

# BMJ Open Prevalence and risk factors of senile pruritus: a systematic review and meta-analysis

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## ABSTRACT

**Objectives** To systematically assess the prevalence and risk factors for senile pruritus (SP) in the elderly ( $\geq 60$  years of age).

**Design** A meta-analysis was used to pool the prevalence and risk factors for SP estimated from individual studies. Four subgroup analyses were conducted to explore the prevalence for SP in different age, sex, research sites and region.

**Setting, participants and measures** SP reduces quality of life in the elderly, yet the worldwide prevalence is unclear. Moreover, the risk factors for SP are controversial. Data from cross-sectional studies, case-control studies, longitudinal studies and cohort studies that reported the prevalence or the risk factors for SP were collected by searching nine electronic databases up to October 2020, including Web of Science, PubMed, Embase, Cochrane Library, CINAHL, CBM, CNKI, Wanfang and VIP. Two reviewers independently screened studies according to the inclusion and exclusion criteria, extracted data and assessed methodological quality. Data analysis was performed using Stata V.15.1 software.

**Results** Seventeen studies involving 28 666 participants were included. The overall pooled prevalence of SP was 21.04% (95% CI 11.37% to 32.72%). In addition, the results showed that smoking, excessive drinking and monophagism were possible risk factors for SP, with pooled ORs of 1.26 (95% CI 1.14 to 1.40), 25.03 (95% CI 18.28 to 34.25) and 1.22 (95% CI 1.12 to 1.33), respectively.

**Conclusions** The overall prevalence of SP was high. Smoking, excessive drinking and monophagism were possible risk factors for SP.

**PROSPERO registration number** CRD42019143295.

## INTRODUCTION

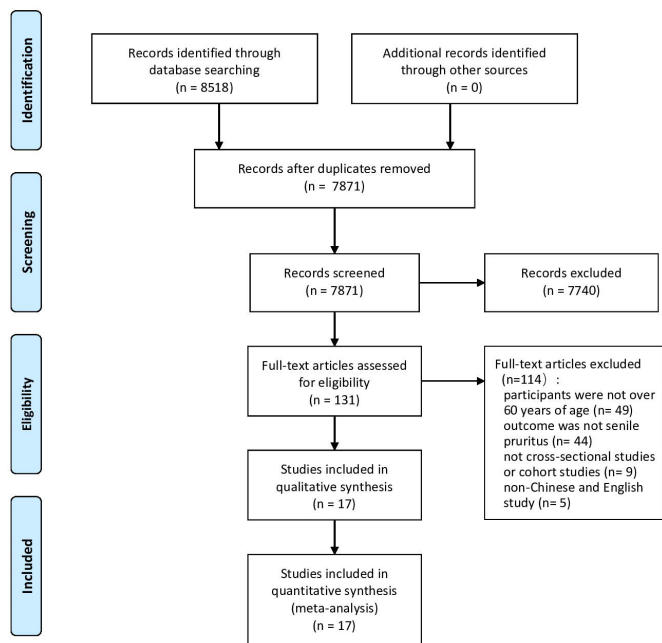
The geriatric population ( $\geq 60$  years of age) has been growing steadily worldwide in recent decades. It is estimated that the geriatric population will account for 20% of the world's population by the middle of this century.<sup>1–3</sup> Ageing results in numerous adverse changes in the structure and function of multiple human organs, including the skin.<sup>4</sup> Senile pruritus (SP) is defined as generalised pruritus in patients without primary skin lesions.<sup>5–8</sup> Pruritus is the most common skin disorder in the geriatric population.<sup>9</sup> It

## Strengths and limitations of this study

- To our knowledge, this study is the first systematic review and meta-analysis providing comprehensive assessment on the prevalence of senile pruritus (SP) in worldwide.
- The risk factors of SPs are evaluated.
- This systematic review and meta-analysis, covering five different countries, was composed of 17 studies, with 28 666 participants were included.
- The definitions of SP differed across the included studies.

can lead to an unpleasant cutaneous sensation, which provokes the desire to scratch (itchiness) and is accompanied by skin lesions, pain and infection.<sup>10</sup> Furthermore, it can lead to adverse consequences for patients' psychological health and quality of life, including anxiety, depression, disruption of normal sleep patterns and poor daytime concentration.<sup>10 11</sup> Therefore, investigating the prevalence of SP is essential for informing policymakers, clinicians, and the general population.

