Incidence, Prevalence, and Mortality of People with Psoriasis and Psoriatic Arthritis in Taiwan: A Nationwide Cohort Study

Ireny Y. K. ISKANDAR1,2, Teng-Chou CHEN2, Li-Chia CHEN2, Meng-Sui LEE3,4, Yen-Yun YANG5, Ting-Chun WANG6, Yu-Chun HSIEH6, K. Arnold CHAN5,6, Christopher E. M. GRIFFITHS7,8 and Darren M. ASHCROFT2,8,9, on behalf of the Global Psoriasis Atlas

1Centre for Occupational and Environmental Health, Division of Population Health, Health Services Research and Primary Care, 2Centre for Pharmacoepidemiology and Drug Safety, Division of Pharmacy and Optometry, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK; 3Department of Dermatology, National Yang-Ming University, 4Department of Medical Research, National Taiwan University Hospital, 5Health Data Research Centre, National Taiwan University, Taipei, Taiwan, 6Dermatology Centre, Salford Royal NHS Foundation Trust, 7National Institute for Health and Care Research (NIHR) Manchester Biomedical Research Centre, Manchester Academic Health Science Centre and 8NIHR, School for Primary Care Research, University of Manchester, Manchester, UK

There is a recognized need to better understand changes in the epidemiology of psoriasis and psoriatic arthritis (PsA) over time in Asia. Using the Taiwan National Health Insurance claim records this population-based study examined changes in the prevalence, incidence, and mortality rates in patients with psoriasis or psoriatic arthritis in Taiwan over 12 years. Patients with ≥1 diagnosis code for psoriasis or psoriatic arthritis, recorded either by dermatologists or rheumatologists, were identified. Annual age- and sex-standardized prevalence and incidence rates were calculated using the Taiwan general population as reference. To investigate mortality, each patient in the incident cohort was matched to 10 comparators from the general population by sex and age (at diagnosis). The risk of mortality between study cohorts and comparators was analysed by Cox proportional hazard regression. The prevalence of psoriasis (0.18–0.86%) and psoriatic arthritis (0.01–0.08%) increased steadily between 2006 and 2017. The incidence rates, however, remained stable (psoriasis: 62–65 per 100,000 person-years; psoriatic arthritis: 6–5 per 100,000 person-years). The risk of all-cause mortality for patients with psoriasis (hazard ratio 1.16; 95% confidence interval: 1.13–1.19) was higher than the general population, despite a decreasing trend over time in the all-cause mortality rates for both groups. The steady increase in the prevalence of psoriasis despite stable incidence rates suggests that improvements in life expectancy may be the key determinant of this increase.

Key words: psoriasis; psoriatic arthritis; epidemiology; incidence; prevalence; mortality.

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Corr: Ireny Y. K. Iskandar, Centre for Occupational and Environmental Health, Division of Population Health, Health Services Research and Primary Care, School of Health Sciences, The University of Manchester, Devas Street, Ellen Wilkinson Building, Manchester, M13 9PL, UK. E-mail: ireny.iskandar@manchester.ac.uk

Psoriasis is a chronic, immune-mediated inflammatory skin condition (1), which is now considered a systemic disease associated with psychological, metabolic, arthritic, and cardiovascular comorbidities (2). Consequently, lifespan is reduced (3). In 2014, the World Health Organization (WHO) recognized psoriasis as a serious non-communicable disease (4) and the accompanying WHO report (2016) emphasized the need to better understand the global burden of the disease (4). In Taiwan, the National Health Insurance (NHI) provides a wide range of health services and treatments to patients with psoriasis and psoriatic arthritis (PsA) (5). However, with a rapidly ageing population and increasing medical expenditures in Taiwan, there is a recognized need to further understand the epidemiology of psoriasis and PsA.

