Alcohol-Related Mortality in Patients With Psoriasis
A Population-Based Cohort Study

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IMPORTANCE People diagnosed with psoriasis have an increased risk of premature mortality, but the underlying reasons for this mortality gap are unclear.

OBJECTIVE To investigate whether patients with psoriasis have an elevated risk of alcohol-related mortality.

DESIGN, SETTING, AND PARTICIPANTS An incident cohort of patients with psoriasis aged 18 years and older was delineated for 1998 through 2014 using the Clinical Practice Research Datalink (CPRD) and linked to Hospital Episode Statistics (HES) and Office for National Statistics (ONS) mortality records. Patients with psoriasis were matched with up to 20 comparison patients without psoriasis on age, sex, and general practice.

MAIN OUTCOMES AND MEASURES Alcohol-related deaths were ascertained via the Office for National Statistics mortality records. A stratified Cox proportional hazard model was used to estimate the cause-specific hazard ratio for alcohol-related death, with adjustment for socioeconomic status.

RESULTS The cohort included 55,537 with psoriasis and 854,314 patients without psoriasis. Median (interquartile) age at index date was 47 (27) years; 408,230 of total patients (44.9%) were men. During a median (IQR) of 4.4 (6.2) years of follow-up, the alcohol-related mortality rate was 4.8 per 10,000 person-years (95% CI, 4.1-5.6; n = 152) for the psoriasis cohort, vs 2.5 per 10,000 (95% CI, 2.4-2.7; n = 1118) for the comparison cohort. The hazard ratio for alcohol-related death in patients with psoriasis was 1.58 (95% CI, 1.31-1.91), and the predominant causes of alcohol-related deaths were alcoholic liver disease (65.1%), fibrosis and cirrhosis of the liver (23.7%), and mental and behavioral disorders due to alcohol (7.9%).

CONCLUSIONS AND RELEVANCE People with psoriasis have approximately a 60% greater risk of dying due to alcohol-related causes compared with peers of the same age and sex in the general population. This appears to be a key contributor to the premature mortality gap. These findings call for routine screening, identification and treatment, using the Alcohol Use Disorders Identification Test (AUDIT-C) in both primary and secondary care to detect alcohol consumption and misuse among people diagnosed with psoriasis.

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Psoriasis is a common, currently incurable, immunemediated skin disease, with a prevalence of between 0.9% and 8.5% in Western countries.1 Recently, we have shown that, despite an overall decrease in mortality over the last 15 years, people with psoriasis nonetheless still die prematurely vs individuals without the disease.2 These findings call for a greater understanding of excess mortality linked with psoriasis.3 Excessive alcohol consumption is recognized in as many as one-third of patients with moderate to severe psoriasis.4-6 Furthermore, there is a correlation between increased alcohol intake and extent of body surface area involvement by psoriasis.5,7 Patients with increased alcohol intake may also report significantly higher levels of anxiety, depression, and psychosocial challenges.8 Consequently, alcohol misuse may be considered as a maladaptive behavior, used by affected individuals to manage their psychological distress.

Earlier studies found that people affected by severe psoriasis had a greater prevalence of, and elevated risk of, dying of liver disease9,9 and of gastrointestinal disease.10 However, only 2 studies11,12 from the United States and Finland specifically examined death due to cirrhosis or alcohol-related mortality in people with psoriasis. These studies are at least 2 decades old and they examined patients with severe psoriasis identified from hospital settings.11,12 To our knowledge, no study has specifically investigated the relative risk of dying from alcohol-related causes among people with psoriasis in the general population.

### Methods

**Data Source and Study Design**

This cohort study was carried out using the UK Clinical Practice Research Datalink (CPRD). The CPRD contains complete patient information from 711 participating general practices in the United Kingdom, with diagnoses, test results, prescriptions and hospital referrals recorded. Read coding is used to record diagnoses within CPRD.13 We examined the 398 CPRD practices in England that were also linked to the national Hospital Episode Statistics (HES) and the Office for National Statistics (ONS) mortality records. Linkage is available at individual-level for those patients registered at practices that have consented to data linkage. Linkage between data sets is undertaken using a deterministic linkage algorithm, based on a patient’s exact National Health Service (NHS) identification number, sex, date of birth, and residential postcode. The study was approved by the Independent Scientific Advisory Committee (ISAC) for Medicines and Healthcare products Regulatory Agency database research (ISAC approval 15_033R) and is reported in line with the recommendations of the RECORD statement.14 This population-based study was conducted using anonymized electronic health records that were extracted by a third party and deidentified before they were made available for research purposes. Hence, patient consent was not required.

