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Incidence, sociodemographic factors and treatment penetration of rheumatoid arthritis and psoriatic arthritis in Norway

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Abstract

Objectives: To evaluate nationwide incidence, sociodemographic associations and treatment penetration of rheumatoid arthritis (RA) and psoriatic arthritis (PsA) in Norway.

Methods: The study combined data from nationwide registries on the total Norwegian adult population (age ≥18). From the Norwegian Patient Registry, incident RA and PsA cases during 2011–2015 were identified with records of first and second healthcare episodes listing RA/PsA diagnostic codes, and ≥1 episode in an internal medicine or rheumatology unit with RA/PsA code during the two-year period after the first episode. Dispensed DMARD prescriptions were obtained from the Norwegian Prescription Database. Persons with dispensed DMARD prescriptions or biologic DMARDs given in hospitals >12 months before the index date were excluded.

Results: Incidence of RA/PsA in Norway was 42/26 per 100,000 person-years (55/28 among women and 28/23 among men). RA peak incidence was observed at ages 70–79 in both sexes, whereas the peak incidence of PsA occurred at ages 50–59. Age- and sex-standardized incidences of RA and PsA were lower among persons with higher education levels. Within a year from the index date, 82.4/57.4% of RA/PsA patients used synthetic DMARDs while 9.4/9.5% used biologic DMARDs.

Conclusions: Register-based incidence estimates for RA and PsA in Norway are similar to other Nordic countries, but slightly higher than in previous Norwegian studies. Furthermore, we found that higher socioeconomic status was associated with lower incidence of both RA and PsA. Although conventional synthetic DMARDs were less often used in early PsA than RA, frequency of biologic DMARD prescriptions was comparable.

Keywords: rheumatoid arthritis, psoriatic arthritis, epidemiology, antirheumatic agents, incidence

Introduction

Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are among the most common chronic inflammatory joint diseases and affect 1–2% of the North-European population[1-4]. Their patterns of disease frequency are considerably different: RA has a clear female predilection and peak incidence at approximately age 70, whereas PsA affects persons with psoriasis with an even sex ratio, and incidence peaks from 40–60.

Incidence and prevalence of RA and PsA are known to have high geographic variability[5-7], with a higher burden of RA detected in Western Europe and North America compared to Eastern Europe, Asia and Africa[5], and a higher burden of PsA in Northern Europe compared to Southern Europe[6]. However, even within a certain geographic area, variability in incidence estimates arises from different methodologies and inclusion criteria between studies[8]. For example, previous attempts to estimate the burden of PsA in Norway have yielded incidences ranging from 6.9/100,000 person-years (PY) in a single regional rheumatology department in Northern Norway[9] to 41.3/100,000 PY based on a questionnaire and verification of diagnosis from hospital records in Central Norway[4]. In addition to incidence estimates in entire populations, identifying subgroups with higher incidences of RA and PsA is important. A gradient of better outcomes with higher socioeconomic status exists for many aspects of health[10]. Evidence suggests that risk of RA is lower among people with high education levels[11, 12], but otherwise research on the associations of socioeconomic factors and incidence of RA and PsA is limited.

An important goal in the treatment of inflammatory joint diseases is early diagnosis. With this in mind, the ACR/EULAR classification criteria for RA were published in 2010[13]. The current, most widely used classification criteria for PsA (ClASsification for Psoriatic ARthritis, CASPAR) were introduced in 2006[14]. Presumably because of a shift towards earlier detection as well as true changes in disease frequency, the epidemiological patterns of both RA and PsA have been changing over time. A recent Danish registry study showed a clear increase in PsA incidence from 7.3 to 27.3/100,000 PY between 1997 and 2010[15]. In contrast, during the 1970s and 1980s, RA incidence seems to have declined[16, 17], whereas more recent studies have mixed results, reporting only a slight to no decrease or even an increase in RA incidence[18-21]. Furthermore, treatment patterns in both RA and PsA have intensified with the

expansion of the armamentarium of disease-modifying antirheumatic drugs (DMARDs) and the treat-to-target approach, emphasized by both RA and PsA treatment recommendations[22, 23]. For these reasons, updated estimates of RA and PsA incidence as well as real-life treatment patterns are warranted[11, 12].

The aim of this study was to provide nationwide and contemporary estimates of RA and PsA incidence in Norway during 2011–2015 and to assess variation in incidence by sociodemographic and geographic factors. We also assess penetration of DMARDs in RA and PsA inception cohorts.

Methods

Data sources

The study was conducted within the Norwegian Cardio-Rheuma Register, which is a nationwide register study with linkage of data on the total adult Norwegian population (age ≥18) between 2008 and 2017 from multiple registries.

Data on episodes in specialized healthcare were retrieved from the Norwegian Patient Registry (NPR), organized under the Norwegian Directorate of Health. NPR holds individual-level information on all specialized healthcare episodes in Norway, both public and private, included in the public reimbursement policy since 2008[24]. Data on primary healthcare is not included in NPR. For all inpatient, day, and outpatient episodes, NPR includes an unlimited number of diagnostic codes, given as ICD-10 codes during the whole study period between 2008 and 2017. NPR also includes medical procedure codes according to the Norwegian classification of medical procedures (NCMP), such as biologic DMARDs given in hospitals. Data quality in NPR is good with regard to completeness of diagnostic codes: in 2015 public somatic hospital records, the main diagnosis was recorded in 100% of contacts[25].

