CHAPTER 1

Epidemiology and economic aspects

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Epidemiology

Epidemiologic research should be understood in the light of its main interest, that is, prevention of the disease and its consequences in man.

Descriptive epidemiology

The measures employed are incidence and prevalence. A first step in descriptive epidemiology is to obtain a valid definition of what constitutes a “case.” Quite surprisingly, up to now, no widely employed diagnostic criteria have been developed for clinical and population based studies of psoriasis. The first diagnosis made by a physician and the first appearance of skin lesions as reported by the patient have both been taken as markers of “onset” in epidemiologic studies.

Incidence—there are few studies

In a pilot study conducted in Rochester, Minnesota, in the period 1980–1983, incident cases were defined as patients requiring, for the first time in their life, medical care for a condition diagnosed as psoriasis. The age- and sex-adjusted (1980 US white population) annual incidence rate was 60.4 per 100,000 people. The crude rates were 54.4 for men and 60.2 for women. In another study from the United States, a cohort of 1633 adult subjects was followed up from 1970 to 2000. Rates adjusted to the 2000 US population increased significantly over time from 50.8 in the period 1970–1974, to 100.5 per 100,000 in the period 1995–1999. In a third study from the United States, a cohort of people younger than 18 years was followed up between 1970 and 1999. The overall incidence of psoriasis age- and sex-adjusted to the 2000 US population was 40.8 per 100,000. The incidence increased steadily with increasing age. Moreover, incidence increased in most recent years in both boys and girls. In a study based on data from the United Kingdom General Practice Research Database (UKGPRD) where cases were recorded by general practitioners from January 1996 to December 1997, a rate as high as 14 per 10,000 person-years was estimated, much higher than rates in the United States.
Prevalence
Each new case (incident case) enters the prevalence pool and remains there until either recovery or death. If recovery and death are not frequent, even low incidence rates (such as those calculated for psoriasis) produce a high prevalence. Prevalence measures may be relative to a point in time (point prevalence) or to a longer period (period and lifetime prevalence). Prevalence of psoriasis “ever experienced” in the past at any age (i.e. lifetime prevalence) approximates the cumulative incidence in that age group, that is, the proportion of the birth cohort developing the disease until the time of survey, provided that psoriasis does not affect mortality per se and that the recall of past episodes is complete.

Results of selected studies of the prevalence of psoriasis in defined populations provide estimates ranging from 0.05% in China to 4.8% in Norway (Table 1.1). Besides geographic variations, these estimates are expected to change according to the period considered, that is, point prevalence vs “lifetime prevalence.” In addition, variations may be expected to arise from differences in case definition and ascertainment, and from differences in age distribution of dynamic populations.

Ethnic and geographic variations
It appears that Mongoloid races in the Far East of Asia have remarkably low prevalence rates. Lower prevalence rates have also been documented in African Americans compared with Caucasians in United States. Duffy et al. analyzed cumulative incidence in 3808 twin pairs and documented significantly higher prevalence rates in southern states of Australia with respect to northern areas. Geographical variations were also described in Norway with the northern regions of Troms and Finmark showing higher rates, and Hedmark and Oppland regions in the south of the country showing lower rates.

Sex and age variations
Most prevalence studies suggest that psoriasis tends to be slightly more prevalent among men than among women. The few studies available providing age-specific incidence rates of psoriasis suggest that incidence increases more or less steadily with age up to the seventh decade of life. If psoriasis appeared throughout life, then both point prevalence and lifetime prevalence would increase with age. However, prevalence estimates in several studies do not increase with age and even decrease, suggesting higher mortality rates in older psoriatics compared with the general population. It has been reported that age at onset in large series of psoriatic patients has a bimodal distribution. This has been taken as evidence for etiologic heterogeneity, and type I and type II psoriasis have been proposed. In fact, variations in numerator data, that is, the number of people experiencing onset at different ages, may simply reflect the age distribution of the population of origin.
Familial aggregation
A history of psoriasis in first degree relatives is given by 20–30% of psoriatics. In a study, the prevalence of psoriasis increased with the number of first-degree relatives affected from 3% with no relative affected to about 40% with two relatives affected.

