ORIGINAL ARTICLE

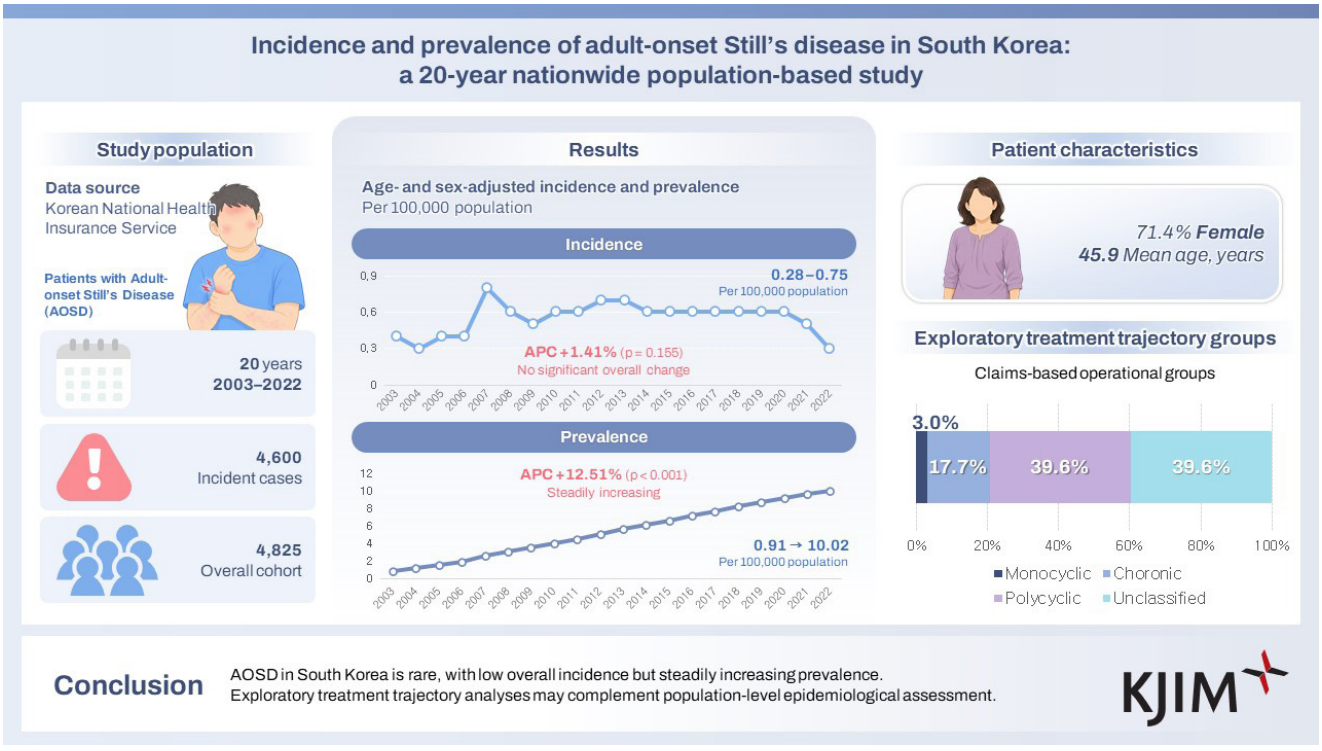
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KJIM

Incidence and prevalence of adult-onset Still's disease in South Korea: a 20-year nationwide population-based study

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Background/Aims: Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder with limited population-based epidemiological data. We estimated the nationwide incidence and prevalence of AOSD in South Korea and assessed temporal trends. As a secondary exploratory aim, we also examined claims-based treatment trajectories.

Methods: We conducted a nationwide retrospective cohort study using Korean National Health Insurance Service claims data from 2002 to 2022. Annual incidence and prevalence were age- and sex-standardised to the 2019 Korean population. Temporal trends were evaluated using log-linear regression and one-joinpoint analyses. Patients were additionally grouped according to claims-based medication trajectories.

Results: Among 15,000 individuals with an AOSD diagnostic code, 4,825 met the case definition; 4,600 incident cases diagnosed during 2003–2022 were included. Age- and sex-adjusted annual incidence remained below 1 per 100,000 pop-

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ulation (0.28–0.75), with no significant overall temporal change (annual percent change [APC], 1.41%; 95% confidence interval [CI], –0.58 to 3.44; $p = 0.155$). Age- and sex-adjusted prevalence increased from 0.91 per 100,000 in 2003 to 10.02 per 100,000 in 2022 (APC, 12.51%; 95% CI, 10.56 to 14.50; $p < 0.001$). Across successive 5-year periods, the proportion of female patients decreased from 72.9% to 66.1%, whereas mean age at diagnosis increased from 41.7 to 47.5 years. Under prespecified operational rules, 3.0% of patients were grouped as monocyclic, 39.6% as polycyclic, 17.7% as chronic, and 39.6% as unclassified.

Conclusions: AOSD in South Korea is rare, with low overall incidence but steadily increasing prevalence. Exploratory treatment trajectory analyses may complement population-level epidemiological assessment.

Keywords: Still's disease, adult-onset; Epidemiology; Administrative claims, healthcare

INTRODUCTION

Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder with a poorly defined global epidemiological profile [1,2]. Because of its low prevalence and the paucity of large-scale, population-based studies, most available data come from hospital-based case series, small cohorts, or regional surveys, which limits generalisability. Reported incidence ranges from 0.16 to 0.62 per 100,000 persons [3-6], and prevalence from 0.10–0.34 per 100,000 in Poland to 6.77 per 100,000 in Türkiye [4,6,7], supporting the classification of AOSD as an orphan disease. AOSD typically affects young adults and may show a bimodal age distribution, with peaks at 15–25 and 36–46 years [2]. Most studies report a female predominance, with female-to-male ratios of 1.4:1 to 3.2:1 [6-11], although slight male predominance has been observed in cohorts from Northern Norway and Italy [5,12,13], suggesting regional or methodological variability.

The disease course of AOSD is commonly classified according to the scheme proposed by Cush et al. [14] in 1987, based on longitudinal follow-up of 21 patients. Three patterns were described: monocyclic (a single self-limited systemic flare), polycyclic (recurrent flares separated by remission), and chronic articular (persistent progressive arthritis). The reported distribution of these patterns varies widely across studies and is strongly influenced by study design and follow-up duration [2,3,8,15]. In Korea, two single-centre studies yielded conflicting results: one found a predominance of the monocyclic pattern, with relatively few polycyclic cases [8], whereas the other reported nearly equal proportions of monocyclic and polycyclic courses [8,16]. Similar heterogeneity in disease-course patterns has been described in other countries [5,6,15,17].

In light of these uncertainties, robust nationwide data on the epidemiology of AOSD are still lacking. Using National Health Insurance Service (NHIS) claims data and an operational case definition, our primary aim was to estimate the annual incidence and prevalence of AOSD in South Korea and to assess temporal trends. As a secondary exploratory aim, we also investigated claims-based treatment trajectories in patients with AOSD.

METHODS

Study design, database, and study population

We conducted a nationwide retrospective cohort study using claims data from the Korean NHIS from 2002 to 2022 (Supplementary Fig. 1). The NHIS database contains information on healthcare utilisation and reimbursement for virtually the entire Korean population; 97% are covered by the NHIS and the remaining 3% by the Medical Aid programme [18]. Claims were obtained from the qualification and contribution files, death registry, claims statements, treatment and diagnosis details, prescription records, and medical institution registry. Available variables included sex, birth year, region, principal and up to five secondary diagnosis codes, treatment dates, and detailed prescription data (dose, duration, drug class). Mid-year population denominators were obtained from the Korean Statistical Information Service (KOSIS).

All inpatient and outpatient claims from medical institutions between 2002 and 2022 were screened. We first identified records with a principal or secondary diagnostic code for AOSD (International Classification of Diseases [ICD]

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M06.1, M06.10–M06.19; Supplementary Table 1). To enhance diagnostic specificity, a conservative case definition was applied, combining diagnostic codes with treatment intensity and duration: (1) the first AOSD code (index date) recorded at a general or tertiary hospital; (2) ≥ 3 outpatient visits or ≥ 1 hospital admission with AOSD within 3 months of the index date; and (3) prescription of prednisolone ≥ 15 mg/day (or equivalent) for ≥ 3 consecutive days within 14 days of the index date. Patients were excluded if, within ± 3 months of the index date, they had diagnostic codes for (i) other autoimmune diseases (Korean Standard Classification of Diseases, KCD M02, M03, M05–M09, M30–M35, M45, K50, K51) or (ii) malignancy (KCD C00–C97) (Supplementary Table 2). To support the validity of the claims-based case definition, we also applied the same algorithm stepwise to the single-centre electronic medical record (EMR) dataset of Konyang University Hospital for the same study period. Patients with at least one AOSD code were identified, after which the washout period, healthcare-utilisation criterion, steroid criterion, and exclusion criteria were sequentially applied using EMR records. Manual chart review was performed to examine the clinical validity of the identified cases and to assess reasons for exclusion or potential misclassification, particularly in relation to the exclusion-based diagnostic process of AOSD.

The study was approved by the Institutional Review Board of Konyang University Hospital (IRB No. KYUH 2024-06-003), and all procedures followed relevant ethical guidelines using anonymised claims data.

Epidemiological metrics

Incidence rate

To identify newly diagnosed cases, we applied a oneyear washout period and excluded data from 2002 from incidence calculations. Annual incident cases between 2003 and 2022 were defined as patients with their first qualifying AOSD diagnosis in a given year and no AOSD code in the preceding 12 months. In accordance with current disease definitions, which classify patients < 16 years of age as having juvenileonset Still's disease, individuals aged 0–14 years were excluded from the denominator [19]. Those aged 15 years were retained because population data were available in fiveyear age bands, although this group may include a small proportion of paediatriconset cases. The annual incidence rate was calculated as:

- *Incidence rate = (number of new AOSD cases in year X / mid-year population aged ≥ 15 years in year X)* × *100,000*

Prevalence rate

Annual prevalence was defined as the number of patients with at least one AOSD claim that satisfied the case definition during a given calendar year, divided by the midyear population aged ≥ 15 years for that year:

- *Prevalence rate = (number of AOSD cases in year X / total mid-year population aged ≥ 15 years in year X)* × *100,000*

Age- and sex-standardisation

To facilitate comparisons over time and between subgroups, we performed direct standardisation using the 2019 Korean mid-year population as the reference population. The 2019 population was selected as a representative mid-period reference for the study period to avoid undue influence of early- or late-period demographic structures. Age- and sex-specific rates were applied to the standard population, and the weighted values were summed to obtain age-adjusted, sex-adjusted, and age- and sex-adjusted incidence and prevalence rates:

- *Standardised rate* = Σ *(age- and sex-specific rate* × *standard population proportion)*

Descriptive characteristics of incident cases

Patients identified as incident cases were further analysed for demographic and clinical characteristics at diagnosis. Incident AOSD cases were stratified into four consecutive 5-year intervals (2003–2007, 2008–2012, 2013–2017, and 2018–2022). We extracted sex, age (mean ± standard deviation [SD]), and insurance type (National Health Insurance vs. Medical Aid). Initial pharmacotherapy was defined as any prescription for corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologic DMARDs (bDMARDs), targeted synthetic DMARDs (tsDMARDs), or other immunosuppressants within the first 3 months after the index date; both drug classes and individual agents were recorded (Supplementary Table 3).

Exploratory claims-based treatment trajectory grouping

As a secondary exploratory analysis, patients in the overall AOSD cohort (n = 4,825) were grouped according to longi-

tudinal medication-use patterns in the claims setting using prespecified operational rules (Table 1). Prescription records were converted into daily-level data, overlapping prescription days were merged, and the last treatment date was determined from the final prescription while accounting for drug-specific dosing intervals (e.g., weekly dosing for methotrexate). AOSD-related medications considered for this grouping included corticosteroids, csDMARDs, bDMARDs, tsDMARDs, and other immunosuppressants; NSAIDs were excluded. Patients were grouped as monocyclic, polycyclic, chronic, or unclassified according to treatment duration and medication-free intervals as defined in Table 1. These categories were intended as pragmatic claims-based proxies for longitudinal medication trajectories rather than clinically validated disease-course subtypes. To provide supplementary clinical context, we additionally compared these operational categories with chart-reviewed disease-course patterns in the single-centre EMR dataset.

Statistical analysis

Annual trends in AOSD incidence and prevalence were evaluated using age-adjusted, sex-adjusted, and age- and sex-adjusted rates per 100,000 population from 2003 to 2022. For each annual rate series, we modelled the natural logarithm of the rate as a linear function of calendar year. Annual percent change (APC) and 95% confidence intervals (CIs) were derived from the year coefficient (β) as (e^{β}–1) × 100.

To assess changes in temporal trends, a one-joinpoint segmented log-linear model was fitted to each series. Candidate joinpoints were examined across calendar years, requiring at least three observations in each segment. The optimal joinpoint was selected using the Bayesian information criterion, and the segmented model was compared with the corresponding linear model by analysis of variance. APCs were then estimated separately for the periods before and after the identified joinpoint.

The annual numbers of incident and prevalent AOSD cases and the baseline demographic and clinical characteristics of the incident cohort were summarised descriptively. Categorical variables were expressed as frequencies and percentages, and continuous variables as means with SD or medians with interquartile ranges, as appropriate. Baseline demographic and clinical characteristics across the exploratory claims-based treatment trajectory groups were also summarised descriptively for supplementary presentation

Table 1. Prespecified operational rules for exploratory claims-based treatment trajectory grouping in AOSD

Disease course	Time frame (initial period)	Medication use (initial treatment)	Medication use (follow-up period)	Interpretation
Monocyclic[a]	In the first year following the index date	Total of ≥ 180 days of prescriptions for ≥ 1 AOSD-related medications[b]	No further prescriptions for any AOSD-related medication for the subsequent 72 months or until the end of observation, whichever came first, after the last medication date (prescription date plus supply days)	Sustained treatment-free period during follow-up
Polycyclic[a]	In the first year following the index date	Total of ≥ 180 days of prescriptions for ≥ 1 AOSD-related medications	Re-initiation of ≥ 1 AOSD-related medication after a drug-free interval of ≥ 6 months before the end of observation	Treatment re-initiation after a prolonged drug-free interval
Chronic[a]	In the first year following the index date	Total of ≥ 300 days of prescriptions for ≥ 1 AOSD-related medication	–	Sustained high treatment burden during the first year
Unclassified[a]	–	–	–	Did not meet criteria for any of the predefined operational treatment trajectory groups

AOSD, adult-onset Still's disease; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs, biologic disease-modifying anti-rheumatic drugs; tsDMARDs, targeted synthetic disease-modifying anti-rheumatic drugs.
[a]Operational group.
[b]AOSD-related medications include corticosteroids, csDMARDs, bDMARDs, tsDMARDs, and immunosuppressants.

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only. All analyses were conducted using SAS version 7.15 (SAS Institute Inc., Cary, NC, USA) and R version 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Incident cases of AOSD

A total of 15,000 individuals with an AOSD diagnostic code were identified between 2002 and 2022. After applying the predefined inclusion and exclusion criteria, 4,825 patients formed the final AOSD cohort (Fig. 1). For epidemiological analyses of incidence and prevalence, data from 2002 were excluded, yielding 4,600 eligible patients diagnosed between 2003 and 2022.

