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# The epidemiology of psoriasis

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This review will focus on the incidence and prevalence of psoriasis, the risk factors for psoriasis and diseases that may be associated with psoriasis. Psoriasis is a heterogeneous disease and, for the purposes of this review, the focus will be plaque psoriasis. Prevalence studies indicate that psoriasis is a common disease and its frequency varies based on age, ethnicity and geography. Family history is the strongest risk factor for the development of psoriasis. Additionally, emerging evidence suggests that some potentially modifiable exposures such as smoking, alcohol, stress and obesity may increase a patient's risk of developing psoriasis. The evolving literature suggests that psoriasis is associated with multiple other diseases including cancer, cardiovascular, autoimmune and psychiatric disease. Epidemiological studies of psoriasis contribute to measuring the public health burden of this disease and guide the care of patients with psoriasis through a better understanding of its natural history.

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Psoriasis is a common chronic inflammatory disease of the skin. Recent studies have demonstrated that psoriasis can have substantial impacts on quality of life, even in patients with relatively limited affected body surface area [1]. Additionally, studies have demonstrated that psoriasis has substantial economic costs, both to patients and the health-care system [2]. Although the cause of this disease remains unknown, the evolving evidence suggests that psoriasis is a complex disorder caused by the interaction of multiple genes, the immune system and environmental factors [3,4].

The epidemiology of psoriasis has been the focus of several reviews [5–8]. Epidemiology is the study of the distribution (e.g., incidence and prevalence) and determinants (e.g., risk factors) of disease frequency in human populations [9,10]. This review will focus on the incidence and prevalence of psoriasis, its risk factors and diseases that may be associated with its natural history.

## Incidence

Incidence is defined as the proportion of individuals at risk in a population that develop a disease of interest in a specified

time period. In contrast to prevalence, which measures existing cases, incidence quantifies the number of new cases of disease that develop in a population at risk during a specific time period [10]. There is currently only one study that examines the incidence rate of psoriasis [11]. This population-based study was conducted using the medical records linkage data resource for the population of Rochester (MN, USA) at the Mayo Clinic. Since not all patients with psoriasis, especially if mild, seek medical attention for their disease, this study may, in fact, underestimate the true incidence of psoriasis. Estimates were based on a total of 132 newly diagnosed cases of psoriasis that were identified during a 4-year period (1980–1983). The overall annual crude incidence rate was 57.6 per 100,000 population; for men, the rate was 54.4 per 100,000 and for women, 60.2. The overall average annual sex- and age-adjusted (1980 US white population) incidence rate was 60.4 per 100,000 people. The highest overall rate of incidence (112.6/100,000 population) was in the 60–69-year-old age group. In men, the average annual incidence of psoriasis increased with age, whereas in women, rates increased until age 69, and

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decreased thereafter. Most of the cases of psoriasis diagnosed in this study (58%) were mild, defined as less than 10% body surface area (BSA).

### Prevalence

Prevalence is defined as the proportion of individuals in a population who have the disease of interest in a specified time period. When measures are relative to a point in time this is referred to as point prevalence; when relative to a longer period, this is referred to as period or lifetime prevalence. Studies of the prevalence of psoriasis have varied in their definition of prevalence (i.e., point prevalence vs lifetime prevalence). Also, the case definition of psoriasis (e.g., self report vs physician diagnosis), the population and ages studied, and the sampling techniques have all varied across studies and may impact on the

prevalence rates. Epidemiological studies from around the world have estimated the prevalence of psoriasis to be anywhere from 0.6 to 4.8% (TABLE 1).

### Impact of geography & ethnicity on prevalence of psoriasis

The prevalence of psoriasis appears to vary based on the geographical region studied and the population groups (e.g., ethnic groups) studied within that region. For example, in a study of twin pairs in Australia, researchers demonstrated that psoriasis occurred more frequently in southern states when compared with the warmer northern states [32]. The same type of geographic variation was noted in a study in Norway, which showed higher prevalence rates in the northern and cooler parts of the country and lower rates in the southern regions relative to the rest of the country [33]. Additionally, several studies

