



Study Report

P5-C2-001

DARWIN EU[®] - Characterising the use of JAK inhibitors in Europe: A Drug Utilisation Study Update

20/08/2026

Version 4.0

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Public

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Study title¹	DARWIN EU® - Characterising the use of JAK inhibitors in Europe: a Drug Utilisation Study Update
Study report version	V4.0
Date	20/08/2026
EUPAS number	EUPAS1000000998
Active substance	JAK inhibitor (abrocitinib, baricitinib, filgotinib, tofacitinib, upadacitinib)
Medicinal product	N/A
Research question and objectives	This study aimed to identify and characterise new JAK inhibitor (JAKi) initiation. The specific objectives were: 1. To estimate the incidence of new JAKi initiation, overall and for each individual JAKi ingredient. 2. To characterise individuals initiating treatment for each individual JAKi, overall and stratified by indication.
Countries of study	Croatia, Denmark, Finland, Germany, Spain, Sweden
Authors	Elin Rowlands (e.rowlands@darwin-eu.org) Amy Lam (a.lam@darwin-eu.org) Daniel Prieto-Alhambra (d.prietoalhambra@darwin-eu.org)

¹This is a routinely repeated study from P3-C1-001 with [EUPAS1000000424](#).

LIST OF ABBREVIATIONS

Acronyms/term	Description
ATC	Anatomical Therapeutic Chemical
CI	Confidence Interval
CIPH	Croatian Institute of Public Health
CDM	Common Data Model
DARWIN EU®	Data Analysis and Real-World Interrogation Network
DDD	Defined Daily Dose
DK-DHR	Danish Data Health Registries
DKMA	Danish Medicines Agency
DRE	Digital Research Environment
DUS	Drug Utilisation Study
ED	Emergency Department
EHR	Electronic Health Records
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
Erasmus MC	Erasmus Medical Center
EU	European Union
EUPAS	EU Post-Authorisation Studies Register
FDA	Food and Drug Administration
FinOMOP-THL	Finnish Care Register for Health Care
FISABIO	Fundació per al Foment de la Investigació Sanitària i Biomèdica de la Comunitat Valenciana
GDPR	General Data Protection Regulation
GP	General Practitioner
HARPER	HARmonized Protocol Template to Enhance Reproducibility
HI-SPEED	Health Impact - Swedish Population Evidence Enabling Data-linkage
IQR	Interquartile Range
IQVIA DA Germany	IQVIA Disease Analyzer Germany
ICD	International Classification of Diseases
IPCI	Integrated Primary Care Information
IRB	Institutional Review Board
JAKi	Janus kinase inhibitor/s
LOINC	Logical Observation Identifiers Names and Codes
MACE	Major Adverse Cardiovascular Event
NAJS	Croatian National Public Health Information System
NLHR	Norwegian Linked Health Registry Data
OHDSI	Observational Health Data Sciences and Informatics

Acronyms/term	Description
OMOP	Observational Medical Outcomes Partnership
ORAL	Oral Rheumatoid Arthritis Trial
Q25	25 th Percentile
Q75	75 th Percentile
RxNorm	Medical prescription normalised
SD	Standard Deviation
SMPA-GU	Swedish Medical Products Agency - Gothenburg University
SNOMED	Systemized Nomenclature of Medicine
TNF	Tumour Necrosis Factor
VID	Valencia Health System Integrated Dataset

1. TITLE

DARWIN EU® - Characterising the use of JAK inhibitors in Europe: A Drug Utilisation Study Update

2. DESCRIPTION OF THE STUDY TEAM

Study team role	Names	Organisation
Principal Investigator	Elin Rowlands Daniel Prieto-Alhambra	University of Oxford
Data Scientist	Kim López-Güell Edward Burn	University of Oxford
Clinical Domain Expert	Amy Lam	University of Oxford
Statistician	Daniel Prieto-Alhambra	University of Oxford
Study Manager	Natasha Yefimenko Nosova	Erasmus MC
Data source	Names	Data Partner Organisation*
Croatian National Public Health Information System (NAJS)	Marko Čavlina Antea Jezidžić Anamaria Jurčević Karlo Pintarić Ivan Pristaš Jakov Vuković	Croatian Institute of Public Health (CIPH)
Danish Data Health Registries (DK-DHR)	Elvira Bräuner Susanne Bruun	Danish Medicines Agency (DKMA)
Finnish Care Register for Health Care (FinOMOP-THL)	Toni Lehtonen	FinOMOP
IQVIA Disease Analyzer Germany (IQVIA DA Germany)	Ellen Gerritsen Akram Mendez Gargi Jadhav Dina Vojinovic	IQVIA
Valencia Health System Integrated Dataset (VID)	Celia Robles Cabaniñas Fran Llopis Cardona Gabriel Sanfèlix Gimeno	Fundació per al Foment de la Investigació Sanitària i Biomèdica de la Comunitat Valenciana (FISABIO)
Health Impact - Swedish Population Evidence Enabling Data-linkage (HI-SPEED)	Huiqi Li Fredrik Nyberg Rickard Ljung Talbäck Mats Marcel Ballin	Swedish Medical Products Agency - Gothenburg University (SMPA-GU)

*Data partners do not have an investigator role. Data partners execute code at their data source, review, and approve their results.

3. ABSTRACT

Rationale and background

Janus kinase inhibitors (JAKi) are increasingly used for the treatment of several autoimmune conditions, including rheumatoid arthritis and inflammatory bowel disease. To support the design and feasibility of future safety studies, the current study aimed to identify the incidence of new JAKi initiation over time and to characterise JAKi initiation in Europe. This is a rerun of a previous study with the same aim, expanding on the countries and time period covered by the previous report.

Objectives

The specific objectives of this study were:

1. To estimate the incidence of new JAKi initiation, overall and for each individual JAKi ingredient.
2. To characterise individuals initiating treatment for each individual JAKi, overall and stratified by indication.

Methods

This was a descriptive study.

Population

The drug use incidence cohort included all individuals present in the selected data sources from 1st January 2018 (or 1st January 2019 for HI-SPEED) until the end of available data, with at least 365 days of prior data.

The individual-level characterisation cohorts included all new JAKi initiations during the study period with at least 365 days of prior data visibility.

Variables

Drugs of interest: abrocitinib, filgotinib, baricitinib, upadacitinib, tofacitinib

Potential indications: alopecia areata, atopic dermatitis, axial spondylitis, inflammatory bowel disease, juvenile arthritis, juvenile idiopathic arthritis, psoriatic arthritis, rheumatoid arthritis, and unknown

Other characteristics of individuals initiating JAKi: age, sex, and time from first diagnosis of indication to JAKi therapy initiation.

Treatment characteristics: treatment duration

Data sources

Six data sources from six European countries (Croatia, Denmark, Sweden, Finland, Germany, Spain) were used, covering both primary and secondary care settings.

Statistical analysis

Incidence of JAKi initiation, overall and for each individual JAKi ingredient, was calculated annually as the number of JAKi initiations per 100,000 person-years of the population at risk of exposure during the period for each calendar year, with 95% Poisson exact confidence intervals. For each JAKi ingredient, new individuals initiating JAKi were characterised in terms of age at initiation, sex, history of diagnoses of potential indication, and prior use of other JAKi ingredients, overall and stratified by potential indication. Time from first diagnosis of potential indication to first JAKi initiation and treatment duration of the first treatment era were reported for each JAKi ingredient, stratified by indication. Treatment duration was summarised, providing the minimum, p25, median, p75, and maximum duration.

Results

Among the 5 included JAKi ingredients, upadacitinib had the highest count of individuals initiating treatment across the data sources, ranging from 710 in DK-DHR to 5,635 in HI-SPEED. Abrocitinib had the lowest count and its use was observed in only two data sources: 167 from FinOMOP-THL and 94 from VID.

The median age of initiation was lowest for abrocitinib, with most starting therapy before age 40. Most other individuals initiating JAKi were aged 41 – 60 years old. The majority of individuals initiating treatment were female, for all JAKi except abrocitinib.

Treatment duration was highly variable, with median treatment duration ranging from 6 – 12 months for abrocitinib to 7 – 24 months for tofacitinib. Median time from potential indication diagnosis to JAKi initiation was also highly variable, typically between 5 – 20 months, with marked differences between data sources and indications.

The majority of individuals initiating JAKi had a history of rheumatoid arthritis as their likely indication, except for abrocitinib, where over 90% of individuals had a record of atopic dermatitis. Inflammatory bowel disease was the second most commonly recorded. In general, at least 90% of individuals initiating JAKi had a history of at least one potential indication in all data sources.

Discussion

The use of JAKi as a class increased over time, largely driven by an increased uptake of newly approved JAKi (upadacitinib and filgotinib) and of newly approved indications. The results of this study show that a comparative safety study on JAKi use among younger individuals with atopic dermatitis or inflammatory bowel disease might be feasible, depending on other feasibility considerations such as comparator and outcome capture. Larger sample sizes may be achievable for baricitinib, tofacitinib, and upadacitinib; however, abrocitinib remains sparsely used and only in a few countries. Additionally, filgotinib is primarily used to treat rheumatoid arthritis and is therefore not commonly used in younger populations.

4. AMENDMENTS AND UPDATES

None.

5. MILESTONES

Study deliverable	Timelines (planned*)	Timelines (actual)
Final Study Protocol	April 2026	26 May 2026
Creation of Analytical code	April 2026	May 2026
Execution of Analytical Code on the data	May 2026	01 June 2026
Draft Study Report	June 2026	09 July 2026
Final Study Report	July 2026	22 July 2026

*Planned dates are dependent on obtaining approvals from the internal review boards of the data sources and deliverables review rounds.

6. RATIONALE AND BACKGROUND

Janus kinase inhibitor (JAKi) therapy has been gaining popularity for the treatment of several autoimmune conditions, including rheumatoid arthritis, inflammatory bowel disease, and atopic dermatitis. The first JAKi, tofacitinib, was approved by the European Medicines Agency (EMA) for the management of rheumatoid arthritis in 2017.[1] A Food and Drug Administration (FDA) requested study (the Oral Rheumatoid Arthritis Trial (ORAL) Surveillance trial) showed a higher risk of major adverse cardiovascular events (MACE), cancer, and adjudicated opportunistic infection with tofacitinib compared to tumour necrosis factor (TNF) inhibitors in individuals aged 50 years or older with at least one cardiovascular risk factor.[2, 3]

Further research has been conducted on the safety profile of JAKi for other indications, including psoriatic arthritis, ulcerative colitis, and atopic dermatitis.[4 – 6] It was shown that risk of venous thrombotic events of JAK inhibitor initiation was similar to placebo in individuals with atopic dermatitis and ulcerative colitis.[5, 6] Incidence of adverse events, including herpes zoster infection and thrombotic events, remained similar with longer follow-up up to two years in psoriatic arthritis individuals with JAK inhibitor.[4] A meta-analysis focusing on the JAKi initiation for immune-mediated skin conditions, including atopic dermatitis, alopecia areata, and vitiligo, also showed no significant difference between JAKi and placebo or active comparators in the composite outcome of MACE and all-cause mortality, as well as risk of venous thrombotic events.[7]

More recently, several real-world studies have begun to provide complementary evidence to clinical trials. An international cohort study using data from rheumatoid arthritis registries found no increased risk of MACE during the first two years of treatment with JAKi compared with TNF inhibitors.[8] Similarly, a cohort study on individuals with inflammatory bowel disease using claims data from the United States found no increased risk of MACE, venous thromboembolism, or serious infections with JAK inhibitors compared with TNF antagonists after adjustment for baseline characteristics.[9] However, the available evidence, especially in indications other than rheumatoid arthritis and inflammatory bowel disease, has been limited by short duration of follow-up and limited sample size, and more research is needed to understand the safety profile in these populations. Since new indications were approved relatively recently and the use of JAKi within those indications has so far not been that common, the sample size under such indications is an issue that hampers future research. Therefore, a study in a federated network, such as DARWIN EU®, where patients are pooled over data sources, might be a solution.

The current study aimed to identify the incidence of new JAKi initiation over time and to characterise new use of JAKi in Europe to inform the feasibility of future safety studies.

This present study is a routine repeated study of a previous DARWIN EU® Network study, *P3-C1-001 - Characterising the use of JAK inhibitors in Europe: a Drug Utilisation Study* ([EUPAS1000000424](#)), covering the period from 2017 to 2024. This present study was repeated to include more recent data and additional data sources.

7. RESEARCH QUESTION AND OBJECTIVES

Research question

This study aimed to identify the incidence of new JAKi initiation over time and to characterise new JAKi initiations in Europe to inform the feasibility of future safety studies.

Research objectives

The specific objectives of this study were:

1. To estimate the incidence of new JAKi initiation, overall and for each individual JAKi ingredient.
2. To characterise individuals initiating treatment for each individual JAKi, overall and stratified by indication.

8. RESEARCH METHODS

8.1. Study design

A descriptive cohort study was conducted using routinely collected health data from six European data sources.

The incidence of new JAKi initiation was estimated.

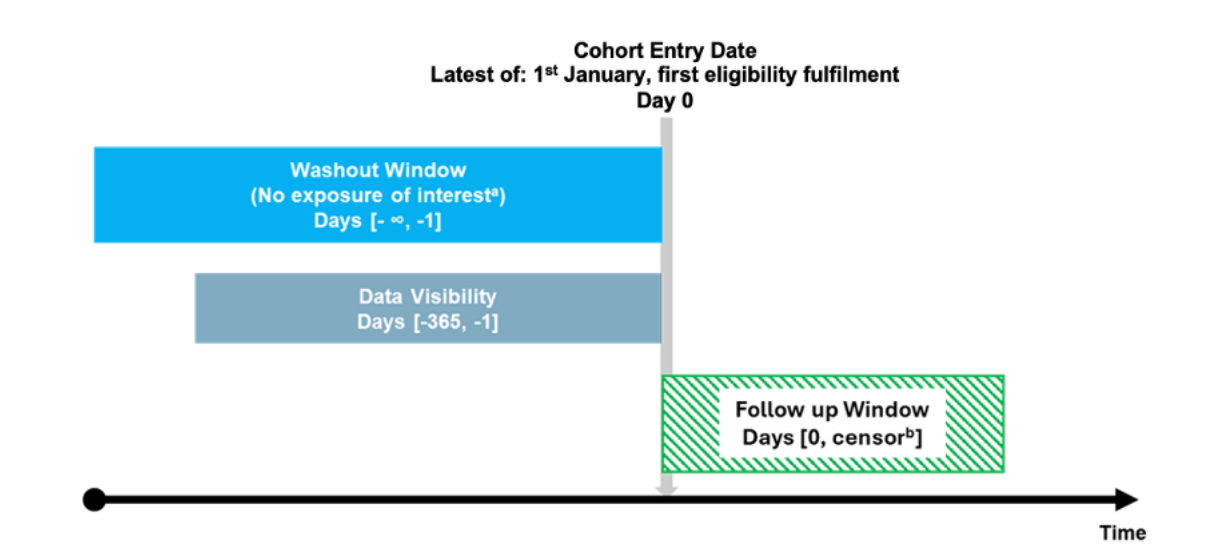


Figure 1. HARPER study design diagram Objective 1 - JAKi initiation incidence.

- a. Exposures of interest: any JAKi, individual JAKi ingredient.
 - b. Earliest of: 31st December of each year, loss of follow-up, end of data availability, initiation of exposure of interest.
- HARPER = HARmonized Protocol Template to Enhance Reproducibility; JAKi = Janus kinase inhibitor/s.

Individuals initiating JAKi were characterised.

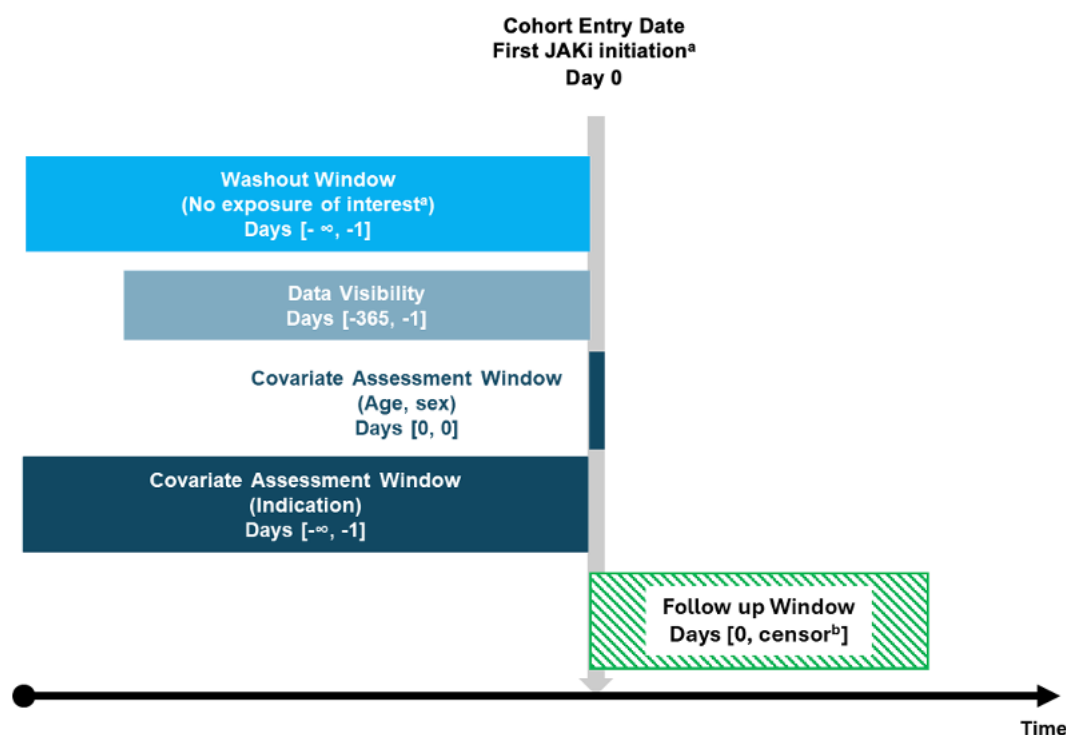


Figure 2. HARPER study design diagram Objective 2 - Individual-level characterisation.

a. Exposures of interest: any JAKi, individual JAKi ingredient.

b. Earliest of: end of treatment with index exposure of interest, death, loss to follow-up, end of data availability.