To date, there are important knowledge gaps in understanding the natural history and disease burden of psoriasis and PsA in Asia (6, 7). Specifically, previous studies from Taiwan have provided limited information on the epidemiology of psoriasis and PsA based on age and sex, and on the temporal trends of the incidence and prevalence (8–11). A recent study has reported excess mortality in patients with psoriasis and PsA compared with the general population (12). Nevertheless, no studies have examined temporal trends in all-cause mortality in patients with psoriasis and PsA in Taiwan. It is critical to determine temporal trends as they will impact on disease prevalence. To date, no studies have simultaneously explored longitudinal trends in incidence, prevalence and mortality in patients with psoriasis or PsA in Taiwan.

SIGNIFICANCE

In 2014, the WHO recognized psoriasis as a serious non-communicable disease and its report emphasized the need to better understand the global burden of the disease. However, epidemiological information on psoriasis or psoriatic arthritis in Asia is limited. This population-based study found that, over 12 years, the incidence of psoriasis and psoriatic arthritis in Taiwan remained stable; however, the prevalence increased steadily over time. The steady increase in prevalence of psoriasis despite stable incidence rates suggests that improvements in life expectancy may be the key determinant of this increase.

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Understanding the epidemiology of psoriasis and PsA in Taiwan is vital in order to quantify the social and economic burden of the disease and to inform policy decisions on the delivery of healthcare services and resource allocation to reduce the morbidity associated with the conditions (4, 13). Therefore, the aim of this study was to investigate the epidemiology of psoriasis and PsA in Taiwan. The specific objectives of the study were to determine trends in the incidence, prevalence and mortality of patients with psoriasis and PsA in Taiwan and examine how these epidemiological factors changed over time.

METHODS

Study design and data source

This population-based cohort study used the Taiwan NHI claim database and death certificates from 1 January 2006 to 31 December 2017. The publicly funded NHI programme (launched in 1995) provides a comprehensive benefit package, including outpatient and inpatient services, prescription drugs, Chinese herbal remedies, and Western and preventive medicine to 99.9% of the 23.5 million people in Taiwan (5). The NHI research database (derived from claims data of NHI beneficiaries) was established in 2002 and continues to be maintained for research purposes by Taiwan’s National Health Research Institutes. In this study data, including diagnosis codes, demographic characteristics, and dates of services provided, were available from the NHI research database from different clinical settings (outpatient and inpatient services and emergency department visits). Personal data regarding patients or care providers, including medical institutions and physicians, was pseudonymized; therefore the requirement for informed consent was waived. The institutional review board of the National Taiwan University Hospital approved the study protocol (NTUH-REC number: 201808083W).

Study population

Patients of all ages registered with the Taiwan NHI programme with at least 1 diagnosis code for psoriasis or PsA made by either a dermatologist or a rheumatologist were eligible for this study. The study cohort was identified using the International Classification of Diseases, 9th (ICD-9; used from 2006 to 2015) and 10th (ICD-10; used from 2016 to 2017) editions codes for psoriasis (ICD-9: 696.1; ICD-10: L40.0, L40.4, L40.9) and PsA (ICD-9: 696.0; ICD-10: L40.5, L40.51, L40.52, L40.53, L40.54, L40.59).

To ensure reliable and complete incidence data and avoid misclassification of prevalent cases as incident ones, the lookback period for identifying incident cases was from 2006 and the incidence analysis was limited to the period between 2009 and 2017. In each year, incident cases were defined as patients with a first recorded diagnosis code for psoriasis or PsA. The index date was the date of the first recorded diagnosis, and individuals were considered prevalent cases from that date onwards. Prevalent cases were those with at least 1 diagnosis code before the end of each year. A sensitivity analysis using ≥2 diagnosis codes assigned by any medical speciality was also conducted for incidence and prevalence evaluation.

To investigate the associations between psoriasis and PsA and all-cause mortality, each person in the incidence cohort was matched by sex and age on the index date to 10 people without prior history of psoriasis and PsA. The matched cohort was assigned the same index date to ensure that patients with or without psoriasis and PsA were followed up over similar periods. The study cohorts were followed from the index date until death, de-registration from the NHI, or end of the study period (31 December 2017), whichever came first. Furthermore, the matched cohort was censored when they received a psoriasis or PsA diagnosis that was confirmed by a dermatologist or a rheumatologist.