**Table 1. Summary of studies on the prevalence of psoriasis.**

Geographical area	Author	Diagnostic method	Number of subjects in study population (age groups)	Measure (age)*	Prevalence estimate (%)	Ref.
UK	Gelfand <i>et al</i>	PR	7,533,475 (all ages)	LT	1.5	[12]
China	Yip	SR	670,000	LT	0.05–0.8	[13]
Sweden	Lindegård	PR	159,200	PP (10 years)	2.3	[14]
USA	Koo	SR	50,000 (all ages)	LT	2.6	[15]
Sweden	Hellgren	PR	38,670 (>6 years)	PT	2.0	[16]
USA	Stern <i>et al</i>	SR	27,220 (>18 years)	LT	2.2	[17]
USA	Johnson	PR	20,749 (1–74 years)	PT	1.4	[18]
Norway	Kavli <i>et al</i>	SR	14,667 (20–54 years)	LT	4.8	[19]
Spain	Ferrandiz <i>et al</i>	SR	12,938 (all ages)	LT	1.2–1.4	[20]
Faroe Islands	Lomholt	PR	10,984	PT	2.8	[21]
Norway	Braathan <i>et al</i>	SR	10,576 (all ages)	LT	1.4	[22]
Croatia	Barisic-Drusko <i>et al</i>	PR	8416 (>18 years)	PT	1.5	[23]
Billesdon, Leicestershire (UK)	Nevitt	SR and PR	5395 (all ages)	PT	1.5	[24]
Denmark	Brandrup <i>et al</i>	SR	3892 (16–99 years)	LT	3.2 (male) 2.5 (female)	[25]
Italy	Naldi <i>et al</i>	SR	3660 (>45 years)	PT	3.1	[26]
Norway (Lapps)	Falk	PR	2963 (all ages)	LT	1.4	[27]
USA - African Americans	Gelfand <i>et al</i>	SR	2443 (>18 years)	LT	1.3	[28]
England	Rea <i>et al</i>	SR and PR	2180 (15–74 years)	PT	1.6	[29]
Norway (Lapps)	Kavli <i>et al</i>	PR	2000	PP (4 years)	0.6	[30]
Busselton, Australia	Quirk	PR	1037 (adults)	PT	2.3	[31]

\*All study populations' age ranges are identified unless otherwise unknown.

LT: Lifetime prevalence; PP: Period prevalence; PR: Physician report; PT: Point prevalence; SR: Self report.

have indicated that ethnic factors (i.e., genetic and behavioral factors) may influence the prevalence of psoriasis. Prevalence rates range from no cases in the Samoan population to nearly 12% in Arctic Kazach'ye [34]. This observation suggests that both genetic and environmental factors are important in determining the prevalence of psoriasis. In a study of 25,000 Latin American Indians, researchers showed that psoriasis was virtually nonexistent in this ethnic group [35]. Also, in a recent population-based study, Gelfand and colleagues showed that the prevalence of psoriasis amongst African Americans (1.3%) is lower than that in the white American population (2.5%) within the USA.

These observations of the variation in psoriasis prevalence based on geographical and ethnic factors suggest a possible role for the physical environment (e.g., climate), genetic factors and behavioral patterns or other exposures in the development of psoriasis.

#### **Impact of gender & age on incidence & prevalence of psoriasis**

The onset of psoriasis can occur from birth to advanced ages. The accurate determination of age of onset in studies is notoriously problematic as researchers typically rely on patient recall, which may be unreliable [7]. Also, studies relying on the first visit or diagnosis by a physician may be unreliable as patients may, in fact, have the disease long before they seek medical care [5]. Despite these problems with accurate ascertainment, many large studies show that the age of onset of psoriasis (i.e., incidence) has a bimodal distribution, peaking in early adult life (late teens to 20s) and then again in later adult life (50s and 60s) [5,36–39]. Many hypothesize that this bimodal distribution in psoriasis incidence represents two clinical presentations of psoriasis; so-called Type I and Type II. Type I is believed to occur before the age of 40 years and is thought to account for more than 75% of cases [5,39]. Patients with this type of psoriasis tend to have more severe disease and more relatives affected than Type II disease [40,41]. Also, these patients tend to have a higher association with human leukocyte antigen (HLA)-Cw6 than patients with Type II disease [7,42]. Type II disease is thought to represent those psoriasis patients that present after the age of 40 years.

Most studies suggest that psoriasis may be slightly more prevalent among males compared with females [7]. However, in young patients (<20 years) the prevalence of psoriasis is greater in females than in males, suggesting an earlier age of onset of psoriasis in females compared with males [12,39]. A study on the natural history of psoriasis in the USA based on mailed questionnaires to dermatologists also described an earlier age of psoriasis onset in female patients [43]. These findings may reflect an interaction between gender, age and the susceptibility to developing psoriasis.

Prevalence data indicate that the frequency of psoriasis decreases in older individuals. In a study of psoriasis prevalence in Spain, psoriasis decreased in individuals over 70 years of age [20]; the same was reported in a population-based study

conducted in the UK [12]. Also, in Braathen's study of psoriasis prevalence in Norway, prevalence rates were shown to decrease with increasing age once patients reached 49 years of age [33]. The cause for the decrease in prevalence of psoriasis in older individuals has not been elucidated. It is possible that psoriasis goes into remission in older individuals or otherwise does not come to medical attention and is therefore not captured by some approaches to measuring prevalence. It is also possible that psoriasis prevalence may decrease in older individuals due to a higher mortality rate from associated comorbidities and behaviors.