HARPER = HARmonized Protocol Template to Enhance Reproducibility; JAKi = Janus kinase inhibitor/s.

8.2. Follow-up

For treatment initiation incidence estimation (Objective 1)

Eligible individuals began to contribute person-time from the latest of the following: (1) study start date, (2) date at which the observation period starts (i.e. 1st January of each year), or (3) date when eligibility criteria are first fulfilled.

Study participants stopped contributing person-time at the earliest date of the following: (1) date on which the observation period ends (i.e. 31st December of each year), (2) end of data availability, or (3) date of first JAKi exposure, if applicable (outcome of the incidence analysis).

For individual-level characterisation (Objective 2)

Eligible individuals were followed from the date of first JAKi exposure until the earliest of: (1) end of index JAKi treatment exposure, (2) death, (3) loss to follow-up, or (4) end of data availability.

8.3. Study population with inclusion and exclusion criteria

For treatment initiation incidence estimation (Objective 1)

All individuals available in the respective data sources during the study period, with at least 365 days of data visibility, were included.

Different exclusion criteria were applied, corresponding to each outcome of the JAKi exposure incidence rate analysis (as defined in [Section 8.6.2](#)). For incidence of first JAKi ever initiation, individuals with any JAKi

exposure before the index date were excluded. For incidence of individual JAKi ingredient (abrocitinib/baricitinib/filgotinib/upadacitinib/tofacitinib) initiation, only individuals with respective JAKi exposure before the index date were excluded.

For individual-level characterisation (Objective 2)

All individuals available in the respective data sources during the study period who newly initiated JAKi and had at least 365 days of data visibility before JAKi initiation were included. Individuals with specific JAKi exposure before the start of the study period were excluded.

8.4. Study setting and data sources

This study was conducted using six data sources onboarded into the DARWIN EU® Network of Data Partners from six European countries. These data sources were selected based on geographic representativeness and availability of data on JAK inhibitors. The selected data sources cover Croatia, Denmark, Finland, Germany, Spain, and Sweden. The results generated from these data sources cover regions of Northern, Central, and Southern Europe. All data were *a priori* mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM).

Table 1. Description of selected data sources.

Country	Name of Data source	Health Care setting	Type of Data	Number of individuals	Calendar period covered by each data source	Contributing to
Croatia	NAJS	Primary care GP, secondary care specialist, hospital inpatient care	Electronic health records (EHR), registries, other	4.8M	02/2014 – 06/2025	Objectives 1 and 2
Denmark	DK-DHR	Community pharmacists, secondary care specialist, hospital inpatient care	EHR, registries, other	8.7M	01/1995 – 10/2025	Objectives 1 and 2
Finland	FinOMOP-THL	Primary care GP, primary care specialist, secondary care specialist, hospital inpatient care	EHR, registries	6.8M	01/2011 – 12/2024	Objectives 1 and 2
Germany	IQVIA DA Germany	Primary care GP, primary care specialist	EHR	43.7M	02/1992 – 06/2025	Objectives 1 and 2
Spain	VID	Primary care GP, primary care specialist, secondary care specialist, hospital inpatient care, other	EHR, registries	6.0M	01/2009 – 12/2024	Objectives 1 and 2
Sweden	HI-SPEED	Primary care GP, secondary	Registries	12.1M	01/2015 – 08/2025	Objectives 1 and 2

Country	Name of Data source	Health Care setting	Type of Data	Number of individuals	Calendar period covered by each data source	Contributing to
		care specialist, hospital inpatient care				

DK-DHR = Danish Data Health Registries; EHR = Electronic Health Records; FinOMOP-THL = Finnish Care Register for Health Care; GP = General Practitioner; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset.

The previous study on the same objectives included the following data sources: FinOMOP-THL (01/2017 – 10/2024), IPCI (01/2017 – 06/2024), IQVIA DA Germany (01/2017 – 06/2024), NLHR (01/2017 – 12/2023), and VID (01/2018 – 12/2021). See the full protocol and documentation for that study [here](#).

Data sources selection

These data sources fulfilled the criteria required in terms of data quality, completeness, timeliness, and representativeness for a drug utilisation study while covering different regions of Europe. See more details on the fitness for use assessment in [Annex II](#).

8.5. Study period

The study period ranged from 1st January 2018 for all data sources, except HI-SPEED, for which the study period started on 1st January 2019, and followed until end of available data for each included data source (see [Table 1](#)).

8.6. Variables

8.6.1. Exposure

No exposure variable was defined for Objective 1.

Exposure of interest in the individual-level characterisation (Objective 2) was the initiation of treatment (first ever use) of the following JAKi: abrocitinib, baricitinib, filgotinib, tofacitinib, and upadacitinib.

The concept sets (i.e. the list of codes used to identify the conditions and drugs of interest) used for this study are described in [Annex IV](#). These codes were refined during the study execution, following the standard DARWIN EU® phenotyping processes, which involved the review of code lists by clinical experts and the review of phenotypes after their execution in the participating data sources.

8.6.2. Outcome

For Objective 1, the incident use of JAKi was the outcome in the analyses.

For the incidence of first JAKi ever initiation, the outcome was defined as first prescription/dispensation of any JAKi. For incidence of individual JAKi ingredient (abrocitinib, baricitinib, filgotinib, tofacitinib, upadacitinib) initiation, the outcome was defined as first prescription/dispensation of the respective individual JAKi ingredient, allowing the previous use of other JAKi.

The concept sets used for the identification of outcomes are described in [Annex IV](#). These codes were refined during the study execution, following the standard DARWIN EU® phenotyping processes, which involved the review of code lists by clinical experts and the review of phenotypes after their execution in the participating data sources.

8.6.3. Covariates, including confounders, effect modifiers, and other variables

Objective 2:

The covariates for this objective were as follows:

- Sex
 - Female/male
- Age at JAKi initiation (index date), namely:
 - Mean/median age
 - Proportion of individuals stratified within age groups (0 – 3, 4 – 12, 13 – 18, 19 – 40, 41 – 60, >60).
- Pre-specified indicated condition for JAKi, defined by condition recorded before the index date (yes/no for each indication). Potential indications of JAKi were defined by any records of the above-mentioned pre-specified conditions before the first exposure of specific individual JAKi ingredients. Multiple indications were allowed per individual.
 - Alopecia areata
 - Atopic dermatitis
 - Axial spondylitis
 - Inflammatory bowel disease
 - Juvenile arthritis
 - Juvenile idiopathic arthritis
 - Psoriatic arthritis
 - Rheumatoid arthritis
 - Unknown indication (defined as none of the predefined indications were found)
- Time from first recorded indication diagnosis to first JAKi initiation, estimated separately for each prespecified indication (more than one per individual possible) and presented in months.
- Duration of index JAKi treatment era (months).
- Prior use of other JAKi (yes/no) and the number of JAKi ingredients used before the index JAKi initiation

The following covariates were used for stratification in the individual-level characterisation.

- Predefined potential indications.

The concept sets used for the identification of covariates were validated for the previous study (P3-C1-001) and are described in [Annex IV](#). However, an additional validation was conducted using the current vocabularies to identify and incorporate any new, relevant concepts. This validation followed the standard DARWIN EU® phenotyping processes, which involved the review of code lists by clinical experts and the review of phenotypes after their execution in the participating data sources.

8.7. Study size

No sample size was calculated for this study. As this is a feasibility assessment study, results based on all available data are presented. Based on the feasibility assessment, the expected number of individuals to be involved in each data source would be approximately between 2800 (NAJS) to 12800 (HI-SPEED).

8.8. Data transformation

Analyses were conducted separately for each data source. Before study initiation, test runs of the analytics were performed on a subset of the data sources or on a simulated set of patients, and quality control checks were performed. Once all the tests were passed (see [Annex III](#)), the final package was released in the version-controlled Study Repository for execution against all the participating data sources.

The data partners locally executed the analytics against the OMOP CDM in R Studio then reviewed and approved the by default aggregated results before returning them to the Coordination Centre. Sometimes multiple execution iterations were performed, and additional fine tuning of the code base was needed. A service desk was available during the study execution for support.

The study results of all data sources were checked after which they were made available to the team in the Digital Research Environment (DRE), and the Dissemination Phase started. All results were locked and timestamped for reproducibility and transparency. To prevent confidentiality issues, cell counts lower than 5 were reported as "<5".

8.9. Statistical methods

8.9.1. Main summary measures

The R package *IncidencePrevalence* was used to derive the incidence of JAKi initiation in the population level drug utilisation study (DUS),[10] while R package *CohortCharacteristics* was used for the individual-level characterisation and *DrugUtilisation* for treatment characterisation in the individual-level DUS.[11, 12] All packages mentioned were developed by DARWIN EU®.

Incidence of new JAKi initiation

Incidence of new JAKi initiation (measured as prescription or dispensation), overall and for each individual JAKi ingredient, was calculated annually as the number of individuals with a first JAKi prescription/dispensation per 100,000 person-years of the population at risk of exposure during the period for each calendar year. Those study individuals who entered the denominator population contributed time-at-risk up to their first use during the study period or if they did not have a drug exposure, they contributed time-at-risk, as described above in [Section 8.2](#). Incidence rates are given together with 95% Poisson exact confidence intervals. Illustration of the calculation of incidence use of the medicines of interest is shown in [Figure 3](#).

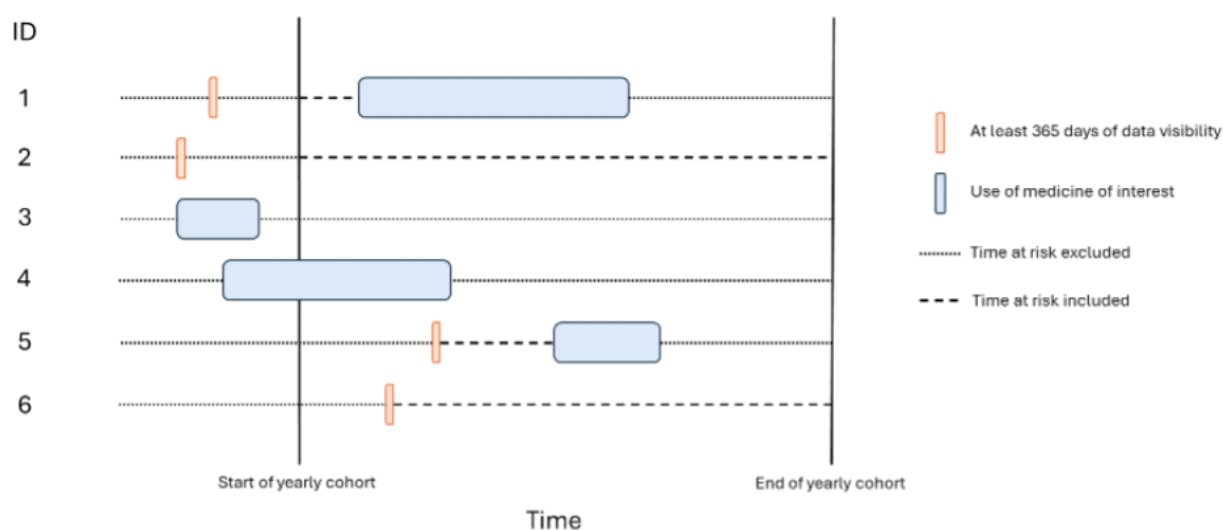


Figure 3. Illustration of the calculation of incidence on use of medicines of interest.

Individuals (ID 1, 2) with sufficient data visibility were included in the incidence calculation contributing to the time-at-risk (denominator). Individuals contributed time-at-risk until initiation of the drug of interest (ID 1) or the end of follow-up for a yearly cohort (ID 2). Individuals with exposure to JAKi before the start of the yearly cohort (ID 3) or with exposure at the start of the yearly cohort (ID 4) were not included in the annual incidence calculation. Individuals only contributed time-at-risk if they had sufficient data visibility. Therefore, as illustrated by IDs 5 and 6, individuals were only included and contributed to the denominator from the point with at least 365 days of data visibility.

For the incidence of each individual JAKi ingredient, only use of the specific individual JAKi ingredient was considered. These individuals with previous exposure to other JAKi were allowed to be included in the denominator during the calculation of population-level incidence. Each analysis on individual JAKi ingredients was independent of other JAKi exposures. In other words, individuals with exposure to different JAKi were counted multiple times in different analyses.

Individual-level characteristics

Individuals initiating JAKi were characterised in terms of age, sex, and time from first diagnosis of prespecified indication to first JAKi exposure. Treatment characterisation included indication and duration of treatment. Reporting on individual-level characterisation was stratified by each individual JAKi ingredient and indication.

Duration of Treatment

Duration of JAKi therapy was defined as follows: exposure begins on the date of the first prescription, e.g. the index date the individuals entered the cohort. For each prescription, the estimated duration of use was retrieved from the drug exposure table in the data sources, using the start and end date of the exposure (see [Annex II](#) for explanation of how prescription end-dates are obtained in each data source). Subsequent prescriptions were combined into continuous exposed episodes (treatment eras) if the distance in days between the end of the first exposure and start of the second exposure was ≤ 90 days. Treatment duration was summarised, providing the minimum, p25, median, p75, and maximum duration.

8.9.2. Missing values

The assumption was made that the absence of a prescription/dispensation record indicated that an individual did not receive the respective drug. For indications, it was assumed that the absence of a record of the respective condition of interest meant that JAKi were not prescribed for that indication.

8.10. Deviations from the protocol

Treatment duration was available in all data sources, except DK-DHR, where treatment end date was unavailable in the majority of JAKi prescriptions. Consequently, results on treatment duration in DK-DHR are not reported in the results tables.

9. RESULTS

The full set of results for this study is available through an interactive web-application Shiny app: [EUPAS1000000998](https://eupas1000000998.shinyapps.io/).

9.1. Participants

A total of 4,619,076 individuals from NAJS, 6,175,427 from DK-DHR, 6,536,600 from FinOMOP-THL, 14,357,543 from IQVIA DA Germany, 5,772,378 from VID, and 11,372,272 from HI-SPEED were eligible for the incidence analyses (denominator population) (please see population attrition in the Shiny app).

9.2. Main results

9.2.1. Incidence of new JAKi initiation

Different JAKi were approved in Europe at different times, initially mainly for rheumatoid arthritis, followed by an expansion in indications (**Table 2**).

Table 2. Year of marketing authorisation approval and indications of JAKi by EMA.

	JAKi ingredient				
	Tofacitinib	Baricitinib	Upadacitinib	Filgotinib	Abrocitinib
Year of marketing authorisation approval	2017	2017	2019	2020	2021
First approved indications	Rheumatoid arthritis	Rheumatoid arthritis	Rheumatoid arthritis	Rheumatoid arthritis	Atopic dermatitis
Later approved indications	Psoriatic arthritis; Ulcerative colitis (2018) Axial spondylitis; Juvenile idiopathic arthritis (2021)	Atopic dermatitis (2020) Alopecia areata (2022) Juvenile idiopathic arthritis (2023)	Atopic dermatitis; Axial spondylitis; Psoriatic arthritis (2021) Ulcerative colitis (2022)	Ulcerative colitis (2021)	

JAKi = Janus kinase inhibitor/s; EMA = European Medicines Agency.

Among the 5 included JAKi ingredients, upadacitinib had the highest count of individuals initiating treatment across the data sources, ranging from 710 in DK-DHR to 5,635 in HI-SPEED, which adds up to a total number of 17,657 individuals. Abrocitinib had the lowest count and was only observed in two data sources: 167 from FinOMOP-THL and 94 from VID. Across data sources, HI-SPEED had the highest number of individuals initiating JAKi, ranging from 1,357 for filgotinib to 5,635 for upadacitinib. NAJS had the lowest number of individuals initiating JAKi, ranging from 206 for filgotinib to 1,449 for upadacitinib.

After excluding individuals without 365 days of prior data visibility, sex information, or observation time during the study period, as well as excluding individuals who initiated JAKi treatment before the study start,

the number of individuals initiating JAKi varied from 94 (VID) to 167 (FinOMOP-THL) for abrocitinib; 980 (NAJS) to 2,691 (HI-SPEED) for baricitinib; 35 (DK-DHR) to 1,357 (HI-SPEED) for filgotinib; 571 (NAJS) to 2,555 (HI-SPEED) for tofacitinib; and 710 (DK-DHR) to 5,635 (HI-SPEED) for upadacitinib (**Figure 4**).

