is known about how many individuals develop the symptom within a specified period of time. To our knowledge there are no data on the incidence of chronic pruritus in the general population.

In order to learn more about risk factors for chronic pruritus, it is necessary to examine associated factors longitudinally. However, to our knowledge, no longitudinal study on the occurrence of chronic pruritus and its risk factors has been conducted to date. So far, cross-sectional data on sociodemographic factors have failed to show a consistent pattern of associations (4, 6, 7), while studies examining other associations (e.g. psychosocial) usually look at a limited number of variables simultaneously (8–11) or at associations in discrete patient samples (12–14).

The aim of this study was to provide first estimates of the 12-month incidence of chronic pruritus and additional estimates of its prevalence in the general population. A second aim was comprehensively to explore cross-sectional associations of prevalent chronic pruritus with potential risk factors for chronic pruritus. Thirdly, the longitudinal associations of baseline demographic data with pruritus incidence were analysed.

METHODS

Study population

The study was approved by the ethics committee of the University of Heidelberg (S-120/2008) and conducted in accordance with the World Medical Association's Declaration of Helsinki. Results are reported in line with the "Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)" recommendations (15). A cohort of 1,190 participants in an earlier cross-sectional study on the prevalence of chronic pruritus (baseline study in 2008 to 2009, $n = 2{,}540$) (4) who had consented to be contacted again, were approached for follow-up one year later. In the baseline study, 4,503 individuals with a minimum age of 18 years had been randomly drawn from the registration offices of 2 cities in Southwestern German (Heidelberg and Ludwigshafen) and 6 surrounding rural communities. A total of 2,540 individuals participated in the baseline survey (response rate 57.8%). Of these, 1,190 consented to take part

in future surveys and received the follow-up questionnaire one year later (2009 to 2010).

Procedure

The questionnaire was sent by post. All non-respondents received one postal reminder after 2 months. Non-respondents after the first reminder were either contacted by telephone (if their telephone number was listed in the telephone directory or the individual had provided it in the previous survey) or received a second postal reminder including a shortened version of the questionnaire (if no telephone number could be obtained).

Questionnaire

The questionnaire assessed the occurrence of chronic pruritus at present, during the last 12 months and ever. These questions were taken directly from a previously validated questionnaire for the assessment of the prevalence of chronic pruritus (16). Furthermore, the questionnaire contained German versions of the Hospital Anxiety and Depression Scale (HADS) (17), a health anxiety scale (Whiteley-7-index) (18, 19), a social support scale (F-SOZU-K14) (20) and the Neuroticism scale of a short-form Big Five instrument (BF-16 AM) (21).

The questionnaire contained a number of items measuring lifestyle variables. Weight ("How much do you weigh?" in kg) and height ("How tall are you?" in cm) were assessed to calculate the body mass index (BMI). Exercise was measured by the item "Do you regularly exercise" (yes/no). We also asked participants whether they slept sufficiently ("Do you think you get enough sleep?" (yes/no), whether they smoked (yes/no), how many units of alcohol they consumed per week (1 unit = 10 ml of alcohol based on number of beers (500 ml at 4.9%), glasses of wine (200 ml at 11%) and shots of spirits (20 ml at 37.5%)), work or worked in a job with regular sun-exposure (yes/no), have or had hobbies involving regular ultraviolet light (UV) exposure (yes/no), whether they applied skin-care products (e.g. emollients) regularly (yes/no), used appropriate sun-protection measures (e.g. sunscreen, hat) regularly when in the sun (yes/no), and how many sunburns have occurred (< 5, 5–10, more > 10).