Study outcomes

The annual prevalence of psoriasis and PsA were derived by dividing the number of prevalent cases for each year by all Taiwan NHI registrants in that particular calendar year. The annual incidence of psoriasis and PsA were calculated by dividing the number of incident cases by their person-time at risk. The person-time at risk was calculated from the start of each calendar year or the day of registration of each incident case until the index date, death, or end of each calendar year, whichever came first. Patients with prior codes for psoriasis and PsA were excluded from the denominator and numerator in determining the annual incidence.

Annual mortality rates among incident cases and their matched comparators were derived by dividing the number of deaths occurred in that calendar year by their person-time at risk. The person-time at risk was calculated from the index date until death, de-registration from the NHI, first psoriasis or PsA diagnosis confirmed by a dermatologist or a rheumatologist (for comparators), or end of the calendar year in question, whichever came first.

Statistical analyses

Annual prevalence (percentage and 95% confidence intervals (95% CIs)) and incidence (per 100,000 person-years and 95% CIs) were estimated and stratified by age and sex. Age- and sex-standardized prevalence was estimated by the direct standardization method (14) using the Taiwan population as reference (15).

Cox proportional hazards regressions were used to investigate mortality, comparing the patients with psoriasis and PsA with their matched comparators. The regression models included index year (as a continuous variable), sex, and age at index date. The proportional hazards assumption was assessed by examining scatterplots of the model coefficients over time and statistical testing based on weighted residuals. All analyses were carried out using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

During the study period, Taiwan NHI registrants increased from 22,502,536 in 2006 to 23,583,524 in 2017 (Table SI). The number of individuals with psoriasis increased from 40,420 in 2006 to 2016,657 in 2017. Overall, 123,303 incident psoriasis cases were diagnosed in 2009 or later (Table I). The number of individuals with PsA included in the study increased from 1,786 in 2006 to 18,209 in 2017. Overall, 12,933 incident PsA cases were diagnosed in 2009 or later (Table I).

Annual incidence and prevalence of psoriasis

The standardized prevalence rates for clinically diagnosed psoriasis increased steadily, from 0.18% to 0.86% between 2006 and 2017. However, the incidence of psoriasis remained stable between 62 (95% CI 61–64) and 65 (95% CI 64–66) per 100,000 person-years during 2009 and 2017. Overall, the prevalence and incidence of psoriasis were consistently higher in males than females (Table I, Fig. 1).
Incidence of psoriasis plotted against age showed a modest bimodal pattern with the frequency of age at first diagnosis peaking at the age of 30–39 years and 80–89 years, characteristic of early-onset (type I) and late-onset (type II), respectively, with a higher proportion of new cases presenting after age 40 years (i.e. late-onset, Fig. 2a). Age-specific incidence rates of psoriasis remained relatively stable within the various age strata from 2009 to 2017 (Fig. 3a), with the incidence among children (0–19 years) much lower compared with adults (Fig. 3a, Table SIII).

The prevalence of psoriasis increased with age (Fig. 2b). Interestingly, the prevalence was comparable between boys and girls (0–19 years old); however, in adults, the prevalence was much higher in males compared with females (Fig. 2b). Age-specific prevalence rates of psoriasis remained relatively stable from 2006 to 2017 among children (0–19 years), but increased steadily in all other age groups particularly among those aged ≥90 years old (Fig. 3b, Table SIII).

Similar rates and trends in incidence and prevalence were observed in the sensitivity analysis (Tables SII and SIV).

### Annual incidence and prevalence of psoriatic arthritis

The standardized prevalence rates for clinically diagnosed PsA increased steadily from 0.01% to 0.08% between 2006 and 2017. However, the incidence of PsA remained stable between 6 (95% CI 6–6) and 5 (95% CI: 4–5) per 100,000 person-years.
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100,000 person-years during 2009 and 2017 (Table I). No difference in the prevalence and incidence of PsA were found between the sexes (Table I, Fig. S1).