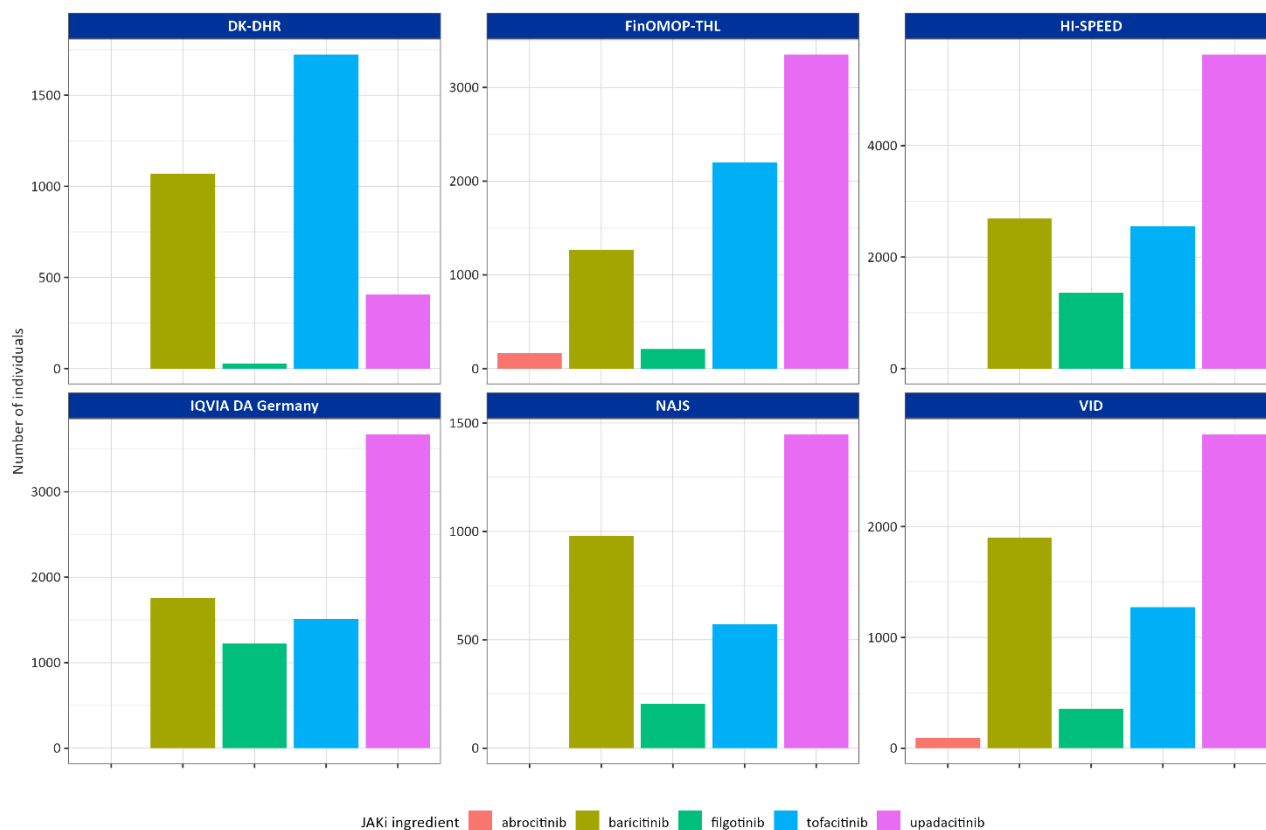


Figure 4. Number of individuals initiating each JAKi ingredient during the study period.

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; JAKi = Janus kinase inhibitor/s

The incidence of JAKi initiation as a class increased over the study period (**Figure 5**).

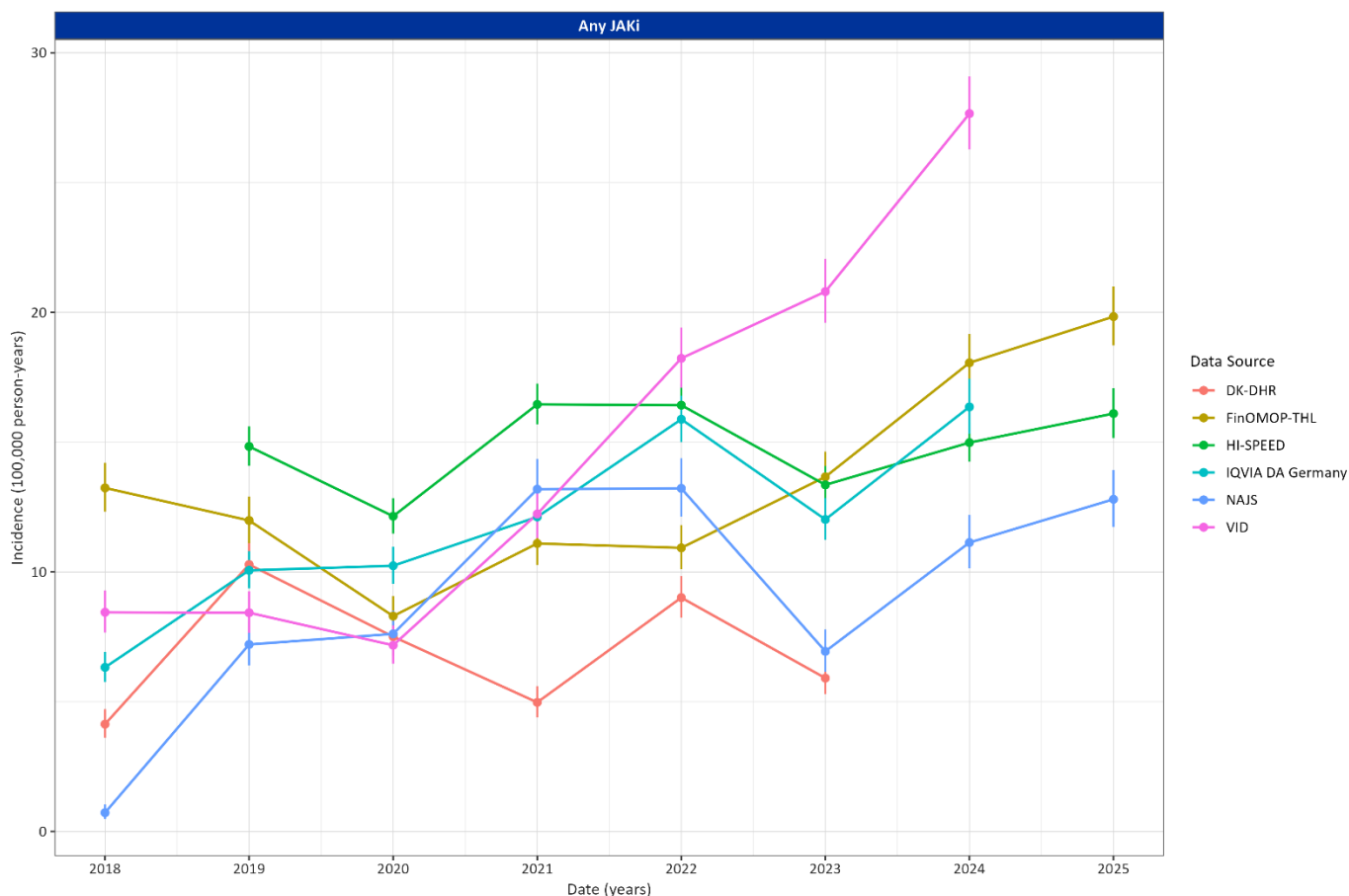


Figure 5. Incidence of first ever JAKi initiation.

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; JAKi = Janus kinase inhibitor/s

When considering the incidence of individual JAKi ingredient initiation, without the previous use of any JAKi, early rising trends were observed for tofacitinib in all data sources, except HI-SPEED, and for baricitinib in IQVIA DA Germany, NAJS, and VID. These early trends likely reflect the fact that these were the first JAKi ingredients authorised. Following the authorisation of filgotinib and upadacitinib (2019 – 2020), there was a plateau or decrease in baricitinib and tofacitinib initiation (**Figure 6, Table S2**).

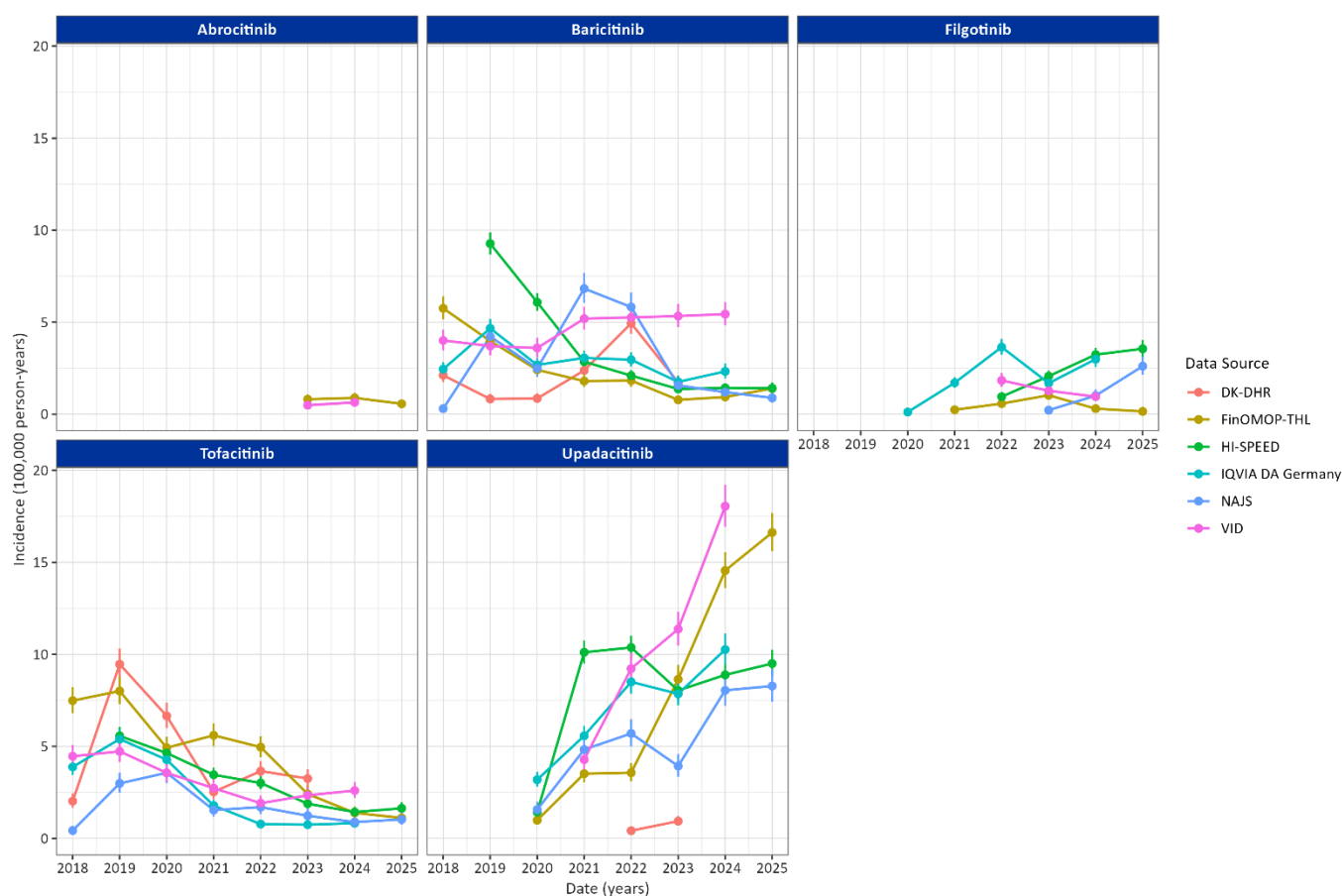


Figure 6. Incidence of first ever JAKi initiation, stratified by ingredient.

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; JAKi = Janus kinase inhibitor/s.

The overall increase in JAKi use over the study period was driven primarily by upadacitinib, and, to some extent, filgotinib. Abrocitinib use was only observed in FinOMOP-THL and VID, with very low counts and starting from 2022.

Further consideration was given to the incidence of initiation of individual JAKi ingredients among those without prior exposure to the same ingredient (but allowing the previous use of other JAKi). Trends of incidence of initiation for each individual JAKi in these analyses were similar to those seen in individuals not previously exposed to any JAKi (**Figure 7, Table S3**).

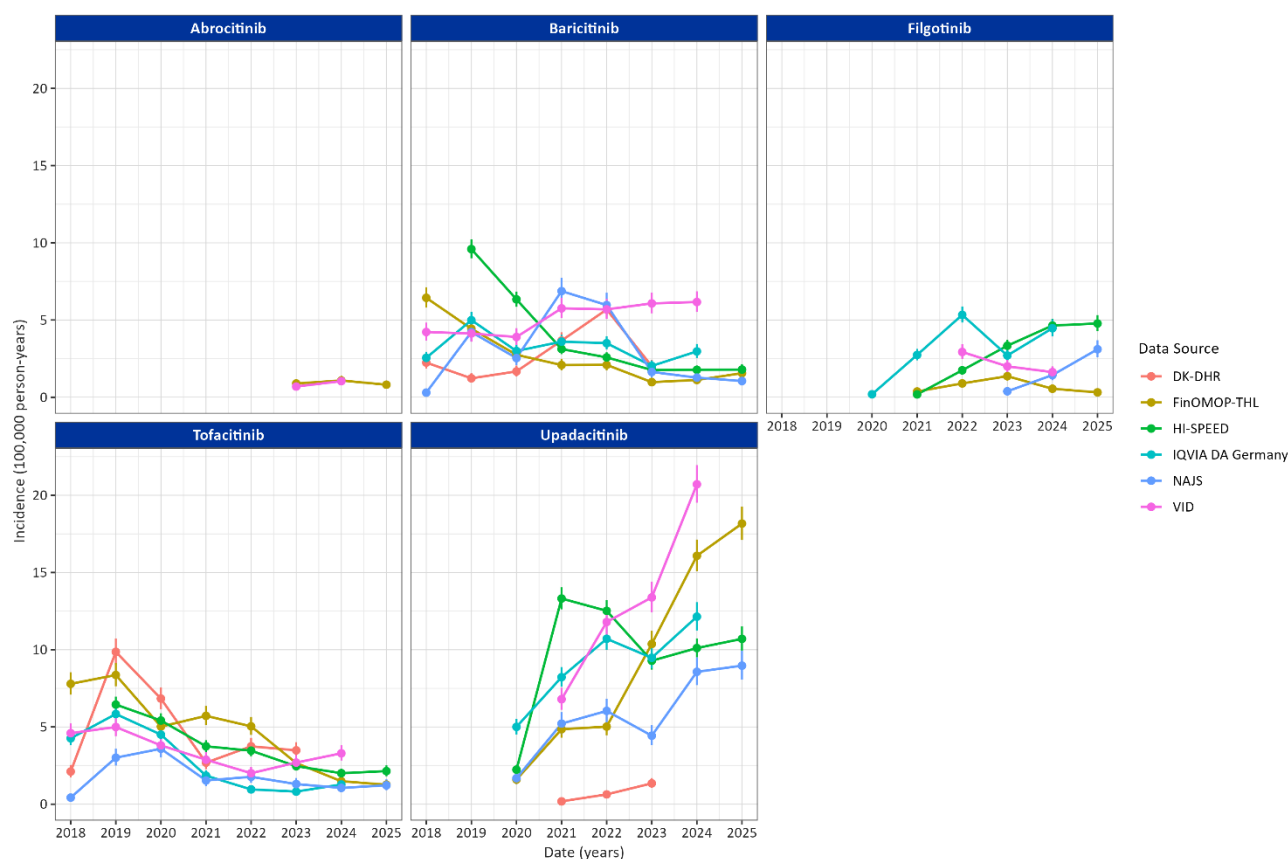


Figure 7. Incidence of first use of each JAKi, regardless of prior exposure to other JAKi ingredients.

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; JAKi = Janus kinase inhibitor/s.

9.2.2. Characteristics of individuals initiating JAKi

Individual-level characterisation for each JAKi ingredient during the study period among those without prior exposure to that same JAKi ingredient was performed and is detailed in [Tables 3 to 7](#). Overall, individuals initiating abrocitinib were the youngest, with most aged 19 – 40 years old. The majority of individuals initiating the other four JAKi ingredients were aged 41 – 60, except for baricitinib in IQVIA DA Germany, where they were mostly aged 61 or older.

Abrocitinib

Individuals initiating abrocitinib had a median age of 34 (Interquartile range (IQR) 24 – 44) in FinOMOP-THL and 36 (23 – 47) in VID and were predominantly male in both data sources (53.9% and 55.3%, respectively). Median treatment duration was 12 (IQR 5 – 23) months in FinOMOP-THL and 6 (2 – 10) months in VID. Of all individuals initiating abrocitinib, 99.4% in FinOMOP-THL and 92.6% in VID had a history of atopic dermatitis as their likely indication. Additionally, all individuals initiating abrocitinib with alopecia areata also had atopic dermatitis.

Among the individuals initiating abrocitinib in FinOMOP-THL, 10.8% had previously used baricitinib, and 15.7% had previously used upadacitinib; however, the vast majority (80.8%) had not received any JAKi prior to initiating abrocitinib. In VID, 9.6% had previously used baricitinib and 30.9% had previously used upadacitinib; therefore, the proportion of abrocitinib initiators with no prior history of JAKi use was lower

(64.9%). Additionally, the median time from diagnosis of atopic dermatitis to abrocitinib initiation was 60 (30 – 101) months in FinOMOP-THL and 104 (37 – 168) months in VID.

Table 3. Characterisation of individuals initiating abrocitinib, overall and stratified by indication.