The prevalence of SP has been reported around the world, ranging from 41% in Thailand,<sup>12</sup> 40.6% in America,<sup>13</sup> 18.9% in Italy<sup>14</sup> and 14.2% in China.<sup>15</sup> However, these studies were limited by sample size and regional differences, and therefore do not represent the prevalence of SP worldwide. Furthermore, several studies conducted surveys on inpatients or outpatients to report the prevalence of SP.<sup>1 11 16 17</sup> Inpatients or outpatients do not represent the whole elderly population, making the results less representative of the actual prevalence of SP in the community. For these reasons, the precise prevalence and characteristics of the population are unknown worldwide. Furthermore, the risk factors for SP have been reported extensively, but with controversial conclusions.<sup>18 19</sup> For example, Yang *et al* indicated that smoking was associated with SP (OR 2.23, 95% CI 1.35 to



**Figure 1** Flow chart of the study selection process.

17.40).<sup>18</sup> However, Chen *et al* reported that smoking was not associated with SP (OR 1.25, 95% CI 0.99 to 1.35).<sup>19</sup>

In this study, we conducted a systematic review and meta-analysis to synthesise the prevalence of SP in different ages, sexes and regions based on the general population and to evaluate the risk factors for SP.

## MATERIALS AND METHODS

### Protocol registration

This study was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.<sup>20</sup>

### Search strategy

Nine databases were searched in this study, including Web of Science, PubMed, Embase, Cochrane Library, CINAHL, CBM, CNKI, Wanfang and VIP. The following strategy was used in the searches: (Pruritus OR Itching) AND (Senile OR Aging OR Aged OR Geriatrics) AND (Incidence OR Epidemiology OR Prevalence OR Risk factors). Complete details of the search strategy are available in online supplemental table S1. All of the databases were searched from their inception dates to the 24 October 2020. Additional relevant literature was included following a manual search of the included studies reference lists.

### Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) the study design was either cross-sectional study, case-control study, cohort study or longitudinal study; (2) participants were greater than or equal to 60 years of age; (3) exact diagnostic criteria for SP were provided and (4) prevalence or risk factors for SP were reported. The exclusion criteria were as follows: (1) the study populations were inpatients

and outpatients; (2) the prevalence or risk factor effect value (mainly referred to as OR in this study) of SP was not clearly reported in the original study, and the data provided by the original study couldn't calculate the prevalence or risk factor effect value of SP; (3) republished literature and (4) or studies published in a language other than Chinese or English.

### Quality of the studies

Two independent reviewers assessed the quality of the included studies according to 11 criteria recommended by the American Agency for Healthcare Research and Quality. The criteria included assessment of selection bias, performance bias, attrition bias, detection bias and publication bias. An item would be scored '1' if it was answered 'YES', and if it was answered 'NO' or 'UNCLEAR', then the item scored '0',<sup>21</sup> providing a maximum score of 11.

### Data extraction

Study selection and data extraction were independently conducted by two reviewers. Any disagreement was resolved by discussion the two reviewers or a third reviewer. The articles were first screened by the title and abstract, and then full-text documents were reviewed for inclusion if they reported the prevalence and risk factors for SP. By using a standardised and pilot-tested form, two reviewers independently extracted data from eligible studies, including the title, first author name, publication year, study location, age, sample size, diagnostic criteria, prevalence and risk factors for SP.

### Data analysis

Double arcsine transformation was used to convert the prevalence of SP so that the data can follow an approximately normal distribution.<sup>22</sup> The ORs with their corresponding 95% CIs were selected to assess the effect size of risk factors for SP. Heterogeneity among studies was tested by Cochrane's Q and  $I^2$  statistics. Heterogeneity was recognised as significant when  $I^2 > 50\%$ . A fixed-effect model (Mantel and Haenszel method) was used if  $I^2 \leq 50\%$ , otherwise a random-effects model (DerSimonian and Laird method) was used.<sup>23</sup> Forest plots were constructed for a visual display of the pooled results if necessary. Four subgroup analyses were conducted to explore the prevalence for SP in different age, sex, research sites and region. Sensitivity analysis were assessed by excluding single studies. Publication bias was assessed by using Begg's and Egger's tests.<sup>24</sup> Tests of publication bias and sensitivity analysis were not conducted in the risk factor analysis section due to the limited number of studies included. Statistical analyses were conducted using STATA V.15.1 (Stata).