The psoriasis cohort comprised adult patients (18 years and older), identified in the CPRD, with their first diagnosis of psoriasis between January 1, 1998, and March 3, 2014. Patients were eligible for linkage to the HES and ONS mortality records and were registered in the practice for at least 1 year prior to being diagnosed with psoriasis. The index date was set as the first diagnosis recorded during the study window. Up to 20 comparison patients, without a diagnosis of psoriasis, were matched by age, sex, and general practice on index date. The reason for matching with this number of unaffected comparison patients was the rarity of alcohol-related death as an outcome, to thereby maximize statistical power and precision and to preclude the occurrence of very small cell values among the comparison cohort. The comparison patients were required to have been in contact with the general practice within 6 months of the index date of the patients with psoriasis to whom they were matched. The selection of patients with and without psoriasis from the same population at risk and identifying them from the same general practice and during the same time window was implemented to thereby avoid potential selection, information, and detection biases. All patients included in the study were followed-up from the index date to the end of the study observation period (March 31, 2014), or to the last date of data collection from the practice, the date the patient transferred out of the practice or died, whichever came first.

**Area-Level Socioeconomic Status**

The residential postcodes of patients were linked to the Index of Multiple Deprivation (IMD) 2010.15 The IMD is an area-level weighted combination of the following seven domains of deprivation: income, employment, health and disability, education skills and training, barriers to housing and services, living environment, and crime. It is calculated at the Lower-layer Super Output Areas (LSOA) level covering approximately 1500 residents. The IMD scores were aggregated into quintiles, where 1 corresponded to the least deprived area and 5 to the most deprived area.

**Measurement of Alcohol Consumption**

Information on alcohol consumption was extracted using an existing algorithm modified for this study (eFigure 1 in the Supplement). In summary, the most recent record, prior to or recorded on the index date, was used to determine the alcohol consumption level. If no information on alcohol consumption was available, this was set to “missing.” Alcohol consumption level was categorized as follows: nondrinkers, former

### Key Points

**Question** Do people with psoriasis have an elevated risk of alcohol-related mortality?

**Findings** In this population-based cohort study, the adjusted hazard ratio of alcohol-related mortality for patients with psoriasis was 1.58 (95% CI, 1.31-1.91) compared with patients without psoriasis.

**Meaning** The elevated risk of alcohol-related mortality found in people with psoriasis calls for routine screening, identification, and treatment using the simple Alcohol Use Disorders Identification Test (AUDIT-C) in both primary and secondary health care to detect alcohol consumption and misuse among people diagnosed with psoriasis.
Alcohol-Related Mortality and Clinical Management

Cause-specific mortality was determined via linkage of patient electronic health records (primary care: CPRD; secondary care: HES) with ONS mortality records. In the United Kingdom, death certificates are completed by an attending registered medical practitioner, and this information is captured nationally by the ONS. Death certificates are divided into 2 parts, containing the underlying cause of death (part 1) and diseases that may have contributed to the death (part 2). We identified alcohol-related deaths via the underlying cause of death code, according to International Classification of Diseases, Ninth Revision (ICD-9) and International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), as recommended by the ONS. The ONS definition of alcohol-related deaths only includes those causes regarded as resulting directly from harmful alcohol consumption (Figure 2 in the Supplement) and does not include other diseases where alcohol has been shown to make some etiological contribution, such as cancers of the mouth, esophagus, and liver, or suicide.

Among those who died of alcohol-related causes, the proportion of people, who had previously: (1) been classified as heavy drinkers; (2) prescribed treatment for alcohol dependence (acamprosate, disulfiram, nalmefene and naltrexone); (3) coded for being offered psychological support for alcohol dependence in primary care; or (4) had an admission to hospital for chronic causes, directly attributable to alcohol, were calculated. All of the code lists used are available from http://www.clinicalcodes.org.