#### **Natural history**

Clinical manifestations of psoriasis are heterogeneous, ranging from limited to very extensive disease. In a recent study of psoriasis patients, selected from the USA population via random digit dialing, 57.4% had less than 1% BSA involved, 26.4% had 1–2% BSA, 12.6% had 3–10% BSA and 3.6% reported more than 10% BSA affected by this disease [44]. Psoriasis is frequently reported to wax and wane over time with episodes of remissions and exacerbations [42]. The timing and causes of these cycles are unknown. Some patients develop remissions without treatment from their physicians while others remain stable or worsen over time [40]. In a recent study evaluating the natural course of psoriasis in the placebo arms of randomized clinical trials for plaque-type psoriasis, this heterogeneity is highlighted [45]. In this systematic review of 27 studies, five reported the average change from baseline in placebo patients to be zero, while 13 reported worsening of psoriasis, no change or minimal improvement (<10%). Three studies reported 11–18% improvement on average, four reported 22–28.7% improvement, one reported 36.4% improvement and one reported 47% improvement. No explanations for differences in outcome could be detected in terms of the duration of the study, the initial severity of the psoriasis or the treatments in the placebo groups. Epidemiological studies are necessary to better determine the natural history and risk factors for psoriasis exacerbation and remission.

#### **Risk factors for development of psoriasis**

Numerous studies have attempted to define the risk factors for developing psoriasis. In order to minimize bias and establish a temporal relationship, population-based case-control studies of patients with incident (i.e., newly developed) psoriasis are necessary to identify potential risk factors for developing this disease. A case-control study is an observational, analytical study in which subjects are selected based on whether they have (cases) or do not have (controls) a particular disease under study. These groups are then compared with respect to the proportion of their having a history of an exposure or characteristic of interest (i.e., risk factor) that predates the disease. In a population-based study, the cases are broadly representative of all of the cases in the community and the controls are derived from the same source population from which the cases were identified in order to minimize bias [10]. Family history (genetics) is the most well established risk factor for

developing psoriasis. Several studies have also examined infections, smoking and alcohol consumption as potential risk factors for psoriasis. Very few studies have examined dietary factors and have yielded conflicting results [8].

### Family history & genetics

Repeated observations of familial clustering in psoriasis patients have been observed for many years [16,46]. Approximately 40% of patients with psoriasis or psoriatic arthritis have a family history of these disorders amongst first-degree relatives [47]. This, in addition to high concordance rates amongst monozygotic twins, has suggested the existence of a genetic component to the disease [48]. For example, the concordance rate for monozygotic twins is approximately 70% compared with 20% amongst dizygotic twins [48,49]. Despite these findings, the disease risk among patient siblings is relatively low. Psoriasis develops in as many as half of the siblings when both parents have psoriasis, falls to 16% when only one parent is affected, and 8% when neither parent is affected but there is an affected sibling [50]. The etiology of psoriasis is complex and requires the interaction between environmental factors or triggers and inheritance susceptibility alleles [3,4,51].

From studies scanning entire genomes to identify those co-inherited by sibling pairs, repeated studies have identified a region of chromosome 6p21 as a contributor to psoriasis susceptibility [51–54]. This susceptibility locus on 6p21 is referred to as psoriasis susceptibility 1 locus (PSORS1), and its demonstration in multiple independent studies seems to indicate a pathogenic role for this region [51,53,55]. The PSORS1 segment is contained in the class I major histocompatibility complex (MHC) region, which encodes class I MHC antigens that play a role in immune system self-recognition and self-tolerance [56–59]. HLA-C is thought to be contained within this interval and has been considered a likely susceptibility gene for some time [60]. In fact, highly significant associations between the HLA-Cw6 allele and psoriasis have been repeatedly reported and may predispose to early disease [60–62]. Genome-wide scans have also identified a number of non-MHC susceptibility loci, but these are not well validated as they have often been observed only once [54,63]. PSORS2, in region 17q25, is an exception and has been replicated in more than two studies [64–66]. Recently, an additional gene locus for psoriasis susceptibility was discovered on chromosome 17q25 [67]. This locus, a runt-related transcription factor 1 (RUNX1) binding-site variant, encodes for hematopoietic cell development and the development of T cells in the thymus [67,68].

### Infections

Bacterial and viral infections may be linked to psoriasis. Unfortunately, large epidemiological studies looking at this association, especially in the case of plaque-type psoriasis, are lacking [7]. Lindegard and colleagues showed that patients who had been hospitalized for psoriasis were more likely to have also been hospitalized for a viral infection than the general population [14]. Most studies exploring this association in

the case of plaque psoriasis are based on case reports. Case reports have raised the hypothesis that subclinical streptococcal infection and local skin infections with *Staphylococcus aureus*, *Malassezia furfur* and *Candida albicans* may play a role in exacerbation of chronic plaque psoriasis; however, analytical studies are necessary to investigate these hypotheses [69–71].