## RESULTS

### Study description

A total of 8518 records were identified from the 9 databases, of which 647 were duplicates. After screening

**Table 1** Characteristics of included studies

Authors	Publication years	Study area	Diagnostic criteria	Sample size	Prevalence (%)	Risk factors
Dalgard <i>et al</i> <sup>34</sup>	2004	Norway	①	3876	6.91	NA
Li <i>et al</i> <sup>25</sup>	2000	China	NA	534	12.36	NA
Xue <sup>27</sup>	2008	China	NA	311	19.29	NA
Ni <i>et al</i> <sup>28</sup>	2012	China	④	426	5.63	NA
Zhang <sup>29</sup>	2012	China	NA	1283	9.90	NA
Li <i>et al</i> <sup>30</sup>	2014	China	⑤	500	33.40	NA
Wu and Zhang <sup>31</sup>	2014	China	⑤	1286	42.38	NA
Yang <i>et al</i> <sup>32</sup>	2014	China	NA	5000	33.84	NA
Tseng <i>et al</i> <sup>35</sup>	2014	China	NA	313	7.35	NA
Miller <i>et al</i> <sup>36</sup>	2016	Denmark	①	8252	6.31	NA
Kara <i>et al</i> <sup>37</sup>	2017	Turkey	NA	105	19.05	NA
Cowdell <i>et al</i> <sup>38</sup>	2017	Britain	⑥	1116	9.32	NA
Dyhre-Petersen and Gazerani <sup>39</sup>	2019	Denmark	⑦	45	28.89	NA
Ge <i>et al</i> <sup>26</sup>	2006	China	②	1236	66.91	Age, xerosis, astringency
Yang <i>et al</i> <sup>18</sup>	2009	China	③	3785	61.98	Less water intake; bathing with soap; baths too much; smoking; malignant tumour.
Chen <i>et al</i> <sup>19</sup>	2015	China	④	200	10.50	Bathing with soap; smoking; chronic illness; excessive drinking; monophagism; Insomnia; contact with animal
Hou and Zhang <sup>33</sup>	2016	China	④	398	18.09	Smoking; chronic illness; excessive drinking; monophagism; insomnia; contact with animal

Diagnostic criteria: ① self-reported skin complaints scale; ② participants  $\geq 60$  years, an itch lasting more than 2 weeks, pruritus of whole body or multiple parts, no primary rash, no other pruritic skin disease, no obvious liver and kidney damage, diabetes and mental disease; ③ dermatology and venereology; ④ clinical dermatology; ⑤ dermatovenerology; ⑥ self-report skin diseases scale;<sup>38</sup> ⑦ self-report skin diseases scale. NA, not available.

titles and abstracts, 7740 records were excluded with reasons of age, outcome, study design. Full-text documents of 131 records were screened, and 114 studies were excluded with reasons listed as follows: participants were not  $\geq 60$  years of age (n=49), outcome was not SP (n=44), not cross-sectional, case-control, cohort or longitudinal study (n=9), non-Chinese and English study (n=5), duplicate publication (n=7). In summary, 17 studies were eligible and included in the meta-analysis finally (figure 1).

### Characteristics of the included studies

The characteristics of the 17 studies are summarised in table 1. Eleven articles were written in Chinese,<sup>18 19 25–33</sup> and six were written in English.<sup>34–39</sup> Thirteen studies were conducted in Asia<sup>18 19 25–33 35 37</sup> and four in Europe.<sup>34 36 38 39</sup> Sample sizes ranged from 45<sup>39</sup> to 8252.<sup>36</sup> Four of the 17 studies reported the risk factors for SP.<sup>18 19 26 33</sup>

### Risk of bias assessment

Results of the risk of bias assessment are listed in online supplemental table S2. Higher scores indicative of less bias and more quality. Article quality was assessed as follows: 0–3 indicates a low quality, 4–7 indicates a moderate quality and 8–11 indicates a high quality.<sup>40</sup> Study quality was found to be moderate in 11 studies and high in the other six studies.

### Prevalence of SP

Seventeen studies, involving 28 666 participants reported the prevalence of SP, ranging from 5.63% to 66.91%. A random-effects model-based meta-analysis showed that the pooled prevalence of SP was 21.04% (95% CI 11.37% to 32.72%). Subgroup analyses indicated that the pooled prevalence of SP for people aged 60–69, 70–79, 80–89 and  $\geq 90$  years old were 11.98% (95% CI 3.91% to 23.62%), 26.79% (95% CI 8.71% to 50.36%),