Analytic epidemiology
The causative model of psoriasis involves interaction between genetic predisposition and environmental factors.
Genetic factors
Heritability quantifies the overall role of genetic factors when a multifactorial model of inheritance is postulated. Measures of the heritability of psoriasis have been provided based on population data and the analysis of concordance of twins. The estimates ranged from 0.5 to 0.9.

Personal habits
Smoking has been consistently linked with psoriasis. Studies that examine the exposure before the onset of psoriasis and control for confounding factors offer the more convincing evidence. There are indications that the risk for smoking may vary according to gender, with it being higher in women. Smoking and alcohol may alter the expression of psoriasis (e.g. pattern distribution, clinical varieties) and its clinical course. Smoking has been linked with acral lesions. Alcohol has been associated with severity of psoriasis and treatment failures.

Body weight and diet
It is well established that increased body mass index (BMI) and increased waist circumference are risk factors for developing psoriasis (Table 1.2). The association has been documented also in infantile psoriasis. Scanty data are available concerning diet. In an Italian case-control study, the risk of psoriasis increased with increasing BMI and was inversely related to the consumption of carrots, tomatoes and fresh fruit, and to the index of beta-carotene intake.

Drugs and infections
Several drugs, such as lithium salts, beta-adrenergic blocking agents, and antimalarials, have been reported to be responsible for the onset or exacerbation of psoriasis, but the evidence is inconclusive. An infection with β-haemolytic streptococci often precedes the first manifestation of guttate psoriasis. Furthermore, a cohort study in the United States, involving 265,000 members of the Harvard Community Health Plan, demonstrated that chronic HIV infection is linked to a higher risk of psoriasis (relative risk 3.5). The risk increases with the progression of the disease from the asymptomatic phase to full-blown AIDS.

Psychosocial factors
Psychosomatic factors are deemed to play a role in psoriasis, and stressful life events have been linked with the risk of incident psoriasis. A major problem in this area is that virtually all the research is based on the recall of past events. People have a strong tendency to seek explanations in order to account for what happens to them, and stress is commonly used for this.
### Table 1.2  Summary of main recent epidemiologic studies on risk factors for incident psoriasis.

<table>
<thead>
<tr>
<th>Country (year)</th>
<th>Study design</th>
<th>Study subjects</th>
<th>Factors analyzed</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy (2005)</td>
<td>Case-control</td>
<td>560 newly diagnosed cases and 690 controls with other skin diseases</td>
<td>Alcohol, smoking, BMI, stressful life events</td>
<td>OR increased in smokers and ex-smokers, 1.7 and 1.9 respectively. Stronger association in women as compared with men and in pustular psoriasis. OR 1.6 and 1.9 for overweighed and obese, respectively. OR increased for increased stressful life-event score.</td>
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<tr>
<td>UK (2007)</td>
<td>Cohort and nested case-control</td>
<td>3994 cases and 10,000 controls</td>
<td>Skin infection, smoking</td>
<td>Infection OR 2.1. Smoking OR 1.4.</td>
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<tr>
<td>UKGPRD</td>
<td>USA (2007) Cohort</td>
<td>79,722 nurses</td>
<td>BMI, waist circumference, weight change</td>
<td>RR increases from 1.40 for BMI 21.0–22.9, to 2.69 for BMI &gt;35.0. Weight gain from the age of 18 years, higher waist circumference, hip circumference, and waist–hip ratio were all associated with a higher risk of incident psoriasis.</td>
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<tr>
<td>Nurse Health Study II</td>
<td>USA (2007) Cohort</td>
<td>78,532 nurses</td>
<td>Smoking</td>
<td>RR 1.78 for current smokers and 1.37 for past smokers. Increased risk with increased number of cigarettes smoked per day. The risk in former smokers decreases almost to that of never smokers 20 years after cessation.</td>
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<td>Nurse Health Study II</td>
<td>UK (2008) Case-control</td>
<td>36,702 cases and matched controls</td>
<td>Beta-blockers and other anti-hypertensive drugs</td>
<td>No association.</td>
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<tr>
<td>UKGPRD</td>
<td>Sweden (2009) Case-control</td>
<td>373 cases and matched controls</td>
<td>Smoking, BMI, alcohol</td>
<td>Smoking OR 1.7. BMI 9% increased risk per unit increase.</td>
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<tr>
<td>Denmark (2010)</td>
<td>Cohort</td>
<td>309,152 school children</td>
<td>Increase in BMI</td>
<td>Psoriasis in adulthood associated with increased BMI at age 12 and 13 in females only.</td>
</tr>
<tr>
<td>Turkey (2011)</td>
<td>Case-control</td>
<td>537 cases and 511 controls younger than 18 years</td>
<td>Passive smoking, BMI, stressful life events</td>
<td>Passive smoking OR 2.9. Life events OR 2.9. BMI (&gt;26) OR 2.5.</td>
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</table>
Natural history and prognosis
Limited data are available concerning long-term outcome and prognosis. An analysis over a 20-year follow-up period of patients enrolled in the psoralen and ultraviolet-A light (PUVA) cohort study documented that, on average, individuals with moderate to severe disease remained at these same levels for 11 or more years, and that, in spite of looking for a cure, consistent control of their psoriasis often had not been achieved.