In the case of guttate psoriasis, studies suggest that upper respiratory infections, especially *Streptococcus pyogenes*, are strongly associated with the onset and flaring of this disease [34,70,72]. Recently, a case-control study of guttate psoriasis showed a high increased odds ratio (OR: 8; 95% CI: 2.8–22.5) for a recent history of acute pharyngitis [73].

An association between severe psoriasis and HIV infection has also been well established [70,74]. This seems counter-intuitive as the authors hypothesize that psoriasis is a CD4<sup>+</sup> T-cell-mediated disease, and HIV-infected patients are deficient in these cell types [75]. Despite this, case reports have shown that CD4<sup>+</sup> cells are actively recruited into skin lesions, as they are in skin lesions of HIV-negative psoriasis patients [76]. Additionally, HIV may act as a superantigen to activate T cells [77]. A cohort study of patients enrolled in the Harvard Community Health Plan showed that psoriasis occurs at a higher rate in HIV-infected patients than in patients without a known diagnosis of HIV. The study showed that the risk of psoriasis increased with progression of the disease from asymptomatic HIV to full-blown AIDS (relative risk [RR] pre-HIV: 0.8; HIV: 2.3; AIDS: 9.5) [78]. Psoriasis has also been shown to regress in terminal AIDS [79].

### Lifestyle

#### Smoking

Several studies have investigated smoking as a risk factor for developing psoriasis. In a case-control study of male patients in Finland, data were gathered on smoking at least 12 months prior to the onset of psoriasis. This study of 144 psoriasis patients and 285 controls showed no significant association between smoking and the onset of psoriasis [80]. In contrast, a subsequent study in Italy, evaluating 215 newly diagnosed cases of psoriasis, did show an association between those who smoked 15 cigarettes or more before diagnosis (OR: 2.1; 95% CI: 1.1–4.0), with the suggestion of a dose–response effect [81]. In 1992, researchers in the UK evaluated 108 patients with new psoriasis and compared rates with matched controls in the community. They showed a significant association between smoking prior to onset and psoriasis (OR: 3.75; 95% CI: 1.68–9.47), as well as a dose–response effect [82]. Poikolainen and colleagues found a significant association (OR: 3.3; 95% CI: 1.4–7.9) between new onset psoriasis and smoking in women that predated the psoriasis, despite having failed to show an association in men a few years prior [83]. In 1998, Naldi and colleagues performed a case-control study involving 471 newly diagnosed psoriasis patients and evaluated smoking prior to onset, which also found an increased psoriasis onset in female smokers (OR: 3.2 [no CIs reported] for smoking >15 cigarettes/day). Additionally, this study showed an

increased risk in male smokers but to a lesser extent than in women (OR: 1.6 [no CIs reported] for smoking >15 cigarettes/day) [84]. Most recently, Naldi performed a case-control study exploring the association between smoking habits and psoriasis onset in 560 patients [85]. His study showed overall that the OR for psoriasis was greater in current (OR: 1.7; 95% CI: 1.1–3.0) and former smokers (OR: 1.9; 95% CI: 1.3–2.7) than in never smokers. He also described gender differences. Male former smokers were at an increased risk (OR: 2.1; 95% CI: 1.3–3.5) for developing psoriasis, whereas this was not the case in females (OR: 1.2; 95% CI: 0.6–2.2). In current smokers, however, there was a higher risk in women than in men (for whom risk estimates correspond to no effect at all). In this study, there was no evidence of a dose–response effect.

The role of smoking as a risk factor for psoriasis remains elusive. It has often been implicated in both the pathogenesis and progression of the disease, but conclusive data on its role is currently lacking. A strong association with palmoplantar pustulosis and smoking has been documented in the medical literature and is worth noting, but the relationship between smoking and plaque psoriasis remains controversial [86]. Overall, the conflicting data emphasize the need for more population-based case-control studies to clarify this association. It is of interest to clarify the impact of smoking on the natural history of psoriasis and response to therapy, as well as to determine if having psoriasis makes a person more likely to smoke. Some studies show that whether or not smoking causes psoriasis, cessation probably does not alter the course of the disease [81,84]. Also, once psoriasis has developed, there may be a subsequent association between smoking, alcohol and negative life events [83].