From the Norwegian National Population Register, administered by the Norwegian Tax Administration, we obtained data on date of birth, death and immigration/emigration, sex, municipality of residence, marital status and registration status (resident of Norway or not) as per January 1 each year for individuals who have resided in Norway. Statistics Norway

provided annual data on highest education level and total income. The Norwegian Prescription Database (NorPD) at the Norwegian Institute of Public Health contains data on dispensed prescriptions according to anatomical therapeutic classification (ATC) codes. Data on over-the-counter drugs are not included in NorPD.

The data from the registries were linked by a personal pseudonym based on the unique Norwegian national identity number, and the final dataset was assigned a project-specific serial number by the register keeper (NorPD).

Study population and definitions

The years 2008–2010 served as a washout period to identify prevalent RA/PsA patients, and incident patients were identified from 2011 to 2015. Incident cases in 2016–2017 were not included because a full 2-year time window for diagnostic codes was not available.

Identification of patients relied on ICD-10 codes M05-M06 for RA and M07.0-M07.3 or L40.5 for PsA (Figure 1). No gold standard for ICD-code-based RA and PsA case definitions exists, but higher validity has been demonstrated if a diagnosis is set in specialized care vs. primary care, by internists or rheumatologists compared to other physicians, and when diagnostic codes are required more than once[26-29].

Our base case definition for RA/PsA was based on all of the following four requirements (Figure 1):

1) First inpatient or outpatient episode in NPR with diagnostic ICD-10 code for RA/PsA as main or contributory diagnosis (index date),

2) Second episode with ICD-10 code for RA/PsA within the two-year period following the index date,

3) ≥1 episodes in internal medicine/rheumatology with RA/PsA diagnostic code within the two-year period, and

4) persons who had dispensed DMARD prescriptions or biologic DMARDs given in hospitals >12 months before the index date were regarded as prevalent and thus excluded (list of ATC and NCMP codes given in Supplementary Table S1).

We evaluated the robustness of this case definition with two reference definitions, the "broad" and "strict" definitions. The broad definition was the same as the base case, but criterion 3 was excluded. The strict case definition incorporated the base case definition and a requirement of ≥3 episodes with a recorded diagnostic code for RA/PsA in NPR (Figure 1).

To estimate treatment penetration, we report the proportion of patients with dispensed prescriptions and/or biologic DMARDs given in hospitals during the 12 and 24 months following the index date (ATC and NCMP codes in Supplementary Table S1).

Seropositivity in RA was defined by ICD-10 codes (M05 for seropositive and M06 for seronegative RA). If both M05 and M06 were present, RA cases were defined as seropositive if the number of episodes with recorded M05 code was equal or higher than the number with M06.

Education level was grouped into three: "below upper secondary education", "upper secondary education or post-secondary non-tertiary education", or "higher education". Marital status was categorized as never married, married (or registered partner), or previously married (divorced or widow/widower). Total annual income level was categorized into low, intermediate, and high, with the cut points set to 33rd and 66th percentiles and redefined annually to account for increasing income.

Ethical considerations

The dataset consists of routinely recorded administrative data and no written consent from study subjects was necessary. Approval was obtained from the Norwegian General Data Protection Regulation (16/00482-11/CDG), the South East Health Authority Ethical Committee (2016/588), the Data Protection Officer at Oslo University Hospital (2016/924) and at Diakonhjemmet Hospital (7/12-2019).

Statistical analysis

Crude incidence rates from 2011 to 2015 were calculated with the number of PY at risk in the denominator, which was estimated by calculating the number of people in Norway aged ≥18 each year 2011–2015 multiplied by one year, but excluding cases with prevalent RA/PsA. Standardized incidence rates were calculated using the direct standardization

method with five-year age strata (18–24, 25–29, … 90+). The Norwegian population aged ≥18 on January 1, 2015, was used as the standard population, and 95% confidence intervals (CI) for incidence rates were calculated assuming a Poisson distribution. Statistical analyses were computed using R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

Between 2011 and 2015, we identified 8,116 RA patients and 5,051 PsA patients fulfilling the base case definition (Figure 1). When using the broad case definition, we identified 18%/12% more RA/PsA cases, and by using the strict case definition, 12%/22% less RA/PsA cases. Baseline characteristics of RA and PsA patients were comparable across definitions (Table 1), with RA patients being on average older at the index date and more often female, compared to PsA patients.

Incidence

During 19,434,531 PY, RA incidence per 100,000 PY was 41.8 (95% CI 40.9–42.7) for the base case definition, and the estimate was relatively stable across the three case definitions (49.2 (95% CI 48.2–50.2) for broad definition, and 36.7 (95% CI 35.9–37.6) for strict definition). For seropositive RA (base case definition), incidence per 100,000 PY was 26.7 (95% CI 26.0–27.4) and for seronegative RA 15.1 (95% CI 14.5–15.6). During 19,485,795 PY, PsA incidence per 100,000 PY was 25.9 (95% CI 25.2–26.6) when using the base case definition, 29.0 (95% CI 28.2–29.7) for the broad definition and 20.2 (95% CI 19.6–20.8) for the strict definition.

In sex-specific analyses (base case definition), RA incidence per 100,000 PY was twice as high among women as among men (55.3 (95% CI 53.8–56.8) vs 28.2 (95% CI 27.2–29.3), respectively), whereas PsA incidence among women was 1.2-fold compared to that among men (28.4 (95% CI 27.4–29.5) vs. 23.4 (95% CI 22.5–24.4), respectively). The number of incident cases by calendar year when applying the three case definitions is shown in Supplementary Figure S1.