Supplementary EMR-based validation of the operational definition

We applied the same stepwise operational definition to the single-centre EMR dataset of Konyang University Hospital as a supplementary validation analysis (Supplementary Table 4). Of 82 patients with at least one AOSD code recorded between 2002 and 2022, 71 remained after the 1-year washout period and 61 after application of the healthcare-utilisation criterion. After the steroid criterion was applied, 41 patients remained, among whom 28 were confirmed as having AOSD on chart review (positive predictive value [PPV], 68.3%). After application of the exclusion criteria, 24 patients remained, including 20 chart-confirmed AOSD cases (PPV, 83.3%). Among the 17 patients excluded at the final step, 8 were judged to have true AOSD on detailed chart review.

Epidemiological metrics

Incidence rate

Crude annual incidence rates were below 1 per 100,000 population in all study years, ranging from 0.31 to 0.70 per 100,000 population (Supplementary Table 5, Supplementary Fig. 2). Crude annual incidence rate was 0.39 per 100,000 population in 2003 and 0.34 per 100,000 population in 2022. In sex-stratified analyses, incidence was consistently higher in females than in males. Age-specific incidence was highest in adults aged 30–39 and 40–49 years and lowest in adolescents and adults aged ≥ 70 years.

Prevalence rate

Crude annual prevalence increased steadily throughout the study period, from 0.97 per 100,000 population in 2003 to 9.82 per 100,000 population in 2022 (Supplementary Table 6, Supplementary Fig. 3). In sex-stratified analyses, prevalence was consistently higher in females than in males. Age-spe-

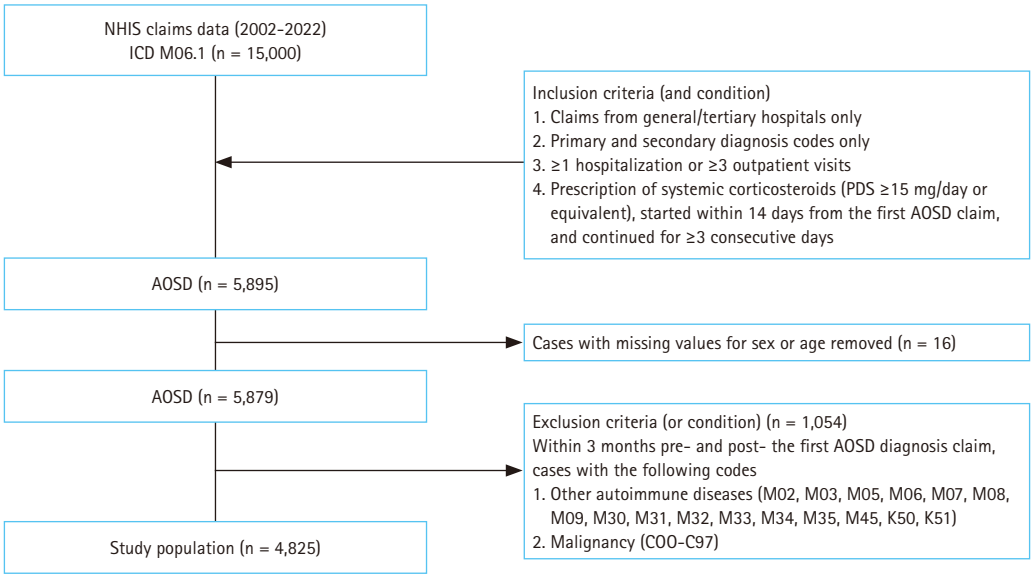


Figure 1. Flow diagram of patient selection for adult-onset Still's disease (AOSD) from the Korean National Health Insurance Service (NHIS) database. The diagram illustrates the stepwise identification of patients with adult-onset Still's disease using diagnostic codes, treatment criteria, and exclusion rules applied to nationwide claims data between 2002 and 2022. ICD, International Classification of Diseases; PDS, prednisolone.

cific prevalence was highest among individuals aged 30–39 years and lowest among adolescents and those aged ≥ 80 years.

Adjusted rates

Age-adjusted, sex-adjusted, and age- and sex-adjusted rates, standardised to the 2019 Korean population, are presented in Table 2 and Figure 2. Across all study years, differences between adjustment methods were small (≤ 0.06 per 100,000 for incidence and ≤ 0.20 per 100,000 for prevalence). For incidence, age- and sex-adjusted rates remained below 1 per 100,000 population, ranging from 0.28 in 2004 to 0.75 in 2007. For prevalence, adjusted rates increased steadily from approximately 0.91 per 100,000 population in 2003 to 10.02 per 100,000 population in 2022, with only modest variation according to the adjustment method.

Annual trends in incidence and prevalence

From 2003 to 2022, the APC in the age- and sex-adjusted incidence rate was 1.41% (95% CI, –0.58 to 3.44; p = 0.155). In the one-joinpoint segmented analysis, the optimal joinpoint for the age- and sex-adjusted incidence rate was identified in 2007, with APCs of 20.97% before 2007 and –1.17% after 2007 (ΔBIC = –12.60; $p = 3.29 \times 10^{-4}$). Over the same period, the APC in the age- and sex-adjusted prevalence rate was 12.51% (95% CI, 10.56 to 14.50; $p = 3.34 \times 10^{-11}$). In the one-joinpoint segmented analysis, the optimal joinpoint for the age- and sex-adjusted prevalence rate was identified in 2009, with APCs of 27.81% before 2009 and 7.96% after 2009 (ΔBIC = –56.67; $p = 1.90 \times 10^{-12}$). APC estimates for the age-adjusted and sex-adjusted incidence and prevalence rates are provided in Supplementary Table 7.

Table 2. Age-, sex-, and age- and sex-adjusted incidence and prevalence rates of AOSD per 100,000 in South Korea (2003–2022)[a)]

Year	Adjusted incidence rate (per 100,000)			Adjusted prevalence rate (per 100,000)		
	Age-adjusted	Sex-adjusted	Age- and sex-adjusted	Age-adjusted	Sex-adjusted	Age- and sex-adjusted
2003	0.37	0.39	0.37	0.92	0.96	0.91
2004	0.28	0.31	0.28	1.18	1.25	1.17
2005	0.40	0.43	0.40	1.56	1.66	1.55
2006	0.44	0.46	0.44	1.95	2.08	1.94
2007	0.76	0.70	0.75	2.67	2.74	2.65
2008	0.55	0.53	0.55	3.15	3.21	3.13
2009	0.54	0.52	0.53	3.63	3.68	3.61
2010	0.57	0.57	0.57	4.10	4.16	4.07
2011	0.56	0.56	0.56	4.58	4.65	4.56
2012	0.69	0.66	0.68	5.18	5.22	5.16
2013	0.66	0.64	0.65	5.72	5.76	5.70
2014	0.59	0.57	0.59	6.22	6.25	6.21
2015	0.57	0.57	0.57	6.67	6.71	6.66
2016	0.64	0.63	0.63	7.19	7.23	7.18
2017	0.60	0.60	0.60	7.70	7.74	7.69
2018	0.63	0.63	0.63	8.24	8.26	8.23
2019	0.61	0.61	0.61	8.74	8.74	8.74
2020	0.57	0.57	0.57	9.25	9.21	9.26
2021	0.52	0.53	0.52	9.71	9.60	9.72
2022	0.34	0.35	0.34	10.01	9.82	10.02

AOSD, adult-onset Still's disease.
[a)]Direct standardisation to the 2019 Korean population was applied to obtain age-adjusted, sex-adjusted, and age-and sex-adjusted rates.

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Demographic and clinical characteristics

The baseline demographic and clinical characteristics of incident AOSD patients according to diagnosis period are presented in Table 3. A total of 4,600 incident patients were identified between 2003 and 2022, including 901 in 2003–2007, 1,187 in 2008–2012, 1,310 in 2013–2017, and 1,202 in 2018–2022. Overall, 3,283 patients (71.4%) were female, and the mean age at diagnosis was 45.9 years (SD, 16.8). The proportion of female patients was 72.9%, 74.8%, 72.1%, and 66.1% across the four periods, respectively, and the corresponding mean ages at diagnosis were 41.7, 45.5, 47.7, and 47.5 years. Overall, 4,476 patients (97.3%) were health insurance beneficiaries, 124 (2.7%) received medical aid, and 444 (9.7%) had disability.

During the first three months after diagnosis, 3,178 patients (69.1%) received csDMARDs, 1,378 (30.0%) immunosuppressants, 311 (6.8%) bDMARDs, and 15 (0.3%) tsDMARDs. Methotrexate (57.7%) and hydroxychloroquine (33.8%) were the most commonly used csDMARDs, whereas cyclosporine (18.4%) and tacrolimus (8.7%) were the most frequently used immunosuppressants. Tocilizumab was the most commonly used bDMARD (5.2%). NSAIDs and corticosteroids were prescribed in 97.0% and 97.6% of patients, respectively.

Corticosteroids and NSAIDs dominated initial therapy throughout (> 90%), with csDMARDs stabilising at around 70% after early expansion (Supplementary Fig. 4). Immunosuppressant use increased progressively (24.3% to 33.7%), reflecting steroid-sparing strategies. The use of bDMARDs increased from 1.6% to 14.0% after 2006, particularly following the introduction of tocilizumab (Supplementary Fig. 5).

Exploratory claims-based treatment trajectory groups

Among the 4,825 patients in the overall AOSD cohort, the prespecified operational rules grouped 146 patients (3.0%) as monocyclic, 1,913 (39.6%) as polycyclic, 855 (17.7%) as chronic, and 1,911 (39.6%) as unclassified (Fig. 3). Because these categories were derived from claims-based medication trajectories rather than direct clinical assessment, they are presented as exploratory descriptive groupings rather than clinically validated disease-course subtypes. The detailed baseline characteristics according to these operational groups are provided in the Supplementary Materials as descriptive data only (Supplementary Table 8).

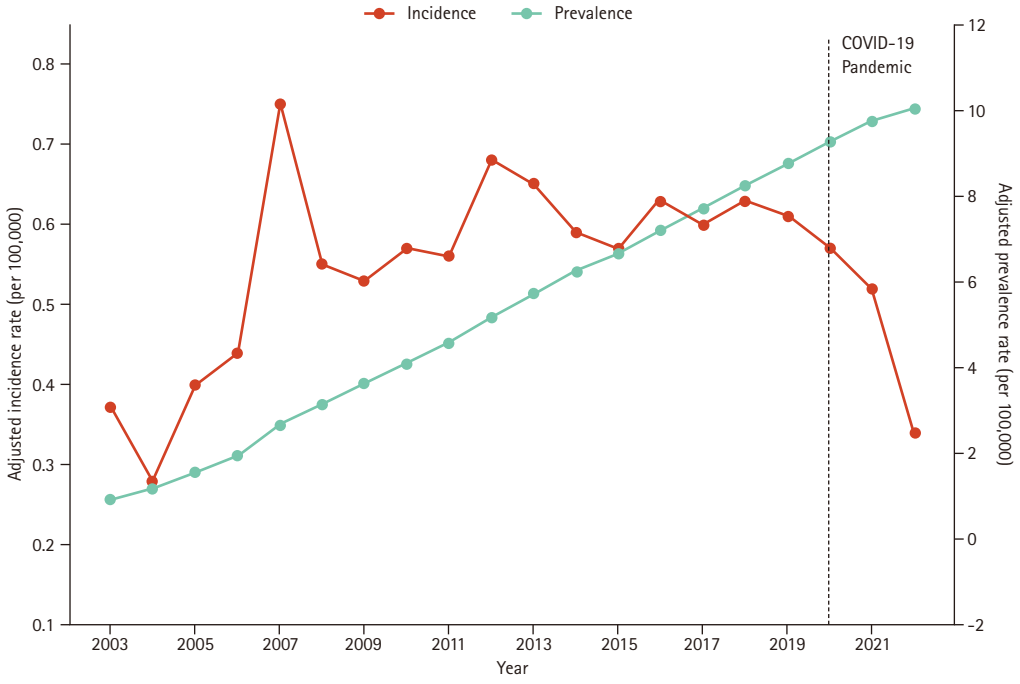


Figure 2. Trends in age- and sex-adjusted incidence and prevalence rates of adult-onset Still's disease in South Korea, 2003–2022. Annual incidence and prevalence rates were estimated using nationwide claims data and standardised to the mid-year Korean population by age and sex. Rates are presented per 100,000 persons. Age- and sex-adjusted annual incidence rates (red line). Age- and sex-adjusted annual prevalence rates (green line).

Table 3. Baseline demographic and clinical characteristics of AOSD patients (2003–2022) using 5 year-incidence intervals

	Total	2003–2007	2008–2012	2013–2017	2018–2022
Number of incident patients	4,600	901	1,187	1,310	1,202
Female	3,283 (71.4)	657 (72.9)	888 (74.8)	944 (72.1)	794 (66.1)
Age at diagnosis	45.9 ± 16.8	41.7 ± 15.5	45.5 ± 16.4	47.7 ± 17.0	47.5 ± 17.3
Age at diagnosis by age group					
15–19	187 (4.1)	45 (5.0)	54 (4.5)	48 (3.7)	40 (3.3)
20–29	711 (15.5)	168 (18.6)	171 (14.4)	176 (13.4)	196 (16.3)
30–39	912 (19.8)	241 (26.7)	234 (19.7)	237 (18.1)	200 (16.6)
40–49	849 (18.5)	170 (18.9)	242 (20.4)	236 (18.0)	201 (16.7)
50–59	862 (18.7)	136 (15.1)	246 (20.7)	259 (19.8)	221 (18.4)
60–69	653 (14.2)	95 (10.5)	131 (11.0)	206 (15.7)	221 (18.4)
70–79	341 (7.4)	41 (4.6)	89 (7.5)	119 (9.1)	92 (7.7)
≥ 80	85 (1.8)	5 (0.6)	20 (1.7)	29 (2.2)	31 (2.6)
Type of insurance					
Health insurance	4,476 (97.3)	881 (97.8)	1,148 (96.7)	1,274 (97.3)	1,173 (97.6)
Medical aid	124 (2.7)	20 (2.2)	39 (3.3)	36 (2.7)	29 (2.4)
Disability present	444 (9.7)	122 (13.5)	121 (10.2)	112 (8.5)	89 (7.4)
Use of medication[a)]					
Any csDMARDs	3,178 (69.1)	605 (67.1)	830 (69.9)	917 (70.0)	826 (68.7)
Methotrexate	2,652 (57.7)	458 (50.8)	674 (56.8)	791 (60.4)	729 (60.6)
Sulfasalazine	450 (9.8)	130 (14.4)	130 (11.0)	115 (8.8)	75 (6.2)
Hydroxychloroquine	1,556 (33.8)	426 (47.3)	497 (41.9)	407 (31.1)	226 (18.8)
Leflunomide	598 (13.0)	125 (13.9)	173 (14.6)	154 (11.8)	146 (12.1)
Any immunosuppressants	1,378 (30.0)	209 (23.2)	326 (27.5)	421 (32.1)	422 (35.1)
Azathioprine	474 (10.3)	82 (9.1)	129 (10.9)	149 (11.4)	114 (9.5)
Cyclosporine	848 (18.4)	148 (16.4)	198 (16.7)	255 (19.5)	247 (20.5)
Tacrolimus	399 (8.7)	25 (2.8)	94 (7.9)	130 (9.9)	150 (12.5)
Any bDMARDs	311 (6.8)	9 (1.0)	47 (4.0)	88 (6.7)	167 (13.9)
Adalimumab	20 (0.4)	0 (0.0)	6 (0.5)	8 (0.6)	6 (0.5)
Infliximab	47 (1.0)	8 (0.9)	23 (1.9)	10 (0.8)	6 (0.5)
Golimumab	2 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)
Tocilizumab	241 (5.2)	0 (0.0)	19 (1.6)	69 (5.3)	153 (12.7)
Anakinra	3 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.2)
Abatacept	17 (0.4)	2 (0.2)	8 (0.7)	5 (0.4)	2 (0.2)
Rituximab	7 (0.2)	0 (0.0)	0 (0.0)	4 (0.3)	3 (0.2)
Any tsDMARDs	15 (0.3)	0 (0.0)	3 (0.3)	6 (0.5)	6 (0.5)
Tofacitinib	7 (0.2)	0 (0.0)	3 (0.3)	4 (0.3)	0 (0.0)
Baricitinib	7 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	5 (0.4)
Upadacitinib	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Any NSAIDs	4,460 (97.0)	889 (98.7)	1,180 (99.4)	1,272 (97.1)	1,119 (93.1)
Any corticosteroids	4,491 (97.6)	888 (98.6)	1,174 (98.9)	1,283 (97.9)	1,146 (95.3)

Values are presented as number (%) or mean ± standard deviation.
AOSD, adult-onset Still's disease; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs, biologic disease-modifying anti-rheumatic drugs; tsDMARDs, targeted synthetic disease-modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs.
[a)]Medication used during the first three months after AOSD diagnosis in the patient cohort from the specified 5-year period.