#### Alcohol

To date, the data on alcohol as a risk factor for psoriasis have been conflicting. As in the case of smoking, a cause–effect relationship is most strongly supported by studies that evaluate incident cases of psoriasis and a drinking history that predates its onset. Few epidemiological studies exist to date that satisfy both criteria. In a case-control study limited to male patients from Finland, alcohol consumption, reported at least 12 months prior, was linked to the onset of psoriasis in young and middle-aged men [80]. This study also suggested that psoriasis may, in fact, lead to sustained drinking and that alcohol may worsen psoriasis. In a follow-up study performed by the same group, this association was re-examined in 55 female patients with new onset psoriasis and no association was found with alcohol consumption [83]. However, the study did suggest disease worsening related to alcohol consumption, as it had in men. In an Italian case-control study, researchers examined incident cases of psoriasis in both males and females [81]. They showed no overall association with alcohol when smoking was controlled for [81]. This finding was confirmed in a case-control study of Australian twins, where researchers found no difference in terms of alcohol consumption between discordant twins when evaluating the origin of psoriasis [32]. Interestingly, in a subsequent study in Italy, Naldi and colleagues did show an association between alcohol

consumption and psoriasis [87]. The risk was shown to vary with gender, with men who drink more than two drinks per day having an increased risk (OR: 1.9; 95% CI: 1.0–3.3). There was no significant association in female drinkers.

In addition to the case-control studies discussed above, there have been numerous cross-sectional studies of the prevalence of alcohol consumption in patients with psoriasis. Cross-sectional studies cannot establish a temporal relationship and, therefore, it is difficult to determine from these studies if alcohol leads to psoriasis or if having psoriasis leads to greater alcohol intake. Many of the early studies failed to show an association between alcohol consumption and plaque-type psoriasis, but alcohol-related liver abnormalities were noted more commonly in psoriasis patients than the general population [88–90]. Despite this initial data, many subsequent studies showed a positive association between psoriasis prevalence and alcohol consumption. A study by Higgins and colleagues showed that the prevalence of psoriasis was increased among patients who abuse alcohol [91]. In a study of psoriasis patients in China, alcohol consumption was significantly associated with psoriasis prevalence in both males (OR: 4.17; 95% CI: 2.79–6.23) and females (OR: 6.6; 95% CI: 2.4–19.63), but results were not adjusted for smoking (also significantly associated with psoriasis in this study) [92]. In a population survey of 10,576 individuals in Norway, 149 psoriasis patients were shown to drink more often and in larger amounts than their nonpsoriatic counterparts [22]. In a population-based study, alcohol was shown to be a significant risk factor for mortality among patients with psoriasis [93]. Finally, alcohol has been associated with disease severity (worsening of skin disease after drinking in men and women) and treatment failures [80,83,94]. It is possible that alcohol may alter the expression of psoriasis and its clinical course [7]. Regardless of whether or not alcohol is associated with psoriasis, it is difficult currently to tease out whether alcohol itself contributes to the morbidity of psoriasis or whether drinking in some way interacts with therapy or patient compliance. Additional studies are necessary to better determine the impact of alcohol on the risk of developing psoriasis, as well as the impact of alcohol consumption on the natural history of psoriasis.

#### Drugs

Drug exposure has not been well defined as a risk factor for new onset (i.e., incident) psoriasis. Most published studies examine the impact of drugs on exacerbating psoriasis and are based on case reports and case series. The most frequently reported offenders of drug-exacerbated psoriasis are lithium,  $\beta$ -adrenergic blocking agents and antimalarials [7,70,95]. Drugs less commonly implicated, but reported in case reports, are numerous. Those reported to exacerbate psoriasis include digoxin, potassium iodide, procaine, amiodarone, salicylate, clonidine, penicillin, tetracycline, bupropion, terbinafine and sulphonamides [95–97]. In addition, withdrawal of systemic corticosteroids, as well as efalizumab, have been shown to induce flares in psoriasis patients [70,97–99]. A major limitation of these studies is that a control group is lacking and, therefore, disease exacerbation may

be due to chance or other factors. Additionally, if these drugs truly exacerbate psoriasis, the true risk of such an event for a patient with psoriasis who needs one of these drugs for medical reasons is unknown.

### **Comorbidities associated with psoriasis**

There have been increasing reports that psoriasis may be associated with a higher rate of comorbidities, such as cancer, cardiovascular disease, obesity, autoimmune disease and psychiatric disease. It is unclear if these associations are due to the pathophysiology of psoriasis, the treatment of psoriasis or psoriasis-associated behaviors (e.g., smoking and alcohol). These associations are important as they are part of the burden of psoriasis and can be potentially important in managing and counseling patients, as well as interpreting safety data of systemic medications used to treat psoriasis.