RA peak incidence was at 70–79 years in both sexes, whereas PsA incidence peaked at 50–59, with smaller variation in incidence across age groups (Figure 2). RA was the predominant diagnosis among older adults. Among those under age 55, PsA incidence was higher than RA incidence among men and almost as high as RA incidence among women. Variation in incidence by case definition was higher in older age groups.

Geographic and sociodemographic variation

Crude and age- and sex-standardized incidence of RA and PsA (base case definition) was lower among those with higher education levels (Supplementary Figure S2 and Figure 3). This difference was apparent in both seropositive and seronegative RA patients (results not shown). Crude incidence of RA and PsA was lower among high- and low-income tertiles than among the intermediate tertile, but after standardization with age, sex and education, only the CIs of low and intermediate groups were not overlapping. Except for the lower incidence of PsA among those who were never married compared to those who were previously married, we found no significant differences in age-, sex-, and education level-standardized incidence of RA and PsA by marital status. Crude and standardized PsA incidence varied considerably between health regions, with the highest incidence in Central Norway and the lowest in Southern and Eastern Norway. RA incidence was slightly lower in Southern and Eastern Norway compared to Central and Western Norway.

Treatment penetration

The penetration of dispensed DMARD prescriptions one and two years after the index date is shown in Table 2. Methotrexate was the most commonly used DMARD in both diseases. Among RA patients and to a lesser extent among PsA patients, penetration of conventional synthetic DMARDs decreased among those above 70 (Figure 4). Methotrexate was the most commonly used conventional synthetic DMARD across age groups (Supplementary Table 2). The proportion of patients with dispensed prescriptions of biologic DMARDs (mostly TNF inhibitors) was comparable in RA and PsA (Table 2). When comparing 10-year age groups between diseases, however, the proportion of biologic DMARD users was somewhat higher among RA patients compared to PsA patients, with a steady decrease with increasing age. The proportion of glucocorticoid users increased with age in both RA and PsA. Supplementary Table S3 shows treatment penetration with conventional synthetic and

biologic DMARDs within one year after the index date by education level, income and health region. Biologic DMARD use was more common among RA patients with higher education and income level.

Discussion

Shedding light on the epidemiology and burden of two of the most common inflammatory joint diseases in Norway, our study provides nationwide contemporary estimates of RA and PsA incidence and their variation with sociodemographic and geographic factors. Our estimates are well aligned with recent Nordic registry studies[11, 15, 30], providing external validation for our findings. Furthermore, the age and sex distribution of RA and PsA followed previously described patterns[11, 31], with RA's peak incidence in the eighth decade and a female–male ratio of 2:1, and peak incidence of PsA in the sixth decade with a female–male ratio of 1.2:1. Although RA incidence was substantially higher than PsA incidence among older adults, the difference was smaller in younger age groups. PsA was more common than RA among men under age 55, highlighting the burden of PsA among the working-age population.

Our findings are highly consistent with previous European population-based studies reporting RA incidence of 30–50/100,000 PY[11, 20, 30]. In contrast, PsA incidence estimates have varied strongly across geographic regions from 3.0 to 41.3/100,000 with a pooled incidence of 8.3/100,000 and with high between-study heterogeneity[6]. Thus, our estimate falls on the high end of previous observations. Furthermore, the incidence of PsA has increased over time. A recent Danish nationwide register study explored secular trends in PsA incidence and discovered a dramatic increase from 7.3 to 27.3/100,000 between 1997 and 2010[15]. A population-based study from Olmsted County, Minnesota, detected a 4% annual rise in PsA incidence in 1970–1999, but incidence remained stable from 2000 to 2017 (8.5/100,000)[32]. A smaller increase in PsA incidence from 9 to 13/100,000 has been reported in Finland from 2000 to 2014[33]. The case definition was based on medication reimbursements in the Finnish study, and thus patients with no DMARD treatment are likely to be underrepresented[33]. The increase in PsA incidence may be related to a true change in PsA frequency or increased recognition of PsA among general practitioners, dermatologists and rheumatologists.

To our knowledge, no Norwegian studies have reported RA incidence in the 2000–2010s nor PsA incidence in the 2010s, reflecting the importance of updated estimates. Our incidence estimate for RA, 42/100,000 PY, was somewhat higher compared to studies from the 1990s in Oslo county (25.7/100,000)[34] and in Troms county (28.7/100,000)[3]. This may be a sign of an increasing incidence of RA in Norway, but may also be related to methodological issues: our study relied on ICD-10 codes in nationwide registries, whereas previous studies used ARA 1987 classification criteria, which have later been criticized as lacking sensitivity in identifying early RA patients. The introduction of the more sensitive ACR/EULAR 2010 classification criteria[13] may have led to an increase in RA diagnoses by refocusing attention on earlier diagnoses, and by allowing more patients with unclassified inflammatory joint disease to be classified as RA[35]. We found considerably higher PsA incidence (26/100,000 PY) compared to a previous study in Northern Norway between 1978 and 1996 (6.9/100,000)[9], supporting a similar increase in PsA diagnoses in Norway to those described in other countries[15, 33].