Statistical Analysis

For the descriptive analysis, continuous variables were summarized using the median and interquartile range (IQR), whereas discrete variables were reported as percentages per exposure group. All-person and sex-specific alcohol-related death rates per 10 000 person-years, with 95% CIs and median age at death (IQR), were calculated for patients with and without psoriasis. Cumulative incidence functions were calculated for alcohol-related deaths, and deaths due to all other causes combined (other causes of death). A stratified Cox proportional hazard model was fitted to estimate the cause-specific hazard ratio (HR) and 95% CI. The model was adjusted for socioeconomic status, measured according to IMD quintile. Additionally, the following 3 models were fitted separately: interactions between psoriasis and age, sex, and IMD quintile. A sensitivity analysis was performed to assess the robustness of the results, by restricting the analysis to patients not prescribed methotrexate as this could be a potential confounder, given the hepatotoxic effects of this drug. All statistical analyses were performed using Stata version 14 (StataCorp).

Results

In all, 55 537 patients with incident psoriasis, and 854 314 patients in the matched comparison cohort, met the eligibility criteria and were included in the analysis (Figure 3 in the Supplement). Median (IQR) age at index date was 47 (27) years (Table 1). Patient postcode-level IMD was similarly distributed. At baseline, there was a higher prevalence of being recorded as a heavy drinker in the psoriasis cohort (9.3%) vs the comparison cohort (4.8; 95% CI, 4.1-5.6) vs the comparison cohort (2.5; 95% CI, 2.4-2.7). Patients with psoriasis died from alcohol-related causes on average 3 years younger than those without psoriasis who died from these causes: median (IQR) age at death 55 (16) years vs 58 (17) years, respectively (Table 2). Furthermore, women with psoriasis died from alcohol-related causes at approximately 5 years younger than women without psoriasis who died from these causes. Three diagnostic codes were predominant among the alcohol-related deaths in the psoriasis cohort: alcoholic liver disease (99 cases [65.1%]), fibrosis and cirrhosis of the liver excluding biliary cirrhosis (36 cases [23.7%]), and mental and behavioral disorders due to alcohol misuse (12 cases [7.9%]). These 3 causes together accounted for 147 (96.7%) of the 152 deaths among the individuals diagnosed with psoriasis. The equivalent percentage (92.1%; 1030 of 1118) was lower in the comparison cohort, but the same 3 types of alcohol-related death predominated.
The electronic health records revealed that most patients who died of alcohol-related causes in the psoriasis cohort or in the comparison cohort had at least 1 lifetime hospital admission for a chronic alcohol-related condition (85.5% and 79.0%, respectively). Among those patients who died due to alcohol-related disease 82.2% in the psoriasis group and 75.5% in the comparison group had been classified as heavy drinkers in their primary care medical records. However, 17.8% of patients who died of alcohol-related causes in the psoriasis cohort and 24.3% in the comparison cohort, never received a lifetime diagnosis of excessive alcohol consumption, or a prescription in primary care for alcohol dependence. Only a small proportion of these patients received pharmacotherapy for alcohol dependence or was coded as being offered psychological support (Table 3).

The cause-specific hazard of alcohol-related death was increased by 58% (HR, 1.58; 95% CI, 1.31-1.91) in the psoriasis cohort vs the comparison cohort, and the cause-specific hazard of other causes of death was lower by 19% (HR, 0.81; 95% CI, 0.78-0.83), as reported in Table 4. For patients with psoriasis, the cumulative incidence of alcohol-related death tended to increase much more rapidly than in the comparison group across the follow-up period. The 16-year cumulative incidence of alcohol-related death in the psoriasis and comparison cohorts were 0.007% (95% CI, 0.005-0.009) and 0.005% (95% CI, 0.003-0.005), respectively (Figure). There was no evidence of variability in relative risk by age (P = .45), sex (P = .59), or IMD quintile (P = .28). The sensitivity analysis, excluding people prescribed methotrexate, confirmed that psoriasis was associated with an elevated alcohol-related mortality risk (HR, 1.66; 95% CI, 1.37-2.01).

Table 2. Event Counts and Crude Incidence Rates of Alcohol-Related Death in the Psoriasis and Comparison Cohorts