### **Cancer**

Several studies have investigated the risk of cancer in patients with psoriasis. In a Finnish study, patients hospitalized for psoriasis had a 30% increased risk for cancer compared with the general Finnish population [100]. In this study, the risk for lung and laryngeal cancer, as well as Hodgkin's and non-Hodgkin's lymphoma (NHL), was increased. In a study by Bofetta and colleagues evaluating a Swedish cohort, researchers found an increased risk for cancer in patients hospitalized for psoriasis compared with the general Swedish population [101]. Interestingly, malignancies that increased were those associated with alcohol and tobacco. Examples of cancers found to be increased were cancers of the oral cavity, liver, pancreas, breast, vulva, penis, bladder and kidney. Frenz and Olsen also reported increased rates for malignancy in patients hospitalized for psoriasis in Denmark [102]. Nonmelanoma skin cancers and lung cancer were thought to account for most of this increased risk amongst both men and women. In a study of Medicaid patients in the USA, Margolis and colleagues showed an increased risk of malignancy in psoriasis patients considered to have severe disease (receiving systemic agents) when compared with patients with hypertension [103]. This study also showed a slightly increased risk for overall malignancy in psoriasis patients considered to have less severe disease. Nonmelanoma skin cancer and lymphoproliferative malignancies accounted for much of the increased risk of cancer in this study. More recently, a population-based cohort study in the UK showed a statistically significant increased rate of developing lymphoma in psoriasis patients over the age of 65 years when compared with controls without psoriasis [104]. Also, Zhang and colleagues recently performed a case-control study investigating the role of prior medical conditions in the etiology of NHL in women [105]. This study did not demonstrate an increased risk related to psoriasis when evaluating all NHL cases, but did demonstrate an increased risk in women specifically related to the T-cell NHL subtype. Other investigators have found no increased risk for systemic malignancies or lymphoma in psoriasis patients [106–109]. In general, discrepancies in findings may

relate to differences in study designs, differences in study populations and comparison groups, varying levels of statistical power, and issues of selection and information bias.

### **Cardiovascular disease**

Several studies have described an association between psoriasis and cardiovascular disease. Reed, a pathologist, was probably among the first to associate vascular disease with psoriasis [110]. He observed an increased rate of myocardial infarction, pulmonary emboli and pulmonary infarcts as a cause of death in his patients with psoriatic arthritis. Thereafter, McDonald and Calbresi reported finding an increased prevalence of cardiovascular disease in patients with psoriasis versus patients with other cutaneous disease in their case-control study of 323 psoriasis patients [111–114]. Ena and colleagues observed an increased prevalence of ischemic heart disease, hypertension, hypercholesterolemia and hypertriglyceridemia in their hospitalized psoriasis patients when compared with controls hospitalized for other dermatologic conditions [115]. Lindegard studied a cohort of 159,200 native Swedes, of which 372 had been hospitalized for psoriasis, and found a statistically significant association between psoriasis and hospitalization for hypertension in males and hospitalization for myocardial infarction in females [14]. In a study of German patients, Henseler and colleagues also noted an increased prevalence of hypertension and heart failure in patients hospitalized for psoriasis [116]. Also, Mallbris and colleagues found an association between cardiovascular mortality and severe psoriasis, measured as repeated hospital admissions with a diagnosis of psoriasis [117]. The standardized mortality ratio (SMR) among outpatients with psoriasis was 0.94 (95% CI: 0.89–0.99), whereas the SMR among patients admitted at least once for psoriasis was increased by 50% (SMR: 1.52; 95% CI: 1.44–1.60). In contrast, Stern and colleagues prospectively evaluated 1380 psoralen and long-wave ultraviolet radiation (PUVA) patients and found no evidence of increased cardiovascular mortality in these patients when compared with the general population based on expected rates from the United States National Center for Health Statistics [118].

### **Obesity**

Several studies have shown an association between obesity and psoriasis. In a case-control study, patients with new onset psoriasis were more likely to be obese compared with patients visiting a dermatologist for a skin problem other than psoriasis. This association persisted even when controlling for age, marital status, hospitalization, education, smoking and alcohol [85]. This study confirmed their earlier study finding of a positive association between psoriasis onset and body mass index (BMI) [119]. These studies suggest that obesity may predispose patients to developing psoriasis. Several cross-sectional studies have also shown an association between psoriasis and obesity, although some results have been conflicting. For example, Lindegard and colleagues showed that female patients hospitalized for psoriasis had a higher prevalence of obesity compared with the general population, but found no association in male patients hospitalized for psoriasis [14]. Henseler and colleagues described an increased prevalence of obesity in

patients hospitalized for psoriasis compared with patients hospitalized for skin diseases other than psoriasis [116]. Finally, a cohort study of 17,032 women in England and Scotland, followed for the pattern of referral to hospital for skin disorders, showed no association between BMI, obesity and psoriasis [120].