Our study confirms that the risk of RA is lower among people with higher education levels[11, 36] and extends previous knowledge by showing that the same applies to PsA. A recent Mendelian randomization analysis supported an inverse causative association of education level and RA[12]. In general, educational health inequalities may be explained by behavioural, material and psychosocial risk factors[37]. Both RA and PsA occur due to a combination of genetics; constitutional risk factors such as age, sex and obesity; and environmental factors. The best-documented environmental risk factor for seropositive RA is smoking. In contrast, although smoking increases the risk of psoriasis, results of smoking and risk for PsA are mixed[38, 39]. Our findings may be explained partly by less frequent smoking among those with higher education[40]. Obesity and heavy alcohol consumption, which are linked to lower education, are also risk factors for PsA and may explain our results[8, 41]. Lower education level is not only associated with higher RA risk but also with reduced access to biologic DMARDs[42] and even RA-related mortality[43]. We suggest that socioeconomic status may be considered in implementation of strategies to increase population awareness of inflammatory joint diseases and modifiable risk factors.

We found considerable differences in age-, sex- and education level-standardized incidence of PsA between health regions, with the highest incidence in Central Norway and the lowest in Southern and Eastern Norway. For RA, these differences were substantially smaller. Geographic differences in other health outcomes in Norway such as mortality[44] have been explained by differences in sociodemographic factors and smoking. Prevalence of obesity may be higher in rural vs. urban areas[45] and thus affect risk of PsA. HLA-B27, a genetic risk factor for spondyloarthropathies, is highly prevalent in Northern Norway, and a north–south gradient of HLA-B27 subtypes in Norway has been suggested[46]. In addition, variation in PsA incidence may partly be explained by differences in use of diagnostic codes between rheumatology centres. Of note, our estimate of PsA incidence in Central Norway (39/100,000 PY) was very well aligned with the results of Nord-Trøndelag Health Study 3 (HUNT 3) from Central Norway 2006–2008 (41/100,000 PY). In the HUNT study, PsA diagnoses were validated from medical records and 95.6% fulfilled CASPAR criteria, thus indirectly supporting our case identification method.

We describe real-world treatment patterns of early RA and PsA, based on both dispensed prescriptions and biologic DMARDs given in hospitals. Conventional synthetic DMARD penetration in the total RA cohort within one year from the index date was 82%, but closer to 90% among younger patients and dropping to 50% among those ≥80. Across all age groups, methotrexate was the most commonly used synthetic DMARD. In comparison, a Swedish register-based study showed 84% treatment penetration with synthetic DMARDs[11], whereas over 90% used synthetic DMARDs in a Finnish early RA cohort with case definition relying on medication reimbursements[47]. Glucocorticoids, which have been dose-dependently linked to many detrimental outcomes such as mortality, infections, osteoporosis and cardiovascular disease, were more often used by older RA and PsA patients. While contraindications for DMARDs may be more prevalent among elderly patients, the drastic drop in DMARD penetration accompanied with an increased use of glucocorticoids among 80-year-olds may represent a gap in RA care.

For PsA, approximately 50–60% of patients were started on a conventional synthetic DMARD across all age groups. This reflects the heterogeneity of PsA, and although a significant proportion of PsA patients do well with only NSAIDs, the majority needed

antirheumatic therapy. The 15% rate of biologic DMARD initiation within the first 2 years was similar in RA and PsA, highlighting the role of PsA as a contributor to medication costs in inflammatory joint diseases. Biologic DMARD initiation was highly age-dependent in both diseases, with as many as one in four RA patients and one in six PsA patients in the youngest age group and <10% in patients older than 60 initiating a biologic DMARD within one year of the index date.

In epidemiological studies, case definition is crucial. Our case definition reflects patients with clinically relevant symptoms who require follow-up in specialized care. When we compared our base case definition to broader and stricter definitions, our incidence estimates were relatively robust. We relied on two or more RA/PsA diagnostic codes recorded in specialized care, and in our base case and strict definition, a requirement of an RA/PsA diagnostic code recorded in a rheumatology or internal medicine unit. Despite these measures shown to increase validity of ICD-10 code-based definitions[26-29], misclassification of NPR diagnoses is a potential source of bias. The lack of knowledge on fulfilment of classification criteria for RA[13] and PsA[14] is a limitation. PsA especially is heterogeneous in clinical presentation, and studies examining PsA prevalence among psoriasis populations have found that underdiagnosis of mild PsA is very common[48]. Furthermore, we did not have data on serology of patients, and our definition of RA patients' serological status based on ICD-10 codes is a rough approximation.

Another challenge to assessing the incidence of a relapsing-remitting disease based on administrative data is how to accurately estimate time of diagnosis. We used a three-year washout period to identify prevalent cases based on DMARD prescriptions and hospital records. To prevent misclassification of prevalent cases as incident cases, we excluded all patients with DMARDs more than one year prior to their first recorded RA/PsA diagnostic code. Although our PsA incidence estimate was stable between 2011 and 2015, our RA incidence estimate slightly declined, which may not represent a true trend but misclassification of prevalent cases as incident cases during the earlier years. Longer washout periods of ≥5 years may reduce this bias as shown in systemic lupus erythematosus[49]. Despite this, when limiting RA incidence analysis to 2013–2015 with a five-year washout period, our incidence estimate remained similar (39 vs 42/100,000 PY).

In conclusion, our contemporary estimates of RA and PsA incidence are somewhat higher than in previous Norwegian studies but well-aligned with more recent Nordic studies. Importantly, higher socioeconomic status seems to be associated with lower risk of both RA and PsA, even in a high-income setting like Norway. Our findings may aid in predicting the need for the rheumatology workforce as well as the development of screening and prevention strategies for RA and PsA.