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Psoriasis Cohort</th>
<th>Comparison Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients per cohort, No.</td>
<td>55,537</td>
<td>854,314</td>
</tr>
<tr>
<td>Follow-up, median (IQR), y</td>
<td>6.4 (5.0)</td>
<td>6.1 (4.3)</td>
</tr>
<tr>
<td>Person-years, No.</td>
<td>318,435</td>
<td>4,455,669</td>
</tr>
<tr>
<td>No. of alcohol-related deaths, No. (%)</td>
<td>152 (0.3)</td>
<td>1118 (0.1)</td>
</tr>
<tr>
<td>Alcohol-related mortality rate (95% CI)*</td>
<td>4.8 (4.1-5.6)</td>
<td>2.5 (2.4-2.7)</td>
</tr>
<tr>
<td>Female</td>
<td>3.9 (3.1-5.0)</td>
<td>1.9 (1.7-2.1)</td>
</tr>
<tr>
<td>Male</td>
<td>5.7 (4.6-7.0)</td>
<td>3.3 (3.0-3.5)</td>
</tr>
<tr>
<td>Age at death for alcohol-related death, median (IQR), y</td>
<td>55 (16)</td>
<td>58 (17)</td>
</tr>
<tr>
<td>Female</td>
<td>55 (18)</td>
<td>60 (18)</td>
</tr>
<tr>
<td>Male</td>
<td>56 (14)</td>
<td>57 (16)</td>
</tr>
</tbody>
</table>

Abbreviation: IQR, interquartile range.

*Crude mortality rates per 10,000 person-years.

Discussion

Main Findings

People diagnosed with psoriasis had a greater risk of dying, on average 3 years younger, due to alcohol-related causes, compared with the general population. Moreover, although there was no evidence of a variation in relative risk by sex, women with psoriasis died of alcohol-related causes at considerably younger age (approximately 5 years) than women without psoriasis who died from these causes. The cumulative incidence functions also showed that the incidence of alcohol-related mortality increased much more rapidly during follow-up in patients with psoriasis. Similar findings were evident after excluding patients, who were prescribed methotrexate in primary care.

Comparison to Other Studies

Consistent with other studies, we found a raised prevalence of alcohol misuse in the psoriasis cohort.7 Our results are also consistent with those that found an increased mortality risk due to liver disease in patients with psoriasis.9,10,20 In examining cause-specific mortality, these earlier studies found that people affected by psoriasis had a greater risk of dying from liver disease, with a standard mortality ratio of 4.04 (95% CI 2.76-5.70) if they had the most severe form of the disease,9 or with a HR of 2.00 (95% CI 1.34-2.99) for mild psoriasis, and 4.26 (95% CI 1.87-9.73) for severe psoriasis.10 Higher mortality rates from gastrointestinal diseases have also been reported among patients with mild (0.9 per 1000 person-years, 95% CI 0.9-1.0) and severe (1.8 per 1000 person-years, 95% CI 1.6-2.0) psoriasis, compared to 0.4 per 1000 person-years (95% CI 0.4-0.4) in the general population.20 Similar to findings reported by Stern and Lange (1988)19 and Poikolainen et al. (1999),20 we found that the risk of death, due to cirrhosis and other causes, directly attributable to alcohol misuse, is greater in people with psoriasis than it is in those without the condition. The first study, using a cohort of 1380 people with moderate-to-severe psoriasis, exposed to Photochemotherapy (PUVA), and which investigated specific causes of death, found that psoriasis was positively associated with death due to cirrhosis (standard mortality ratio, 4.7; 95% CI, 3.1-6.8).11 The second study,12 analyzing more than 5000 patients hospitalized for psoriasis, reported elevated mortality, directly attributable to alcohol (standard mortality ratio 4.46; 95% CI, 3.60-5.45 for men and standard mortality ratio, 5.60; 95% CI, 2.98-8.65 for women).

Strengths and Limitations of the Study

Major strengths of this study included the linkage of primary care electronic health records to national mortality records to
are commonly managed through shared-care arrangements between hospital and primary care health care providers. Second, we were unable to examine risk of alcohol-related mortality by severity of psoriasis, as validated measures of disease severity are not routinely recorded in patient electronic health records in primary care.

### Interpretation of the Findings

Individuals with psoriasis face psychological distress and psychosocial challenges, often as a consequence of the stigmatizing nature of the disease, and these in turn can lead to chronic alcohol misuse and dependence. Highlighting the dual stigma of psoriasis and problem drinking is important. Alcohol misuse is perceived as a self-inflicted lifestyle choice rather than a disease. Hence, patients are often reticent to acknowledge the problem. People affected by psoriasis have a higher prevalence of excessive alcohol consumption and an elevated risk of dying due to alcohol-related causes compared with the general population of the same age and sex, independent of socioeconomic status. Our findings also highlight that alcohol misuse often remains unidentified and undertreated in primary care.