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DISCUSSION

This nationwide claims-based study provides the first population-level estimates of the epidemiology and treatment characteristics of AOSD in South Korea. The age- and sex-adjusted incidence of AOSD remained low and largely stable over time, ranging from 0.28 to 0.75 per 100,000 population, whereas prevalence increased steadily from 0.91 per 100,000 in 2003 to 10.02 per 100,000 in 2022. AOSD showed a clear female predominance (71.4%) and occurred most commonly in younger to middle-aged adults. Treatment patterns were characterised by consistently high use of corticosteroids and NSAIDs (> 90%), together with increasing use of immunosuppressants and biologic agents over time. As a secondary exploratory analysis, we also examined claims-based treatment trajectories derived from longitudinal medication-use patterns, which provided additional descriptive information on population-level treatment patterns.

Defining AOSD in administrative claims data is inherently challenging because detailed clinical manifestations and laboratory findings are unavailable, precluding direct application of classification criteria such as the Yamaguchi criteria. Previous claims-based studies have therefore used heterogeneous operational definitions. In a Japanese administrative database study, AOSD cases were defined using diagnostic codes together with imaging studies, blood-culture testing, glucocorticoid treatment, and hospitalisation criteria [10]. By contrast, a US study using Truven MarketScan data identified AOSD primarily on the basis of diagnostic codes, age eligibility, insurance continuity, and exclusion of other rheumatic or autoinflammatory diseases [11]. To

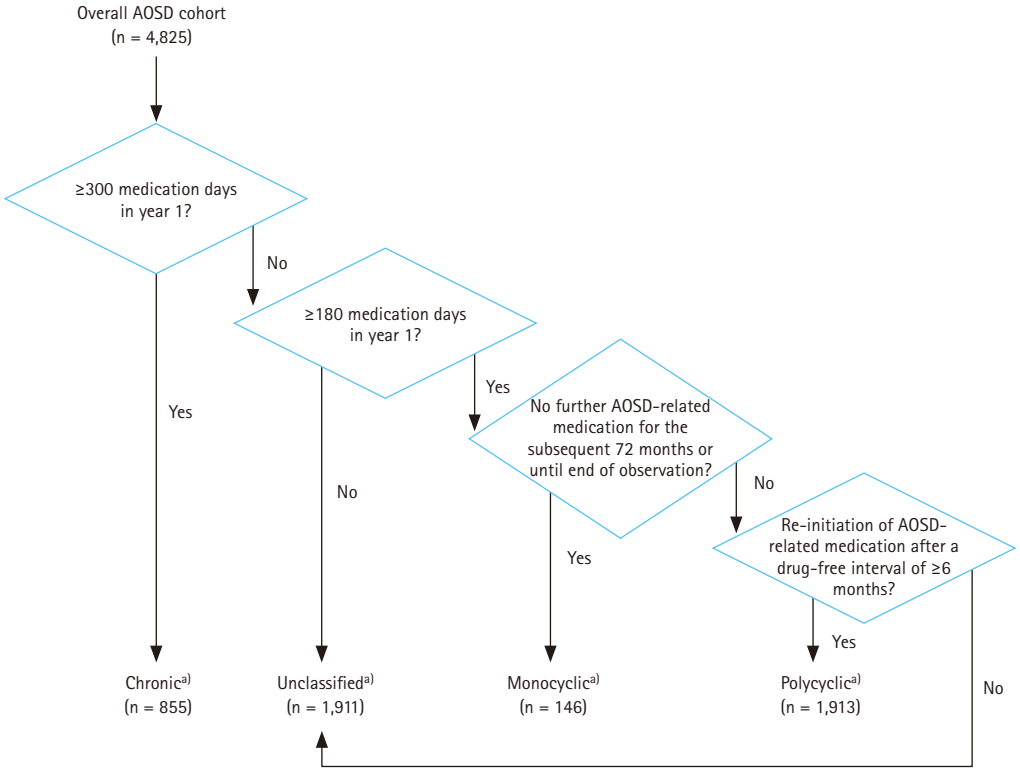


Figure 3. Operational classification of adult-onset Still's disease (AOSD) patients into treatment trajectory groups based on longitudinal medication-use patterns identified from claims data. Operational classification of AOSD patients into treatment trajectory groups based on claims-based medication trajectories. Chronic cases were defined as patients who received ≥ 300 days of prescriptions for ≥ 1 AOSD-related medication within the first year after the index date. Among the remaining patients, those who received ≥ 180 days of AOSD-related medication within the first year were further classified as monocyclic if no additional prescriptions for any AOSD-related medication were recorded during the subsequent 72 months or until the end of follow-up, whichever came first. Polycyclic cases were defined as patients who met the same initial treatment criterion but subsequently re-initiated ≥ 1 AOSD-related medication after a drug-free interval of ≥ 6 months before the end of follow-up. Patients who did not meet any of these criteria were classified as unclassified. These categories should be interpreted as prespecified operational groups rather than clinically validated disease-course subtypes. [a)]Operational groups defined using prespecified claims-based medication trajectory rules.

our knowledge, however, no previous study has formally assessed the validity of a claims-based operational definition for AOSD against chart-reviewed clinical data. This gap in the literature likely reflects the rarity of AOSD, its heterogeneous disease course, and marked inter-individual variation in treatment patterns.

We therefore adopted a conservative operational definition that combined repeated diagnostic coding with healthcare-utilisation and glucocorticoid treatment criteria. In the present study, patients were required to have repeated AOSD-coded healthcare encounters and to receive prednisolone ≥ 15 mg/day (or equivalent) for at least 3 consecutive days within 14 days of the index date. Textbook guidance indicates that most patients with AOSD require glucocorticoids, usually at an initial prednisolone dose of 0.5–1 mg/kg/day [20]. On this basis, we considered a threshold of 15 mg/day to be clinically plausible while remaining broad enough to capture treated cases in routine practice. To support the validity of this definition, we additionally applied the same stepwise algorithm to a single-centre EMR dataset and performed manual chart review. This supplementary analysis showed that the healthcare-utilisation and steroid criteria enriched clinically plausible AOSD cases, with a PPV of 68.3% before the exclusion step and 83.3% after the exclusion step. These findings suggest that the present operational definition may be useful as a conservative, relatively high-specificity approach for epidemiological research.

At the same time, the supplementary EMR-based validation highlighted an important limitation of the exclusion rule. Although the final exclusion step improved the PPV, it also excluded a substantial number of chart-confirmed AOSD cases. This is clinically understandable because AOSD is fundamentally a diagnosis of exclusion. During the initial diagnostic work-up, patients frequently receive provisional differential diagnostic labels for conditions with overlapping systemic or articular manifestations, including lupus, viral exanthem, rheumatoid arthritis, reactive arthritis, and spondyloarthritis. In our chart review, such codes were recorded not only by rheumatologists but also by physicians in other departments. Accordingly, exclusion codes recorded around the index date may reflect provisional diagnostic considerations rather than confirmed alternative diagnoses. Thus, while the present operational definition may be useful as a conservative and relatively high-specificity definition for epidemiological analyses, it may also under-ascertain some true AOSD cases in EMR-based validation.

The choice of a ± 3-month exclusion window should therefore be interpreted as a pragmatic balance rather than a definitive threshold. A longer exclusion window might theoretically reduce some misclassification by capturing more alternative diagnoses; however, our available aggregated data indicated that extending the exclusion window from ± 3 months to ± 6 months and ± 12 months reduced the eligible cohort by 7.4% and 16.9%, respectively. The reduction was even greater in the most recent years, suggesting that a broader exclusion window could materially alter both cohort size and composition. Given the rarity of AOSD, excessive contraction of the cohort may compromise the stability and interpretability of period-specific estimates. For these reasons, we considered ± 3 months to represent a practical compromise between limiting potential misclassification and preserving cohort feasibility.

The 1-year washout period is another important methodological consideration. We acknowledge that this duration may not fully exclude all prevalent or polycyclic cases in a relapsing disease such as AOSD. In our single-centre EMR review, one patient had a documented visit before 2002 but re-presented in 2008 and would therefore have been classified as incident under a 1-year washout definition. In addition, one chart-confirmed polycyclic case relapsed after 5.3 years, illustrating the difficulty of distinguishing late relapse from truly incident disease using any fixed washout period. A longer washout period might reduce some misclassification, but would not eliminate this problem entirely and would further reduce the size of an already rare incident cohort. We therefore used a 1-year washout period as a pragmatic approach while acknowledging the possibility of residual misclassification.

The age- and sex-adjusted annual incidence of AOSD ranged from 0.28 to 0.75 per 100,000 population. These values are comparable to previous estimates from France (0.16 per 100,000) [3], Japan (0.22 per 100,000) [4,5], and Northern Norway (0.4 per 100,000) [5], and broadly similar to the estimate reported from Northwestern Thrace, Türkiye (0.62 per 100,000) [6]. The age- and sex-adjusted prevalence increased steadily over time, reaching 10.02 per 100,000 in 2022. In the present study, we restricted the cohort to patients diagnosed at general or tertiary hospitals because these settings are the most likely to recognise AOSD and to undertake the extensive exclusion work-up required for diagnosis. In practice, many lower-level hospitals in South Korea do not have rheumatologists on staff, and diagnostic

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recognition may therefore vary according to healthcare setting. The increase in incidence observed around 2007–2008 should also be interpreted with caution, as it may partly reflect changes in diagnostic coding practice, claims capture, or diagnostic recognition rather than a true epidemiological shift. In particular, greater recognition of AOSD in higher-level hospitals and improved exclusion-based work-up may have contributed to increased ascertainment during this period. By contrast, the rare disease registration programme was introduced later, with registration beginning in June 2009 and cost-sharing reduction from July 2009, suggesting that the earlier increase was unlikely to be fully attributable to registration-related policy changes.

Our findings support the well-documented female predominance of AOSD, with female-to-male incidence and prevalence rate ratios ranging from approximately 2.6 to 3.7:1 across the study period. This is consistent with international reports describing female predominance, although the reported magnitude has varied across settings [6-11]. This pattern, although less pronounced than that seen in systemic lupus erythematosus, may reflect genetic and environmental factors as well as sex-specific differences in disease presentation [21]. The age distribution in our cohort also corresponded broadly to previous descriptions of peak incidence in younger to middle-aged adults, with the highest rates observed among individuals aged 30–49 years. Although a bimodal distribution has been suggested in some previous studies, we did not observe a secondary peak in older adults, possibly owing to differences in population structure, case ascertainment, or diagnostic practice.

The nationwide NHIS dataset offered an important advantage over single-centre or small hospital-based cohorts by enabling population-level assessment of epidemiological patterns and treatment trajectories over a prolonged period. Although claims data lack detailed clinical information, they allow comprehensive capture of healthcare utilisation and prescription records across virtually the entire Korean population, thereby reducing referral and institutional selection biases that may affect hospital-based studies.

Although AOSD and systemic-onset juvenile idiopathic arthritis are increasingly discussed within a unified Still's disease spectrum [22-25], epidemiological data are still largely generated, coded, and interpreted within age-specific clinical and administrative frameworks. In this context, the present study was specifically designed to evaluate adult-onset AOSD in a nationwide claims-based setting. Its contribution should therefore be interpreted primarily as providing population-level reference data for adult-onset AOSD in South Korea.

Using the medication-trajectory-based operational rules, 3.0% of patients were grouped as monocyclic, 39.6% as polycyclic, 17.7% as chronic, and 39.6% as unclassified. However, these categories were derived from longitudinal medication-use patterns observable in claims data rather than from direct assessment of disease activity, remission, relapse, or articular progression. Accordingly, they should be interpreted as exploratory claims-based treatment trajectory groups rather than as clinically established disease-course subtypes. This distinction is important because the distribution of these operational groups was sensitive to the prespecified thresholds, and a substantial proportion of patients remained unclassified. Supplementary EMR-based chart review also showed limited agreement between the claims-based categories and chart-reviewed clinical course, with concordance being highest for the chronic category and lower for monocyclic and polycyclic patterns. Taken together, these findings indicate that claims data alone may be insufficient to support clinically robust disease-course classification in AOSD. Although such grouping may still provide descriptive information on population-level medication trajectories, its direct clinical interpretability is limited, and any subgroup-based inference should be made cautiously.

In the present study, disease course was operationally approximated from medication trajectories because direct clinical assessment of remission and relapse was not possible in claims data. This approach enabled long-term population-level follow-up, but it was sensitive to the thresholds applied. For example, lowering the initial medication-duration threshold for entry into the monocyclic/polycyclic pathway from 180 days to 90 days increased the proportion of monocyclic cases from 3.0% to 9.1%. Supplementary EMR-based chart review also showed that concordance was highest for the chronic category, whereas clinically monocyclic and polycyclic cases were more frequently reclassified as chronic or unclassified by the operational definition. Among 13 clinically monocyclic cases, the median duration of AOSD-related medication exposure was 304 days (range, 63–397); 7 exceeded the 300-day threshold used for chronic classification, and 3 did not meet the 180-day threshold required to enter the monocyclic/polycyclic pathway. Similarly, some clinically polycyclic cases were not captured because the drug-free interval did not reach 6 months despite

subsequent treatment re-initiation. These findings further support cautious interpretation of the operational groups derived from medication trajectories in claims data.

Throughout the study period, treatment patterns in AOSD were characterised by early use of anti-inflammatory agents. Corticosteroids and NSAIDs were used in over 90% of patients, consistent with Japanese data in which glucocorticoid monotherapy accounted for 65.5% of first-line regimens and glucocorticoid plus NSAID combinations for 6.4% [7]. csDMARDs were prescribed within 3 months of diagnosis in over 60% of Korean cases, suggesting broader early use of steroid-sparing therapy than has been reported in Japanese administrative data [10]. Use of non-biologic immunosuppressants also increased over time, indicating greater adoption of multi-agent treatment strategies. Most bDMARDs and tsDMARDs remain off-label for AOSD. Tocilizumab, the only biologic approved for AOSD by the Ministry of Food and Drug Safety in Korea, became available in 2018 and likely contributed to the observed increase in bDMARD use in recent years. However, despite the 2024 EULAR/PReS recommendations supporting early interleukin (IL)-1 or IL-6 inhibition [25], current Korean reimbursement policies require prolonged failure of corticosteroids and csDMARDs, substantially limiting timely access to biologic therapy.