Data availability statement

The data underlying this study cannot be shared because release could compromise privacy of study subjects.

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Tables

Table 1. Patient characteristics. Characteristics of incident RA and PsA cases based on three different definitions, and proportion of cases with overlapping rheumatic diseases.

	Rheumatoid arthritis			Psoriatic arthritis		
Definition	**Broad**	**Base case**	**Strict**	**Broad**	**Base case**	**Strict**
N	9,548	8,116	7,146	5,638	5,051	3,937
Women, n (%)	6,468 (67.7)	5,377 (66.3)	4,754 (66.5)	3,158 (56.0)	2,778 (55.0)	2,133 (54.2)
Age at index date, median (IQR)	61.6 (49.6-71.6)	60.9 (48.8-70.9)	60.5 (48.5-70.1)	50.9 (40.9-60.3)	50.5 (40.6-59.8)	50.0 (40.3-59.4)
RF positive, n (%)	6,163 (64.5)	5,188 (63.9)	4753 (66.5)	NA	NA	NA
Episodes with RA/PsA diagnostic code within 2 yrs from index date, median (IQR)	5 (3-8)	5 (3-8)	6 (4-9)	4 (3-6)	4 (3-7)	5 (4-7)
≥2 diagnostic codes for other RMDs[a], n (%)						
Rheumatoid arthritis	NA	NA	NA	326 (5.8)	273 (5.4)	229 (5.8)
Psoriatic arthritis	318 (3.3)	241 (3.0)	176 (2.5)	NA	NA	NA
Axial spondyloarthritis[b]	191 (2.0)	136 (1.7)	97 (1.4)	256 (4.5)	239 (4.7)	175 (4.4)
Systemic connective tissue disorders[c]	376 (3.9)	314 (3.9)	267 (3.7)	124 (2.2)	112 (2.2)	89 (2.3)
Enteropathic arthritis[d]	3 (0.0)	3 (0.0)	3 (0.0)	22 (0.4)	22 (0.4)	18 (0.5)
Any of the above	845 (8.9)	657 (8.1)	517 (7.2)	685 (12.1)	609 (12.1)	482 (12.2)

[a]Overlap with other rheumatic diseases was defined as presence of diagnostic codes for the disease of interest on ≥2 occasions in NPR
[b]Diagnostic codes M45, M46.0, M46.1, M46.9
[c]M30-M36, comprising polyarteritis nodosa and related conditions, other necrotising vasculopathies, systemic lupus erythematosus, dermatopolymyositis, systemic sclerosis, other systemic involvement of connective tissue (incl. Sjögren's syndrome), and systemic disorders of connective tissue in diseases classified elsewhere
[d]M07.4, M07.5

Abbreviations: SD, standard deviation; IQR, interquartile range; RF, rheumatoid factor; RMD, rheumatic disease; NPR, National Patient Register

Table 2. Use of DMARDs and glucocorticoids among early RA and PsA cases. Proportion of RA and PsA cases (base case definition) with dispensed prescriptions for DMARDs and/or oral glucocorticoids. For biologic DMARDs, hospital-given infusions were also included.

	Rheumatoid arthritis		Psoriatic arthritis	
	12 months	**24 months**	**12 months**	**24 months**
Any conventional synthetic DMARD	6687 (82.4)	6860 (84.5)	2897 (57.4)	3183 (63.0)
Methotrexate	6228 (76.7)	6436 (79.3)	2637 (52.2)	2932 (58.0)
Leflunomide	389 (4.8)	590 (7.3)	228 (4.5)	347 (6.9)
Sulfasalazine	745 (9.2)	1034 (12.7)	330 (6.5)	456 (9.0)
Hydroxychloroquine	574 (7.1)	745 (9.2)	24 (0.5)	28 (0.6)
Any biologic DMARD	759 (9.4)	1228 (15.1)	479 (9.5)	764 (15.1)
TNF-inhibitors	690 (8.5)	1136 (14.0)	471 (9.3)	751 (14.9)
Oral glucocorticoids	5858 (72.2)	6199 (76.4)	1446 (28.6)	1804 (35.7)
Any DMARD or glucocorticoids	7493 (92.3)	7634 (94.1)	3377 (66.9)	3715 (73.5)

Abbreviations; DMARD, disease-modifying antirheumatic drug; TNF, tumour necrosis factor