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Abrocitinib - Overall								
Number individuals	–	N	0	0	167	0	94	0
Age	–	Median [Q25 – Q75]	–	–	34 [24 – 44]	–	36 [23 – 47]	–
		Mean (SD)	–	–	35 (13)	–	37 (15)	–
		Range	–	–	16 to 74	–	15 to 79	–
Sex	Female	N (%)	–	–	77 (46.1%)	–	42 (44.7%)	–
Treatment duration (months)*	–	Median [Q25 – Q75]	–	–	12 [5 – 23]	–	6 [2 – 10]	–
		Mean (SD)	–	–	14 (10)	–	7 (5)	–
Potential indications	Alopecia areata	N (%)	–	–	<5	–	5 (5.3%)	–
	Atopic dermatitis	N (%)	–	–	166 (99.4%)	–	87 (92.6%)	–
	Axial spondylitis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Inflammatory bowel disease	N (%)	–	–	<5	–	<5	–
	Juvenile arthritis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Juvenile idiopathic arthritis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Psoriatic arthritis	N (%)	–	–	0 (0.0%)	–	<5	–
	Rheumatoid arthritis	N (%)	–	–	0 (0.0%)	–	<5	–
Time from indication diagnosis to JAKi initiation (months)	Alopecia areata	Median [Q25 – Q75]	–	–	–	–	66 [14 – 131]	–
	Atopic dermatitis	Median [Q25 – Q75]	–	–	60 [30 – 101]	–	104 [37 – 168]	–
	Axial spondylitis	Median [Q25 – Q75]	–	–	–	–	–	–
	Inflammatory bowel disease	Median [Q25 – Q75]	–	–	–	–	–	–
	Juvenile arthritis	Median [Q25 – Q75]	–	–	–	–	–	–
	Juvenile idiopathic arthritis	Median [Q25 – Q75]	–	–	–	–	–	–

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Prior JAK inhibitor use	Psoriatic arthritis	Median [Q25 – Q75]	–	–	–	–	61 [52 – 112]	–
	Rheumatoid arthritis	Median [Q25 – Q75]	–	–	–	–	46 [37 – 54]	–
	Baricitinib	N (%)	–	–	18 (10.8%)	–	9 (9.6%)	–
	Filgotinib	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Tofacitinib	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Upadacitinib	N (%)	–	–	26 (15.6%)	–	29 (30.9%)	–
	No previous JAKi use	N (%)	–	–	135 (80.8%)	–	61 (64.9%)	–
Number of prior JAKi ingredients initiated	–	Median [Q25 – Q75]	–	–	0 [0 – 0]	–	0 [0 – 1]	–
Abrocitinib - Alopecia areata								
Number individuals	–	N	–	–	<5	–	5	–
Age	–	Median [Q25 – Q75]	–	–	–	–	37 [32 – 54]	–
		Mean (SD)	–	–	–	–	42 (14)	–
		Range	–	–	–	–	26 to 59	–
Sex	Female	N (%)	–	–	<5	–	–	–
Treatment duration (months)*	–	Median [Q25 – Q75]	–	–	–	–	10 [4 – 12]	–
		Mean (SD)	–	–	–	–	9 (7)	–
Co-morbid conditions	Atopic dermatitis	N (%)	–	–	<5	–	5 (100.0%)	–
	Axial spondylitis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Inflammatory bowel disease	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Juvenile arthritis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Juvenile idiopathic arthritis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Psoriatic arthritis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Rheumatoid arthritis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Abrocitinib - Atopic dermatitis								
Number individuals	–	N	–	–	166	–	87	–
Age	–	Median [Q25 – Q75]	–	–	34 [24 – 44]	–	35 [24 – 46]	–
		Mean (SD)	–	–	35 (13)	–	36 (13)	–
		Range	–	–	16 to 74	–	15 to 64	–
Sex	Female	N (%)	–	–	77 (46.4%)	–	39 (44.8%)	–
Treatment duration (months)*	–	Median [Q25 – Q75]	–	–	12 [5 – 23]	–	7 [2 – 11]	–
		Mean (SD)	–	–	14 (10)	–	7 (5)	–
Co-morbid conditions	Alopecia areata	N (%)	–	–	<5	–	5 (5.7%)	–
	Axial spondylitis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Inflammatory bowel disease	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Juvenile arthritis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Juvenile idiopathic arthritis	N (%)	–	–	0 (0.0%)	–	0 (0.0%)	–
	Psoriatic arthritis	N (%)	–	–	0 (0.0%)	–	<5	–
	Rheumatoid arthritis	N (%)	–	–	0 (0.0%)	–	<5	–

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; SD = Standard Deviation; Q25 = 25th Percentile; Q75 = 75th Percentile; JAKi = Janus kinase inhibitor/s.

– is used when data is not available.

*Treatment duration was available in all data sources, except DK-DHR, where treatment end date was unavailable in the majority of JAKi prescriptions.

Baricitinib

The median age of individuals initiating baricitinib ranged from 53 (44 – 61) years old in VID to 61 (52 – 70) in IQVIA DA Germany. There was a predominance of female individuals initiating baricitinib in all data sources, ranging from 66.9% in NAJS to 78.9% in FinOMOP-THL. Median treatment duration ranged from 4 (0 – 27) months in NAJS to 24 (11 – 50) months in FinOMOP-THL.

Baricitinib was initially approved to treat rheumatoid arthritis in 2017. Subsequently, it was approved for treatment use of atopic dermatitis in 2020, alopecia areata in 2022, and juvenile idiopathic arthritis in 2023. This is reflected in the study results, with rheumatoid arthritis being the most frequently identified potential indication (ranging from 54.7% in NAJS to 80.9% in FinOMOP-THL). Atopic dermatitis was also commonly identified (from 8.2% in HI-SPEED to 12.6% in NAJS), as was juvenile idiopathic arthritis (from 1.1% in IQVIA DA Germany to 11.9% in FinOMOP-THL), and alopecia areata (from 2.3% in NAJS to 20.8% in VID).

The median age of individuals with prior history of rheumatoid arthritis ranged from 55 (48 – 62) in VID to 62 (54 – 71) in IQVIA DA Germany, and the proportion of females was between 75.6% (VID) and 87.3% (NAJS). Treatment duration varied from 10 (3 – 26) months in IQVIA DA Germany to 24 (12 – 58) months in FinOMOP-THL. Time from diagnosis of rheumatoid arthritis to baricitinib initiation varied from 45 (35 – 60) months in FinOMOP-THL to 144 (78 – 220) months in DK-DHR.

Individuals with prior history of atopic dermatitis were typically younger (median age ranging from 32 (22 – 50) in FinOMOP-THL to 45 (31 – 58) in IQVIA DA Germany) and the proportion of females was lower (from 54.2% in IQVIA DA Germany to 61.8% in FinOMOP-THL) compared with individuals with a prior history of rheumatoid arthritis. Treatment duration was typically shorter, varying from 5 (2 – 11) months in IQVIA DA Germany to 14 (6 – 24) months in FinOMOP-THL. Time from diagnosis of atopic dermatitis to baricitinib initiation was slightly shorter than for rheumatoid arthritis, varying from 43 (16 – 113) months for IQVIA DA Germany to 117 (36 – 229) months in DK-DHR.

Similarly, individuals with prior history of juvenile idiopathic arthritis were typically younger (median age ranging from 24 (17 – 41) in HI-SPEED to 39 (26 – 50) in VID) than those with prior history of rheumatoid arthritis; however, the proportion of females was slightly higher (from 80.0% in FinOMOP-THL to 90.0% in IQVIA DA Germany). They also had a shorter treatment duration, varying from 8 (3 – 13) months in IQVIA DA Germany to 16 (3 – 54) months in NAJS. Time from diagnosis of juvenile idiopathic arthritis to baricitinib initiation was longer than for rheumatoid arthritis, varying from 52 (18 – 109) months in IQVIA DA Germany to 183 (83 – 225) months in DK-DHR.

Individuals with a prior history of alopecia areata were typically younger than individuals with prior history of rheumatoid arthritis (from 34 (21 – 52) in HI-SPEED to 53 (40 – 60) in IQVIA DA Germany), and the proportion of females was slightly lower (from 60.7% in DK-DHR to 78.7% in FinOMOP-THL). Additionally, they also had shorter treatment duration (from 4 (2 – 11) months in IQVIA DA Germany to 20 (1 – 37) months in NAJS). Time from diagnosis of alopecia areata to baricitinib initiation was shorter than for rheumatoid arthritis, varying from 18 (5 – 58) months in FinOMOP-THL to 84 (23 – 125) months in DK-DHR. Additionally, a significant proportion of individuals with alopecia areata also had a record of atopic dermatitis (from 17.4% in VID to 45.8% in IQVIA DA Germany) and rheumatoid arthritis (from 16.3% in HI-SPEED to 60.9% in NAJS).

The proportion of individuals initiating baricitinib who had previously received a different JAKi varied significantly by data source. Prior use of tofacitinib varied from 1.1% in NAJS to 18.5% in DK-DHR. Similarly, prior use of upadacitinib varied from 0.6% in DK-DHR to 5.4% in HI-SPEED. However, in all data sources, the vast majority of baricitinib initiators had no previous use of other JAKi recorded (from 80.8% in DK-DHR to 97.7% in NAJS).

Table 4. Characterisation of individuals initiating baricitinib, overall and stratified by indication.

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Baricitinib - Overall								
Number individuals	–	N	980	1,170	1,264	1,753	1,900	2,691
Age	–	Median [Q25 – Q75]	59 [50 – 68]	58 [45 – 66]	55 [41 – 66]	61 [52 – 70]	53 [44 – 61]	57 [42 – 68]
		Mean (SD)	58 (15)	55 (17)	52 (17)	60 (15)	51 (14)	54 (19)
		Range	16 to 94	8 to 93	3 to 92	6 to 93	1 to 90	1 to 93
Sex	Female	N (%)	656 (66.9%)	855 (73.1%)	997 (78.9%)	1,330 (75.9%)	1,283 (67.5%)	2,019 (75.0%)
Treatment duration (months)*	–	Median [Q25 – Q75]	4 [0 – 27]	–	24 [11 – 50]	8 [3 – 23]	10 [3 – 26]	11 [4 – 30]
		Mean (SD)	17 (23)	–	33 (27)	16 (19)	18 (19)	20 (21)
Potential indications	Alopecia areata	N (%)	23 (2.3%)	28 (2.4%)	61 (4.8%)	59 (3.4%)	396 (20.8%)	166 (6.2%)
	Atopic dermatitis	N (%)	123 (12.6%)	122 (10.4%)	152 (12.0%)	177 (10.1%)	226 (11.9%)	220 (8.2%)
	Axial spondylitis	N (%)	22 (2.2%)	32 (2.7%)	20 (1.6%)	29 (1.7%)	33 (1.7%)	70 (2.6%)
	Inflammatory bowel disease	N (%)	16 (1.6%)	59 (5.0%)	21 (1.7%)	14 (0.8%)	19 (1.0%)	40 (1.5%)
	Juvenile arthritis	N (%)	19 (1.9%)	93 (7.9%)	151 (11.9%)	20 (1.1%)	56 (2.9%)	238 (8.8%)
	Juvenile idiopathic arthritis	N (%)	19 (1.9%)	88 (7.5%)	150 (11.9%)	20 (1.1%)	55 (2.9%)	228 (8.5%)
	Psoriatic arthritis	N (%)	10 (1.0%)	94 (8.0%)	32 (2.5%)	54 (3.1%)	51 (2.7%)	190 (7.1%)
	Rheumatoid arthritis	N (%)	536 (54.7%)	839 (71.7%)	1,023 (80.9%)	1,417 (80.8%)	1,284 (67.6%)	1,821 (67.7%)
Time from indication diagnosis to JAKi initiation (months)	Alopecia areata	Median [Q25 – Q75]	58 [33 – 67]	84 [23 – 125]	18 [5 – 58]	26 [10 – 90]	61 [19 – 121]	38 [20 – 72]
	Atopic dermatitis	Median [Q25 – Q75]	76 [24 – 93]	117 [36 – 229]	59 [26 – 83]	43 [16 – 113]	82 [27 – 116]	55 [17 – 79]
	Axial spondylitis	Median [Q25 – Q75]	34 [26 – 59]	150 [81 – 262]	41 [22 – 59]	85 [30 – 129]	69 [27 – 112]	47 [27 – 58]
	Inflammatory bowel disease	Median [Q25 – Q75]	54 [39 – 70]	127 [78 – 196]	39 [23 – 56]	34 [23 – 68]	70 [37 – 116]	48 [32 – 68]
	Juvenile arthritis	Median [Q25 – Q75]	58 [32 – 82]	182 [80 – 254]	63 [45 – 109]	52 [18 – 109]	73 [42 – 112]	56 [46 – 71]

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Juvenile idiopathic arthritis	Median [Q25 – Q75]	58 [32 – 82]	183 [83 – 255]	62 [45 – 109]	52 [18 – 109]	74 [44 – 112]	56 [46 – 71]
	Psoriatic arthritis	Median [Q25 – Q75]	41 [22 – 61]	101 [55 – 172]	41 [30 – 58]	54 [34 – 90]	59 [24 – 108]	48 [28 – 62]
	Rheumatoid arthritis	Median [Q25 – Q75]	59 [48 – 75]	144 [78 – 220]	45 [35 – 60]	57 [29 – 106]	78 [29 – 118]	52 [37 – 63]
Prior JAK inhibitor use	Abrocitinib	N (%)	0 (0.0%)	0 (0.0%)	<5	0 (0.0%)	<5	0 (0.0%)
	Filgotinib	N (%)	0 (0.0%)	0 (0.0%)	<5	38 (2.2%)	8 (0.4%)	23 (0.9%)
	Tofacitinib	N (%)	11 (1.1%)	216 (18.5%)	105 (8.3%)	98 (5.6%)	114 (6.0%)	69 (2.6%)
	Upadacitinib	N (%)	15 (1.5%)	7 (0.6%)	23 (1.8%)	69 (3.9%)	63 (3.3%)	144 (5.4%)
	No previous JAKi use	N (%)	957 (97.7%)	945 (80.8%)	1,111 (87.9%)	1,531 (87.3%)	1,718 (90.4%)	2,451 (91.1%)
Number of prior JAKi ingredients initiated	–	Median [Q25 – Q75]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]
Baricitinib - Alopecia areata								
Number individuals	–	N	23	28	61	59	396	166
Age	–	Median [Q25 – Q75]	49 [38 – 60]	46 [25 – 54]	41 [29 – 50]	53 [40 – 60]	46 [36 – 55]	34 [21 – 52]
		Mean (SD)	50 (16)	42 (19)	39 (14)	50 (15)	44 (15)	36 (18)
		Range	24 to 81	10 to 74	11 to 75	10 to 83	3 to 81	3 to 82
Sex	Female	N (%)	18 (78.3%)	17 (60.7%)	48 (78.7%)	44 (74.6%)	263 (66.4%)	120 (72.3%)
Treatment duration (months)*	–	Median [Q25 – Q75]	20 [1 – 37]	–	11 [4 – 22]	4 [2 – 11]	10 [5 – 17]	9 [4 – 19]
		Mean (SD)	22 (23)	–	15 (14)	9 (11)	12 (12)	13 (11)
Co-morbid conditions	Atopic dermatitis	N (%)	8 (34.8%)	6 (21.4%)	14 (23.0%)	27 (45.8%)	69 (17.4%)	53 (31.9%)
	Axial spondylitis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5	5 (1.3%)	<5
	Inflammatory bowel disease	N (%)	0 (0.0%)	<5	<5	0 (0.0%)	8 (2.0%)	<5
	Juvenile arthritis	N (%)	0 (0.0%)	<5	5 (8.2%)	<5	<5	12 (7.2%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Juvenile idiopathic arthritis	N (%)	0 (0.0%)	<5	5 (8.2%)	<5	<5	12 (7.2%)
	Psoriatic arthritis	N (%)	0 (0.0%)	<5	0 (0.0%)	<5	5 (1.3%)	<5
	Rheumatoid arthritis	N (%)	14 (60.9%)	6 (21.4%)	13 (21.3%)	18 (30.5%)	82 (20.7%)	27 (16.3%)
Baricitinib - Atopic dermatitis								
Number individuals	–	N	123	122	152	177	226	220
Age	–	Median [Q25 – Q75]	35 [26 – 54]	37 [25 – 49]	32 [22 – 50]	45 [31 – 58]	44 [23 – 56]	33 [21 – 53]
		Mean (SD)	40 (18)	39 (16)	36 (18)	46 (20)	40 (20)	36 (20)
		Range	17 to 90	8 to 85	5 to 81	6 to 91	1 to 86	2 to 87
Sex	Female	N (%)	73 (59.3%)	67 (54.9%)	94 (61.8%)	96 (54.2%)	133 (58.8%)	132 (60.0%)
Treatment duration (months)*	–	Median [Q25 – Q75]	9 [3 – 19]	–	14 [6 – 24]	5 [2 – 11]	8 [3 – 18]	8 [3 – 17]
		Mean (SD)	14 (15)	–	18 (16)	9 (11)	13 (14)	12 (13)
Co-morbid conditions	Alopecia areata	N (%)	8 (6.5%)	6 (4.9%)	14 (9.2%)	27 (15.3%)	69 (30.5%)	53 (24.1%)
	Axial spondylitis	N (%)	0 (0.0%)	0 (0.0%)	<5	<5	<5	<5
	Inflammatory bowel disease	N (%)	<5	6 (4.9%)	5 (3.3%)	0 (0.0%)	6 (2.7%)	<5
	Juvenile arthritis	N (%)	<5	6 (4.9%)	26 (17.1%)	<5	5 (2.2%)	12 (5.5%)
	Juvenile idiopathic arthritis	N (%)	<5	6 (4.9%)	26 (17.1%)	<5	<5	12 (5.5%)
	Psoriatic arthritis	N (%)	0 (0.0%)	<5	<5	5 (2.8%)	14 (6.2%)	6 (2.7%)
	Rheumatoid arthritis	N (%)	22 (17.9%)	17 (13.9%)	41 (27.0%)	17 (9.6%)	69 (30.5%)	25 (11.4%)
Baricitinib - Axial spondylitis								
Number individuals	–	N	22	32	20	29	33	70
Age	–	Median [Q25 – Q75]	58 [52 – 64]	53 [41 – 58]	50 [34 – 56]	58 [51 – 68]	57 [49 – 62]	52 [32 – 60]
		Mean (SD)	58 (12)	51 (12)	45 (16)	59 (12)	55 (13)	48 (18)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Range	26 to 77	23 to 74	11 to 67	39 to 87	16 to 79	14 to 81
Sex	Female	N (%)	16 (72.7%)	21 (65.6%)	14 (70.0%)	19 (65.5%)	22 (66.7%)	48 (68.6%)
Treatment duration (months)*	–	Median [Q25 – Q75]	11 [1 – 27]	–	24 [11 – 69]	7 [3 – 17]	9 [2 – 21]	10 [3 – 27]
		Mean (SD)	17 (20)	–	38 (33)	13 (14)	17 (19)	19 (22)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5	5 (15.2%)	<5
	Atopic dermatitis	N (%)	0 (0.0%)	0 (0.0%)	<5	<5	<5	<5
	Inflammatory bowel disease	N (%)	<5	<5	<5	0 (0.0%)	0 (0.0%)	<5
	Juvenile arthritis	N (%)	<5	<5	7 (35.0%)	0 (0.0%)	<5	14 (20.0%)
	Juvenile idiopathic arthritis	N (%)	<5	<5	7 (35.0%)	0 (0.0%)	<5	14 (20.0%)
	Psoriatic arthritis	N (%)	<5	6 (18.8%)	<5	<5	<5	10 (14.3%)
	Rheumatoid arthritis	N (%)	18 (81.8%)	20 (62.5%)	15 (75.0%)	26 (89.7%)	22 (66.7%)	26 (37.1%)
Baricitinib - Inflammatory bowel disease								
Number individuals	–	N	16	59	21	14	19	40
Age	–	Median [Q25 – Q75]	58 [51 – 67]	54 [43 – 64]	56 [44 – 67]	60 [56 – 67]	50 [36 – 61]	60 [46 – 70]
		Mean (SD)	58 (15)	54 (16)	52 (19)	61 (7)	50 (21)	57 (16)
		Range	22 to 85	23 to 91	16 to 78	51 to 75	7 to 85	21 to 86
Sex	Female	N (%)	10 (62.5%)	41 (69.5%)	16 (76.2%)	12 (85.7%)	10 (52.6%)	34 (85.0%)
Treatment duration (months)*	–	Median [Q25 – Q75]	6 [1 – 26]	–	12 [3 – 24]	5 [1 – 13]	12 [2 – 18]	8 [3 – 15]
		Mean (SD)	17 (22)	–	18 (16)	15 (23)	13 (13)	14 (17)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	<5	<5	0 (0.0%)	8 (42.1%)	<5
	Atopic dermatitis	N (%)	<5	6 (10.2%)	5 (23.8%)	0 (0.0%)	6 (31.6%)	<5
	Axial spondylitis	N (%)	<5	<5	<5	0 (0.0%)	0 (0.0%)	<5