Several limitations should be acknowledged. First, case ascertainment was based on an operational definition applied to administrative claims data, in which detailed clinical manifestations, laboratory findings, and disease activity measures were unavailable. Consequently, established classification criteria such as the Yamaguchi criteria could not be directly applied. Although we used a conservative definition combining repeated diagnostic coding, healthcare utilisation, glucocorticoid treatment, and exclusion criteria, some degree of misclassification is inevitable. In particular, this approach may have under-ascertained mild cases, provisional diagnoses, and cases managed outside general or tertiary hospitals. Supplementary single-centre EMR validation supported the use of this definition as a relatively high-specificity approach, but also showed that the exclusion rule could remove some true AOSD cases because codes recorded around the index date may reflect provisional differential diagnoses rather than confirmed alternative diagnoses. In addition, because the analyses were originally conducted using 5-year age-band denominators from KOSIS within a closed NHIS environment, patients aged 15 years could not be separately identified in the aggregated dataset; accordingly, limited inclusion of cases at the boundary between paediatric- and adult-onset disease cannot be excluded. Secondly, the 1-year washout period may not have fully excluded all prevalent or polycyclic cases, and some residual misclassification of incident cases is therefore possible. Although a longer washout period might reduce some misclassification, it would also further reduce the size of an already rare incident cohort. In addition, because the study was conducted within a closed NHIS analysis environment and only aggregated outputs were available, additional patient-level sensitivity analyses using alternative washout periods or exclusion windows could not be performed. Thirdly, the exploratory treatment trajectory groups were inferred from medication trajectories rather than direct clinical assessment, and supplementary EMR review showed only limited agreement with chart-reviewed disease course. These operational categories should therefore be interpreted only as pragmatic claims-based proxies for longitudinal treatment patterns, not as clinically validated disease-course phenotypes. Furthermore, because the NHIS database is based on reimbursed claims, non-reimbursed prescriptions or treatments may not have been fully captured. This may have influenced both case ascertainment and the operational classification of disease course based on medication trajectories. Our dataset also did not capture exact corticosteroid doses, and the analysis of medication use was restricted to the first 3 months after diagnosis in order to describe initial treatment patterns. Later treatment escalation, including delayed initiation of biologics or tsDMARDs, may therefore not have been fully captured. Finally, temporal changes in coding practice, claims capture, and healthcare access may also have influenced the observed trends over time, and their contribution could not be fully distinguished from true epidemiological change in the present dataset.

In conclusion, this nationwide study provides population-based estimates of the epidemiology and treatment characteristics of AOSD in South Korea. Incidence remained low and largely stable, whereas prevalence increased steadily over time. Exploratory claims-based treatment trajectory groups could be described at the population level, but their clinical interpretability was limited, and they should not be regarded as validated disease-course subtypes. These findings may contribute to a better understanding of the epidemiological burden and clinical course of this rare condition and may inform future research and health policy planning.

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KEY MESSAGE

1. Between 2003 and 2022, 4,600 incident AOSD cases were identified in South Korea, with an age- and sex-adjusted annual incidence ranging from 0.28 to 0.75 per 100,000 population.
2. Age- and sex-adjusted prevalence increased steadily over time, from 0.91 per 100,000 population in 2003 to 10.02 per 100,000 population in 2022.
3. Exploratory claims-based treatment trajectory groups could be derived from longitudinal medication-use patterns, but these should not be interpreted as clinically validated disease-course subtypes.

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CRedit authorship contributions
Mihye Kwon: conceptualization, methodology, resources, investigation, data curation, formal analysis, validation, software, writing - original draft, funding acquisition; Chung-il Joung: methodology, writing - review & editing; Jee Young Hong: methodology, formal analysis, software; Younghee Jung: conceptualization, writing - review & editing, funding acquisition

Conflicts of interest
The authors disclose no conflicts.

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Data availability statement
All data supporting the findings of this study are presented in the main tables, figures, and supplementary materials. Due to NHIS data policies and the closed-server analysis environment, the underlying raw data are not publicly available.

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Supplementary Table 1. Diagnostic KCD codes used for inclusion and exclusion of AOSD

ICD codes	Disease
Inclusion criterion	
M06.1	AOSD
M06.10	AOSD, multiple sites
M06.11	AOSD, shoulder region
M06.12	AOSD, upper arm
M06.13	AOSD, forearm
M06.14	AOSD, hand
M06.15	AOSD, pelvic region and thigh
M06.16	AOSD, lower leg
M06.17	AOSD, ankle and foot
M06.18	AOSD, other specified sites
M06.19	AOSD, unspecified site
Exclusion criterion	
M02	Reactive arthropathies
M03	Post-infective and reactive arthropathies in disease classified elsewhere
M05	Seropositive rheumatoid arthritis
M06	Other (excluding M06.1)
M07	Psoriatic and enteropaethic arthropathies
M08	Juvenile arthritis
M09	Juvenile arthritis in diseases classified elsewhere
M30	Polyarteritis nodosa and related conditions
M31	Other necrotizing vasculopathies (including Wegener's granulomatosis, Aortic arch syndrome [Takayasu], Giant cell arteritis with polymyalgia rheumatica, Microscopic polyangiitis)
M32	Systemic lupus erythematosus
M33	Dermato-polymyositis
M34	Systemic sclerosis
M35	Other systemic involvement of connective tissue (including Sicca syndrome [Sjogren], Other overlap syndromes, Behcet's disease, Polymyalgia rheumatic)
M45	Ankylosing spondylitis
K50	Crohn's disease [regional enteritis]
K51	Ulcerative colitis
C00-C97	Various malignancies

This table lists the Korean Standard Classification of Diseases (KCD) codes used to identify AOSD and to exclude alternative inflammatory, autoimmune, or malignant conditions during cohort construction.
ICD, International Classification of Diseases; AOSD, adult-onset Still's disease.

Supplementary Table 2. Operational definition of the study population

Step	Description
Data source	NHIS claims data (2002–2022), medical institutions only (excluding traditional medicine, dental, pharmacy)
Initial cohort	All patients with KCD M06.1 or M06.10–M06.19 as principal or secondary diagnosis
Number identified	15,000
Inclusion criteria	1. AOSD code first recorded at a general or tertiary hospital 2. ≥ 3 outpatient visits or ≥ 1 hospitalisation within 3 months 3. Prednisolone ≥ 15 mg/day (or equivalent corticosteroid) ≥ 3 days within 14 days of index date
Exclusion criteria	1. Autoimmune disease diagnosis (Table 2–3) within ± 3 months 2. Malignancy diagnosis (C00–C97) within ± 3 months

This table summarises the stepwise operational definition of the study population derived from the Korean National Health Insurance Service (NHIS) claims data, including inclusion and exclusion criteria applied to identify patients with AOSD.
KCD, the Korean Standard Classification of Diseases; AOSD, adult-onset Still's disease.

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Supplementary Table 3. Therapeutic agents and routes of administration considered in the analysis

Category	Drug name and unit	Route
csDMARD	Methotrexate 2.5 mg	Oral
	Methotrexate 10 mg, 15 mg, 20 mg, 25 mg (50 mg/mL)	Inj
	Leflunomide 10 mg, 20 mg	Oral
	Hydroxychloroquine sulfate 0.1 g, 0.2 g, 0.4 g, 0.15 g, 0.3 g	Oral
	Sulfasalazine 0.5 g	Oral
Immuno-suppressant	Tacrolimus hydrate (as tacrolimus 0.25 mg, 0.5 mg, 1 mg, 2 mg, 5 mg)	Oral
	Cyclosporine 0.1 g, 25 mg	Oral
	Microemulsion cyclosporine 5 g (0.1 g/mL)	Oral
	Microemulsion cyclosporine 0.1 g, 25 mg, 50 mg	Oral
	Azathioprine 25 mg, 50 mg	Oral
bDMARD	Adalimumab 40 mg (100 mg/mL), 20 mg (0.1 g/mL), 40 mg (50 mg/mL)	Inj
	Etanercept 25 mg (50 mg/mL), 50 mg (50 mg/mL), 25 mg (25 mg/mL)	Inj
	Infliximab 0.12 g (0.12 g/mL), 0.1 g	Inj
	Golimumab 50 mg (0.1 g/mL), 0.1 g (0.1 g/mL), 50 mg (12.5 mg/mL)	Inj
	Abatacept 0.125 g (0.125 g/mL), 0.25 g	Inj
	Rituximab 0.1 g (10 mg/mL), 0.5 g (10 mg/mL), 1.4 g (0.12 g/mL)	Inj
	Tocilizumab 0.162 g (0.18 g/mL), 80 mg (20 mg/mL), 0.2 g (20 mg/mL), 0.4 g (20 mg/mL)	Inj
	Anakinra 0.1 g	Inj
tsDMARD	Tofacitinib citrate (as tofacitinib 5 mg, 10 mg, 11 mg)	Oral
	Baricitinib 2 mg, 4 mg	Oral
	Upadacitinib hemihydrate (as upadacitinib 15 mg, 30 mg)	Oral
	Filgotinib maleate (as filgotinib 0.1 g, 0.2 g)	Oral
Steroid	Betamethasone 0.5 mg	Oral
	Deflazacort 6 mg	Oral
	Dexamethasone 0.5 mg, 0.75 mg	Oral
	Fludrocortisone acetate 100 ug	Oral
	Hydrocortisone 5 mg, 10 mg	Oral
	Methylprednisolone 1 mg, 4 mg	Oral
	Prednisolone 5 mg	Oral
	Triamcinolone 1 mg, 2 mg, 4 mg	Oral
	Methylprednisolone sodium succinate (as methylprednisolone 40 mg 0.125 g, 0.5 g)	Inj
	Betamethasone sodium phosphate (as betamethasone 4 mg (4 mg/mL))	Inj
	Dexamethasone disodium phosphate 4.37 mg (4.37 mg/mL), 5 mg (5 mg/mL)	Inj
NSAID	Aceclofenac 0.1 g, 0.2 g	Oral
	Naproxen 0.5 g, 1 g	Oral
	Naproxen sodium 0.275 g	Oral
	Celecoxib 0.1 g, 0.2 g, 0.4 g	Oral
	Meloxicam 7.5 mg, 15 mg	Oral
	Nabumetone 0.5 g	Oral
	Ibuprofen 0.2 g, 0.4 g, 0.6 g	Oral
	Dexibuprofen 0.15 g, 0.3 g, 0.4 g	Oral

Supplementary Table 3. Continued

Category	Drug name and unit	Route
	Diclofenac potassium 50 mg	Oral
	Diclofenac sodium 25 mg, 50 mg	Oral
	Etodolac 0.2 g, 0.4 g, 0.6 g	Oral
	Ketorolac tromethamine 10 mg	Oral
	Loxoprofen sodium hydrate (as loxoprofen sodium 60 mg, 90 mg)	Oral
	Piroxicam 10 mg, 20 mg	Oral
	Piroxicam β-cyclodextrin (as piroxicam 10 mg)	Oral
	Polmacoxib 2 mg	Oral
	Etoricoxib 30 mg	Oral
	Pelubiprofen 30 mg, 45 mg	Oral
	Talniflumate 0.37 g	Oral
	Morniflumate 0.35 g	Oral
	Zaltoprofen 80 mg	Oral

The table details disease-related medications used for treatment classification, including conventional synthetic, biologic, and targeted synthetic disease-modifying anti-rheumatic drugs, corticosteroids, and non-steroidal anti-inflammatory drugs, together with their routes of administration.

csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; Inj, injection; bDMARDs, biologic disease-modifying anti-rheumatic drugs; tsDMARDs, targeted synthetic disease-modifying anti-rheumatic drugs; NSAID, non-steroidal anti-inflammatory drug.

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Supplementary Table 4. Stepwise implementation of the claims-based operational definition for AOSD in the single-centre EMR dataset and chart-review findings

Step	Operational definition applied	No. remaining	No. excluded at this step	Chart-confirmed AOSD among remaining, n/N (%)	Non-AOSD on chart review among remaining, n/N (%)	PPV (%)	Main chart-review observations
1	≥ 1 AOSD diagnostic code recorded during 2002–2022	82	–	NA	NA	NA	Initial EMR capture included provisional or rule-out diagnoses.
2	After 1-year washout period	71	11	NA	NA	NA	Patients with possible prevalent disease during the washout period were excluded.
3	After healthcare-utilisation criterion: ≥ 3 outpatient visits or ≥ 1 hospital admission with AOSD within 3 months of the index date	61	10	NA	NA	NA	Most excluded patients had only a single rule-out AOSD code without subsequent AOSD-related evaluation, treatment, or follow-up. A few were followed at outside hospitals and visited this centre only for laboratory testing or preoperative consultation.
4	After steroid criterion: prednisolone ≥ 15 mg/day (or equivalent) for ≥ 3 consecutive days within 14 days of the index date	41	20	28/41 (68.3)	13/41 (31.7)	68.3	The medication criterion enriched clinically plausible AOSD cases.
5	After exclusion criteria: autoimmune disease or malignancy code within ± 3 months of the index date	24	17	20/24 (83.3)	4/24 (16.7)	83.3	The exclusion criteria improved PPV, but also excluded some true AOSD cases.
-	Patients excluded at Step 5	17	–	8/17 (47.1)	9/17 (52.9)	NA	Among patients excluded at the final step, 8 were judged to have true AOSD on detailed chart review, indicating loss of true cases related to the exclusion-based nature of AOSD diagnosis.

Patients with at least one AOSD diagnostic code recorded between 2002 and 2022 were identified first, after which the 1-year washout period, healthcare-utilisation criterion, steroid criterion, and exclusion criteria were sequentially applied. Manual chart review was used to assess the clinical plausibility of the identified cases and to examine reasons for exclusion or misclassification.

Notes:

1. Chart review was performed primarily for patients meeting the code, healthcare-utilisation, and steroid criteria, and for those excluded at the final exclusion step.
2. Patients excluded by the healthcare-utilisation criterion were mostly those with a single provisional or rule-out AOSD code and no subsequent AOSD-related evaluation, treatment, or follow-up; a small number were being followed at outside hospitals and visited the study centre only for laboratory testing or preoperative consultation.
3. Because AOSD is a diagnosis of exclusion, codes for lupus, viral exanthem, rheumatoid arthritis, reactive arthritis, spondyloarthritis, other autoimmune diseases, or malignancy recorded around the index date often reflected provisional differential diagnoses rather than confirmed alternative diagnoses.
4. Among the 41 patients who met the code, healthcare-utilisation, and steroid criteria, application of the exclusion criteria yielded 20 true positives, 4 false positives, 8 false negatives, and 9 true negatives on chart review. Accordingly, within this subset, the conditional sensitivity, specificity, negative predictive value, and accuracy of the exclusion step were 71.4%, 69.2%, 52.9%, and 70.7%, respectively.

AOSD, adult-onset Still's disease; EMR, electronic medical record; PPV, positive predictive value; NA, not assessed.