The questionnaire also contained questions about previous medical diagnoses of the respondent. Individuals were asked to indicate whether any of the following conditions had ever been diagnosed by a physician: hypertension, heart attack, stroke, diabetes, liver disease, kidney disease, hyper- or hypothyroidism, allergy, rhino-conjunctivitis, eczema, mental illness, cancer or any other illness. In addition, regular intake of medication, presence of dry skin, and skin type according to Fitzpatrick (22) were assessed. For the purpose of the manuscript these 3 variables and the diagnoses are subsumed under medical variables. Skin type according to the Fitzpatrick scale measures several factors, such as genetic disposition and reaction to sun-exposure (very fair = type 1 to black = type 6). For the purpose of the present study (European sample) only types 1 to 4 were assessed.

Finally, sociodemographic variables (age in years, gender (male vs. female), occupational status (working, retired or other), schooling (elementary, secondary ordinary or secondary advanced school leaving certificate), ethnic origin (German vs. non-German), place of residence (rural vs. urban) and marital status (with partner vs. without partner) were measured.

Statistical analyses

Statistical analyses were conducted using SPSS 19 (IBM SPSS Statistics). Data are given as absolute and relative frequencies (categorical variables), or by means and standard deviations (continuous variables), and 95% confidence intervals (CI) were computed. Comparisons between respondents, on the one hand, and non-respondents and those refusing to participate, on the other hand, were carried out by independent *t*-tests for the continuous variable age and by χ^2 test for the sex distribution. Longitudinal associations of incident chronic pruritus with sociodemographic variables and cross-sectional associations of prevalent lifetime chronic pruritus with medical variables, lifestyle and psychosocial variables were analysed by univariate and multivariate robust Poisson-regression analysis yielding risk-ratios or prevalence-ratios, respectively. It is recommended to estimate prevalence ratios obtained by a robust method in lieu of odds ratios in cross-sectional analyses when the prevalence of the characteristic in question is high (23). *p*-values < 0.05 were considered to indicate statistical significance.

RESULTS

Response rate, drop-out analyses and sample description

Of those alive ($n = 1{,}135$ of 1,190; 95%) at follow-up, 943 returned the follow-up questionnaire; a response rate of 83.1%. Eighteen (1.6%) individuals refused participation in the follow-up study while 174 (15.3%) had not responded after 3 contact attempts (Tables I and II). Those returning the questionnaire differed significantly from non-respondents in terms of age and from those refusing to participate in terms of gender (Table I). The demographic characteristics of the sample are given in Table III. We observed a preponderance of females in the sample.

Incidence and prevalence of chronic pruritus

Table IV provides the estimates for these 2 epidemiological parameters. Of those individuals who had been free of the symptom at baseline (12 months prior to the follow-up study ($n = 651$)), 7% reported chronic pruritus at follow-up; an incidence rate of 70 per 1,000 person-years (12-month incidence = 7%). The 12-month incidence of chronic pruritus increased somewhat with each reminder (apart from the third postal reminder) (Table II). Prevalence of chronic pruritus was estimated in the whole sample that was available at follow-up ($n = 943$). Of the total sample 15.4% reported current chronic pruritus, 18.2% chronic pruritus during the previous 12 months, and 25.5% chronic pruritus to have ever occurred (Table IV).

Table I. *Attrition and drop-out analyses (n=1,190)*

	n (%)	Age, years Mean ± SD	Sex (Female %)
Total contacted	1,190 (100)	53.9 ± 17.4	57.4
Excluded	55 (4.6)		
Deceased	15 (1.3)	58.5 ± 21.3	46.7
Unknown address	36 (3.0)	45.2 ± 17.1	50.0
Unable to participate[a]	4 (0.3)	85.5 ± 11.0	50.0
Total included	1,135 (100)		
Agreed to participate (participants)	943 (83.1)	56.0[b] ± 16.5	58.0[b]
Refused to participate	18 (1.6)	50.1 ± 17.2	27.8[b]
Did not respond	174 (15.3)	43.7[b] ± 17.3	60.1[b]

[a]Due to severe dementia or earning disabilities. [b]Significantly different at $p < 0.001$.
SD: standard deviation.