Only a very small proportion of individuals who died from alcohol-related causes were prescribed pharmacotherapy or coded as being offered psychological support. Nonetheless, the majority of these patients had previously been hospitalized for alcohol-related problems. These findings concur with those from a recent study on prescribing patterns for alcohol dependence in the United Kingdom, which concluded that only 12% of people with alcohol dependence were prescribed treatment in primary care. In recent years, the National Institute for Health and Care Excellence (NICE) guidelines in England and systematic reviews of the evidence-base have recommended a combination of pharmacotherapy and psychological counseling, neither of which are regularly deployed for people with alcohol dependence.

### Alcohol Treatment Services and Implications for Clinicians

There is also a need to detect and intervene earlier in liver disease and the main determinant of long-term survival for these patients is to abstain from drinking. Screening and brief interventions, in both primary and secondary health care, and hospital alcohol care teams help patients achieve abstinence, improve health harms and prognosis, and remove the stigma of self-inflicted disease. Our study has reinforced the findings from the National Confidential Enquiry into Patient Outcome and Death report, highlighting the long-term nature of missed opportunities, such as delays in referral of patients for specialist alcohol and liver care, and missed opportunities for brief interventions during previous admissions.
Conclusions

Our findings also indicate that health care practitioners, with responsibility for the care of patients with psoriasis, should be more aware of the psychological difficulties that this group of patients face. Routine screening, identification and treatment, using the simple, shortened form (AUDIT-C) of the Alcohol Use Disorders Identification Test screening tool, developed by the World Health Organization to detect the early signs of hazardous, harmful, and dependent alcohol consumption, should be implemented in both primary and secondary care to detect alcohol misuse among all people diagnosed with psoriasis. This is critical in hospital dermatology departments, where the most severe cases of psoriasis, in whom alcohol consumption is highest, are cared for. Moreover, there is also an urgent need for effective alcohol and addiction treatment services to be developed, so as to address both health harms and to overcome the stigma experienced by patients with both psoriasis and alcohol problems.

REFERENCES


Joseph Goldberger—Public Health Champion and Investigator of Pellagra

Kishore L. Jayakumar, BS; Robert G. Micheletti, MD

Joseph Goldberger, MD (1874-1929), was an American physician whose commitment to public health led him to risk his own health and to confront the medical and political establishments of his day. In 1899, not long after graduating from Bellevue Hospital Medical College, Goldberger joined the US Marine Hospital Service (later the Public Health Service). Initially, his duties included inspecting immigrants in the Port of New York, but he soon became fascinated by epidemiology and infectious diseases. As a quarantine officer, Goldberger traveled extensively to study outbreaks of yellow fever, dengue fever, and typhus, and managed to contract each of these on his visits.1

In 1914, Surgeon General Rupert Blue appointed Goldberger, who was battling an epidemic of diphtheria in Detroit, to investigatepellagra, which had become a national scourge, disproportionately affecting rural areas and the impoverished.1 In a medical era dominated by bacteriology, the prevailing theory postulated that pellagra was an infectious disease. Goldberger, however, rejected this theory, noting that it failed to explain why prisoners and children in orphanages were often affected while staff members at these institutions were spared. Instead, he hypothesized that differences in diet were responsible.1

To confirm his hypothesis, he arranged for children in 2 Mississippi orphanages to receive a more balanced diet.2 Among the children with pellagra, nearly all were cured, and among the healthy children, no new cases developed. When he performed another study at the Georgia State Sanitarium, he obtained similar results. Having demonstrated that a varied diet could cure pellagra, he then established that an unvaried diet could induce it. In 1915, cooperating with Mississippi Governor Earl Brewer, Goldberger arranged a study at the Rankin State Prison Farm. Prisoners who volunteered to restrict their diet were promised pardons. Although no cases occurred in the control group, 6 of the 11 healthy volunteers in the experimental group developed pellagra, with one declaring, "I have been through a thousand hells."3 Despite this evidence, critics still disputed Goldberger’s conclusions, claiming that the experiment’s ulterior purpose was to pardon white-collar prisoners who were friends of the governor, that the poor diet had merely sensitized prisoners to the actual cause of pellagra, and that Goldberger was a Northerner intent on disparaging the South.3

Frustrated but not deterred, Goldberger sought to dispel any notion of a pathogenic cause of pellagra. In 1916, he hosted “filth parties,” in which blood, stool, and secretions from patients with pellagra were administered to healthy volunteers, including himself and his wife. Though some developed gastroenteritis, none developed pellagra.4

Today, we remember not only Goldberger’s heroic efforts in promoting public health but also the lesson that neither popular opinion nor political motivations should impede the assimilation of sound scientific findings.

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