Supplementary Table 5. Crude annual incidence rates of adult-onset Still's disease per 100,000 population in South Korea, 2003–2022

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Inc	Population[a)]	n	Inc	Population[a)]	n	Inc
2003	15–19	3239195.5	11	0.34	1686289.5	6	0.36	1552906	5	0.32
	20–29	8060752	31	0.38	4124486	5	0.12	3936266	26	0.66
	30–39	8874752	45	0.51	4532981.5	17	0.38	4341770.5	28	0.64
	40–49	8000165	23	0.29	4073330.5	6	0.15	3926834.5	17	0.43
	50–59	4609403.5	18	0.39	2293593.5	2	0.09	2315810	16	0.69
	60–69	3565444.5	15	0.42	1626634.5	6	0.37	1938810	9	0.46
	70–79	1670598.5	5	0.30	615188.5	1	0.16	1055410	4	0.38
	80–	593572	1	0.17	171218	0	0.00	422354	1	0.24
	Overall	38613883	149	0.39	19123722	43	0.22	19490161	106	0.54
2004	15–19	3159628	11	0.35	1651535	5	0.30	1508093	6	0.40
	20–29	7871498.5	20	0.25	4032239.5	0	0.00	3839259	20	0.52
	30–39	8899294.5	41	0.46	4536677	9	0.20	4362617.5	32	0.73
	40–49	8190223	20	0.24	4171055	3	0.07	4019168	17	0.42
	50–59	4785259.5	12	0.25	2387756.5	2	0.08	2397503	10	0.42
	60–69	3640880	11	0.30	1669139	1	0.06	1971741	10	0.51
	70–79	1766471	4	0.23	656945	0	0.00	1109526	4	0.36
	80–	627303.5	0	0.00	182682	0	0.00	444621.5	0	0.00
	Overall	38940558	119	0.31	19288029	20	0.10	19652529	99	0.50
2005	15–19	3137402.5	10	0.32	1646915.5	0	0.00	1490487	10	0.67
	20–29	7697454	39	0.51	3948404.5	14	0.35	3749049.5	25	0.67
	30–39	8859245.5	49	0.55	4514206	10	0.22	4345039.5	39	0.90
	40–49	8325045	35	0.42	4239407.5	12	0.28	4085637.5	23	0.56
	50–59	5079573	23	0.45	2537545	5	0.20	2542028	18	0.71
	60–69	3674783.5	11	0.30	1693834.5	1	0.06	1980949	10	0.50
	70–79	1889790.5	1	0.05	711598.5	1	0.14	1178192	0	0.00
	80–	658063.5	1	0.15	192403.5	1	0.52	465660	0	0.00
	Overall	39321357.5	169	0.43	19484315	44	0.23	19837042.5	125	0.63
2006	15–19	3168789.5	3	0.09	1668896.5	1	0.06	1499893	2	0.13
	20–29	7556958	46	0.61	3883476.5	11	0.28	3673481.5	35	0.95
	30–39	8789633.5	43	0.49	4472326.5	11	0.25	4317307	32	0.74
	40–49	8417973	40	0.48	4293361.5	16	0.37	4124611.5	24	0.58
	50–59	5411366.5	25	0.46	2702636	8	0.30	2708730.5	17	0.63
	60–69	3701994	17	0.46	1717420.5	5	0.29	1984573.5	12	0.60
	70–79	2019757.5	7	0.35	771737.5	2	0.26	1248020	5	0.40
	80–	692157.5	0	0.00	201817.5	0	0.00	490340	0	0.00
	Overall	39758629.5	181	0.46	19711672.5	54	0.27	20046957	127	0.63
2007	15–19	3261491.5	10	0.31	1722228.5	3	0.17	1539263	7	0.45
	20–29	7404698.5	32	0.43	3812687	8	0.21	3592011.5	24	0.67
	30–39	8714447.5	63	0.72	4431071	19	0.43	4283376.5	44	1.03

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Supplementary Table 5. Continued

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Inc	Population[a)]	n	Inc	Population[a)]	n	Inc
	40–49	8498413	52	0.61	4333765.5	16	0.37	4164647.5	36	0.86
	50–59	5701710	58	1.02	2851682	16	0.56	2850028	42	1.47
	60–69	3789398.5	41	1.08	1769336.5	16	0.90	2020062	25	1.24
	70–79	2145193	24	1.12	832056.5	5	0.60	1313136.5	19	1.45
	80–	733241.5	3	0.41	213069.5	0	0.00	520172	3	0.58
	Overall	40248593.5	283	0.70	19965896.5	83	0.42	20282697	200	0.99
2008	15–19	3359504	7	0.21	1779842.5	3	0.17	1579661.5	4	0.25
	20–29	7273831.5	42	0.58	3751232	14	0.37	3522599.5	28	0.79
	30–39	8570849	47	0.55	4366438	11	0.25	4204411	36	0.86
	40–49	8602964.5	36	0.42	4377870	9	0.21	4225094.5	27	0.64
	50–59	5991650	36	0.60	3002131	6	0.20	2989519	30	1.00
	60–69	3909749.5	32	0.82	1837225.5	8	0.44	2072524	24	1.16
	70–79	2269325.5	12	0.53	893793.5	4	0.45	1375532	8	0.58
	80–	784942.5	4	0.51	226892.5	2	0.88	558050	2	0.36
	Overall	40762816.5	216	0.53	20235425	57	0.28	20527391.5	159	0.77
2009	15–19	3444215	8	0.23	1829732.5	4	0.22	1614482.5	4	0.25
	20–29	7126950	34	0.48	3682226.5	6	0.16	3444723.5	28	0.81
	30–39	8420913.5	51	0.61	4295222	9	0.21	4125691.5	42	1.02
	40–49	8700671.5	44	0.51	4424692.5	10	0.23	4275979	34	0.80
	50–59	6324325	39	0.62	3170223.5	11	0.35	3154101.5	28	0.89
	60–69	4006144	24	0.60	1894727	9	0.48	2111417	15	0.71
	70–79	2405239.5	10	0.42	961241.5	1	0.10	1443998	9	0.62
	80–	844310.5	6	0.71	243694	1	0.41	600616.5	5	0.83
	Overall	41272769	216	0.52	20501759.5	51	0.25	20771009.5	165	0.79
2010	15–19	3519339.5	12	0.34	1870870	4	0.21	1648469.5	8	0.49
	20–29	6927508.5	33	0.48	3590734	9	0.25	3336774.5	24	0.72
	30–39	8324779	54	0.65	4244773.5	14	0.33	4080005.5	40	0.98
	40–49	8715638.5	54	0.62	4434091	11	0.25	4281547.5	43	1.00
	50–59	6726715.5	42	0.62	3369420	9	0.27	3357295.5	33	0.98
	60–69	4092724.5	22	0.54	1946827.5	5	0.26	2145897	17	0.79
	70–79	2536642	16	0.63	1027907	5	0.49	1508735	11	0.73
	80–	907282	4	0.44	261387	1	0.38	645895	3	0.46
	Overall	41750629.5	237	0.57	20746010	58	0.28	21004619.5	179	0.85
2011	15–19	3544677	12	0.34	1882478	6	0.32	1662199	6	0.36
	20–29	6759635	34	0.50	3513629.5	13	0.37	3246005.5	21	0.65
	30–39	8226191	42	0.51	4193210	13	0.31	4032981	29	0.72
	40–49	8709044.5	53	0.61	4435055	10	0.23	4273989.5	43	1.01
	50–59	7175713	58	0.81	3592136.5	13	0.36	3583576.5	45	1.26
	60–69	4150537.5	17	0.41	1983827	3	0.15	2166710.5	14	0.65
	70–79	2671439	18	0.67	1096506.5	4	0.36	1574932.5	14	0.89

Supplementary Table 5. Continued

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Inc	Population[a)]	n	Inc	Population[a)]	n	Inc
	80–	968750	2	0.21	278706	1	0.36	690044	1	0.14
	Overall	42205987	236	0.56	20975548.5	63	0.30	21230438.5	173	0.81
2012	15–19	3508863.5	15	0.43	1859556	6	0.32	1649307.5	9	0.55
	20–29	6643071	28	0.42	3462091.5	9	0.26	3180979.5	19	0.60
	30–39	8133117.5	40	0.49	4143116	10	0.24	3990001.5	30	0.75
	40–49	8713418.5	55	0.63	4437926.5	12	0.27	4275492	43	1.01
	50–59	7537308.5	71	0.94	3776652.5	14	0.37	3760656	57	1.52
	60–69	4217734.5	36	0.85	2025528.5	10	0.49	2192206	26	1.19
	70–79	2845487	33	1.16	1183270	6	0.51	1662217	27	1.62
	80–	1037190.5	4	0.39	300498.5	3	1.00	736692	1	0.14
	Overall	42636191	282	0.66	21188639.5	70	0.33	21447551.5	212	0.99
2013	15–19	3446369.5	15	0.44	1818948.5	6	0.33	1627421	9	0.55
	20–29	6575859.5	33	0.50	3438603	10	0.29	3137256.5	23	0.73
	30–39	8018833	58	0.72	4085613	17	0.42	3933220	41	1.04
	40–49	8756553	35	0.40	4452693.5	11	0.25	4303859.5	24	0.56
	50–59	7786323	49	0.63	3909234	10	0.26	3877089	39	1.01
	60–69	4343385	48	1.11	2094829	9	0.43	2248556	39	1.73
	70–79	2994554	30	1.00	1258609	8	0.64	1735945	22	1.27
	80–	1115768	5	0.45	327384.5	0	0.00	788383.5	5	0.63
	Overall	43037645	273	0.63	21385914.5	71	0.33	21651730.5	202	0.93
2014	15–19	3364378.5	9	0.27	1767803	3	0.17	1596575.5	6	0.38
	20–29	6585186	36	0.55	3455017.5	10	0.29	3130168.5	26	0.83
	30–39	7847118	44	0.56	4000924.5	13	0.32	3846193.5	31	0.81
	40–49	8810883	42	0.48	4474484	10	0.22	4336399	32	0.74
	50–59	8000583	52	0.65	4020936.5	12	0.30	3979646.5	40	1.01
	60–69	4529945	45	0.99	2194268	10	0.46	2335677	35	1.50
	70–79	3081420	17	0.55	1305431.5	2	0.15	1775988.5	15	0.84
	80–	1206729	4	0.33	359793.5	1	0.28	846935.5	3	0.35
	Overall	43426242.5	249	0.57	21578658.5	61	0.28	21847584	188	0.86
2015	15–19	3283016	9	0.27	1718355	2	0.12	1564661	7	0.45
	20–29	6639679	35	0.53	3492793	9	0.26	3146886	26	0.83
	30–39	7677906.5	47	0.61	3917273.5	12	0.31	3760633	35	0.93
	40–49	8783313.5	50	0.57	4459325	12	0.27	4323988.5	38	0.88
	50–59	8148783.5	53	0.65	4097254.5	9	0.22	4051529	44	1.09
	60–69	4824617.5	31	0.64	2342575.5	6	0.26	2482042	25	1.01
	70–79	3130969.5	18	0.57	1337821	7	0.52	1793148.5	11	0.61
	80–	1312079.5	5	0.38	398448.5	0	0.00	913631	5	0.55
	Overall	43800365	248	0.57	21763846	57	0.26	22036519	191	0.87
2016	15–19	3185554	6	0.19	1662817	4	0.24	1522737	2	0.13
	20–29	6695952	41	0.61	3526732	19	0.54	3169220	22	0.69

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Supplementary Table 5. Continued

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Inc	Population[a)]	n	Inc	Population[a)]	n	Inc
	30–39	7538707	51	0.68	3850486	18	0.47	3688221	33	0.89
	40–49	8716227	46	0.53	4418589	16	0.36	4297638	30	0.70
	50–59	8247924	56	0.68	4155589	15	0.36	4092335	41	1.00
	60–69	5151263.5	41	0.80	2502779	17	0.68	2648484.5	24	0.91
	70–79	3173638	27	0.85	1369559.5	8	0.58	1804078.5	19	1.05
	80–	1421689.5	8	0.56	439823	1	0.23	981866.5	7	0.71
	Overall	44130955	276	0.63	21926374.5	98	0.45	22204580.5	178	0.80
2017	15–19	3034107.5	9	0.30	1582678.5	7	0.44	1451429	2	0.14
	20–29	6751231.5	31	0.46	3556649	6	0.17	3194582.5	25	0.78
	30–39	7388644	37	0.50	3778264	9	0.24	3610380	28	0.78
	40–49	8640493	63	0.73	4376816.5	27	0.62	4263676.5	36	0.84
	50–59	8329801.5	49	0.59	4198173.5	15	0.36	4131628	34	0.82
	60–69	5438101.5	41	0.75	2648476.5	5	0.19	2789625	36	1.29
	70–79	3272215.5	27	0.83	1426916.5	8	0.56	1845299	19	1.03
	80–	1531888.5	7	0.46	482675	2	0.41	1049213.5	5	0.48
	Overall	44386483	264	0.59	22050649.5	79	0.36	22335833.5	185	0.83
2018	15–19	2872026	10	0.35	1497710	5	0.33	1374316	5	0.36
	20–29	6784375	41	0.60	3572699.5	11	0.31	3211675.5	30	0.93
	30–39	7258542.5	57	0.79	3715496	23	0.62	3543046.5	34	0.96
	40–49	8491462.5	47	0.55	4308537	17	0.39	4182925.5	30	0.72
	50–59	8428191	47	0.56	4239769	12	0.28	4188422	35	0.84
	60–69	5721990	51	0.89	2794221.5	19	0.68	2927768.5	32	1.09
	70–79	3399521	22	0.65	1497789	6	0.40	1901732	16	0.84
	80–	1644088	7	0.43	527239	3	0.57	1116849	4	0.36
	Overall	44600196	282	0.63	22153461	96	0.43	22446735	186	0.83
2019	15–19	2725294.5	12	0.44	1418938	6	0.42	1306356.5	6	0.46
	20–29	6784678	49	0.72	3570498.5	18	0.50	3214179.5	31	0.96
	30–39	7111488	37	0.52	3645955.5	11	0.30	3465532.5	26	0.75
	40–49	8335858.5	47	0.56	4233740.5	20	0.47	4102118	27	0.66
	50–59	8518746.5	45	0.53	4283873	11	0.26	4234873.5	34	0.80
	60–69	6045292.5	52	0.86	2956002.5	15	0.51	3089290	37	1.20
	70–79	3505477.5	23	0.66	1559596	11	0.71	1945881.5	12	0.62
	80–	1769298.5	7	0.40	577222.5	4	0.69	1192076	3	0.25
	Overall	44796134	272	0.61	22245826.5	96	0.43	22550307.5	176	0.78
2020	15–19	2551012.5	7	0.27	1325906	2	0.15	1225106.5	5	0.41
	20–29	6777444.5	43	0.63	3562457	12	0.34	3214987.5	31	0.96
	30–39	6917016.5	42	0.61	3557427	13	0.37	3359589.5	29	0.86
	40–49	8244512.5	43	0.52	4187027	12	0.29	4057485.5	31	0.76
	50–59	8538879	55	0.64	4299675	21	0.49	4239204	34	0.80
	60–69	6440301.5	40	0.62	3150709	14	0.44	3289592.5	26	0.79

Supplementary Table 5. Continued

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Inc	Population[a)]	n	Inc	Population[a)]	n	Inc
	70–79	3603371	21	0.58	1616394	9	0.56	1986977	12	0.60
	80–	1895711.5	4	0.21	627780.5	0	0.00	1267931	4	0.32
	Overall	44968249	255	0.57	22327375.5	83	0.37	22640873.5	172	0.76
2021	15–19	2395066	6	0.25	1242509	2	0.16	1152557	4	0.35
	20–29	6704990	37	0.55	3519240	13	0.37	3185750	24	0.75
	30–39	6753189	44	0.65	3483442.5	14	0.40	3269746.5	30	0.92
	40–49	8152506.5	41	0.50	4140356	17	0.41	4012150.5	24	0.60
	50–59	8541581.5	43	0.50	4309556.5	14	0.32	4232025	29	0.69
	60–69	6879681.5	41	0.60	3367038.5	12	0.36	3512643	29	0.83
	70–79	3673106.5	17	0.46	1658872	8	0.48	2014234.5	9	0.45
	80–	2022853.5	8	0.40	679284	2	0.29	1343569.5	6	0.45
	Overall	45122974.5	237	0.53	22400299	82	0.37	22722676	155	0.68
2022	15–19	2340932.5	5	0.21	1211372.5	3	0.25	1129560	2	0.18
	20–29	6516720.5	26	0.40	3416094.5	5	0.15	3100626	21	0.68
	30–39	6635874.5	20	0.30	3432350.5	5	0.15	3203524	15	0.47
	40–49	8060736.5	23	0.29	4091323.5	7	0.17	3969413	16	0.40
	50–59	8548546.5	31	0.36	4315988.5	11	0.25	4232558	20	0.47
	60–69	7230878	37	0.51	3544507.5	14	0.39	3686370.5	23	0.62
	70–79	3752572.5	9	0.24	1706639.5	3	0.18	2045933	6	0.29
	80–	2170505.5	5	0.23	741237.5	3	0.40	1429268	2	0.14
	Overall	45256766.5	156	0.34	22459514	51	0.23	22797253	105	0.46

Crude annual incidence rates are presented overall and stratified by age group and sex. Population denominators were based on the mid-year population of each corresponding year, excluding individuals aged < 15 years.