Table II. *Response rate progress and its relation to 12-month incidence*

Wave	Sample[a]	Response rate *n* (%)	12-month incidence of chronic pruritus (%)
First postal	1,165	546 (46.9)	5.5 (400)[b]
Second postal	1,157	800 (69.1)	6.9 (566)[b]
Third (postal)	1,151	867 (75.3)	6.6 (607)[b]
Third (telephone)	1,135	943 (83.1)	7.0 (651)[b]

[a]1,190 minus those excluded (deceased, unknown address, unable to participate); [b]individuals without lifetime chronic pruritus at baseline.

Longitudinal associations of incident chronic pruritus with baseline demographics (Table V)

Of the 6 demographic parameters (sex, age, occupational status, schooling, ethnic origin and place of residence) assessed at baseline, only age and occupational status achieved statistical significance in univariate analyses. The risk of chronic pruritus increased by 2% with each additional year of life and was twice as high in retired compared with working individuals. Since age and retirement are inextricably linked we also conducted a multivariable analysis to control for co-variation among predictors. While the direction of association remained the same, the magnitude of the relationships between the variables was no longer large enough to achieve statistical significance in multivariable analysis.

Cross-sectional associations of the lifetime prevalence of chronic pruritus with medical variables, lifestyle and psychosocial variables (Table VI)

Again, we initially conducted univariate analyses to examine potential associations between the lifetime prevalence and each individual variable from the 3 domains (medical variables, lifestyle and psychosocial constructs). The lifetime prevalence of chronic pruritus was significantly increased for individuals reporting hyper- or hypothyroidism, at least one allergy, asthma, eczema, mental illness, taking medication regularly and having dry skin. In comparison with the absence of these conditions the risk increased by between 33% (medication) and almost 300% (eczema).

Of the lifestyle variables, insufficient sleep, smoking and number of sunburns were significantly associated with the lifetime prevalence of chronic pruritus. The risk to smokers of developing pruritus was increased by 34%. There was a positive relationship between the number of sunburns and the risk of chronic pruritus (risk ratio (RR) = 1.20), while sufficient sleep was associated with a 27% decreased risk of chronic pruritus.

Of the assessed psychosocial constructs, anxiety and depression, as measured by the HADS were significantly associated with the lifetime prevalence of chronic pruritus. An increment of one unit in the respective scale scores was associated with a 7% increase for anxiety and a 4% increase for depression.

Again, to adjust for confounding, we conducted multivariable analyses within each of the 3 domains (medical variables, lifestyle and psychosocial constructs). Within the medical variables domain, presence of liver disease (RR = 2.12), asthma (RR = 1.82), eczema (RR = 2.70) and dry skin (RR = 1.89) remained significant correlates

Table III. *Demographics of respondents (*n = *943)*

	Relative frequency (%)	95% CI
Sex		
Female	58.0	54.8–61.1
Male	42.0	38.9–45.2
Age, mean (standard deviation)	56.0 (16.5)	54.9–57.0
Partner		
Schooling		
Elementary	37.0	34.0–40.2
Secondary (ordinary)	24.6	21.9–27.5
Secondary (advanced)	37.6	34.5–40.7
Occupational status		
Working	50.6	47.3–54.0
Retired	37.0	33.9–40.3
Other	12.3	10.2–14.6
Origin		
German	89.9	87.9–91.7
Other	10.1	8.3–12.1

CI: confidence interval.

Table IV. *Prevalence and incidence of chronic pruritus (*n = *943)*

	Relative frequency (%)	95% CI
Prevalence		
Point	15.4	13.2–17.8
12-month	18.2	15.8–20.8
Lifetime	25.5	21.8–27.8
12-month incidence[a]	7.0	5.2–9.2

[a]Based on 651 cases without chronic pruritus at baseline.
CI: confidence interval.