### **Psoriatic arthritis**

Joint diseases are common among patients with psoriasis [121]. Psoriatic arthritis is defined as a rheumatoid factor-negative inflammatory arthritis associated with psoriasis and has emerged as a specific disease, independent from rheumatoid arthritis [122]. Estimates of the prevalence of psoriatic arthritis among patients with psoriasis vary from 6 up to 30% [121,123]. Population-based studies, which are broadly representative of all patients with psoriasis, have found a prevalence of psoriatic arthritis in patients with psoriasis of 6.25% in Olmstead County (MN, USA) and 11% in the continental US population [124]. Additionally, the population- and clinic-based studies have indicated that the prevalence of psoriatic arthritis increases significantly based on the BSA affected by psoriasis [124,125].

Generally, psoriatic arthritis tends to appear several years after the onset of skin lesions in the majority of patients. However, it can precede the skin disease in approximately 13–17% of cases [126]. Nail lesions may help to identify those patients with psoriasis who are at higher risk of developing arthritis as these lesions occur in 80–90% of patients with psoriatic arthritis compared with 46% in those with psoriasis uncomplicated by arthritis [127]. Several patterns of joint involvement in psoriatic arthritis have been identified. These include distal arthritis, asymmetric oligoarthritis, symmetric polyarthritis, arthritis mutilans and spondyloarthropathy. The severity of skin psoriasis does not reliably correlate with the severity of psoriatic arthritis symptoms and signs [127]. Broadly representative population-based studies suggest that the incidence of structural damage in psoriatic arthritis is low (<10%) and that the disease does not impact mortality [123]. Studies from tertiary care centers, which are skewed towards patients with more severe disease, have shown a higher risk of mortality for patients with psoriatic arthritis compared with the expected rates in the community, and higher overall frequencies of destructive joint changes [126,128]. Several HLA types have been associated with psoriatic arthritis, suggesting a genetic predisposition to developing this disease [47,129,130].

### **Autoimmune diseases**

The immunological nature of psoriasis suggests that these patients may be more likely to develop other immune-related diseases. The strongest link so far has been with inflammatory bowel disease, specifically Crohn's disease [131,132]. Similar to psoriasis, Crohn's disease is mediated by an abnormal T-helper (Th)-1 immune response [131]. Studies show that the prevalence of psoriasis in patients with Crohn's disease is higher than chance would allow if they were mutually exclusive diseases [132]. Also, family members affected with Crohn's disease or psoriasis are more likely to have close relatives affected by the other disease than by chance alone [133]. Factors implicated in this association include common

environmental factors, shared pathological mechanisms, as well as heritable genetic factors. Researchers have identified regions on chromosomes 16, 6, 4 and 3 where genetic markers are linked to both psoriasis and Crohn's disease [55,65,132,134–139].

Multiple sclerosis (MS) is another example of an immune-mediated Th-1 disease that has been linked with psoriasis. Studies exploring an association between MS and psoriasis are of special interest as antitumor necrosis factor (TNF)- $\alpha$  therapies used to treat psoriasis (and other autoimmune diseases such as Crohn's disease and rheumatoid arthritis) carry warnings that they may trigger new onset MS, optic neuritis and demyelinating diseases [131]. In a cross-sectional study, Broadly and colleagues found that psoriasis was more common in families of patients with MS compared with control families [140]. Moreover, multiplex families (e.g., families with more than one case of MS) had an even higher odds of having a family member with psoriasis, suggesting a trend towards genetic loading of these diseases. Alemen-Rodriguez and colleagues performed a prevalence study investigating the coexistence of a wide range of autoimmune diseases in first- and second-degree relatives of MS patients [141]. Their study showed that almost 30% of patients with MS had a first- and/or second-degree relative with either MS or another autoimmune disease (most commonly psoriasis, autoimmune thyroid disease or Type 1 diabetes mellitus). Finally, Midgard and colleagues, using a cross-sectional design, found that MS patients had an OR of 2.01 (95% CI: 0.73–5.83) of having psoriasis compared with controls. However, the finding was not statistically significant [142]. These studies suggest a common susceptibility to psoriasis and MS, however, additional studies are necessary to confirm the association.