[a)]The population denominator refers to the mid-year population of each corresponding year, excluding individuals aged 0 to 14 years.

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Supplementary Table 6. Crude annual prevalence rates of adult-onset Still's disease per 100,000 population in South Korea, 2003–2022

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Prev	Population[a)]	n	Prev	Population[a)]	n	Prev
2003	15–19	3239195.5	22	0.68	1686289.5	8	0.47	1552906	14	0.90
	20–29	8060753	96	1.19	4124486	18	0.44	3936267	78	1.98
	30–39	8874753	99	1.12	4532982	25	0.55	4341771	74	1.70
	40–49	8000166	65	0.81	4073331	14	0.34	3926835	51	1.30
	50–59	4609405	47	1.02	2293594	7	0.31	2315811	40	1.73
	60–69	3565446	35	0.98	1626635	11	0.68	1938811	24	1.24
	70–79	1670600	8	0.48	615189	2	0.33	1055411	6	0.57
	80–	593574	1	0.17	171219	0	0.00	422355	1	0.24
	Overall	38613892.5	373	0.97	19123725.5	85	0.44	19490167	288	1.48
2004	15–19	3159628	33	1.04	1651535	13	0.79	1508093	20	1.33
	20–29	7871499	116	1.47	4032240	18	0.45	3839259	98	2.55
	30–39	8899296	138	1.55	4536678	33	0.73	4362618	105	2.41
	40–49	8190224	84	1.03	4171055	16	0.38	4019169	68	1.69
	50–59	4785260	59	1.23	2387757	9	0.38	2397503	50	2.09
	60–69	3640881	45	1.24	1669140	12	0.72	1971741	33	1.67
	70–79	1766472	12	0.68	656946	2	0.30	1109526	10	0.90
	80–	627307	1	0.16	182683	0	0.00	444624	1	0.22
	Overall	38940567	488	1.25	19288034	103	0.53	19652533	385	1.96
2005	15–19	3137403	43	1.37	1646916	13	0.79	1490487	30	2.01
	20–29	7697455	155	2.01	3948405	32	0.81	3749050	123	3.28
	30–39	8859246	187	2.11	4514206	43	0.95	4345040	144	3.31
	40–49	8325046	118	1.42	4239408	28	0.66	4085638	90	2.20
	50–59	5079574	82	1.61	2537545	14	0.55	2542029	68	2.68
	60–69	3674785	55	1.50	1693835	13	0.77	1980950	42	2.12
	70–79	1889791	13	0.69	711599	3	0.42	1178192	10	0.85
	80–	658067	2	0.30	192405	1	0.52	465662	1	0.21
	Overall	39321366.5	655	1.67	19484318.5	147	0.75	19837048	508	2.56
2006	15–19	3168790	45	1.42	1668897	13	0.78	1499893	32	2.13
	20–29	7556959	199	2.63	3883477	43	1.11	3673482	156	4.25
	30–39	8789634	229	2.61	4472327	53	1.19	4317307	176	4.08
	40–49	8417974	158	1.88	4293362	44	1.02	4124612	114	2.76
	50–59	5411368	104	1.92	2702637	22	0.81	2708731	82	3.03
	60–69	3701995	71	1.92	1717421	18	1.05	1984574	53	2.67
	70–79	2019758	18	0.89	771738	4	0.52	1248020	14	1.12
	80–	692159	2	0.29	201819	1	0.50	490340	1	0.20
	Overall	39758636.5	826	2.08	19711677.5	198	1.00	20046959	628	3.13
2007	15–19	3261492	55	1.69	1722229	16	0.93	1539263	39	2.53
	20–29	7404699	229	3.09	3812687	50	1.31	3592012	179	4.98
	30–39	8714448	291	3.34	4431071	72	1.62	4283377	219	5.11

Supplementary Table 6. Continued

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Prev	Population[a)]	n	Prev	Population[a)]	n	Prev
	40–49	8498414	210	2.47	4333766	60	1.38	4164648	150	3.60
	50–59	5701710	162	2.84	2851682	38	1.33	2850028	124	4.35
	60–69	3789400	110	2.90	1769337	32	1.81	2020063	78	3.86
	70–79	2145194	42	1.96	832057	9	1.08	1313137	33	2.51
	80–	733244	5	0.68	213071	1	0.47	520173	4	0.77
	Overall	40248600.5	1104	2.74	19965899.5	278	1.39	20282701	826	4.07
2008	15–19	3359504	62	1.85	1779843	19	1.07	1579662	43	2.72
	20–29	7273832	269	3.70	3751232	64	1.71	3522600	205	5.82
	30–39	8570850	337	3.93	4366439	83	1.90	4204411	254	6.04
	40–49	8602965	245	2.85	4377870	69	1.58	4225095	176	4.17
	50–59	5991652	198	3.30	3002132	44	1.47	2989520	154	5.15
	60–69	3909751	138	3.53	1837226	37	2.01	2072525	101	4.87
	70–79	2269327	53	2.34	893794	13	1.45	1375533	40	2.91
	80–	784945	8	1.02	226894	3	1.32	558051	5	0.90
	Overall	40762826	1310	3.21	20235429.5	332	1.64	20527396.5	978	4.76
2009	15–19	3444215	70	2.03	1829733	23	1.26	1614483	47	2.91
	20–29	7126951	303	4.25	3682227	70	1.90	3444724	233	6.76
	30–39	8420915	386	4.58	4295223	92	2.14	4125692	294	7.13
	40–49	8700673	288	3.31	4424693	79	1.79	4275980	209	4.89
	50–59	6324326	235	3.72	3170224	54	1.70	3154102	181	5.74
	60–69	4006145	162	4.04	1894728	46	2.43	2111417	116	5.49
	70–79	2405241	62	2.58	961242	13	1.35	1443999	49	3.39
	80–	844313	14	1.66	243695	4	1.64	600618	10	1.66
	Overall	41272779	1520	3.68	20501764.5	381	1.86	20771014.5	1139	5.48
2010	15–19	3519340	81	2.3	1870870	27	1.44	1648470	54	3.28
	20–29	6927509	336	4.85	3590734	79	2.20	3336775	257	7.70
	30–39	8324780	437	5.25	4244774	104	2.45	4080006	333	8.16
	40–49	8715639	341	3.91	4434091	89	2.01	4281548	252	5.89
	50–59	6726716	270	4.01	3369420	60	1.78	3357296	210	6.26
	60–69	4092726	181	4.42	1946828	50	2.57	2145898	131	6.10
	70–79	2536643	73	2.88	1027908	18	1.75	1508735	55	3.65
	80–	907285	17	1.87	261389	4	1.53	645896	13	2.01
	Overall	41750637.5	1736	4.16	20746014	431	2.08	21004623.5	1305	6.21
2011	15–19	3544677	93	2.62	1882478	33	1.75	1662199	60	3.61
	20–29	6759636	370	5.47	3513630	92	2.62	3246006	278	8.56
	30–39	8226192	476	5.79	4193211	117	2.79	4032981	359	8.90
	40–49	8709045	393	4.51	4435055	98	2.21	4273990	295	6.90
	50–59	7175714	324	4.52	3592137	71	1.98	3583577	253	7.06
	60–69	4150539	195	4.70	1983828	51	2.57	2166711	144	6.65
	70–79	2671440	90	3.37	1096507	22	2.01	1574933	68	4.32

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Supplementary Table 6. Continued

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Prev	Population[a)]	n	Prev	Population[a)]	n	Prev
	80–	968752	19	1.96	278707	5	1.79	690045	14	2.03
	Overall	42205995	1960	4.64	20975553	489	2.33	21230442	1471	6.93
2012	15–19	3508864	108	3.08	1859556	39	2.10	1649308	69	4.18
	20–29	6643072	398	5.99	3462092	101	2.92	3180980	297	9.34
	30–39	8133119	514	6.32	4143117	127	3.07	3990002	387	9.70
	40–49	8713419	445	5.11	4437927	109	2.46	4275492	336	7.86
	50–59	7537309	393	5.21	3776653	85	2.25	3760656	308	8.19
	60–69	4217736	227	5.38	2025529	60	2.96	2192207	167	7.62
	70–79	2845487	121	4.25	1183270	28	2.37	1662217	93	5.59
	80–	1037192	20	1.93	300499	7	2.33	736693	13	1.76
	Overall	42636197.5	2226	5.22	21188643	556	2.62	21447554.5	1670	7.79
2013	15–19	3446370	122	3.54	1818949	44	2.42	1627421	78	4.79
	20–29	6575861	431	6.55	3438604	111	3.23	3137257	320	10.20
	30–39	8018833	570	7.11	4085613	143	3.50	3933220	427	10.86
	40–49	8756554	479	5.47	4452694	119	2.67	4303860	360	8.36
	50–59	7786325	439	5.64	3909235	94	2.40	3877090	345	8.90
	60–69	4343385	268	6.17	2094829	66	3.15	2248556	202	8.98
	70–79	2994554	144	4.81	1258609	31	2.46	1735945	113	6.51
	80–	1115770	25	2.24	327386	7	2.14	788384	18	2.28
	Overall	43037651.5	2478	5.76	21385918.5	615	2.88	21651733	1863	8.6
2014	15–19	3364379	131	3.89	1767803	47	2.66	1596576	84	5.26
	20–29	6585187	467	7.09	3455018	121	3.50	3130169	346	11.05
	30–39	7847119	612	7.80	4000925	156	3.90	3846194	456	11.86
	40–49	8810884	519	5.89	4474485	129	2.88	4336399	390	8.99
	50–59	8000584	489	6.11	4020937	105	2.61	3979647	384	9.65
	60–69	4529947	310	6.84	2194269	75	3.42	2335678	235	10.06
	70–79	3081421	157	5.10	1305432	29	2.22	1775989	128	7.21
	80–	1206731	29	2.40	359795	8	2.22	846936	21	2.48
	Overall	43426251.5	2714	6.25	21578664	670	3.1	21847587.5	2044	9.36
2015	15–19	3283016	140	4.26	1718355	49	2.85	1564661	91	5.82
	20–29	6639681	501	7.55	3492794	130	3.72	3146887	371	11.79
	30–39	7677907	657	8.56	3917274	167	4.26	3760633	490	13.03
	40–49	8783314	563	6.41	4459325	137	3.07	4323989	426	9.85
	50–59	8148785	538	6.60	4097255	112	2.73	4051530	426	10.51
	60–69	4824618	334	6.92	2342576	79	3.37	2482042	255	10.27
	70–79	3130970	173	5.53	1337821	35	2.62	1793149	138	7.70
	80–	1312082	32	2.44	398450	7	1.76	913632	25	2.74
	Overall	43800373	2938	6.71	21763850	716	3.29	22036523	2222	10.08
2016	15–19	3185554	146	4.58	1662817	53	3.19	1522737	93	6.11
	20–29	6695953	541	8.08	3526733	149	4.22	3169220	392	12.37

Supplementary Table 6. Continued

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Prev	Population[a)]	n	Prev	Population[a)]	n	Prev
	30–39	7538708	708	9.39	3850487	185	4.80	3688221	523	14.18
	40–49	8716228	606	6.95	4418590	151	3.42	4297638	455	10.59
	50–59	8247925	594	7.20	4155589	127	3.06	4092336	467	11.41
	60–69	5151264	368	7.14	2502779	92	3.68	2648485	276	10.42
	70–79	3173639	190	5.99	1369560	41	2.99	1804079	149	8.26
	80–	1421692	38	2.67	439824	8	1.82	981868	30	3.06
	Overall	44130963	3191	7.23	21926379	806	3.68	22204584	2385	10.74
2017	15–19	3034108	154	5.08	1582679	60	3.79	1451429	94	6.48
	20–29	6751232	570	8.44	3556649	155	4.36	3194583	415	12.99
	30–39	7388645	743	10.06	3778265	194	5.13	3610380	549	15.21
	40–49	8640494	668	7.73	4376817	178	4.07	4263677	490	11.49
	50–59	8329803	639	7.67	4198174	141	3.36	4131629	498	12.05
	60–69	5438102	405	7.45	2648477	96	3.62	2789625	309	11.08
	70–79	3272217	213	6.51	1426917	47	3.29	1845300	166	9.00
	80–	1531891	41	2.68	482676	9	1.86	1049215	32	3.05
	Overall	44386491.5	3433	7.73	22050653.5	880	3.99	22335838	2553	11.43
2018	15–19	2872026	164	5.71	1497710	65	4.34	1374316	99	7.2
	20–29	6784376	609	8.98	3572700	166	4.65	3211676	443	13.79
	30–39	7258543	799	11.01	3715496	217	5.84	3543047	582	16.43
	40–49	8491463	713	8.40	4308537	194	4.50	4182926	519	12.41
	50–59	8428193	683	8.10	4239770	153	3.61	4188423	530	12.65
	60–69	5721991	450	7.86	2794222	114	4.08	2927769	336	11.48
	70–79	3399523	225	6.62	1497790	49	3.27	1901733	176	9.25
	80–	1644091	42	2.55	527240	11	2.09	1116851	31	2.78
	Overall	44600206	3685	8.26	22153465	969	4.37	22446741	2716	12.10
2019	15–19	2725295	176	6.46	1418938	71	5.00	1306357	105	8.04
	20–29	6784679	658	9.70	3570499	184	5.15	3214180	474	14.75
	30–39	7111489	833	11.71	3645956	227	6.23	3465533	606	17.49
	40–49	8335859	755	9.06	4233741	212	5.01	4102118	543	13.24
	50–59	8518747	725	8.51	4283873	162	3.78	4234874	563	13.29
	60–69	6045294	494	8.17	2956003	124	4.19	3089291	370	11.98
	70–79	3505478	230	6.56	1559596	59	3.78	1945882	171	8.79
	80–	1769302	45	2.54	577224	14	2.43	1192078	31	2.60
	Overall	44796142.5	3916	8.74	22245830	1053	4.73	22550312.5	2863	12.70
2020	15–19	2551013	183	7.17	1325906	73	5.51	1225107	110	8.98
	20–29	6777445	701	10.34	3562457	196	5.50	3214988	505	15.71
	30–39	6917018	872	12.61	3557428	240	6.75	3359590	632	18.81
	40–49	8244513	798	9.68	4187027	224	5.35	4057486	574	14.15
	50–59	8538879	774	9.06	4299675	181	4.21	4239204	593	13.99
	60–69	6440303	523	8.12	3150710	132	4.19	3289593	391	11.89