Incidence of PsA showed a trend of increasing incidence with age, reaching a peak at the age of 50–59 years, after which it declined (Fig. S2a), while the prevalence of PsA increased with age (Fig. S2b). Interestingly, the prevalence of PsA was comparable between the sexes up to the age of 60–69 years, after which the prevalence was higher in males than females (Fig. S2b). Age-specific prevalence rates of PsA remained relative stable from 2006 to 2017 among children (0–19 years), but increased steadily in all other age groups (Fig. S3b, Table SV).

Similar rates and trends in incidence and prevalence were observed in the sensitivity analysis (Tables SII and SVI).

**All-cause mortality in people with psoriasis and psoriatic arthritis compared against matched comparators**

In total, 123,303 people with psoriasis were matched to 1,232,717 comparators between 2009 and 2017. Males accounted for 58% in both cases and controls, and the mean follow-up time (52 ± 32 months) was similar between cases and comparators (Table II). The results of Cox proportional hazards regressions (Table III) showed an overall reduction in mortality over time for all patients (HR 0.99, 95% CI 0.98–0.99, Fig. S4). After controlling for index year, age and sex, patients with psoriasis had a higher mortality risk than the comparators (1.16, 1.13–1.19). Results from the sensitivity analysis were consistent with the findings from the primary analysis (Table SVII). The findings were similar for the association between PsA and all-cause mortality (Tables SVIII, SIX and Fig. S5).

**DISCUSSION**

This study found the prevalence of clinically diagnosed psoriasis and PsA has increased steadily over 12 years, and the results suggest that psoriasis and PsA affect 0.86% and 0.08%, respectively, of the general population in Taiwan. In contrast, the incidence of psoriasis and PsA remained stable. Age-specific incidence rates remained constant within the various age strata throughout the follow-up period. At the same time, the prevalence increased more steadily in the older age groups than in younger age groups, suggesting an increasing population living longer with psoriasis and PsA. Nevertheless, the risk of all-cause mortality was higher for patients with psoriasis and PsA than in the general population.

An increasing trend in the prevalence of psoriasis and PsA has been observed previously in Taiwan (10, 11)
Studies about the longitudinal incidence of psoriasis and PsA in Taiwan are scarce. Similar to our findings, Wei et al. (11) demonstrated that the incidence of psoriasis remained approximately the same between 2000 and 2013. However, in contrast to our findings, they reported that the incidence of PsA increased from 3.64 to 6.91/100,000 person-years between 2000 and 2013. Nevertheless, between 2009 and 2013, the reported incidence rates for PsA remained stable and are similar to the current findings. It is unclear whether the increase in the incidence rate for PsA between 2000 and 2013 represents true changes in PsA incidence over time, changes in the risk factors (obesity, psychological conditions, and stress) for PsA (19), or changes in the diagnosis pattern and awareness of the disease over time (20).

No difference in the incidence and prevalence of psoriasis between boys and girls was observed, but in adults, higher incidence and prevalence rates were observed in men compared with women. These findings align with most of the previous studies that reported a male predominance in East Asia (21–24). The reason for this is not clear (6). Healthcare service utilization is higher among women than men in Taiwan (9, 25); therefore, the possibility that the male predominance in Taiwan might be due to selection bias is unlikely. Nevertheless, societal taboo (for females) and the difference in self-directed health behaviours (e.g., diet, exercise, smoking or alcohol consumption) are some reasons that have been speculated to account for the difference in the incidence and prevalence observed between the sexes, particularly that this difference is observed in adults and not in children (6). Contrary to Wei et al. (11), the current results suggest no difference in the overall incidence and prevalence of PsA between the sexes. Nevertheless, our findings are in line with previous reports on the epidemiology of PsA (26).