Table V. *Longitudinal univariate and multivariate associations of (baseline) sociodemographic variables with (follow-up) 12-month occurrence of chronic pruritus (incidence) (*n = *651)*

	12-month incidence RR (95% Wald CI)	
	Univariate	Multivariate
Sex		
Male	1.00	1.00
Female	1.26 (0.70–2.28)	1.32 (0.69–2.54)
Age, years	**1.02 (1.01–1.04)**	1.01 (0.97–1.03)
Occupational status		
Working	1.00	1.00
Retired	**1.98 (1.07–3.63)**	1.70 (0.67–4.33)
Other	0.89 (0.31–2.57)	0.88 (0.31–2.50)
Schooling		
Elementary	1.00	1.00
Secondary ordinary	0.73 (0.36–1.51)	0.85 (0.39–1.88)
Secondary advanced	0.58 (0.29–1.14)	0.74 (0.38–1.42)
Other	0.00 (0.00–0.00)	0.00 (0.00–0.00)
Origin		
German	1.00	1.00
Other	0.82 (0.30–2.23)	0.84 (0.31–2.26)
Place of residence		
Urban	1.00	1.00
Rural	0.90 (0.50–1.61)	0.95 (0.53–1.70)

Significant associations in bold type.
CI: confidence interval; RR: risk ratio.

Table VI. *Cross-sectional associations of prevalent chronic pruritus (lifetime) with medical variables, lifestyle and psychosocial variables (univariate and multivariate)*

	Lifetime prevalence PR (95% Wald CI)	
	Univariate	Multivariate[c]
Medical variables		
Hypertension[b]	1.01 (0.77–1.31)	0.93 (0.67–1.28)
Heart attack[b]	0.69 (0.30–1.54)	0.51 (0.20–1.28)
Stroke[b]	0.64 (0.22–1.83)	0.96 (0.37–2.52)
Diabetes[b]	0.90 (0.57–1.42)	1.12 (0.71–1.78)
Liver disease[b]	1.44 (0.74–2.81)	**2.12 (1.13–3.98)**
Kidney disease[b]	1.01 (0.54–1.87)	0.84 (0.45–1.58)
Hyper- or hypothyroidism[b]	**1.61 (1.21–2.13)**	1.20 (0.87–1.64)
Allergy[b]	**1.85 (1.45–2.36)**	1.29 (0.93–1.80)
Asthma[b]	**1.97 (1.39–2.79)**	1.82 (1.22–2.71)
Rhino-conjunctivitis[b]	1.18 (0.85–1.62)	0.70 (0.49–1.02)
Eczema[b]	**3.97 (3.23–4.90)**	2.70 (2.01–3.64)
Mental illness[b]	**2.02 (1.48–2.75)**	1.32 (0.94–1.84)
Cancer[b]	0.65 (0.38–1.14)	0.58 (0.31–1.10)
Other illness[b]	1.26 (0.97–1.64)	1.08 (0.80–1.44)
Medication[b]	**1.33 (1.03–1.72)**	1.34 (0.97–1.85)
Dry skin[b]	**2.44 (1.88–3.17)**	1.89 (1.41–2.55)
Skin type[a]	0.97 (0.82–1.14)	1.01 (0.85–1.20)
Lifestyle		
BMI[a]	1.01 (0.99–1.04)	**1.03 (1.01–1.06)**
Partner[b]	0.78 (0.59–1.04)	0.89 (0.61–1.29)
Exercise	0.98 (0.77–1.26)	1.10 (0.80–1.51)
Sufficient sleep[b]	**0.73 (0.55–0.97)**	0.88 (0.62–1.26)
Smoking[b]	**1.34 (1.02–1.77)**	1.36 (0.96–1.92)
Units of alcohol per week[a]	1.01 (0.99–1.02)	1.01 (0.99–1.02)
UV-exposure at work[b]	0.79 (0.49–1.29)	0.53 (0.26–1.06)
UV-exposure (recreational)[b]	1.16 (0.90–1.50)	1.07 (0.77–1.47)
Regular skin care[b]	1.25 (0.96–1.61)	1.19 (0.88–1.62)
Regular sun protection[b]	1.01 (0.77–1.32)	1.10 (0.78–1.56)
Number of sunburns[a]	**1.20 (1.04–1.40)**	1.12 (0.93–1.34)
Psychosocial		
HADS-A[a]	**1.07 (1.04–1.11)**	1.07 (1.02–1.13)
HADS-D[a]	**1.04 (1.01–1.07)**	1.01 (0.96–1.06)
F-SOZU[a]	0.99 (0.98–1.01)	1.00 (0.99–1.02)
Neuroticism[a]	1.01 (0.98–1.04)	0.98 (0.95–1.02)
Whiteley-7[a]	1.07 (0.99–1.14)	0.99 (0.92–1.09)