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Juvenile arthritis	N (%)	<5	10 (16.9%)	<5	0 (0.0%)	0 (0.0%)	<5
	Juvenile idiopathic arthritis	N (%)	<5	8 (13.6%)	<5	0 (0.0%)	0 (0.0%)	<5
	Psoriatic arthritis	N (%)	0 (0.0%)	5 (8.5%)	<5	0 (0.0%)	0 (0.0%)	<5
	Rheumatoid arthritis	N (%)	11 (68.8%)	42 (71.2%)	16 (76.2%)	12 (85.7%)	8 (42.1%)	26 (65.0%)
Baricitinib - Juvenile arthritis								
Number individuals	–	N	19	93	151	20	56	238
Age	–	Median [Q25 – Q75]	35 [30 – 54]	30 [20 – 44]	28 [18 – 42]	28 [21 – 45]	38 [26 – 49]	23 [17 – 41]
		Mean (SD)	42 (17)	33 (14)	31 (16)	33 (15)	36 (16)	29 (17)
		Range	16 to 71	10 to 78	3 to 71	11 to 68	1 to 64	2 to 78
Sex	Female	N (%)	17 (89.5%)	78 (83.9%)	120 (79.5%)	18 (90.0%)	46 (82.1%)	198 (83.2%)
Treatment duration (months)*	–	Median [Q25 – Q75]	16 [3 – 54]	–	12 [6 – 24]	8 [3 – 13]	13 [5 – 31]	7 [3 – 17]
		Mean (SD)	27 (28)	–	23 (25)	9 (8)	20 (20)	13 (15)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	<5	5 (3.3%)	<5	<5	12 (5.0%)
	Atopic dermatitis	N (%)	<5	6 (6.5%)	26 (17.2%)	<5	5 (8.9%)	12 (5.0%)
	Axial spondylitis	N (%)	<5	<5	7 (4.6%)	0 (0.0%)	<5	14 (5.9%)
	Inflammatory bowel disease	N (%)	<5	10 (10.8%)	<5	0 (0.0%)	0 (0.0%)	<5
	Juvenile idiopathic arthritis	N (%)	19 (100.0%)	88 (94.6%)	150 (99.3%)	20 (100.0%)	55 (98.2%)	228 (95.8%)
	Psoriatic arthritis	N (%)	0 (0.0%)	7 (7.5%)	<5	0 (0.0%)	<5	16 (6.7%)
	Rheumatoid arthritis	N (%)	17 (89.5%)	68 (73.1%)	77 (51.0%)	12 (60.0%)	51 (91.1%)	84 (35.3%)
Baricitinib - Juvenile idiopathic arthritis								
Number individuals	–	N	19	88	150	20	55	228
Age	–	Median [Q25 – Q75]	35 [30 – 54]	30 [20 – 44]	28 [19 – 42]	28 [21 – 45]	39 [26 – 50]	24 [17 – 41]

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Mean (SD)	42 (17)	33 (15)	31 (16)	33 (15)	37 (15)	30 (17)
		Range	16 to 71	10 to 78	3 to 71	11 to 68	5 to 64	4 to 78
Sex	Female	N (%)	17 (89.5%)	74 (84.1%)	120 (80.0%)	18 (90.0%)	45 (81.8%)	192 (84.2%)
Treatment duration (months)*	–	Median [Q25 – Q75]	16 [3 – 54]	–	12 [6 – 24]	8 [3 – 13]	13 [6 – 32]	8 [3 – 17]
		Mean (SD)	27 (28)	–	23 (25)	9 (8)	21 (20)	14 (15)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	<5	5 (3.3%)	<5	<5	12 (5.3%)
	Atopic dermatitis	N (%)	<5	6 (6.8%)	26 (17.3%)	<5	<5	12 (5.3%)
	Axial spondylitis	N (%)	<5	<5	7 (4.7%)	0 (0.0%)	<5	14 (6.1%)
	Inflammatory bowel disease	N (%)	<5	8 (9.1%)	<5	0 (0.0%)	0 (0.0%)	<5
	Juvenile arthritis	N (%)	19 (100.0%)	88 (100.0%)	150 (100.0%)	20 (100.0%)	55 (100.0%)	228 (100.0%)
	Psoriatic arthritis	N (%)	0 (0.0%)	6 (6.8%)	<5	0 (0.0%)	<5	12 (5.3%)
	Rheumatoid arthritis	N (%)	17 (89.5%)	66 (75.0%)	77 (51.3%)	12 (60.0%)	51 (92.7%)	84 (36.8%)
Baricitinib - Psoriatic arthritis								
Number individuals	–	N	10	94	32	54	51	190
Age	–	Median [Q25 – Q75]	62 [56 – 68]	56 [46 – 65]	57 [44 – 62]	59 [53 – 66]	57 [49 – 64]	57 [49 – 66]
		Mean (SD)	63 (9)	55 (14)	54 (16)	60 (11)	56 (12)	56 (14)
		Range	52 to 77	19 to 85	18 to 79	34 to 89	22 to 81	13 to 81
Sex	Female	N (%)	9 (90.0%)	64 (68.1%)	24 (75.0%)	41 (75.9%)	32 (62.7%)	141 (74.2%)
Treatment duration (months)*	–	Median [Q25 – Q75]	10 [5 – 37]	–	24 [6 – 46]	6 [2 – 20]	8 [3 – 24]	7 [3 – 26]
		Mean (SD)	23 (24)	–	27 (27)	14 (18)	18 (21)	17 (20)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	<5	0 (0.0%)	<5	5 (9.8%)	<5
	Atopic dermatitis	N (%)	0 (0.0%)	<5	<5	5 (9.3%)	14 (27.5%)	6 (3.2%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Axial spondylitis	N (%)	<5	6 (6.4%)	<5	<5	<5	10 (5.3%)
	Inflammatory bowel disease	N (%)	0 (0.0%)	5 (5.3%)	<5	0 (0.0%)	0 (0.0%)	<5
	Juvenile arthritis	N (%)	0 (0.0%)	7 (7.4%)	<5	0 (0.0%)	<5	16 (8.4%)
	Juvenile idiopathic arthritis	N (%)	0 (0.0%)	6 (6.4%)	<5	0 (0.0%)	<5	12 (6.3%)
	Rheumatoid arthritis	N (%)	9 (90.0%)	68 (72.3%)	20 (62.5%)	34 (63.0%)	38 (74.5%)	65 (34.2%)
Baricitinib - Rheumatoid arthritis								
Number individuals	–	N	536	839	1,023	1,417	1,284	1,821
Age	–	Median [Q25 – Q75]	59 [52 – 66]	59 [50 – 68]	58 [48 – 67]	62 [54 – 71]	55 [48 – 62]	61 [50 – 71]
		Mean (SD)	59 (11)	58 (14)	56 (15)	62 (13)	54 (11)	59 (15)
		Range	19 to 90	15 to 93	7 to 92	14 to 93	7 to 88	5 to 93
Sex	Female	N (%)	468 (87.3%)	669 (79.7%)	844 (82.5%)	1,120 (79.0%)	971 (75.6%)	1,459 (80.1%)
Treatment duration (months)*	–	Median [Q25 – Q75]	22 [5 – 49]	–	24 [12 – 58]	10 [3 – 26]	14 [5 – 36]	13 [4 – 36]
		Mean (SD)	29 (25)	–	36 (28)	18 (20)	22 (22)	23 (23)
Co-morbid conditions	Alopecia areata	N (%)	14 (2.6%)	6 (0.7%)	13 (1.3%)	18 (1.3%)	82 (6.4%)	27 (1.5%)
	Atopic dermatitis	N (%)	22 (4.1%)	17 (2.0%)	41 (4.0%)	17 (1.2%)	69 (5.4%)	25 (1.4%)
	Axial spondylitis	N (%)	18 (3.4%)	20 (2.4%)	15 (1.5%)	26 (1.8%)	22 (1.7%)	26 (1.4%)
	Inflammatory bowel disease	N (%)	11 (2.1%)	42 (5.0%)	16 (1.6%)	12 (0.8%)	8 (0.6%)	26 (1.4%)
	Juvenile arthritis	N (%)	17 (3.2%)	68 (8.1%)	77 (7.5%)	12 (0.8%)	51 (4.0%)	84 (4.6%)
	Juvenile idiopathic arthritis	N (%)	17 (3.2%)	66 (7.9%)	77 (7.5%)	12 (0.8%)	51 (4.0%)	84 (4.6%)
	Psoriatic arthritis	N (%)	9 (1.7%)	68 (8.1%)	20 (2.0%)	34 (2.4%)	38 (3.0%)	65 (3.6%)

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; SD = Standard Deviation; Q25 = 25th Percentile; Q75 = 75th Percentile; JAKi = Janus kinase inhibitor/s.

– is used when data is not available.

*Treatment duration was available in all data sources, except DK-DHR, where treatment end date was unavailable in the majority of JAKi prescriptions.

Filgotinib

The median age of individuals initiating filgotinib ranged from 47 (37 – 59) years old in FinOMOP-THL to 59 (50 – 68) in IQVIA DA Germany. Similarly, most individuals initiating filgotinib were female, ranging from 66.3% in FinOMOP-THL to 78.6% in NAJS. The median duration of treatment ranged from 6 (3 – 12) months in NAJS to 24 (12 – 33) in FinOMOP-THL.

Filgotinib was approved to treat rheumatoid arthritis in 2020 and was subsequently approved to treat inflammatory bowel disease (specifically ulcerative colitis) in 2021. This is reflected in the study results, with rheumatoid arthritis being the most common indication identified (from 52.3% in HI-SPEED to 85.9% in VID), followed by inflammatory bowel disease (from 12.4% in VID to 41.3% in FinOMOP-THL).

The median age of individuals initiating filgotinib with prior history of rheumatoid arthritis ranged from 55 (45 – 64) in HI-SPEED to 61 (53 – 69) in IQVIA DA Germany, and the proportion of females was between 75.7% (VID) and 92.0% (DK-DHR). Treatment duration varied from 7 (3 – 13) months in NAJS to 24 (6 – 31) months in FinOMOP-THL. Time from diagnosis of rheumatoid arthritis to baricitinib initiation varied from 66 (28 – 114) months in IQVIA DA Germany to 107 [60 – 182] months in DK-DHR.

Individuals with prior history of inflammatory bowel disease were typically younger (median age ranging from 36 (30 – 47) in DK-DHR to 44 (35 – 56) in IQVIA DA Germany) and the proportion of females was lower (from 44.9% in HI-SPEED to 50.0% in FinOMOP-THL and VID) compared with individuals with a prior history of rheumatoid arthritis. Treatment duration was typically shorter, varying from 5 (3 – 7) months in NAJS to 24 (18 – 35) months in FinOMOP-THL. Time from diagnosis of inflammatory bowel disease to filgotinib initiation was similar to that of rheumatoid arthritis, varying from 49 (27 – 87) months for IQVIA DA Germany to 113 (31 – 122) months in NAJS.

Prior use of other JAKi before filgotinib initiation was observed in some individuals. Prior use of baricitinib varied from 7.0% in HI-SPEED to 20.8% in VID, prior use of tofacitinib varied from 9.5% in HI-SPEED to 14.6% in VID, and prior use of upadacitinib varied from 5.8% in NAJS to 20.5% in HI-SPEED. However, in all data sources, the majority of filgotinib initiators had no previous use of other JAKi recorded (from 61.7% in VID to 80.0% in DK-DHR).

Table 5. Characterisation of individuals initiating filgotinib, overall and stratified by indication.

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Filgotinib - Overall								
Number individuals	–	N	206	35	208	1,228	355	1,357
Age	–	Median [Q25 – Q75]	55 [46 – 61]	54 [38 – 66]	47 [37 – 59]	59 [50 – 68]	55 [47 – 62]	49 [35 – 60]
		Mean (SD)	54 (13)	51 (16)	48 (15)	58 (14)	53 (12)	48 (16)
		Range	19 to 77	20 to 77	17 to 78	18 to 89	18 to 80	15 to 89
Sex	Female	N (%)	162 (78.6%)	26 (74.3%)	138 (66.3%)	909 (74.0%)	259 (73.0%)	917 (67.6%)
Treatment duration (months)*	–	Median [Q25 – Q75]	6 [3 – 12]	–	24 [12 – 33]	8 [3 – 18]	10 [5 – 20]	7 [3 – 14]
		Mean (SD)	9 (8)	–	22 (13)	13 (13)	13 (10)	10 (9)
Potential indications	Alopecia areata	N (%)	8 (3.9%)	<5	<5	8 (0.7%)	22 (6.2%)	17 (1.3%)
	Atopic dermatitis	N (%)	18 (8.7%)	0 (0.0%)	9 (4.3%)	13 (1.1%)	19 (5.4%)	39 (2.9%)
	Axial spondylitis	N (%)	6 (2.9%)	<5	6 (2.9%)	25 (2.0%)	10 (2.8%)	39 (2.9%)
	Inflammatory bowel disease	N (%)	37 (18.0%)	8 (22.9%)	86 (41.3%)	210 (17.1%)	44 (12.4%)	523 (38.5%)
	Juvenile arthritis	N (%)	<5	<5	17 (8.2%)	10 (0.8%)	15 (4.2%)	87 (6.4%)
	Juvenile idiopathic arthritis	N (%)	<5	<5	17 (8.2%)	10 (0.8%)	15 (4.2%)	84 (6.2%)
	Psoriatic arthritis	N (%)	<5	5 (14.3%)	5 (2.4%)	56 (4.6%)	10 (2.8%)	95 (7.0%)
	Rheumatoid arthritis	N (%)	173 (84.0%)	25 (71.4%)	115 (55.3%)	977 (79.6%)	305 (85.9%)	710 (52.3%)
Time from indication diagnosis to JAKi initiation (months)	Alopecia areata	Median [Q25 – Q75]	60 [30 – 80]	–	–	74 [23 – 110]	59 [17 – 120]	76 [44 – 87]
	Atopic dermatitis	Median [Q25 – Q75]	84 [45 – 105]	–	57 [15 – 75]	51 [39 – 101]	82 [55 – 105]	58 [42 – 89]
	Axial spondylitis	Median [Q25 – Q75]	80 [55 – 102]	–	79 [35 – 92]	50 [14 – 135]	91 [25 – 139]	69 [33 – 91]