Figures

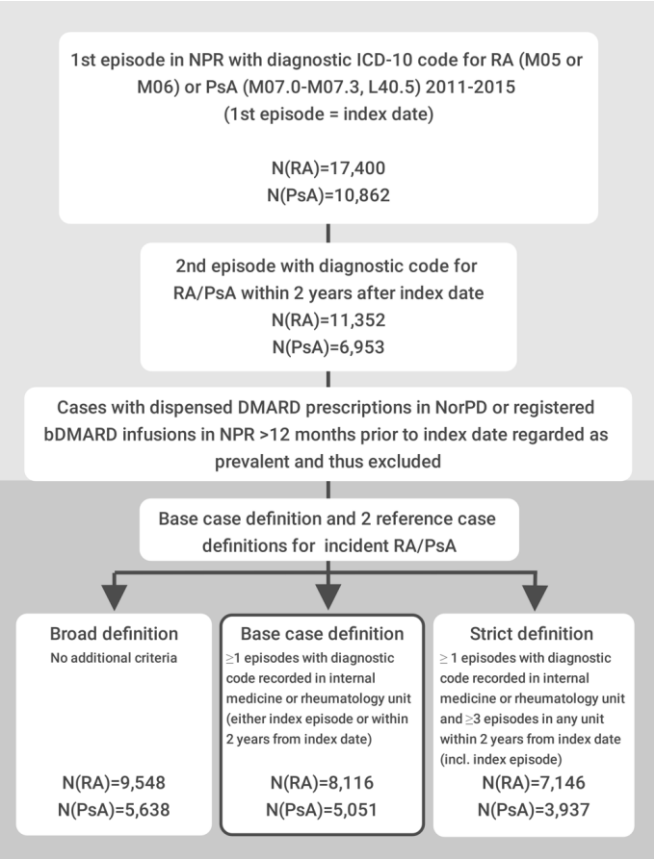


Figure 1. **Study flow chart.** Number of cases with rheumatoid arthritis (RA) and psoriatic arthritis (PsA) according to broad, base case and strict definition are given in the bottom boxes.

Abbreviations: NPR, Norwegian Patient Register; DMARD, disease-modifying antirheumatic drugs; bDMARD, biologic DMARD; NorPD, Norwegian Prescription Database

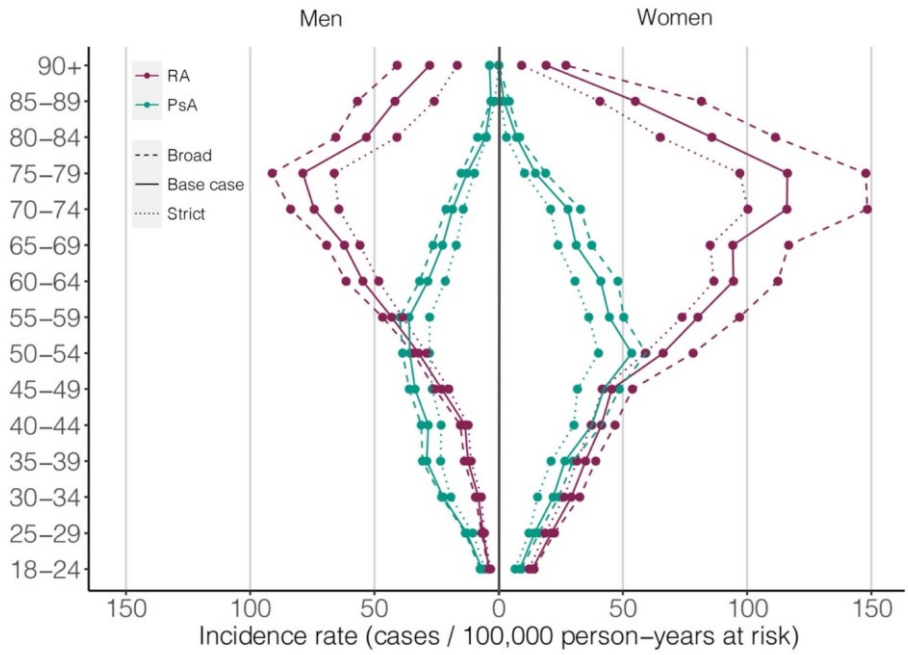


Figure 2. Incidence rate of RA and PsA by age and sex. Incidence of RA and PsA is given in age- and sex-specific strata and three different definitions of index disease.

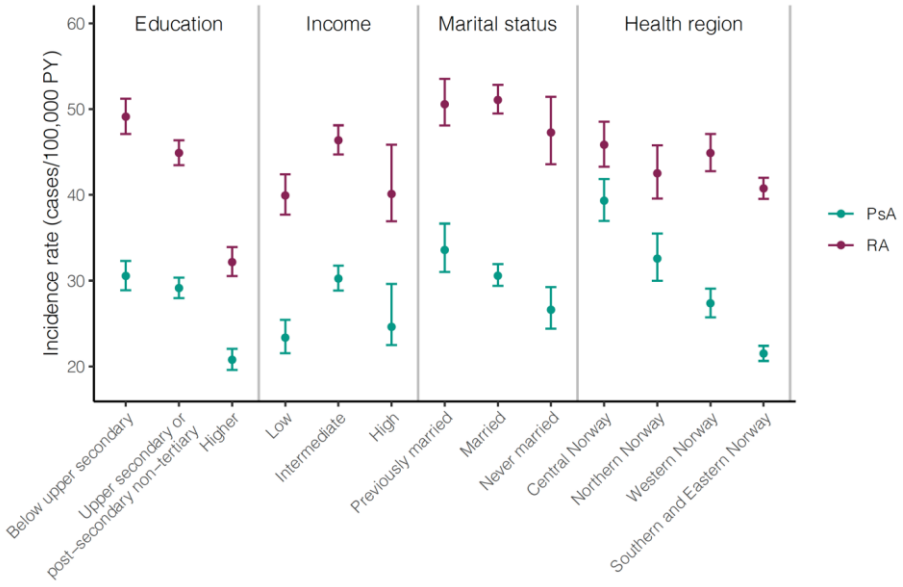


Figure 3. Standardized incidence of RA and PsA by sociodemographic factors and health region.