[a]Continuous correlate in ascending order; [b]reference is absence of condition; [c]3 multivariable robust Poisson regressions within medical, lifestyle and psychosocial sets of variables; significant associations in bold type.
PR: prevalence ratio; CI; confidence interval; BMI: body mass index; UV: ultraviolet; HADS-A: Hospital Anxiety and Depression Scale-A; HADS-D: Hospital Anxiety and Depression Scale-D; F-SOZU: Fragebogen zur sozialen Unterstützung (a social support scale).

of the lifetime prevalence of chronic pruritus. Of the lifestyle variables only the BMI was a significant correlate of lifetime chronic pruritus. One-unit increments in BMI were associated with a 3% increased risk of chronic pruritus. Within the psychosocial constructs only the HADS-A remained a significant correlate in multivariable analyses. A 1-unit increase in HADS-A led to 7% higher risk of developing chronic pruritus.

DISCUSSION

Cumulative incidence and prevalence of the symptom

There appears to be a growing body of evidence indicating a considerable prevalence of the symptom chronic pruritus at the population level (4, 5). The present study also sought to estimate the point-, 12-month- and lifetime-prevalence of the symptom in this cohort. These were 15.4%, 18.2% and 25.5%, respectively. The prevalence estimates closely resemble those obtained in our baseline survey (4) and in a survey conducted in a large working population (5) and again highlight a substantial prevalence of the symptom in the population.

However, so far there have been no studies attempting to quantify the incidence of chronic pruritus. Our study found a 12-month cumulative incidence of the symptom of 7% and is the first study to provide this epidemiological estimate. While the obtained response rate was good, at 83.1%, it must be noted though, that based on the 95% confidence interval, the estimate is also compatible with an incidence of 5.2%. Based on conventionally accepted levels of statistical uncertainty, the true incidence of chronic pruritus may be slightly higher or lower than the reported 7%, as indicated by the corresponding confidence interval of 5.2–9.2%.

Longitudinal relationships

Of the baseline sociodemographic variables only age and retirement were significant longitudinal predictors of follow-up presence of the symptom when analysed alone. but failed to remain significant predictors in multivariable analyses due to their high interrelationship. The (cross-sectional) relationship of itching in general with age is assumed by many, but apparently the empirical base for this assumption is not straightforward. One study found younger age related to acute pruritus (9), the Lambeth study found no significant relationship between prurigo and allied conditions with age (24) while 2 others found positive relationships between chronic pruritus and age (5, 16). Our findings are in line with the latter. Patient samples reporting chronic pruritus tend to be older (25, 26); however, it should be borne in mind that these samples are highly selective, as with advancing age the occurrence of disease (that may be associated with chronic pruritus) also increases. In terms of chronic pruritus the evidence so far suggests a positive relationship with age.

Cross-sectional associations

The literature on factors related to chronic pruritus is growing, but studies often look at discrete factors. The present study was designed to provide data on multiple potential determinants and pave the way for a future prospective analysis of these factors.

Not surprisingly we found positive associations with history of liver disease, asthma, dry skin and eczema. In the latter, pruritus is a defining feature of the condition (27). Hypo- or hyperthyroidism and at least one allergy were also found to be significantly related to the lifetime prevalence of chronic pruritus, but since they failed to

remain significant in multivariable analysis they do not seem to be independently associated with chronic pruritus. Our data also back up previous observations (28, 29) of increased pruritus prevalence among psychiatric conditions; but again, in multivariable analyses the association disappeared. The same applied to medication intake. Independent associations obtained from multivariable analysis were found for liver disease, asthma, eczema and dry skin, suggesting that several of the aforementioned univariate associations are mediated by any of these factors.