Our findings relating to the age of onset of psoriasis, showed a slight bimodal age distribution of psoriasis onset, supporting the notion of “type I” (early-onset) and “type II” (late-onset) variants of the condition. Interestingly, late-onset psoriasis is more common than early-onset type, contrary to the often-quoted convention that 75% of new psoriasis cases present before age 40 years (i.e. early-onset) (27). While the predominance of early-onset psoriasis was confirmed in study populations from dermatology departments, outpatient clinics, and self-reported surveys (28–33); population-based estimates suggested that late-onset psoriasis was more common (34, 35). In addition, the high frequency of late-onset psoriasis among incident cases probably reflects the underlying lower frequency of HLA-Cw6 in the Taiwanese population (36–38). Compared with late-onset psoriasis, HLA-Cw6 is strongly associated with early-onset psoriasis, and its frequency is generally higher in the Caucasian population (27, 37). The discrepancy may also be explained by the underlying population age distribution, with late-onset psoriasis more common in an ageing population (34).

### Table II. Summary of characteristics of patients with psoriasis and their matched control included in the mortality analysis

|                          | Psoriasis cases | Comparators matched on age and sex |
|--------------------------|-----------------|------------------------------------|
| Cases/controls included in the entire study period, n | 123,303         | 1,232,717                          |
| Male patients, n (%)     | 71,873 (58.3)   | 718,481 (58.3)                     |
| Cumulative follow-up, person-years | 528,984         | 5,304,859                          |
| Months of follow-up, mean (SD) | 52.2 (31.6)    | 52.4 (31.6)                        |
| Age group, n (%)         |                 |                                    |
| 0–9 years                | 1,207 (1.0)     | 12,070 (1.0)                       |
| 10–19 years              | 7,128 (5.8)     | 71,279 (5.8)                       |
| 20–29 years              | 17,515 (14.2)   | 175,148 (14.2)                     |
| 30–39 years              | 22,306 (18.1)   | 223,055 (18.1)                     |
| 40–49 years              | 20,245 (16.4)   | 202,431 (16.4)                     |
| 50–59 years              | 22,108 (17.9)   | 221,034 (17.9)                     |
| 60–69 years              | 15,759 (12.8)   | 157,556 (12.8)                     |
| 70–79 years              | 10,598 (8.6)    | 105,910 (8.6)                      |
| 80–89 years              | 5691 (4.6)      | 56,810 (4.6)                       |
| 90–99 years              | 727 (0.6)       | 7234 (0.6)                         |
| ≥100 years               | 19 (0.02)       | 190 (0.02)                         |
| Index year, n (%)        |                 |                                    |
| 2009                     | 13,560 (11.0)   | 135,597 (11.0)                     |
| 2010                     | 12,962 (10.5)   | 129,603 (10.5)                     |
| 2011                     | 13,288 (10.8)   | 132,863 (10.8)                     |
| 2012                     | 14,723 (11.9)   | 147,202 (11.9)                     |
| 2013                     | 14,064 (11.4)   | 140,594 (11.4)                     |
| 2014                     | 13,167 (10.7)   | 131,620 (10.7)                     |
| 2015                     | 13,502 (11.0)   | 134,966 (11.0)                     |
| 2016                     | 13,444 (10.9)   | 134,393 (10.9)                     |
| 2017                     | 14,593 (11.8)   | 145,879 (11.8)                     |

*21 psoriasis diagnosis records (diagnosed by a dermatologist).

and in several other settings, for example in Korea (16, 17) and Germany (18). This observed increase in the prevalence of psoriasis and PsA in Taiwan has previously been speculated to be attributable to changes in lifestyle and environmental factors (obesity, psychological conditions, and stress), or an increased awareness of the disease among physicians and the general population (possibly due to the advent of biologic therapies) (10).

In this study, however, we observed a steady increase in psoriasis and PsA prevalence in the context of a decreasing risk of mortality. As fewer patients die for every incident case over time, we found that the prevalence pool of patients with psoriasis and PsA is increasing steadily. Nevertheless, we found that life expectancy has increased by approximately 3 years and therefore, may not fully explain the observed increase in psoriasis and PsA prevalence. Hence, some of the other reasons that have been highlighted previously to be attributed to the increase in the prevalence of psoriasis and PsA may also help to explain the increase in prevalence observed in our study.