Standardized incidence of RA and PsA (base case definition) with 95% confidence intervals by education level, total income, marital status and health region. For subgroups by education level, we standardized for age in 5-year strata and sex. For subgroups by marital status, income and health region, we standardized for age, sex and education. We used 2015 Norwegian population ≥18 years as the standard, but for subgroups by marital status, standardized incidences were calculated for people aged ≥30 because of the low number of previously married people aged <30.

Abbreviations: PY, person-years

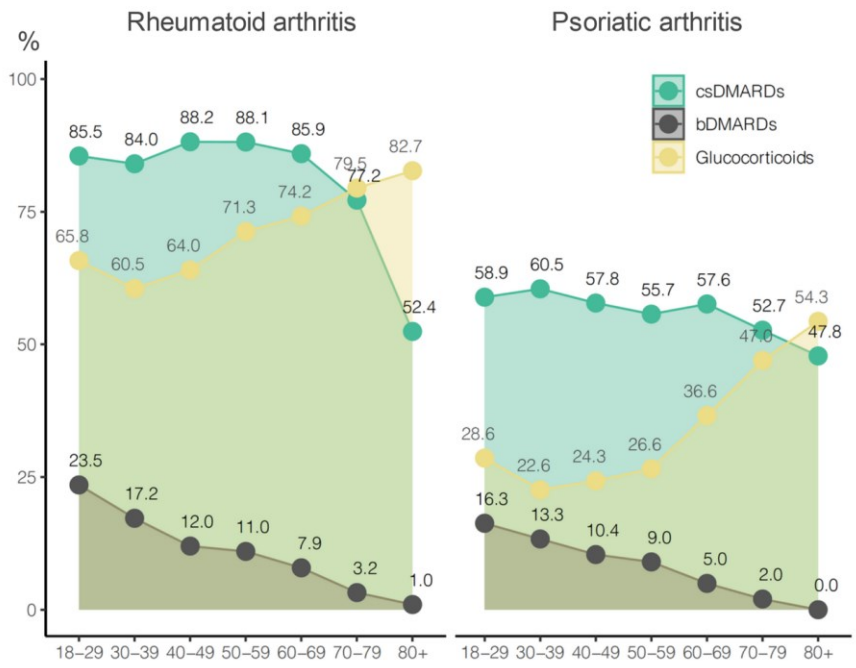
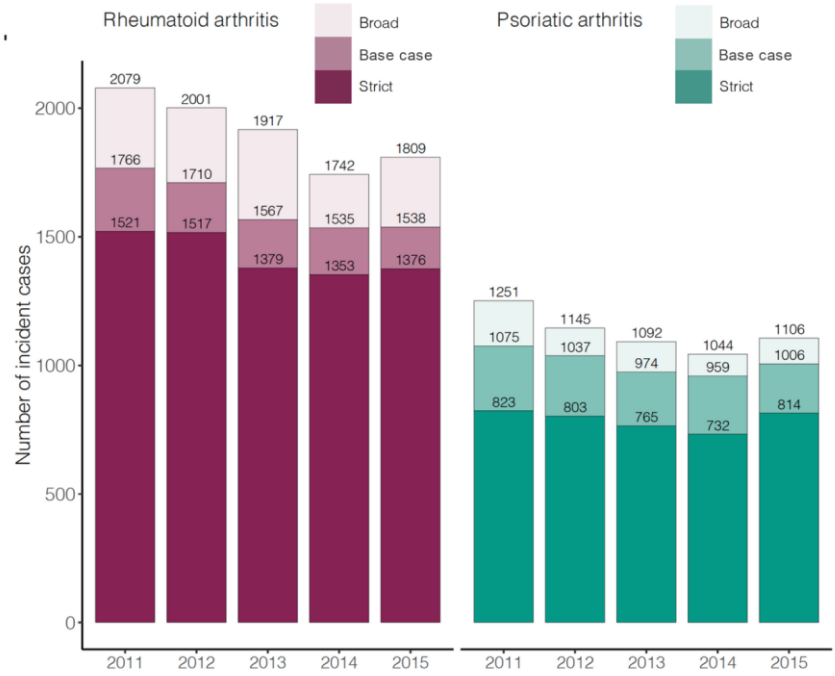


Figure 4. Treatment patterns of early RA and PsA by age. Use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologic DMARDS (bDMARDs) and glucocorticoids among RA and PsA cases (base case definition) within 12 months after index date by age.

Supplemental material

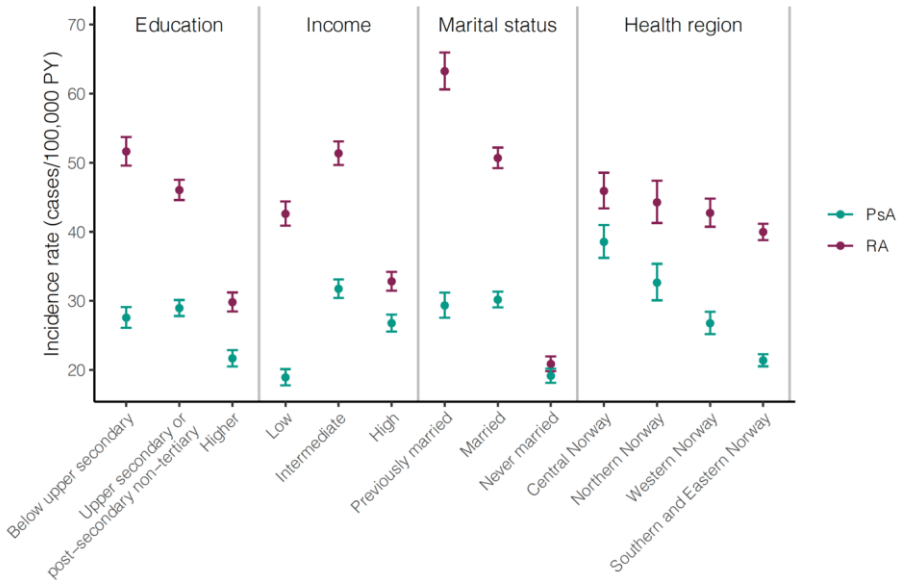
Supplementary table S1. Anatomical Therapeutic Chemical (ATC) codes for dispensed pharmacological prescriptions from pharmacies and Norwegian Classification of Medicinal Procedures (NCMP) codes for biologic drugs given in hospitals