Of the lifestyle variables under investigation, insufficient sleep, smoking and number of sunburns were found to be significantly related to chronic pruritus in univariate analysis. Multivariate analysis revealed that only BMI was independently related to it. To our knowledge this is a novel finding, but the effect is likely to be mediated by other factors. For instance, higher BMI has been linked to psoriasis occurrence in some studies (30–33). However, psoriasis is only one illness that may be accompanied by chronic pruritus.

Of the psychosocial constructs, depression and anxiety were significantly associated with the lifetime prevalence of chronic pruritus when analysed univariately. Due to their high and significant intercorrelation (for instance between HADS-A and HADS-D $r=0.57$, $p<0.001$) the effects could not be replicated in multivariable analysis (only anxiety remained a significant correlate), but a relationship between chronic pruritus and a general psychosocial factor can be assumed. The design of the current study does not permit the establishment of any causal direction, but similar to how psychosocial factors are involved in eczema, influences in both directions are possible and likely (34–36). Future prospective studies may be able to analyse the conditions of how and when psychosocial factors influence chronic pruritus and/or vice versa. For instance, Yamamoto et al. (37) were able to show that depressive symptoms predicted later pruritus in haemodialysis patients, while many studies report a psychological impact of pruritus (4, 11, 38). The present findings extend previous research on acute pruritus (9, 11, 38) to the symptom chronic pruritus.

Limitations

A number of limitations need to be discussed. Firstly, as with all surveys, a selection bias is possible. However, the response rate was good at 83.1%; thus minimizing the likelihood of selection bias. Secondly, as the data were obtained by self-reporting, bias due to social desirability tendencies are possible. Thirdly, incorrect recall due to the lack of a clear-cut definition of the symptom (information bias) cannot be ruled out. Although chronic pruritus is defined at a minimum duration of 6 weeks (3) no other qualifying criteria (e.g. strength, minimum daily duration, etc.) are given in this classification. As such, some respondents may consider slight itching occurring daily over a period of 6 weeks to be chronic pruritus, while others only consider widespread itching over at least 6 weeks that is presented to a physician to constitute the symptom. Pruritus is a subjective experience, but more effort is necessary to provide a clear-cut definition of the symptom to help standardize its reliable assessment. A potential information bias is, however, not limited to the variable chronic pruritus, but may also apply to most variables in this study. Fourthly, we were unable to disentangle potential directions of causality due to the cross-sectional character of the analysed relationships of chronic pruritus with medical variables, lifestyle factors and psychosocial variables; however, another follow-up is underway. Finally, although we achieved good response rates at baseline and follow-up of our population-based sample, we cannot rule out that higher response rates would have yielded slightly different findings and improved generalizability. The impact of selective participation, as discussed previously (4), may also influence the findings of the present follow-up study, such that individuals affected by the symptom may have been more likely to respond.

In conclusion, the present investigation adds to the growing number of epidemiological studies of chronic pruritus and its determinants in the general population. It provides, for the first time, an estimate of the 12-month cumulative incidence and corroborates previous findings on the prevalence of the symptom and its relation to age. In addition, a large number of established and potential correlates were cross-sectionally analysed in a first systematic attempt at synthesizing isolated findings from previous research and at paving the way for a more causal perspective in future longitudinal analyses. Healthcare provision, as well as research aimed at curative and palliative relief, may need to pay more attention to this troublesome symptom considering its high frequency of occurrence in the general adult population. Researchers and clinicians may also need to pay more attention to how certain co-occurrences of medical variables, lifestyle or psychosocial, on the one hand, and chronic pruritus, on the other hand, may in fact be mediated by other factors.

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