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Supplementary Table 6. Continued

Year	Age group	Overall			Male			Female		
		Population[a)]	n	Prev	Population[a)]	n	Prev	Population[a)]	n	Prev
	70–79	3603372	244	6.77	1616395	66	4.08	1986977	178	8.96
	80–	1895714	46	2.43	627782	12	1.91	1267932	34	2.68
	Overall	44968256.5	4141	9.21	22327380	1124	5.03	22640876.5	3017	13.33
2021	15–19	2395066	189	7.89	1242509	75	6.04	1152557	114	9.89
	20–29	6704992	737	10.99	3519241	208	5.91	3185751	529	16.61
	30–39	6753190	916	13.56	3483443	254	7.29	3269747	662	20.25
	40–49	8152507	834	10.23	4140356	238	5.75	4012151	596	14.85
	50–59	8541582	812	9.51	4309557	192	4.46	4232025	620	14.65
	60–69	6879683	549	7.98	3367039	135	4.01	3512644	414	11.79
	70–79	3673107	248	6.75	1658872	65	3.92	2014235	183	9.09
	80–	2022856	47	2.32	679285	11	1.62	1343571	36	2.68
	Overall	45122983	4332	9.60	22400302	1178	5.26	22722681	3154	13.88
2022	15–19	2340933	194	8.29	1211373	78	6.44	1129560	116	10.27
	20–29	6516721	761	11.68	3416095	213	6.24	3100626	548	17.67
	30–39	6635875	934	14.08	3432351	258	7.52	3203524	676	21.10
	40–49	8060737	853	10.58	4091324	243	5.94	3969413	610	15.37
	50–59	8548548	837	9.79	4315989	201	4.66	4232559	636	15.03
	60–69	7230879	579	8.01	3544508	144	4.06	3686371	435	11.80
	70–79	3752573	239	6.37	1706640	60	3.52	2045933	179	8.75
	80–	2170508	49	2.26	741239	13	1.75	1429269	36	2.52
	Overall	45256773.5	4446	9.82	22459518.5	1210	5.39	22797255	3236	14.19

Crude annual prevalence rates are shown overall and stratified by age group and sex. Population denominators correspond to the mid-year population of each year.

[a)]Population refers to the mid-year population of the corresponding year.

Supplementary Table 7. Annual percent changes (APCs) in age-adjusted, sex-adjusted, and age- and sex-adjusted incidence and prevalence rates of adult-onset Still's disease from 2003 to 2022

Outcome	Linear APC, % (95% CI)	*p* value	Joinpoint	APC before	APC after	ΔBIC	Model comparison *p* value
Age-adjusted incidence rate	1.40 (–0.62, 3.46)	0.164	2007	21.33	–1.23	–12.71	3.13 × 10^-4
Sex-adjusted incidence rate	1.23 (–0.49, 2.98)	0.151	2019	3.09	–17.99	–11.81	4.66 × 10^-4
Age- and sex-adjusted incidence rate	1.41 (–0.58, 3.44)	0.155	2007	20.97	–1.17	–12.60	3.29 × 10^-4
Age-adjusted prevalence rate	12.44 (10.49, 14.42)	3.57 × 10^-11	2009	27.46	7.90	–56.69	1.88 × 10^-12
Sex-adjusted prevalence rate	12.04 (10.16, 13.96)	3.77 × 10^-11	2009	26.52	7.66	–53.69	6.76 × 10^-12
Age- and sex-adjusted prevalence rate	12.55 (10.58, 14.56)	3.91 × 10^-11	2009	27.81	7.94	–56.40	2.10 × 10^-12

APCs were estimated using log-linear regression models. Joinpoint APCs were derived from one-joinpoint segmented log-linear models, with the optimal joinpoint selected using the Bayesian information criterion. Model comparison *p* values indicate comparisons between the segmented and linear models. Rates are expressed per 100,000 population.

CI, confidence interval; BIC, Bayesian information criterion.

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Supplementary Table 8. Descriptive baseline demographic and clinical characteristics according to exploratory claims-based treatment trajectory groups in patients with AOSD

Characteristics	Monocyclic[a)]	Polycyclic[a)]	Chronic[a)]	Unclassified[a)]	Total
Incident number (% of all patients)	146 (3.0)	1,913 (39.6)	855 (17.7)	1,911 (39.6)	4,825 (100)
Mean follow-up months (SD)	49.4 (65.7)	125.8 (64.2)	87.0 (67.1)	128.6 (70.7)	117.7 (70.2)
Sex, n (% within operational group)					
Male	54 (4.0)	498 (36.6)	206 (15.2)	601 (44.2)	1,359 (100)
Female	92 (2.7)	1,415 (40.8)	649 (18.7)	1,310 (37.8)	3,466 (100)
Age at diagnosis, mean (SD)	45.4 (17.3)	43.5 (16.1)	49.4 (17.0)	45.8 (16.9)	45.5 (16.7)
Age at diagnosis by age group, n (% within group)					
15–19	6 (4.1)	88 (4.6)	32 (3.7)	72 (3.8)	198 (4.1)
20–29	32 (21.9)	355 (18.6)	104 (12.2)	285 (14.9)	776 (16.1)
30–39	17 (11.6)	405 (21)	128 (15.0)	417 (21.8)	967 (20.0)
40–49	28 (19.2)	376 (19.7)	134 (15.7)	353 (18.5)	891 (18.5)
50–59	24 (16.4)	341 (17.8)	174 (20.4)	352 (18.4)	891 (18.5)
60–69	30 (20.5)	215 (11.0)	188 (22.0)	240 (12.6)	673 (13.9)
70–79	6 (4.1)	119 (6.2)	74 (8.7)	145 (7.6)	344 (7.1)
80–	3 (2.1)	14 (0.7)	21 (2.5)	47 (2.5)	85 (1.8)
Disability status present, n (% of all patients)	7 (1.4)	174 (35.6)	110 (22.5)	198 (40.5)	489 (100)
Type of insurance, n (%)					
Health insurance	141 (3.0)	1,856 (39.5)	836 (17.8)	1,868 (39.7)	4,701 (100)
Medical aid	5 (4.0)	57 (46.0)	19 (15.3)	43 (34.7)	124 (100)
Use of medication, n (% within group)[b)]					
Any csDMARDs	122 (83.6)	1665 (87.0)	796 (93.1)	772 (40.4)	3,355 (69.5)
Methotrexate	115 (78.8)	1,504 (78.6)	752 (88.0)	425 (22.2)	2,796 (57.9)
Sulfasalazine	8 (5.5)	236 (12.3)	130 (15.2)	120 (6.3)	494 (10.2)
Hydroxychloroquine	35 (24.0)	833 (43.5)	335 (39.2)	489 (25.6)	1,692 (35.1)
Leflunomide	19 (13.0)	294 (15.4)	261 (30.5)	65 (3.4)	639 (13.2)
Any immunosuppressants	49 (33.6)	692 (36.2)	431 (50.4)	275 (14.4)	1,447 (30)
Azathioprine	8 (5.5)	243 (12.7)	151 (17.7)	101 (5.3)	503 (10.4)
Cyclosporine	31 (21.2)	453 (23.7)	257 (30.1)	154 (8.1)	895 (18.5)
Tacrolimus	17 (11.6)	155 (8.1)	178 (20.8)	50 (2.6)	400 (8.3)
Any bDMARDs	20 (13.7)	91 (4.8)	179 (20.9)	22 (1.2)	312 (6.5)
Adalimumab	0 (0)	9 (0.5)	9 (1.1)	2 (0.1)	20 (0.4)
Infliximab	1 (0.7)	16 (0.8)	29 (3.4)	2 (0.1)	48 (1.0)
Golimumab	0 (0)	0 (0)	2 (0.2)	0 (0)	2 (0)
Tocilizumab	18 (12.3)	63 (3.3)	145 (17.0)	15 (0.8)	241 (5.0)
Anakinra	0 (0)	1 (0.1)	1 (0.1)	1 (0.1)	3 (0.1)
Abatacept	1 (0.7)	8 (0.4)	8 (0.9)	0 (0)	17 (0.4)
Rituximab	1 (0.7)	1 (0.1)	3 (0.4)	2 (0.1)	7 (0.1)
Any tsDMARDs	2 (1.4)	5 (0.3)	8 (0.9)	0 (0)	15 (0.3)
Tofacitinib	0 (0)	4 (0.2)	3 (0.4)	0 (0)	7 (0.1)
Baricitinib	1 (0.7)	1 (0.1)	5 (0.6)	0 (0)	7 (0.1)

Supplementary Table 8. Continued

Characteristics	Monocyclic[a)]	Polycyclic[a)]	Chronic[a)]	Unclassified[a)]	Total
Upadacitinib	1 (0.7)	0 (0)	0 (0)	0 (0)	1 (0)
Any NSAIDs	132 (90.4)	1,871 (97.8)	823 (96.3)	1,853 (97.0)	4,679 (97.0)
Any corticosteroids	143 (97.9)	1,884 (98.5)	838 (98.0)	1,851 (96.9)	4,716 (97.7)

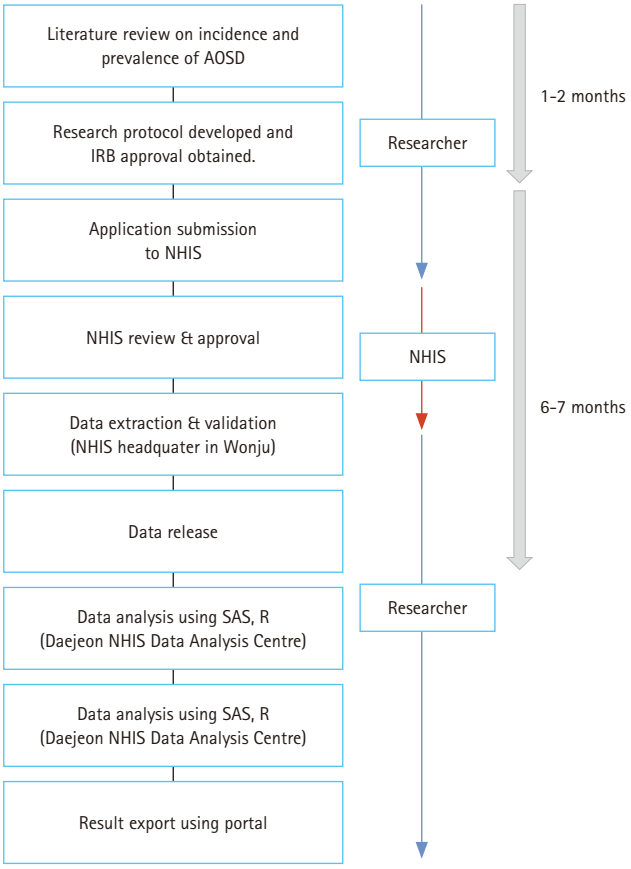
The categories shown in this table were derived from prespecified claims-based operational rules based on longitudinal medication-use patterns. They are presented for descriptive purposes only and should not be interpreted as clinically validated disease-course subtypes of AOSD.

AOSD, adult-onset Still's disease; SD, standard deviation; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs, biologic disease-modifying anti-rheumatic drugs; tsDMARDs, targeted synthetic disease-modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs.

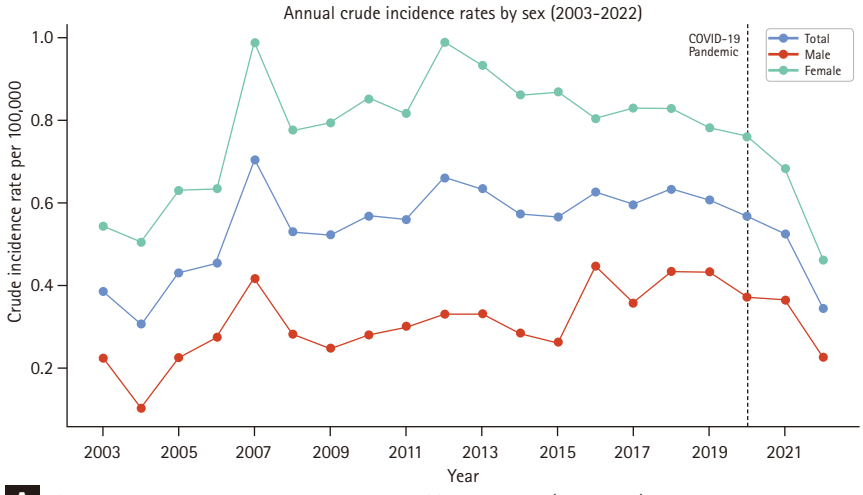
[a)]Operational group.

[b)]Use of medication during the first three months after diagnosis, showing the initial treatment regimen.