Drug	ATC code	NCMP codes	Used to identify prevalent RA	Used to identify prevalent PsA
csDMARDs				
Methotrexate	L04AX03, L01BA01		x	x
Hydroxychloroquine	P01BA02		x	x
Sulfasalazine	A07EC01		x	x
Leflunomide	L04AA13		x	x
Azathioprine	L04AX01		x	x
Cyclosporine	L04AD01			
Gold preparations	M01CB		x	
bDMARDs				
Etanercept	L04AB01	4AB01	x	x
Infliximab	L04AB02	4AB02	x	x
Adalimumab	L04AB04	4AB04	x	x
Certolizumab pegol	L04AB05	4AB05	x	x
Golimumab	L04AB06	4AB06	x	x
Rituximab	L01XC02	1XC02	x	
Tocilizumab	L04AC07	4AC07	x	
Anakinra	L04AC03	4AC03	x	
Abatacept	L04AA24	4AA24	x	x
Secucinumab	L04AC10			x
Ustekinumab	L04AC05			x
Glucocorticoids	H02AB			



	2011	2012	2013	2014	2015	2011	2012	2013	2014	2015
Broad	55.1	52.3	49.3	44.2	45.4	33.1	29.8	28.0	26.4	27.7
Base case	46.8	44.6	40.2	38.9	38.5	28.4	27.0	25.0	24.2	25.1
Strict	40.3	39.6	35.4	34.3	34.4	21.7	20.9	19.6	18.5	20.3

Supplementary Figure S1. Bar plot shows number of incident RA and PsA cases based on three different definitions (broad, base case and strict) by calendar year, and the table below shows respective incidence rates (cases/100,000 person-years at risk)



Supplementary Figure S2. Crude incidence rate of RA and PsA (base case definition) with 95% confidence intervals in subgroups by education level, total income, marital status and health region.

Abbreviations: PY, person-years

Supplementary Table S2. Treatment penetration with the most common conventional synthetic DMARDs within 12 months after index date by age group in both rheumatoid arthritis (RA) and psoriatic arthritis (PsA), given as percentages of the respective age group. RA and PsA cases were defined according to the base case definition.

	Methotrexate	Leflunomide	Sulfasalazine	Hydroxychloroquine
RA				
18-29	72.7	2.1	18.8	7.1
30-39	73.9	3.1	16.4	8.4
40-49	83.4	5.0	10.4	8.4
50-59	84.2	5.9	9.9	8.7
60-69	81.3	4.7	8.1	7.1
70-79	71.3	5.4	5.6	5.2
80+	47.7	3.7	2.3	3.1
PsA				
18-29	51.9	2.8	11.0	0.0
30-39	54.3	3.3	9.5	0.4
40-49	52.2	5.3	7.6	0.5
50-59	51.7	4.7	5.0	0.4
60-69	52.4	5.1	4.1	0.7
70-79	50.0	4.4	2.0	0.7
80+	41.3	6.5	0.0	2.2

Supplementary Table S3. Treatment penetration (%) with conventional synthetic and biologic DMARDs within 12 months after index date by education level, income and health region in rheumatoid arthritis (RA) and psoriatic arthritis (PsA) (base case definition).

		RA			PsA		
		Total, n	csDMARDs, n (%)	bDMARDs, n (%)	Total, n	csDMARDs, n (%)	bDMARDs, n (%)
Education	Below upper secondary	2,417	1,940 (80.3)	174 (7.2)	1,296	741 (57.2)	113 (8.7)
	Upper secondary or post-secondary non-tertiary	3,830	3,204 (83.7)	351 (9.2)	2,415	1,425 (59.0)	235 (9.7)
	Higher	1,800	1,482 (82.3)	221 (12.3)	1,311	710 (54.2)	130 (9.9)
Income	Low	2,304	1,834 (79.6)	179 (7.8)	1,028	568 (55.3)	82 (8.0)
	Intermediate	3,504	2,866 (81.8)	294 (8.4)	2,173	1,251 (57.6)	210 (9.7)
	High	2,257	1,961 (86.9)	286 (12.7)	1,843	1,074 (58.3)	186 (10.1)
Health region	Southern and Eastern Norway	4,363	3,519 (80.7)	467 (10.7)	2,342	1,357 (57.9)	276 (11.8)
	Central Norway	1,230	1,041 (84.6)	86 (7.0)	1,035	643 (62.1)	81 (7.8)
	Western Norway	1,709	1,437 (84.1)	154 (9.0)	1,073	552 (51.4)	72 (6.7)
	Northern Norway	814	690 (84.8)	52 (6.4)	601	345 (57.4)	50 (8.3)