**Table 2** Subgroup analyses by age, sex, research sites and region

Subgroup	Prevalence (%)	95% CI (%)	Heterogeneity	
			I <sup>2</sup> (%)	P value
<b>Age</b>				
60–69	11.98	3.91 to 23.62	98.1	0.000
70–79	26.79	8.71 to 50.36	99.7	0.000
80–89	51.31	47.20 to 96.33	99.6	0.000
≥90	57.53	8.18 to 98.09	99.0	0.000
<b>Sex</b>				
Females	8.26	5.88 to 11.00	87.4	0.000
Males	18.65	0.83 to 51.61	99.9	0.000
<b>Research sites</b>				
Health examination centre	43.83	19.39 to 69.94	99.8	0.000
Nursing homes	16.26	4.55 to 33.29	93.2	0.000
Community	12.21	3.46 to 25.34	99.8	0.000
<b>Region</b>				
Turkey, China	24.34	14.03 to 36.38	99.6	0.000
Norway, Denmark, Britain	8.23	6.36 to 10.35	90.2	0.000

51.31% (95% CI 47.20% to 96.33%) and 57.53% (95% CI 8.18% to 98.09%), respectively. The pooled prevalence of SP was 8.26% (95% CI 5.88% to 11.00%) in females and 18.65% (95% CI 0.83% to 51.61%) in males. The pooled prevalence of SP in health examination centres, nursing homes and communities was 43.83% (95% CI 19.39% to 69.94%), 16.26% (95% CI 4.55% to 33.29%) and 12.21% (95% CI 3.46% to 25.34%), respectively. The pooled prevalence of SP in Turkey and China was 24.34% (95% CI 14.03% to 36.38%). The pooled prevalence of SP in Norway, Denmark and Britain was 8.23% (95% CI 6.36% to 10.35%). The results of subgroup analyses of age, sex, research site and region are shown in [table 2](#).

### Risk factors

Four studies, including 5619 participants, reported the risk factors for SP.<sup>18 19 26 33</sup> There were three studies,<sup>18 19 33</sup> including 4383 participants, that reported the association of smoking and SP. Meta-analyses showed smoking was associated with SP (pooled OR of 1.26 (95% CI 1.14 to 1.40), I<sup>2</sup>=0%). The results of two studies,<sup>19 33</sup> involving 598 participants, suggested that excessive drinking increased the occurrence of SP (pooled OR of 25.03 (95% CI 18.28 to 34.25), I<sup>2</sup>=0%). Two studies<sup>19 33</sup> involving 589 participants reported the association of monophagism and

SP (pooled OR of 1.22 (95% CI 1.12 to 1.33), I<sup>2</sup>=0%) ([table 3](#)).

### Sensitivity analysis

Sensitivity analysis was performed by excluding a single study and showed that the results of the meta-analysis were stable (18.61%–22.23%). Sensitivity analysis was not conducted for the risk factor analysis due to the limited number of studies.

### Publication bias

Publication bias was assessed by using Begg's and Egger's tests. Begg's (Z=0.70, p=0.484) and Egger's test (t=0.26, p=0.796) results showed that the possibility of publication bias was less in the overall prevalence pooled analysis. Publication bias was not assessed in the risk factor analysis due to the limited number of studies.

### DISCUSSION

In this study, 17 studies involving 28 666 participants were included encompassing Norway, China, Denmark, Turkey and Britain. Subgroup analyses found that the difference in the prevalence of SP based on epidemiological factors. Subgroup analyses indicated that a steadily increasing

**Table 3** Pooled risk factors of senile pruritus

No.	Risk factors	OR	95% CI	P value	Heterogeneity	
					I <sup>2</sup> (%)	P value
1	Smoking	1.26	1.14 to 1.40	0.000	0%	0.673
2	Excessive drinking	25.03	18.28 to 34.25	0.000	0%	0.980
3	Monophagism	1.22	1.12 to 1.33	0.000	0%	0.926

prevalence of SP was associated with increasing age. Xerosis is related to ageing and is reported as the most common cause of SP.<sup>41–43</sup> One of the skin's most important functions is to retain water. skin surface lipids and sebum on the skin helps retain water.<sup>44</sup> As skin ages, there is a decrease in lipids and sebum on the skin, leading to suboptimal moisture retention.<sup>42</sup> It was reported that pruritus can also be secondary to diabetes, kidney disease, liver disease, etc.<sup>44 45</sup> Furthermore, pruritus is commonly listed as a medication complication,<sup>46</sup> including ACE inhibitors, salicylates, chloroquine and calcium channel blockers.<sup>44</sup> However, elderly people have more basic diseases and complex medication, which also contributed to the higher incidence of pruritus. Another view is that SP is probably a subclinical neuropathy, degenerative change in peripheral nerve endings may be attributable to age. This age alteration can cause pruritus without specific stimuli.<sup>7</sup> In addition, immunosenescence occurs with ageing and also produces a higher incidence of pruritus.<sup>42</sup> Moreover, decreases in androgen, oestrogen and glucocorticoid in aged people can contribute to SP.<sup>47 48</sup> All these factors will increase the prevalence of SP with age.