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Inflammatory bowel disease	Median [Q25 – Q75]	113 [31 – 122]	70 [28 – 127]	73 [30 – 93]	49 [27 – 87]	78 [43 – 159]	80 [37 – 98]
	Juvenile arthritis	Median [Q25 – Q75]	–	–	94 [81 – 103]	59 [42 – 157]	114 [39 – 131]	101 [90 – 114]
	Juvenile idiopathic arthritis	Median [Q25 – Q75]	–	–	94 [81 – 103]	59 [42 – 157]	114 [39 – 131]	101 [89 – 114]
	Psoriatic arthritis	Median [Q25 – Q75]	–	132 [67 – 179]	15 [8 – 18]	39 [23 – 78]	96 [70 – 172]	74 [38 – 103]
	Rheumatoid arthritis	Median [Q25 – Q75]	107 [55 – 121]	107 [60 – 182]	81 [41 – 95]	66 [28 – 114]	107 [50 – 155]	91 [46 – 106]
Prior JAK inhibitor use	Abrocitinib	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Baricitinib	N (%)	19 (9.2%)	<5	33 (15.9%)	111 (9.0%)	74 (20.8%)	95 (7.0%)
	Tofacitinib	N (%)	20 (9.7%)	<5	27 (13.0%)	123 (10.0%)	52 (14.6%)	129 (9.5%)
	Upadacitinib	N (%)	12 (5.8%)	<5	34 (16.3%)	172 (14.0%)	54 (15.2%)	278 (20.5%)
	No previous JAKi use	N (%)	160 (77.7%)	28 (80.0%)	136 (65.4%)	807 (65.7%)	219 (61.7%)	897 (66.1%)
Number of prior JAKi ingredients initiated	–	Median [Q25 – Q75]	0 [0 – 0]	0 [0 – 0]	0 [0 – 1]	0 [0 – 1]	0 [0 – 1]	0 [0 – 1]
Filgotinib - Alopecia areata								
Number individuals	–	N	8	<5	<5	8	22	17
Age	–	Median [Q25 – Q75]	50 [41 – 67]	–	–	61 [50 – 72]	58 [48 – 62]	43 [35 – 53]
		Mean (SD)	52 (16)	-	-	62 (15)	53 (14)	44 (13)
		Range	32 to 74	–	–	44 to 84	21 to 68	23 to 68
Sex	Female	N (%)	8 (100.0%)	<5	<5	8 (100.0%)	21 (95.5%)	15 (88.2%)
Treatment duration (months)*	–	Median [Q25 – Q75]	9 [3 – 16]	–	–	2 [1 – 10]	7 [4 – 12]	2 [1 – 7]
		Mean (SD)	10 (9)	–	–	9 (14)	9 (7)	6 (8)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Co-morbid conditions	Atopic dermatitis	N (%)	<5	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5	<5
	Axial spondylitis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
	Inflammatory bowel disease	N (%)	<5	0 (0.0%)	<5	<5	<5	6 (35.3%)
	Juvenile arthritis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5
	Juvenile idiopathic arthritis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5
	Psoriatic arthritis	N (%)	0 (0.0%)	<5	0 (0.0%)	<5	<5	<5
	Rheumatoid arthritis	N (%)	7 (87.5%)	0 (0.0%)	0 (0.0%)	6 (75.0%)	21 (95.5%)	10 (58.8%)
Filgotinib - Atopic dermatitis								
Number individuals	–	N	18	0	9	13	19	39
Age	–	Median [Q25 – Q75]	58 [46 – 62]	–	37 [35 – 55]	61 [53 – 66]	56 [52 – 60]	42 [30 – 53]
		Mean (SD)	54 (14)	–	43 (14)	58 (11)	54 (12)	42 (15)
		Range	19 to 77	–	21 to 63	33 to 69	21 to 68	19 to 74
Sex	Female	N (%)	15 (83.3%)	–	8 (88.9%)	8 (61.5%)	16 (84.2%)	32 (82.1%)
Treatment duration (months)*	–	Median [Q25 – Q75]	5 [3 – 11]	–	24 [13 – 36]	6 [1 – 30]	11 [5 – 19]	4 [2 – 10]
		Mean (SD)	7 (6)	–	25 (14)	15 (17)	12 (9)	7 (7)
Co-morbid conditions	Alopecia areata	N (%)	<5	–	0 (0.0%)	0 (0.0%)	<5	<5
	Axial spondylitis	N (%)	<5	–	0 (0.0%)	0 (0.0%)	<5	<5
	Inflammatory bowel disease	N (%)	<5	–	6 (66.7%)	<5	<5	21 (53.8%)
	Juvenile arthritis	N (%)	0 (0.0%)	–	0 (0.0%)	0 (0.0%)	<5	<5
	Juvenile idiopathic arthritis	N (%)	0 (0.0%)	–	0 (0.0%)	0 (0.0%)	<5	<5
	Psoriatic arthritis	N (%)	0 (0.0%)	–	0 (0.0%)	<5	<5	<5
	Rheumatoid arthritis	N (%)	14 (77.8%)	–	<5	11 (84.6%)	16 (84.2%)	14 (35.9%)
Filgotinib - Axial spondylitis								

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Number individuals	–	N	6	<5	6	25	10	39
Age	–	Median [Q25 – Q75]	51 [48 – 61]	-	41 [37 – 50]	53 [44 – 63]	58 [45 – 63]	50 [41 – 56]
		Mean (SD)	56 (12)	-	42 (10)	54 (13)	53 (15)	49 (14)
		Range	46 to 77	-	28 to 56	30 to 81	23 to 67	20 to 87
Sex	Female	N (%)	<5	–	<5	14 (56.0%)	7 (70.0%)	30 (76.9%)
Treatment duration (months)*	–	Median [Q25 – Q75]	6 [4 – 15]	–	11 [3 – 19]	5 [1 – 12]	13 [10 – 19]	8 [4 – 17]
		Mean (SD)	9 (8)	–	14 (14)	10 (12)	14 (6)	12 (11)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5
	Atopic dermatitis	N (%)	<5	-	0 (0.0%)	0 (0.0%)	<5	<5
	Inflammatory bowel disease	N (%)	<5	-	<5	<5	<5	14 (35.9%)
	Juvenile arthritis	N (%)	0 (0.0%)	-	0 (0.0%)	<5	<5	<5
	Juvenile idiopathic arthritis	N (%)	0 (0.0%)	-	0 (0.0%)	<5	<5	<5
	Psoriatic arthritis	N (%)	0 (0.0%)	-	0 (0.0%)	<5	<5	<5
	Rheumatoid arthritis	N (%)	<5	-	<5	18 (72.0%)	8 (80.0%)	10 (25.6%)
Filgotinib - Inflammatory bowel disease								
Number individuals	–	N	37	8	86	210	44	523
Age	–	Median [Q25 – Q75]	42 [30 – 55]	36 [30 – 47]	40 [30 – 47]	44 [35 – 56]	42 [28 – 52]	38 [28 – 49]
		Mean (SD)	44 (17)	38 (12)	41 (14)	45 (14)	42 (15)	40 (14)
		Range	19 to 77	23 to 60	19 to 77	18 to 75	18 to 80	15 to 89
Sex	Female	N (%)	17 (45.9%)	<5	43 (50.0%)	103 (49.0%)	22 (50.0%)	235 (44.9%)
Treatment duration (months)*	–	Median [Q25 – Q75]	5 [3 – 7]	–	24 [18 – 35]	6 [3 – 15]	7 [3 – 11]	6 [3 – 13]
		Mean (SD)	6 (6)	–	24 (11)	11 (11)	9 (7)	10 (9)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Co-morbid conditions	Alopecia areata	N (%)	<5	0 (0.0%)	<5	<5	<5	6 (1.1%)
	Atopic dermatitis	N (%)	<5	0 (0.0%)	6 (7.0%)	<5	<5	21 (4.0%)
	Axial spondylitis	N (%)	<5	0 (0.0%)	<5	<5	<5	14 (2.7%)
	Juvenile arthritis	N (%)	0 (0.0%)	0 (0.0%)	<5	0 (0.0%)	0 (0.0%)	11 (2.1%)
	Juvenile idiopathic arthritis	N (%)	0 (0.0%)	0 (0.0%)	<5	0 (0.0%)	0 (0.0%)	10 (1.9%)
	Psoriatic arthritis	N (%)	<5	0 (0.0%)	0 (0.0%)	<5	0 (0.0%)	9 (1.7%)
	Rheumatoid arthritis	N (%)	<5	<5	<5	13 (6.2%)	6 (13.6%)	26 (5.0%)
Filgotinib - Juvenile arthritis								
Number individuals	–	N	<5	<5	17	10	15	87
Age	–	Median [Q25 – Q75]	-	-	43 [38 – 48]	32 [26 – 41]	46 [30 – 52]	31 [24 – 41]
		Mean (SD)	-	-	44 (14)	33 (8)	42 (14)	34 (12)
		Range	-	-	19 to 68	23 to 45	22 to 63	18 to 72
Sex	Female	N (%)	<5	<5	15 (88.2%)	8 (80.0%)	12 (80.0%)	76 (87.4%)
Treatment duration (months)*	–	Median [Q25 – Q75]	–	–	24 [18 – 24]	6 [4 – 12]	9 [2 – 15]	6 [3 – 14]
		Mean (SD)	–	–	22 (10)	11 (11)	11 (10)	9 (9)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5
	Atopic dermatitis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5	<5
	Axial spondylitis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5	<5	<5
	Inflammatory bowel disease	N (%)	0 (0.0%)	0 (0.0%)	<5	0 (0.0%)	0 (0.0%)	11 (12.6%)
	Juvenile idiopathic arthritis	N (%)	<5	<5	17 (100.0%)	10 (100.0%)	15 (100.0%)	84 (96.6%)
	Psoriatic arthritis	N (%)	0 (0.0%)	<5	0 (0.0%)	0 (0.0%)	<5	11 (12.6%)
	Rheumatoid arthritis	N (%)	<5	<5	12 (70.6%)	8 (80.0%)	12 (80.0%)	43 (49.4%)
Filgotinib - Juvenile idiopathic arthritis								

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Number individuals	–	N	<5	<5	17	10	15	84
Age	–	Median [Q25 – Q75]	–	–	43 [38 – 48]	33 [26 – 41]	46 [30 – 52]	32 [23 – 42]
		Mean (SD)	–	–	43.7 (13.8)	33.2 (8.5)	42.1 (13.8)	34.0 (12.5)
		Range	–	–	19 to 68	23 to 45	22 to 63	18 to 72
Sex	Female	N (%)	<5	<5	15 (88.2%)	8 (80.0%)	12 (80.0%)	73 (86.9%)
Treatment duration (months)*	–	Median [Q25 – Q75]	–	–	24 [18 – 24]	6 [4 – 12]	9 [2 – 15]	6 [3 – 13]
		Mean (SD)	–	–	21.6 (9.9)	10.7 (10.9)	10.7 (9.9)	9.4 (8.8)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
	Atopic dermatitis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	–	–
	Axial spondylitis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	–	–	–
	Inflammatory bowel disease	N (%)	0 (0.0%)	0 (0.0%)	–	0 (0.0%)	0 (0.0%)	10 (11.9%)
	Juvenile arthritis	N (%)	<5	<5	17 (100.0%)	10 (100.0%)	15 (100.0%)	84 (100.0%)
	Psoriatic arthritis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	–	9 (10.7%)
	Rheumatoid arthritis	N (%)	<5	<5	12 (70.6%)	8 (80.0%)	12 (80.0%)	42 (50.0%)
Filgotinib - Psoriatic arthritis								
Number individuals	–	N	<5	5	5	56	10	95
Age	–	Median [Q25 – Q75]	–	54 [36 – 54]	56 [52 – 74]	58 [54 – 64]	55 [51 – 60]	54 [48 – 62]
		Mean (SD)	–	47 (20)	55 (23)	59 (10)	53 (12)	53 (13)
		Range	–	20 to 72	17 to 74	35 to 80	31 to 68	21 to 82
Sex	Female	N (%)	<5	5 (100.0%)	<5	38 (67.9%)	7 (70.0%)	77 (81.1%)
Treatment duration (months)*	–	Median [Q25 – Q75]	–	–	1 [1 – 35]	7 [4 – 15]	5 [2 – 14]	6 [2 – 11]
		Mean (SD)	–	–	16 (21)	11 (11)	8 (8)	9 (9)
Co-morbid indications	Alopecia areata	N (%)	0 (0.0%)	<5	0 (0.0%)	<5	<5	<5

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Atopic dermatitis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5	<5	<5
	Axial spondylitis	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<5	<5	<5
	Inflammatory bowel disease	N (%)	<5	0 (0.0%)	0 (0.0%)	<5	0 (0.0%)	9 (9.5%)
	Juvenile arthritis	N (%)	0 (0.0%)	<5	0 (0.0%)	0 (0.0%)	<5	11 (11.6%)
	Juvenile idiopathic arthritis	N (%)	0 (0.0%)	<5	0 (0.0%)	0 (0.0%)	<5	9 (9.5%)
	Rheumatoid arthritis	N (%)	<5	<5	<5	43 (76.8%)	9 (90.0%)	40 (42.1%)
Filgotinib - Rheumatoid arthritis								
Number individuals	–	N	173	25	115	977	305	710
Age	–	Median [Q25 – Q75]	56 [48 – 61]	56 [42 – 68]	56 [44 – 64]	61 [53 – 69]	56 [49 – 63]	55 [45 – 64]
		Mean (SD)	56 (10)	55 (16)	54 (14)	61 (13)	55 (10)	54 (14)
		Range	20 to 77	20 to 77	17 to 78	22 to 89	21 to 80	19 to 88
Sex	Female	N (%)	147 (85.0%)	23 (92.0%)	90 (78.3%)	776 (79.4%)	231 (75.7%)	593 (83.5%)
Treatment duration (months)*	–	Median [Q25 – Q75]	7 [3 – 13]	–	24 [6 – 31]	8 [3 – 19]	11 [5 – 22]	7 [3 – 15]
		Mean (SD)	9 (8)	–	21 (15)	13 (13)	13 (10)	10 (9)
Co-morbid indications	Alopecia areata	N (%)	7 (4.0%)	0 (0.0%)	0 (0.0%)	6 (0.6%)	21 (6.9%)	10 (1.4%)
	Atopic dermatitis	N (%)	14 (8.1%)	0 (0.0%)	<5	11 (1.1%)	16 (5.2%)	14 (2.0%)
	Axial spondylitis	N (%)	<5	0 (0.0%)	<5	18 (1.8%)	8 (2.6%)	10 (1.4%)
	Inflammatory bowel disease	N (%)	<5	<5	<5	13 (1.3%)	6 (2.0%)	26 (3.7%)
	Juvenile arthritis	N (%)	<5	<5	12 (10.4%)	8 (0.8%)	12 (3.9%)	43 (6.1%)
	Juvenile idiopathic arthritis	N (%)	<5	<5	12 (10.4%)	8 (0.8%)	12 (3.9%)	42 (5.9%)
	Psoriatic arthritis	N (%)	<5	<5	<5	43 (4.4%)	9 (3.0%)	40 (5.6%)

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; SD = Standard Deviation; Q25 = 25th Percentile; Q75 = 75th Percentile; JAKi = Janus kinase inhibitor/s.

– is used when data is not available.

*Treatment duration was available in all data sources, except DK-DHR, where treatment end date was unavailable in the majority of JAKi prescriptions.

Tofacitinib

The median age of individuals initiating tofacitinib ranged from 48 (33 – 59) in HI-SPEED to 58 (48 – 66) in IQVIA DA Germany. The majority of individuals were female (from 61.1% in HI-SPEED to 72.8% in IQVIA DA Germany). The median duration of treatment ranged from 7 (3 – 20) months in IQVIA DA Germany to 24 (12 – 45) in FinOMOP-THL.

Tofacitinib was approved to treat rheumatoid arthritis in 2017 and was subsequently approved to treat psoriatic arthritis and inflammatory bowel disease (specifically ulcerative colitis) in 2018 and axial spondylitis and juvenile idiopathic arthritis in 2021. This is reflected in the study results, with rheumatoid arthritis being the most common indication in all data sources (from 50.0% in FinOMOP-THL to 69.9% in IQVIA DA Germany) except in HI-SPEED, where inflammatory bowel disease was the most common indication (36.8%). Inflammatory bowel disease was also commonly recorded in the remaining data sources, varying from 15.1% in IQVIA DA Germany to 31.6% in FinOMOP-THL. The proportion of individuals initiating tofacitinib with prior history of axial spondylitis varied from 3.7% in DK-DHR to 11.0% in NAJS, while the proportion of individuals with prior history of psoriatic arthritis varied from 10.8% in DK-DHR to 27.4% in HI-SPEED, and for juvenile idiopathic arthritis it varied from 3.9% in VID to 14.0% in FinOMOP-THL.

The median age of individuals initiating tofacitinib with prior history of rheumatoid arthritis ranged from 53 (46 – 59) in VID to 60 (53 – 69) in IQVIA DA Germany, and the proportion of females was between 77.4% (VID) and 82.3% (NAJS). Treatment duration varied from 7 (3 – 21) months in HI-SPEED to 24 (12 – 50) months in FinOMOP-THL. Time from diagnosis of rheumatoid arthritis to tofacitinib diagnosis varied from 42 (30 – 54) months in FinOMOP-THL to 123 (59 – 193) months in DK-DHR.

Individuals initiating tofacitinib with prior history of inflammatory bowel disease were typically younger (median age ranging from 37 (27 – 50) in FinOMOP-THL to 43 (33 – 55) in IQVIA DA Germany, and the proportion of females was lower (from 36.8% in NAJS and FinOMOP-THL to 52.9% in VID) compared with individuals with a prior history of rheumatoid arthritis. Treatment duration was similar, varying from 6 (3 – 17) months in VID to 24 (14 – 43) months in FinOMOP-THL. Time from diagnosis of inflammatory bowel disease to tofacitinib initiation was typically shorter, varying from 48 (21 – 67) months in FinOMOP-THL to 79 (29 – 125) months in VID.

Individuals initiating tofacitinib with prior history of axial spondylitis were typically younger (median age ranging from 42 (32 – 53) in FinOMOP-THL to 52 (41 – 59) in IQVIA DA Germany and the proportion of females was lower (from 55.9% in DK-DHR to 69.8% in NAJS) compared with individuals with a prior history of rheumatoid arthritis. Treatment duration was fairly similar, varying from 5 (3 – 10) in IQVIA DA Germany to 24 (11 – 27) in FinOMOP-THL. Time from diagnosis of axial spondylitis to tofacitinib initiation was typically shorter, ranging from 42 (25 – 110) months in IQVIA DA Germany to 99 (56 – 207) months in DK-DHR.