### **Psychiatric disease**

Multiple studies have examined psychological characteristics of patients with psoriasis but most are only descriptive [143–145]. Case series have reported a wide range of psychological characteristics in psoriasis patients including depression, anxiety, obsessive behavior and difficulty expressing emotions such as anger [146–151]. Studies have indicated a higher prevalence of depression in patients with psoriasis compared with controls. A study comparing 50 patients with psoriasis with 50 healthy controls found that patients with psoriasis had a statistically significantly higher average score on the Beck Depression Inventory (BDI) (16.96 vs 5.48, respectively;  $p < 0.01$ ) [152]. This finding was confirmed in another study in Turkey, which also used the BDI [153]. Depression may be so severe that patients may in fact contemplate suicide [154]. In a study based on the Carroll Rating Scale for Depression, of 217 psoriasis patients, almost 10% reported a wish to be dead and 5.5% reported active suicidal ideation at the time of study [144]. Suicidal ideation is more prevalent in psoriasis inpatients (reported in 7.2%) than outpatients (2.5%) and general medical patients (range: 2.4–3.3%) [143]. These studies highlight the importance of recognizing psychiatric comorbidity, especially depression, among psoriasis patients.

There are several studies that have examined the role of stress in psoriasis [85]. Naldi showed a significant association between stressful life events in the preceding year and psoriasis onset compared

with controls [85]. Stress may also have a deleterious effect on response to therapy [5]. In a study of patients undergoing PUVA therapy, those individuals designated as being pathological worriers cleared significantly more slowly than those considered low worriers [155]. Studies showing either limited or no association with stress have also been published [156,157]. For example, a case-control study of 40 outpatients with either recent onset or exacerbation of psoriasis showed no difference in the mean number of major stress events reported within the preceding year when compared with 116 outpatients with other skin conditions [156,157]. Prospective population-based epidemiological studies examining the onset of psoriasis and stress as a risk factor need to be performed to elucidate this issue further. One major problem with teasing out this relationship is the fact that virtually all research in this field relies on patient recall of past events [7]. This technique is susceptible to recall bias and is notoriously unreliable as patients often seek out explanations in order to try to explain disease processes, and stress is commonly used for this [7].

### Conclusions

Epidemiological studies of psoriasis have yielded important insights into the etiology and natural history of this disease. Studies of the distribution (e.g., incidence and prevalence) of psoriasis show the importance of geography and ethnicity on the odds of developing psoriasis, which suggests that genetic and environmental exposures are important in the pathogenesis of this disorder. Emerging evidence suggests that potentially modifiable exposures, such as smoking, stress and obesity, may increase the risk of developing psoriasis. Additionally, a breadth of studies indicate that psoriasis is associated with a variety of important comorbidities. Future well orchestrated epidemiological studies need to be performed in order to better elucidate the roles played by potential risk factors in this disease process, as well as to clarify the potential importance of concomitant disease processes.

### Expert commentary

The majority of studies of the epidemiology of psoriasis are based on case reports, case series and cross-sectional studies. Several analytical studies (e.g., case-control studies and cohort studies) have been performed to try to identify potentially modifiable risk factors and have often yielded conflicting or inconsistent results. Additionally, most of the case-control studies have been hospital-based or specialty clinic-based and, therefore, broadly representative population-based studies are necessary to confirm potential associations. Prospective data on the determinants of the natural history of psoriasis remission and flare, as well as data on the natural history of diseases that may be associated with psoriasis, are needed. Ideally, studies need to measure multiple potential covariates in order to determine which factors or diseases are independently associated with psoriasis.

### Five-year view

There is enormous scientific opportunity to investigate the epidemiology of psoriasis as there are still wide gaps in our knowledge. Studies in the next 5 years should focus on better

understanding of the natural history of chronic plaque psoriasis in order to identify which patients may experience spontaneous remissions and which patients may experience flares of their disease. Large, broadly representative case-control studies can further investigate potential risk factors for developing psoriasis, and future intervention trials can determine if altering modifiable risk factors such as smoking and obesity leads to a lower risk of psoriasis. Finally, determining the relative importance of psoriasis, its treatments and its associated behaviors on the risk of developing comorbidities such as cardiovascular disease, cancer and other diseases will allow us to better counsel patients with psoriasis and interpret long-term safety data on novel therapies for psoriasis.

### Information resources

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[www.cche.net/usersguides/main.asp](http://www.cche.net/usersguides/main.asp)

### Key issues

- Psoriasis is a common disease, affecting 0.6–4.8% of the population.
- Age, gender, geography and ethnicity are important determining factors in the prevalence of psoriasis.
- Family history is the most well established risk factor for developing psoriasis.
- Emerging evidence suggests that some modifiable conditions such as smoking, stress and obesity may be risk factors for developing psoriasis.
- Psoriasis has been associated with a variety of other comorbidities, such as cardiovascular disease, cancer, autoimmune disease and psychiatric disease.
- Future studies are needed to identify the natural history and determinants of psoriasis remission and flare. Studies are also needed to identify and validate risk factors for psoriasis and to determine if modification of these risk factors lowers the risk of developing psoriasis. Finally, studies examining the impact of psoriasis itself, its treatments and its associated behaviors on the risk of developing associated comorbidities are necessary for counseling patients and interpreting safety data of psoriasis therapies.

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