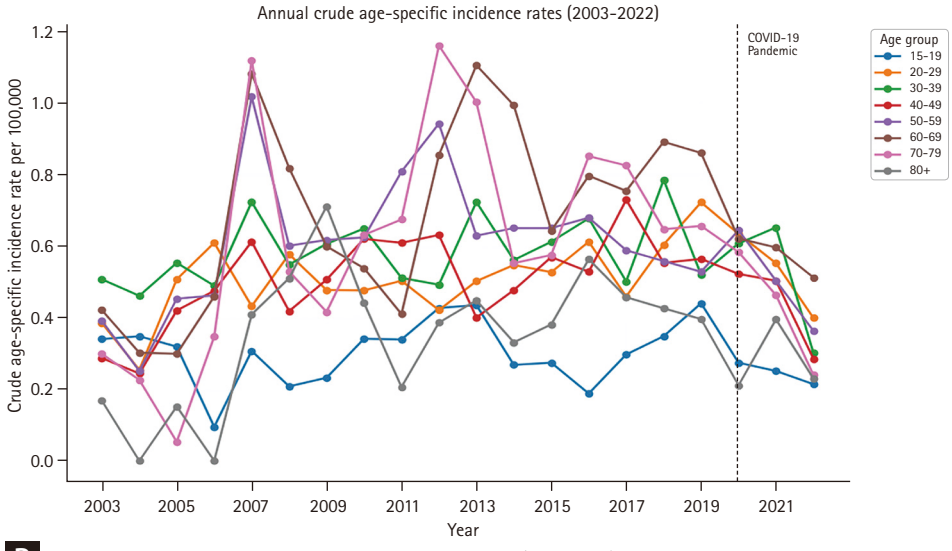
https://doi.org/10.3904/kjim.2026.062



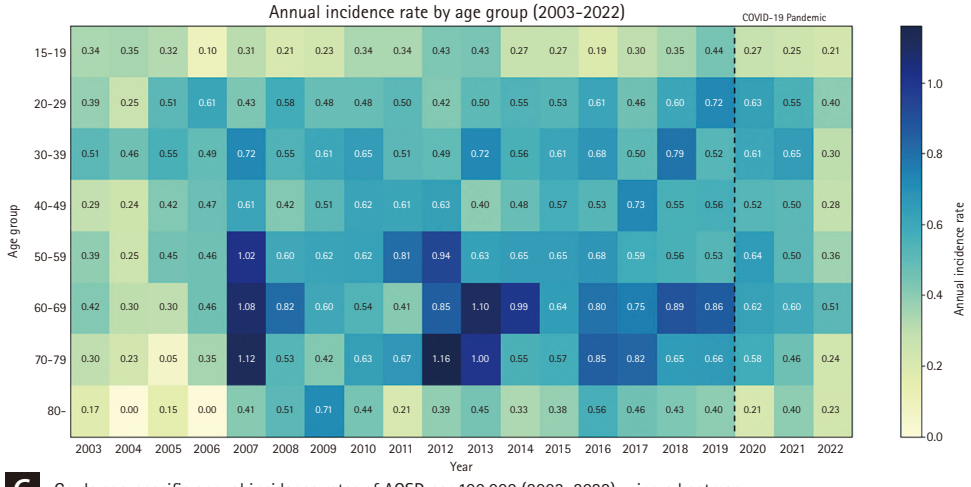
Supplementary Figure 1. Flow diagram of data acquisition and utilisation from the Korean National Health Insurance Service (NHIS). The diagram illustrates the process of data extraction, linkage, and utilisation of nationwide claims data for the identification and analysis of patients with adult-onset Still's disease (AOSD).



A Crude and sex-specific annual incidence rates of AOSD per 100,000 (2003–2022)



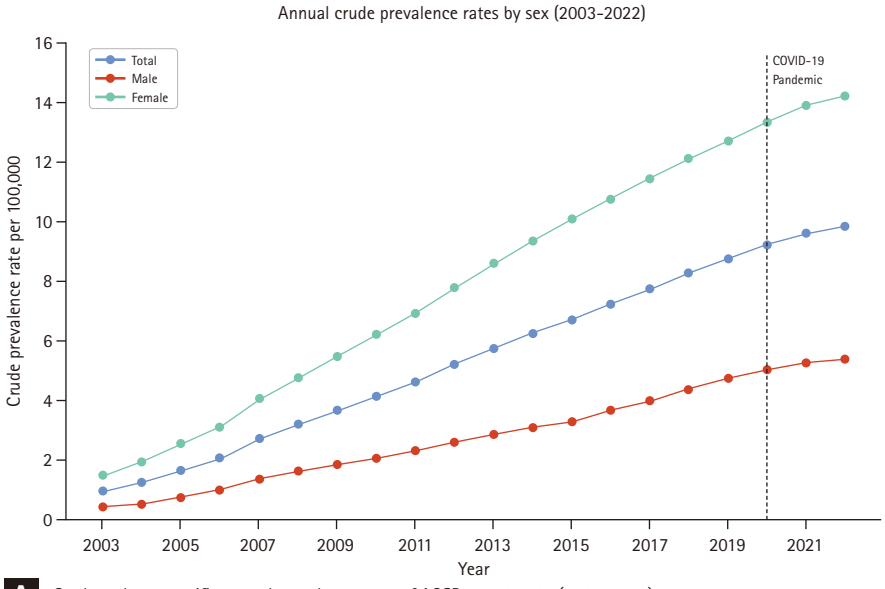
B Crude age-specific annual incidence rates of AOSD per 100,000 (2003–2022)



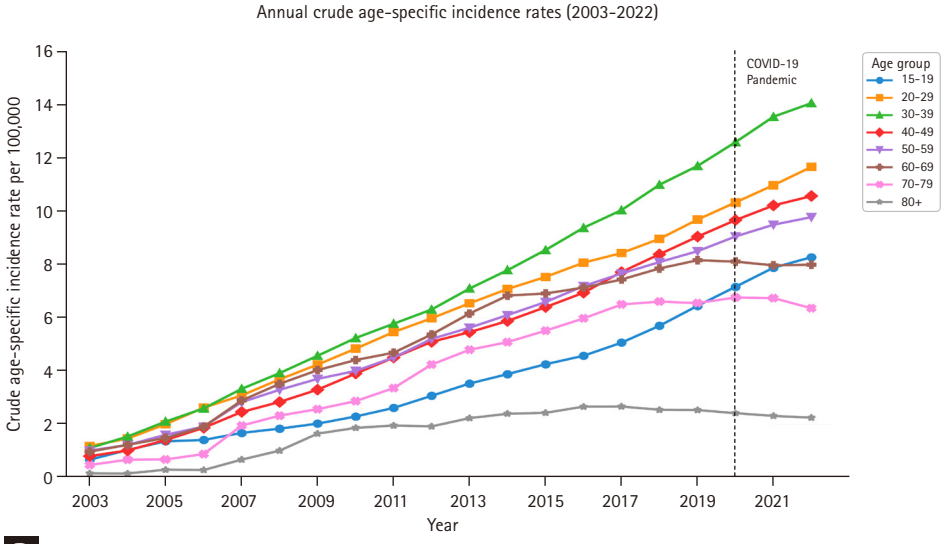
C Crude age-specific annual incidence rates of AOSD per 100,000 (2003–2022) using a heatmap

Supplementary Figure 2. Crude annual incidence rates of adult-onset Still's disease (AOSD) per 100,000 population, 2003–2022. Crude incidence rates are presented overall and stratified by sex and age group. (A) Overall and sex-specific annual incidence rates. (B) Age-specific annual incidence rates. (C) Heatmap of age-specific annual incidence rates.

https://doi.org/10.3904/kjim.2026.062

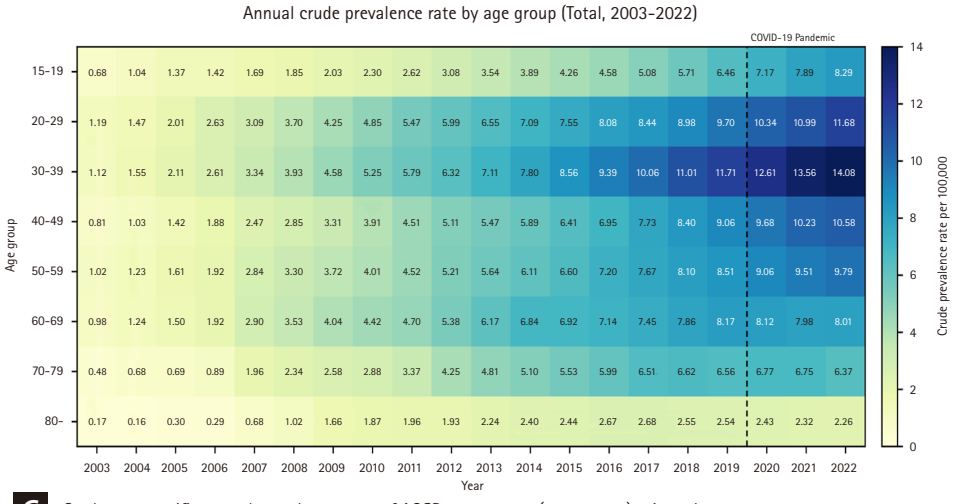


A Crude and sex-specific annual prevalence rates of AOSD per 100,000 (2003–2022)



B Crude age-specific annual prevalence rates of AOSD per 100,000 (2003–2022)

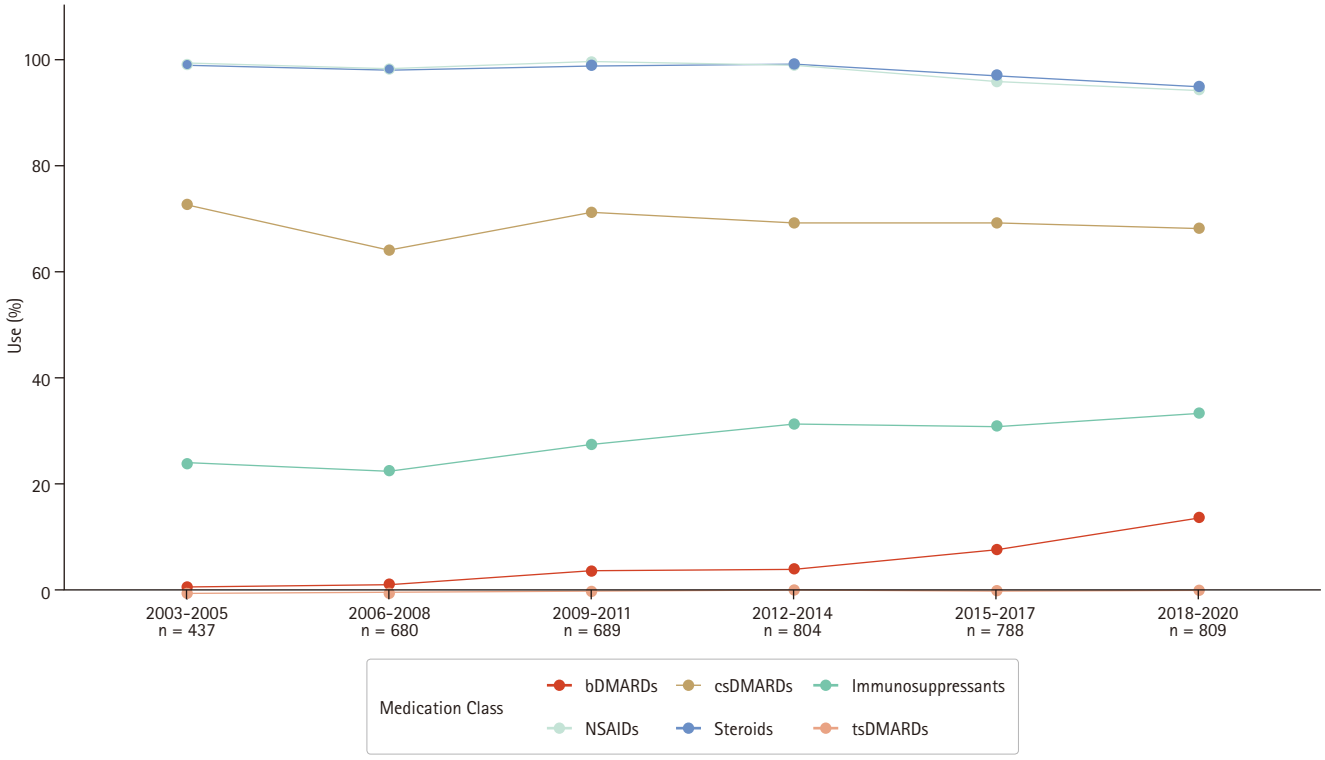
Supplementary Figure 3. Crude annual prevalence rates of adult-onset Still's disease (AOSD) per 100,000 population, 2003–2022. Crude prevalence rates are shown overall and stratified by sex and age group. (A) Overall and sex-specific annual prevalence rates. (B) Age-specific annual prevalence rates. (C) Heatmap of age-specific annual prevalence rates.



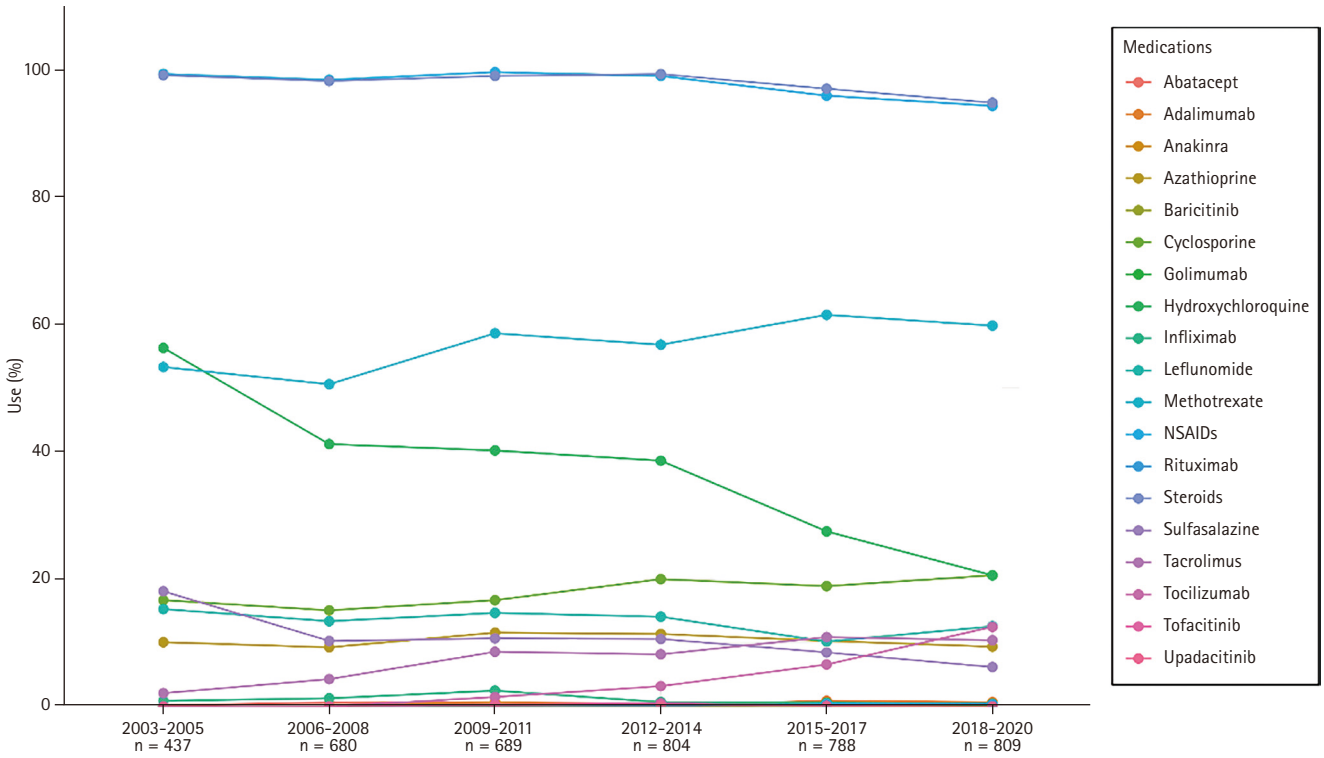
C Crude age-specific annual prevalence rates of AOSD per 100,000 (2003–2022) using a heatmap

Supplementary Figure 3. Continued.

https://doi.org/10.3904/kjim.2026.062



Supplementary Figure 4. Trends in treatment patterns by medication class during the first 3 months after diagnosis of adult-onset Still's disease, 2003–2020. This figure illustrates temporal changes in the use of major medication classes prescribed within the first 3 months after diagnosis. csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs, biologic disease-modifying anti-rheumatic drugs; tsDMARDs, targeted synthetic disease-modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs.



Supplementary Figure 5. Trends in treatment patterns by individual medications during the first 3 months after diagnosis of adult-onset Still's disease, 2003–2020. Temporal trends in the use of individual therapeutic agents prescribed during the early disease period are presented. NSAIDs, non-steroidal anti-inflammatory drugs.

https://doi.org/10.3904/kjim.2026.062