Individuals initiating tofacitinib with prior history of psoriatic arthritis were a similar age to those with prior history of rheumatoid arthritis, with median age varying from 52 (45 – 59) in VID to 56 (48 – 63) in IQVIA DA Germany, while the proportion of females was lower (from 60.0% in NAJS to 74.9% in IQVIA DA Germany). Treatment duration was also similar, varying from 6 (3 – 16) months in IQVIA DA Germany and HI-SPEED to 24 (12 – 46) months in FinOMOP-THL. Time from diagnosis of psoriatic arthritis to tofacitinib initiation was shorter, varying from 40 (22 – 82) months in IQVIA DA Germany to 104 (45 – 167) months in DK-DHR.

Individuals initiating tofacitinib with prior history of juvenile idiopathic arthritis were younger than those with prior history of rheumatoid arthritis (median age ranging from 18 (12 – 28) in FinOMOP-THL to 34 (18 – 48) in VID), and the proportion of females was higher (between 70.0% in VID and 91.7% in IQVIA DA Germany). Treatment duration was similar, varying from 4 (2 – 9) months in IQVIA DA Germany to 24 (12 – 32) month in FinOMOP-THL. Time from diagnosis of juvenile idiopathic arthritis to tofacitinib initiation varied from 47 (21 – 91) months in IQVIA DA Germany to 176 (93 – 247) months in DK-DHR.

Use of other JAKi prior to tofacitinib initiation was very low, with between 84.3% (HI-SPEED) and 96.0% (NAJS and FinOMOP-THL) of individuals having no prior JAKi use.

Table 6. Characterisation of individuals initiating tofacitinib, overall and stratified by indication.

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Tofacitinib - Overall								
Number individuals	–	N	571	1,828	2,199	1,512	1,274	2,555
Age	–	Median [Q25 – Q75]	53 [39 – 62]	54 [39 – 64]	48 [32 – 60]	58 [48 – 66]	50 [41 – 58]	48 [33 – 59]
		Mean (SD)	50 (16)	52 (17)	46 (18)	57 (15)	48 (13)	46 (17)
		Range	9 to 84	9 to 90	2 to 85	3 to 92	1 to 83	1 to 87
Sex	Female	N (%)	391 (68.5%)	1,257 (68.8%)	1,365 (62.1%)	1,101 (72.8%)	868 (68.1%)	1,562 (61.1%)
Treatment duration (months)*	–	Median [Q25 – Q75]	11 [4 – 34]	–	24 [12 – 45]	7 [3 – 20]	8 [3 – 22]	7 [3 – 21]
		Mean (SD)	22 (23)	–	31 (24)	15 (19)	16 (19)	15 (18)
Potential indications	Alopecia areata	N (%)	14 (2.5%)	14 (0.8%)	6 (0.3%)	25 (1.7%)	133 (10.4%)	60 (2.3%)
	Atopic dermatitis	N (%)	35 (6.1%)	30 (1.6%)	96 (4.4%)	10 (0.7%)	125 (9.8%)	80 (3.1%)
	Axial spondylitis	N (%)	63 (11.0%)	68 (3.7%)	85 (3.9%)	69 (4.6%)	113 (8.9%)	214 (8.4%)
	Inflammatory bowel disease	N (%)	155 (27.1%)	491 (26.9%)	695 (31.6%)	228 (15.1%)	280 (22.0%)	940 (36.8%)
	Juvenile arthritis	N (%)	46 (8.1%)	91 (5.0%)	319 (14.5%)	26 (1.7%)	50 (3.9%)	205 (8.0%)
	Juvenile idiopathic arthritis	N (%)	43 (7.5%)	84 (4.6%)	307 (14.0%)	24 (1.6%)	50 (3.9%)	190 (7.4%)
	Psoriatic arthritis	N (%)	75 (13.1%)	198 (10.8%)	341 (15.5%)	275 (18.2%)	233 (18.3%)	699 (27.4%)
	Rheumatoid arthritis	N (%)	345 (60.4%)	1,199 (65.6%)	1,100 (50.0%)	1,057 (69.9%)	721 (56.6%)	694 (27.2%)
Time from indication diagnosis to JAKi initiation (months)	Alopecia areata	Median [Q25 – Q75]	48 [33 – 64]	59 [11 – 109]	18 [8 – 33]	49 [23 – 95]	53 [20 – 87]	42 [16 – 65]
	Atopic dermatitis	Median [Q25 – Q75]	51 [27 – 77]	171 [49 – 247]	36 [16 – 66]	127 [73 – 149]	72 [41 – 109]	44 [25 – 61]
	Axial spondylitis	Median [Q25 – Q75]	55 [29 – 80]	99 [56 – 207]	55 [31 – 80]	42 [25 – 110]	82 [37 – 126]	47 [24 – 74]

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Inflammatory bowel disease	Median [Q25 – Q75]	62 [44 – 86]	74 [21 – 144]	48 [21 – 67]	48 [25 – 93]	79 [29 – 125]	51 [28 – 70]
	Juvenile arthritis	Median [Q25 – Q75]	59 [42 – 97]	175 [88 – 246]	60 [28 – 91]	42 [17 – 89]	72 [48 – 110]	67 [48 – 91]
	Juvenile idiopathic arthritis	Median [Q25 – Q75]	57 [41 – 98]	176 [93 – 247]	61 [27 – 93]	47 [21 – 91]	72 [48 – 110]	67 [47 – 92]
	Psoriatic arthritis	Median [Q25 – Q75]	46 [27 – 64]	104 [45 – 167]	46 [28 – 62]	40 [22 – 82]	58 [28 – 109]	50 [29 – 64]
	Rheumatoid arthritis	Median [Q25 – Q75]	59 [43 – 69]	123 [59 – 193]	42 [30 – 54]	54 [29 – 105]	75 [30 – 112]	53 [33 – 70]
Prior JAK inhibitor use	Abrocitinib	N (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Baricitinib	N (%)	8 (1.4%)	71 (3.9%)	46 (2.1%)	48 (3.2%)	53 (4.2%)	128 (5.0%)
	Filgotinib	N (%)	0 (0.0%)	<5	<5	10 (0.7%)	<5	28 (1.1%)
	Upadacitinib	N (%)	18 (3.2%)	10 (0.5%)	32 (1.5%)	48 (3.2%)	55 (4.3%)	156 (6.1%)
	No previous JAKi use	N (%)	548 (96.0%)	1744 (95.4%)	2112 (96.0%)	1365 (90.3%)	1170 (91.8%)	2154 (84.3%)
Number of prior JAKi ingredients initiated	–	Median [Q25 – Q75]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]
Tofacitinib - Alopecia areata								
Number individuals	–	N	14	14	6	25	133	60
Age	–	Median [Q25 – Q75]	54 [39 – 64]	38 [21 – 58]	25 [17 – 50]	54 [45 – 62]	42 [32 – 52]	38 [24 – 54]
		Mean (SD)	52 (14)	40 (19)	34 (22)	52 (14)	41 (14)	38 (19)
		Range	28 to 70	16 to 66	14 to 65	19 to 79	5 to 67	8 to 78
Sex	Female	N (%)	13 (92.9%)	14 (100.0%)	6 (100.0%)	24 (96.0%)	96 (72.2%)	42 (70.0%)
Treatment duration (months)*	–	Median [Q25 – Q75]	30 [4 – 38]	–	19 [11 – 30]	5 [2 – 9]	9 [4 – 23]	10 [4 – 24]

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Mean (SD)	24 (18)	–	21 (16)	12 (19)	17 (19)	16 (16)
Co-morbid conditions	Atopic dermatitis	N (%)	0 (0.0%)	<5	<5	<5	29 (21.8%)	7 (11.7%)
	Axial spondylitis	N (%)	<5	<5	<5	<5	8 (6.0%)	5 (8.3%)
	Inflammatory bowel disease	N (%)	6 (42.9%)	<5	0 (0.0%)	<5	15 (11.3%)	11 (18.3%)
	Juvenile arthritis	N (%)	0 (0.0%)	<5	<5	0 (0.0%)	5 (3.8%)	9 (15.0%)
	Juvenile idiopathic arthritis	N (%)	0 (0.0%)	<5	<5	0 (0.0%)	5 (3.8%)	9 (15.0%)
	Psoriatic arthritis	N (%)	<5	<5	0 (0.0%)	6 (24.0%)	14 (10.5%)	10 (16.7%)
	Rheumatoid arthritis	N (%)	5 (35.7%)	8 (57.1%)	<5	15 (60.0%)	44 (33.1%)	13 (21.7%)
Tofacitinib - Atopic dermatitis								
Number individuals	–	N	35	30	96	10	125	80
Age	–	Median [Q25 – Q75]	50 [24 – 62]	35 [24 – 56]	32 [20 – 49]	46 [33 – 53]	46 [32 – 57]	36 [21 – 56]
		Mean (SD)	44 (22)	40 (18)	35 (18)	44 (21)	43 (16)	38 (20)
		Range	9 to 77	15 to 80	2 to 74	7 to 80	1 to 73	7 to 76
Sex	Female	N (%)	26 (74.3%)	23 (76.7%)	71 (74.0%)	9 (90.0%)	88 (70.4%)	56 (70.0%)
Treatment duration (months)*	–	Median [Q25 – Q75]	7 [2 – 25]	–	23 [11 – 32]	4 [3 – 10]	9 [4 – 23]	7 [3 – 21]
		Mean (SD)	16 (20)	–	25 (20)	11 (14)	17 (18)	12 (13)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	<5	<5	<5	29 (23.2%)	7 (8.8%)
	Axial spondylitis	N (%)	<5	<5	8 (8.3%)	0 (0.0%)	9 (7.2%)	7 (8.8%)
	Inflammatory bowel disease	N (%)	11 (31.4%)	11 (36.7%)	32 (33.3%)	0 (0.0%)	32 (25.6%)	36 (45.0%)
	Juvenile arthritis	N (%)	9 (25.7%)	<5	34 (35.4%)	<5	8 (6.4%)	17 (21.2%)
	Juvenile idiopathic arthritis	N (%)	8 (22.9%)	<5	32 (33.3%)	<5	8 (6.4%)	16 (20.0%)
	Psoriatic arthritis	N (%)	<5	<5	9 (9.4%)	<5	27 (21.6%)	18 (22.5%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Rheumatoid arthritis	N (%)	21 (60.0%)	14 (46.7%)	42 (43.8%)	5 (50.0%)	51 (40.8%)	17 (21.2%)
Tofacitinib - Axial spondylitis								
Number individuals	–	N	63	68	85	69	113	214
Age	–	Median [Q25 – Q75]	48 [38 – 56]	48 [38 – 56]	42 [32 – 53]	52 [41 – 59]	49 [42 – 55]	46 [34 – 57]
		Mean (SD)	47 (15)	48 (14)	44 (15)	51 (13)	48 (11)	45 (15)
		Range	10 to 75	22 to 81	14 to 80	14 to 90	12 to 77	12 to 83
Sex	Female	N (%)	44 (69.8%)	38 (55.9%)	54 (63.5%)	41 (59.4%)	68 (60.2%)	126 (58.9%)
Treatment duration (months)*	–	Median [Q25 – Q75]	8 [3 – 19]	–	24 [11 – 27]	5 [3 – 10]	6 [3 – 12]	5 [2 – 11]
		Mean (SD)	13 (16)	–	23 (17)	11 (15)	10 (13)	11 (15)
Co-morbid conditions	Alopecia areata	N (%)	<5	<5	<5	<5	8 (7.1%)	5 (2.3%)
	Atopic dermatitis	N (%)	<5	<5	8 (9.4%)	0 (0.0%)	9 (8.0%)	7 (3.3%)
	Inflammatory bowel disease	N (%)	21 (33.3%)	22 (32.4%)	24 (28.2%)	<5	36 (31.9%)	48 (22.4%)
	Juvenile arthritis	N (%)	10 (15.9%)	<5	11 (12.9%)	<5	<5	21 (9.8%)
	Juvenile idiopathic arthritis	N (%)	10 (15.9%)	<5	11 (12.9%)	<5	<5	21 (9.8%)
	Psoriatic arthritis	N (%)	9 (14.3%)	12 (17.6%)	16 (18.8%)	27 (39.1%)	26 (23.0%)	37 (17.3%)
	Rheumatoid arthritis	N (%)	32 (50.8%)	35 (51.5%)	30 (35.3%)	33 (47.8%)	39 (34.5%)	39 (18.2%)
Tofacitinib - Inflammatory bowel disease								
Number individuals	–	N	155	491	695	228	280	940
Age	–	Median [Q25 – Q75]	38 [27 – 51]	37 [26 – 52]	37 [27 – 50]	43 [33 – 55]	42 [31 – 50]	38 [29 – 52]
		Mean (SD)	40 (15)	39 (15)	39 (15)	44 (14)	41 (13)	40 (15)
		Range	16 to 77	9 to 83	9 to 85	20 to 84	12 to 77	7 to 83
Sex	Female	N (%)	57 (36.8%)	249 (50.7%)	256 (36.8%)	97 (42.5%)	148 (52.9%)	414 (44.0%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Treatment duration (months)*	–	Median [Q25 – Q75]	9 [3 – 33]	–	24 [14 – 43]	8 [3 – 23]	6 [3 – 17]	8 [3 – 26]
		Mean (SD)	19 (20)	–	30 (21)	17 (18)	13 (16)	17 (19)
Co-morbid conditions	Alopecia areata	N (%)	6 (3.9%)	<5	0 (0.0%)	<5	15 (5.4%)	11 (1.2%)
	Atopic dermatitis	N (%)	11 (7.1%)	11 (2.2%)	32 (4.6%)	0 (0.0%)	32 (11.4%)	36 (3.8%)
	Axial spondylitis	N (%)	21 (13.5%)	22 (4.5%)	24 (3.5%)	<5	36 (12.9%)	48 (5.1%)
	Juvenile arthritis	N (%)	<5	5 (1.0%)	22 (3.2%)	0 (0.0%)	<5	22 (2.3%)
	Juvenile idiopathic arthritis	N (%)	<5	<5	20 (2.9%)	0 (0.0%)	<5	18 (1.9%)
	Psoriatic arthritis	N (%)	<5	17 (3.5%)	16 (2.3%)	<5	13 (4.6%)	53 (5.6%)
	Rheumatoid arthritis	N (%)	15 (9.7%)	88 (17.9%)	44 (6.3%)	17 (7.5%)	27 (9.6%)	57 (6.1%)
Tofacitinib - Juvenile arthritis								
Number individuals	–	N	46	91	319	26	50	205
Age	–	Median [Q25 – Q75]	21 [16 – 43]	29 [22 – 44]	18 [12 – 28]	22 [16 – 40]	34 [18 – 48]	21 [15 – 33]
		Mean (SD)	28 (17)	33 (14)	22 (14)	29 (18)	34 (17)	25 (13)
		Range	9 to 63	10 to 64	2 to 72	3 to 69	1 to 69	1 to 75
Sex	Female	N (%)	34 (73.9%)	79 (86.8%)	251 (78.7%)	22 (84.6%)	35 (70.0%)	157 (76.6%)
Treatment duration (months)*	–	Median [Q25 – Q75]	9 [5 – 27]	–	24 [12 – 33]	4 [2 – 8]	10 [4 – 18]	6 [3 – 18]
		Mean (SD)	19 (22)	–	25 (16)	9 (17)	15 (16)	12 (14)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	<5	<5	0 (0.0%)	5 (10.0%)	9 (4.4%)
	Atopic dermatitis	N (%)	9 (19.6%)	<5	34 (10.7%)	<5	8 (16.0%)	17 (8.3%)
	Axial spondylitis	N (%)	10 (21.7%)	<5	11 (3.4%)	<5	<5	21 (10.2%)
	Inflammatory bowel disease	N (%)	<5	5 (5.5%)	22 (6.9%)	0 (0.0%)	<5	22 (10.7%)
	Juvenile idiopathic arthritis	N (%)	43 (93.5%)	84 (92.3%)	307 (96.2%)	24 (92.3%)	50 (100.0%)	190 (92.7%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Psoriatic arthritis	N (%)	<5	11 (12.1%)	29 (9.1%)	<5	5 (10.0%)	34 (16.6%)
	Rheumatoid arthritis	N (%)	25 (54.3%)	64 (70.3%)	132 (41.4%)	8 (30.8%)	37 (74.0%)	63 (30.7%)
Tofacitinib - Juvenile idiopathic arthritis								
Number individuals	–	N	43	84	307	24	50	190
Age	–	Median [Q25 – Q75]	21 [16 – 32]	29 [22 – 42]	18 [12 – 28]	20 [15 – 36]	34 [18 – 48]	20 [15 – 33]
		Mean (SD)	26 (16)	33 (14)	22 (14)	27 (18)	34 (17)	25 (14)
		Range	9 to 62	10 to 63	2 to 71	3 to 69	1 to 69	1 to 75
Sex	Female	N (%)	32 (74.4%)	74 (88.1%)	244 (79.5%)	22 (91.7%)	35 (70.0%)	147 (77.4%)
Treatment duration (months)*	–	Median [Q25 – Q75]	9 [5 – 24]	–	24 [12 – 32]	4 [2 – 9]	10 [4 – 18]	6 [3 – 18]
		Mean (SD)	17 (19)	–	24 (15)	10 (17)	15 (16)	12 (14)
Co-morbid conditions	Alopecia areata	N (%)	0 (0.0%)	<5	<5	0 (0.0%)	5 (10.0%)	9 (4.7%)
	Atopic dermatitis	N (%)	8 (18.6%)	<5	32 (10.4%)	<5	8 (16.0%)	16 (8.4%)
	Axial spondylitis	N (%)	10 (23.3%)	<5	11 (3.6%)	<5	<5	21 (11.1%)
	Inflammatory bowel disease	N (%)	<5	<5	20 (6.5%)	0 (0.0%)	<5	18 (9.5%)
	Juvenile arthritis	N (%)	43 (100.0%)	84 (100.0%)	307 (100.0%)	24 (100.0%)	50 (100.0%)	190 (100.0%)
	Psoriatic arthritis	N (%)	<5	8 (9.5%)	22 (7.2%)	<5	5 (10.0%)	24 (12.6%)
	Rheumatoid arthritis	N (%)	23 (53.5%)	60 (71.4%)	129 (42.0%)	6 (25.0%)	37 (74.0%)	61 (32.1%)
Tofacitinib - Psoriatic arthritis								
Number individuals	–	N	75	198	341	275	233	699
Age	–	Median [Q25 – Q75]	56 [46 – 63]	55 [45 – 63]	53 [44 – 61]	56 [48 – 63]	52 [45 – 59]	53 [45 – 62]
		Mean (SD)	54 (12)	54 (14)	51 (15)	55 (12)	52 (11)	53 (14)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Range	24 to 75	18 to 82	9 to 85	17 to 81	12 to 83	11 to 84
Sex	Female	N (%)	45 (60.0%)	140 (70.7%)	212 (62.2%)	206 (74.9%)	153 (65.7%)	468 (67.0%)
Treatment duration (months)*	–	Median [Q25 – Q75]	7 [3 – 28]	–	24 [12 – 46]	6 [3 – 16]	7 [3 – 20]	6 [3 – 16]
		Mean (SD)	20 (24)	–	30 (24)	13 (17)	15 (17)	14 (17)
Co-morbid conditions	Alopecia areata	N (%)	<5	<5	0 (0.0%)	6 (2.2%)	14 (6.0%)	10 (1.4%)
	Atopic dermatitis	N (%)	<5	<5	9 (2.6%)	<5	27 (11.6%)	18 (2.6%)
	Axial spondylitis	N (%)	9 (12.0%)	12 (6.1%)	16 (4.7%)	27 (9.8%)	26 (11.2%)	37 (5.3%)
	Inflammatory bowel disease	N (%)	<5	17 (8.6%)	16 (4.7%)	<5	13 (5.6%)	53 (7.6%)
	Juvenile arthritis	N (%)	<5	11 (5.6%)	29 (8.5%)	<5	5 (2.1%)	34 (4.9%)
	Juvenile idiopathic arthritis	N (%)	<5	8 (4.0%)	22 (6.5%)	<5	5 (2.1%)	24 (3.4%)
	Rheumatoid arthritis	N (%)	35 (46.7%)	132 (66.7%)	102 (29.9%)	110 (40.0%)	90 (38.6%)	133 (19.0%)
Tofacitinib - Rheumatoid arthritis								
Number individuals	–	N	345	1,199	1,100	1,057	721	694
Age	–	Median [Q25 – Q75]	57 [49 – 64]	58 [48 – 67]	57 [46 – 65]	60 [53 – 69]	53 [46 – 59]	57 [46 – 67]
		Mean (SD)	56 (12)	57 (14)	54 (16)	61 (13)	52 (11)	55 (15)
		Range	9 to 78	10 to 90	5 to 84	19 to 92	8 to 83	11 to 87
Sex	Female	N (%)	284 (82.3%)	934 (77.9%)	856 (77.8%)	838 (79.3%)	558 (77.4%)	550 (79.3%)
Treatment duration (months)*	–	Median [Q25 – Q75]	15 [4 – 42]	–	24 [12 – 50]	7 [3 – 23]	9 [3 – 28]	7 [3 – 21]
		Mean (SD)	25 (25)	–	34 (26)	16 (19)	19 (21)	15 (18)
Co-morbid conditions	Alopecia areata	N (%)	5 (1.4%)	8 (0.7%)	<5	15 (1.4%)	44 (6.1%)	13 (1.9%)
	Atopic dermatitis	N (%)	21 (6.1%)	14 (1.2%)	42 (3.8%)	5 (0.5%)	51 (7.1%)	17 (2.4%)
	Axial spondylitis	N (%)	32 (9.3%)	35 (2.9%)	30 (2.7%)	33 (3.1%)	39 (5.4%)	39 (5.6%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Inflammatory bowel disease	N (%)	15 (4.3%)	88 (7.3%)	44 (4.0%)	17 (1.6%)	27 (3.7%)	57 (8.2%)
	Juvenile arthritis	N (%)	25 (7.2%)	64 (5.3%)	132 (12.0%)	8 (0.8%)	37 (5.1%)	63 (9.1%)
	Juvenile idiopathic arthritis	N (%)	23 (6.7%)	60 (5.0%)	129 (11.7%)	6 (0.6%)	37 (5.1%)	61 (8.8%)
	Psoriatic arthritis	N (%)	35 (10.1%)	132 (11.0%)	102 (9.3%)	110 (10.4%)	90 (12.5%)	133 (19.2%)