### Table III. Results of the Cox regression analysis examining the risk of mortality in patients with psoriasis

| Variable    | HR (95% CI) | p-value  |
|-------------|-------------|----------|
| Index year  | 0.99 (0.98–0.99) | <0.0001 |
| Women       | 0.62 (0.61–0.63) | <0.0001 |
| Age         | 1.10 (1.09–1.10) | <0.0001 |
| Psoriasis   | 1.16 (1.13–1.19) | <0.0001 |

*21 psoriasis diagnosis records (diagnosis is made by a dermatologist).

*Age* represents age at index date.

HR: hazard ratio; CI: confidence interval. p-values significant at the 0.05 level in bold.
A higher risk of all-cause mortality for patients with psoriasis and PsA compared with the general population was observed in this study. This finding aligns with several previous studies that reported on excess mortality in patients with psoriasis and PsA compared with the general population (12, 39–41). For example, both all-cause mortality and mortality from malignancies and circulatory system diseases have been reported to be elevated in patients with psoriasis and PsA in Taiwan (12). There is growing evidence suggesting a link between psoriasis and other risk factors, which could lead to a higher risk of mortality. Patients with psoriasis are more likely to have cardiovascular disease, metabolic syndrome, obesity, diabetes mellitus, and malignancies, particularly in those with PsA and severe skin disease (40–44), which could explain the higher mortality risk observed in patients with psoriasis. In addition, patients with psoriasis tend to have higher rates of behavioural risk factors, including smoking and alcohol use (45, 46), which could also explain the higher mortality risk observed in patients with psoriasis.

To our knowledge, this is the first study to examine trends in incidence, prevalence and mortality of patients with psoriasis and PsA over a prolonged period among the general population in Taiwan. Although the size of the database and the use of recent data (2006–2017) enabled us to investigate these trends robustly and provide contemporary population-based estimates of disease epidemiology and trends over time, some limitations remain that should be considered alongside the current findings. Firstly, prevalent cases could have been misclassified as an incident if individuals did not seek healthcare services shortly after the onset of symptoms. Nevertheless, restricting the incidence analysis period between 2009 and 2017 allowed ample time for prevalent cases to aggregate in the database. Secondly, due to left censorship the prevalence of psoriasis and PsA may have been underestimated in 2006; however, this is a general limitation for all studies using secondary databases. Thirdly, the actual age of incidence may be systematically lower than our estimates, but we assume such an error would be consistent and not affect the observed trends. Fourthly, the current study only includes those people who seek medical care and thereby receive a diagnosis of psoriasis or PsA, but milder cases who do not present for medical care might be missed. This, however, would also be true in other patient populations and probably, is of lesser magnitude in the current study considering the unique setting of highly accessible healthcare services in Taiwan. Fifthly, we did not adjust for all potential confounders (such as socioeconomic status, lifestyle factors (e.g. smoking and alcohol drinking), environmental factors (e.g. residence – urban, suburban, or rural) and comorbidities) in the regression models used to investigate mortality, as many of these confounders are not routinely captured in the NHl claims database. Finally, we did not analyse prevalence and incidence by disease severity, as standardized measures of severity are not routinely captured in the NHl claims database.

In conclusion, this national cohort study estimated the prevalence and incidence of clinically recognized psoriasis and PsA and mortality rates in Taiwan over 12 years. There was an increase in the prevalence of diagnosed psoriasis and PsA in Taiwan between 2006 and 2017, which does not appear to be attributable to a corresponding increase in incidence. The study found an increasing population living longer with psoriasis and PsA in Taiwan, which contributes to the increasing prevalence of the conditions. Nevertheless, patients with psoriasis and PsA had a higher risk of mortality compared with the general population. These findings have important implications for healthcare services and resource allocation.

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