The results of subregional analyses found that individuals who were living in Turkey and China were associated with a higher prevalence of SP. Pruritus is influenced by multiple factors, such as genetic, biological, psychological, social, environmental and cultural factors.<sup>49</sup> Different countries vary in society, culture and environment, genetic, biological and psychological factors also differ among populations in different countries. Therefore, the different prevalence among countries is related to the above factors.

The results of subsex found that the prevalence of male is higher. Subresearch sites analyses found that the highest prevalence of SP was found in health examination centres. The reasons for these results are unclear based on the current scientific knowledge available on SP prevalence. Further studies would be helpful in further exploring these phenomena. In conclusion, the prevalence of SP varies among different populations. However, the reasons underlying the differences in prevalence observed in the current study remain unclear. It is suggested that further studies of the prevalence of SP in different populations be conducted in the future.

Meta-analyses showed that smoking, excessive drinking, and monophagism were possible risk factors for SP. It has been shown that smoking can cause nutrient and oxygen deprivation in cutaneous tissues, decreases collagen and elastin fibres in the dermis, and increases keratinocyte dysplasia.<sup>50</sup> These changes reduce skin lipids, sebum and moisture retention, leading to dryness and pruritus of skin.<sup>51 52</sup> Therefore, smoking is a potential risk factor for SP. This study also identified drinking alcohol as a potential risk factor for SP. Studies have demonstrated that alcohol consumption could reduce the concentration of carotenoids in the skin.<sup>53</sup> Carotenoids can neutralise free radicals, delay premature skin ageing and skin diseases caused

by free radicals.<sup>53–55</sup> It could be proposed that alcohol consumption may lead to skin diseases by affecting the concentration of carotenoids. The human body cannot synthesise carotenoids in sufficient amounts without relying on a nutrient rich diet including fruit and vegetables. Therefore, monophagism could contribute to reducing the concentration of carotenoids and it could be considered a risk factors for skin diseases. Regrettably, the specific types of monophagism wasn't pointed out in the included study, which prevented further analysis and discussion. We expect that follow-up studies will explore and investigate this. In addition, point out the participants' dietary structure and specific types of monophagism.

Although this study indicated smoking, excessive drinking and monophagism were associated with an increased risk of SP, all the studies included in the meta-analysis were cross-sectional. Consequently, It is not possible to infer on the causality between exposure and outcomes. Further studies are needed to confirm these findings. In addition to the three risk factors identified through the meta-analyses, the included studies also showed that the risk factors for SP also include age, xerosis, astriction, less water intake, bathing with soap, bathing too frequently, malignant tumour, chronic illness, excessive drinking, insomnia and contact with animals.

To the best of our knowledge, this study is the first to provide a systematic review of SP prevalence and risk factors. However, several limitations of this study should be noted. First, The epidemiological data on SP was only from Norway, China, Turkey, Britain and Denmark, which cannot be generalised to the worldwide population. Second, the methods of identifying SP varied among the included studies, the definitions of SP may not be uniform among investigators and researchers in different countries, the study of different countries may not be unified in assessing the prevalence of SP, making it difficult to analyse the prevalence of SP using a gold standard method. These limitations make we less confident that the final estimate is close to a 'true' estimate. Considering these limitations, further studies will be needed to better understand the prevalence and risk factors of SP worldwide.

## CONCLUSION

In conclusion, this study found the prevalence of SP was 21.04%. Individuals who were older, male or living in Turkey and China were associated with a higher prevalence of SP. Additionally, among health examination centres, nursing homes and communities, the highest detection rate of SP was found in the health examination centres. Smoking, excessive drinking and monophagism were possible individual risk factors for SP.

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**Contributors** SC and FZ contributed equally to this study. SC conceived and participated in the design of this review. SC and FZ performed the literature searches, study selection, data extraction and assessed the risk of bias. SC and FZ drafted the manuscript. YX helped in performing the analysis with constructive discussions. SC revised the final version. All authors read and approved the final manuscript. SC is responsible for the overall content as the guarantor.

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