Although psoriatic arthritis in clinical series represents up to 25% of all patients, population-based estimates suggest that no more than 5–10% of psoriatic patients present seronegative arthritis as an associated feature. Modifiable risk factors for psoriasis, namely smoking and obesity, may influence clinical severity, comorbidities, or response to treatment, and may even be responsible for an increased mortality among psoriatics as compared with the general population. Established psoriasis has been associated with the many components of the metabolic syndrome, including hypertension, dyslipidemia, obesity, and impaired glucose tolerance. Besides cardiovascular disease, a number of other conditions partly associated with smoking or obesity have been linked with psoriasis, including inflammatory bowel disorders, and tumors of specific sites, such as lung cancer, colonic cancer, and kidney cancer. A rare but well-defined association is with celiac disease.

In spite of the need for their continuous use, limited data are available on the long-term impact of treatment modalities for psoriasis. A model example are cohort studies of PUVA therapy which, among the others, enabled elevated risks for nonmelanoma skin cancer (including male genital tumors) to be estimated in PUVA-treated patients. Similar studies are needed for most new therapies, and registries of systemic treatments for psoriasis have recently been established in several countries. A merging of data from these registries to assess the risk for rare events would be desirable.

Social and economic impact
Negative feelings and moral evaluation are associated with skin manifestations. For centuries in many different cultures, skin diseases have been associated with disgrace and danger. A notable association is the connotation of dirtiness, bound up with fears of infection or contagion. The available surveys document that patients with psoriasis commonly experience social stigmatization and overt public rejection. These rejection experiences may result in greater sensitivity to the attitudes of others and further anticipation of rejection. A 1-year prospective study documented that improvement in skin condition did not correlate with feeling less stigmatized in women over 1 year. Feelings of embarrassment or lack of self-confidence can reduce social and even employment opportunities. One study in the United States, using data from the National...
Psoriasis Foundation database, showed that the probability of a low income (<US$30,000) was significantly greater among patients with severe disease than among those with mild psoriasis ($P = 0.0002$). It must also be conceded that low income may lead to behaviors (such as unhealthy alimentary habits and poor compliance) that further exacerbate disease and poor socioeconomic outcomes. The negative impact of psoriasis on relationships is similar to that of other chronic conditions, with relatives of patients reporting social disruption (55%), limitations to holiday plans and leisure activities (44%), and deterioration of close relationships (37%).

**Economic cost**

A systematic literature search dealing with cost-of-illness analyses in psoriasis, that is, analyses assessing direct, indirect and intangible costs, retrieved a total of seven papers. All studies but one were performed before biologics became available. The total annual costs per patient ranged between €1079 and about €23,000. The studies may have underestimated some psoriasis costs not included in their protocols, such as comorbidities and reduction in productivity by families and caregivers. Data from the studies show that the more severe the plaque psoriasis, the higher the direct and indirect costs for its management. Direct costs were higher than indirect costs, hospitalization representing the most significant item. There were considerable discrepancies between the results obtained in the different studies. Reasons for these discrepancies are manifold including differences in the selection of the sample, as well as in the methods for calculating costs. Only the adoption of a common methodology would help to discern differences attributable to different healthcare systems and to identify areas where intervention to optimize costs should be directed. Interestingly, an analysis of trends in the average wholesale price of brand-name psoriasis therapies from 2000 to 2008 demonstrated an average increase of 66%; thus, costs of several brand-name psoriasis drugs greatly outpaced the rates of inflation for all items and all prescription drugs.

**Further reading**