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; SD = Standard Deviation; Q25 = 25th Percentile; Q75 = 75th Percentile; JAKi = Janus kinase inhibitor/s.

– is used when data is not available.

*Treatment duration was available in all data sources, except DK-DHR, where treatment end date was unavailable in the majority of JAKi prescriptions.

Upadacitinib

The median age of individuals initiating upadacitinib ranged from 41 (30 – 54) in FinOMOP-THL to 56 (44 – 64) in IQVIA DA Germany. The majority of the individuals were female (from 52.8% in FinOMOP-THL to 67.7% in HI-SPEED). The median duration of treatment ranged from 7 (3 – 19) in IQVIA DA Germany to 15 (6 – 24) in FinOMOP-THL.

Upadacitinib was approved to treat rheumatoid arthritis in 2019 and was subsequently approved to treat atopic dermatitis, axial spondylitis, and psoriatic arthritis in 2021, and inflammatory bowel disease (specifically ulcerative colitis) in 2022. This is reflected in the study results, with inflammatory bowel disease being the most common indication in DK-DHR and FinOMOP-THL (54.6% and 52.0% respectively), followed by rheumatoid arthritis (36.1% and 29.0%, respectively). In the remaining data sources, rheumatoid arthritis was the most common (from 42.3% in HI-SPEED to 56.2% in IQVIA DA Germany), followed by inflammatory bowel disease (from 13.3% in HI-SPEED to 24.2% in NAJS). Atopic dermatitis was recorded in 7.9% (DK-DHR) to 25.5% (NAJS) of individuals, axial spondylitis in 9.0% (FinOMOP-THL) to 17.7% (NAJS), and psoriatic arthritis in 8.5% (FinOMOP-THL) to 20.5% (HI-SPEED).

The median age of individuals initiating upadacitinib with prior history of rheumatoid arthritis ranged from 53 (42 – 62) in FinOMOP-THL to 59 (51 – 66) in IQVIA DA Germany, and the proportion of females was between 73.4% (DK-DHR) and 83.8% (NAJS). Treatment duration varied from 9 (3 – 23) months in IQVIA DA Germany to 24 (11 – 39) in FinOMOP-THL. Time from diagnosis of rheumatoid arthritis to upadacitinib initiation varied from 59 (28 – 104) months in IQVIA DA Germany to 153 (86 – 222) months in DK-DHR.

Individuals initiating upadacitinib with prior history of inflammatory bowel disease were typically younger (median age ranging from 36 (27 – 49) in DK-DHR to 45 (35 – 53) in VID), and the proportion of females was lower (from 39.7% in FinOMOP-THL to 55.9% in HI-SPEED) compared with those with prior history of rheumatoid arthritis. Treatment duration was shorter, varying from 6 (3 – 9) months in VID to 12 (4 – 20) months in FinOMOP-THL, as was time from inflammatory bowel disease diagnosis to upadacitinib initiation (ranging from 55 (29 – 96) months in IQVIA DA Germany to 109 (44 – 165) months in VID).

Individuals initiating upadacitinib with prior history of atopic dermatitis were typically younger (median age ranging from 27 (22 – 38) in DK-DHR to 44 (30 – 56) in IQVIA DA Germany), and the proportion of females was lower (ranging from 44.3% in IQVIA DA Germany to 57.4% in VID) compared with those with prior history of rheumatoid arthritis. Treatment duration was shorter (ranging from 6 (3 – 17) months in IQVIA DA Germany to 12 (5 – 24) in NAJS), as was time from diagnosis of atopic dermatitis to upadacitinib initiation (ranging from 39 (17 – 91) months in IQVIA DA Germany to 128 (30 – 197) months in DK-DHR).

Individuals initiating upadacitinib with prior history of axial spondylitis were slightly younger (median age ranging from 43 (34 – 53) months in FinOMOP-THL to 52 (43 – 59) month in NAJS), and the proportion of females was lower (from 49.0% in FinOMOP-THL to 66.0% in NAJS) compared with those with prior history of rheumatoid arthritis. Treatment duration was shorter (from 6 (3 – 15) months in IQVIA DA Germany to 17 (5 – 24) months in FinOMOP-THL), as was time from diagnosis of axial spondylitis to upadacitinib initiation (from 46 (17 – 81) months in NAJS to 118 (47 – 178) in DK-DHR).

Individuals initiating upadacitinib with prior history of psoriatic arthritis were a similar age (median age ranging from 51 (42 – 59) in FinOMOP-THL to 57 (49 – 63) in IQVIA DA Germany), and the proportion of females was lower (from 64.8% in HI-SPEED to 75.2% in NAJS) compared with those with prior history of rheumatoid arthritis. Treatment duration was shorter (from 6 (3 – 15) months in IQVIA DA Germany to 22 (7 – 24) months in FinOMOP-THL), as was time from psoriatic arthritis diagnosis to upadacitinib initiation (from 44 (21 – 81) months in IQVIA DA Germany to 106 (50 – 165) months in DK-DHR).

Prior use of baricitinib was observed in 3.9% (NAJS) to 10.6% (DK-DHR), and prior use of tofacitinib was observed in 3.2% (NAJS) to 16.5% (DK-DHR). However, the majority of upadacitinib initiators had no prior JAKi use (from 76.6% (DK-DHR) to 92.6% (NAJS)).

Table 7. Characterisation of individuals initiating upadacitinib, overall and stratified by indication.

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Upadacitinib - Overall								
Number individuals	–	N	1,449	710	3,353	3,675	2,835	5,635
Age	–	Median [Q25 – Q75]	49 [35 – 59]	44 [31 – 56]	41 [30 – 54]	56 [44 – 64]	50 [40 – 58]	51 [37 – 61]
		Mean (SD)	46 (16)	44 (16)	42 (15)	54 (15)	48 (14)	49 (16)
		Range	10 to 85	11 to 84	11 to 85	6 to 95	5 to 90	4 to 93
Sex	Female	N (%)	960 (66.3%)	425 (59.9%)	1,770 (52.8%)	2,398 (65.3%)	1,827 (64.4%)	3,817 (67.7%)
Treatment duration (months)*	–	Median [Q25 – Q75]	10 [4 – 22]	–	15 [6 – 24]	7 [3 – 19]	8 [3 – 17]	8 [3 – 19]
		Mean (SD)	15 (15)	–	17 (14)	13 (14)	11 (11)	13 (14)
Potential indications	Alopecia areata	N (%)	51 (3.5%)	7 (1.0%)	27 (0.8%)	56 (1.5%)	270 (9.5%)	114 (2.0%)
	Atopic dermatitis	N (%)	369 (25.5%)	56 (7.9%)	604 (18.0%)	332 (9.0%)	666 (23.5%)	655 (11.6%)
	Axial spondylitis	N (%)	256 (17.7%)	71 (10.0%)	302 (9.0%)	353 (9.6%)	465 (16.4%)	723 (12.8%)
	Inflammatory bowel disease	N (%)	350 (24.2%)	388 (54.6%)	1,742 (52.0%)	599 (16.3%)	492 (17.4%)	752 (13.3%)
	Juvenile arthritis	N (%)	39 (2.7%)	44 (6.2%)	143 (4.3%)	33 (0.9%)	76 (2.7%)	376 (6.7%)
	Juvenile idiopathic arthritis	N (%)	35 (2.4%)	43 (6.1%)	132 (3.9%)	30 (0.8%)	74 (2.6%)	363 (6.4%)
	Psoriatic arthritis	N (%)	161 (11.1%)	72 (10.1%)	285 (8.5%)	644 (17.5%)	451 (15.9%)	1,153 (20.5%)
	Rheumatoid arthritis	N (%)	666 (46.0%)	256 (36.1%)	973 (29.0%)	2,066 (56.2%)	1,213 (42.8%)	2,382 (42.3%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Time from indication diagnosis to JAKi initiation (months)	Alopecia areata	Median [Q25 – Q75]	60 [28 – 88]	73 [54 – 95]	24 [15 – 50]	43 [21 – 103]	59 [24 – 112]	43 [18 – 71]
	Atopic dermatitis	Median [Q25 – Q75]	84 [44 – 103]	128 [30 – 197]	58 [31 – 97]	39 [17 – 91]	90 [33 – 142]	63 [27 – 91]
	Axial spondylitis	Median [Q25 – Q75]	46 [17 – 81]	118 [47 – 178]	79 [38 – 101]	54 [27 – 105]	78 [36 – 131]	64 [31 – 86]
	Inflammatory bowel disease	Median [Q25 – Q75]	96 [48 – 117]	93 [41 – 188]	67 [25 – 107]	55 [29 – 96]	109 [44 – 165]	81 [42 – 103]
	Juvenile arthritis	Median [Q25 – Q75]	79 [57 – 97]	203 [123 – 294]	92 [76 – 115]	53 [27 – 104]	104 [64 – 138]	82 [70 – 99]
	Juvenile idiopathic arthritis	Median [Q25 – Q75]	83 [57 – 97]	200 [135 – 297]	92 [75 – 115]	61 [27 – 109]	104 [69 – 139]	81 [67 – 98]
	Psoriatic arthritis	Median [Q25 – Q75]	53 [23 – 81]	106 [50 – 165]	66 [32 – 92]	44 [21 – 81]	75 [31 – 126]	67 [33 – 84]
	Rheumatoid arthritis	Median [Q25 – Q75]	70 [38 – 86]	153 [86 – 222]	70 [36 – 89]	59 [28 – 104]	89 [43 – 142]	71 [41 – 84]
Prior JAK inhibitor use	Abrocitinib	N (%)	0 (0.0%)	0 (0.0%)	16 (0.5%)	0 (0.0%)	7 (0.2%)	0 (0.0%)
	Baricitinib	N (%)	57 (3.9%)	75 (10.6%)	172 (5.1%)	239 (6.5%)	256 (9.0%)	365 (6.5%)
	Filgotinib	N (%)	5 (0.3%)	<5	23 (0.7%)	115 (3.1%)	39 (1.4%)	70 (1.2%)
	Tofacitinib	N (%)	46 (3.2%)	117 (16.5%)	292 (8.7%)	292 (8.0%)	273 (9.6%)	333 (5.9%)
	No previous JAKi use	N (%)	1342 (92.6%)	544 (76.6%)	2863 (85.4%)	2863 (77.9%)	2309 (81.4%)	4661 (82.7%)
Number of prior JAKi ingredients initiated	–	Median [Q25 – Q75]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]	0 [0 – 0]
Upadacitinib - Alopecia areata								
Number individuals	–	N	51	7	27	56	270	114

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Age	–	Median [Q25 – Q75]	45 [30 – 56]	38 [30 – 52]	38 [30 – 46]	56 [44 – 64]	50 [41 – 58]	42 [32 – 56]
		Mean (SD)	42 (17)	42 (15)	39 (14)	53 (16)	48 (12)	43 (17)
		Range	11 to 69	25 to 64	17 to 75	17 to 83	13 to 70	11 to 80
Sex	Female	N (%)	36 (70.6%)	5 (71.4%)	18 (66.7%)	49 (87.5%)	230 (85.2%)	87 (76.3%)
Treatment duration (months)*	–	Median [Q25 – Q75]	7 [4 – 15]	–	10 [4 – 23]	8 [2 – 21]	7 [3 – 16]	7 [3 – 16]
		Mean (SD)	12 (11)	–	14 (13)	13 (15)	11 (10)	13 (14)
Co-morbid conditions	Atopic dermatitis	N (%)	20 (39.2%)	<5	12 (44.4%)	15 (26.8%)	75 (27.8%)	34 (29.8%)
	Axial spondylitis	N (%)	7 (13.7%)	<5	<5	<5	40 (14.8%)	13 (11.4%)
	Inflammatory bowel disease	N (%)	13 (25.5%)	<5	11 (40.7%)	12 (21.4%)	46 (17.0%)	13 (11.4%)
	Juvenile arthritis	N (%)	<5	<5	0 (0.0%)	0 (0.0%)	5 (1.9%)	9 (7.9%)
	Juvenile idiopathic arthritis	N (%)	<5	<5	0 (0.0%)	0 (0.0%)	5 (1.9%)	9 (7.9%)
	Psoriatic arthritis	N (%)	8 (15.7%)	<5	<5	5 (8.9%)	41 (15.2%)	14 (12.3%)
	Rheumatoid arthritis	N (%)	15 (29.4%)	<5	5 (18.5%)	27 (48.2%)	117 (43.3%)	33 (28.9%)
Upadacitinib - Atopic dermatitis								
Number individuals	–	N	369	56	604	332	666	655
Age	–	Median [Q25 – Q75]	30 [22 – 46]	27 [22 – 38]	33 [24 – 45]	44 [30 – 56]	41 [23 – 54]	34 [24 – 50]
		Mean (SD)	35 (16)	32 (14)	35 (14)	43 (17)	40 (18)	38 (16)
		Range	10 to 85	12 to 74	11 to 81	11 to 88	5 to 90	4 to 80
Sex	Female	N (%)	209 (56.6%)	28 (50.0%)	329 (54.5%)	147 (44.3%)	382 (57.4%)	374 (57.1%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Treatment duration (months)*	–	Median [Q25 – Q75]	12 [5 – 24]	–	12 [6 – 23]	6 [3 – 17]	8 [3 – 16]	7 [3 – 14]
		Mean (SD)	16 (14)	–	15 (11)	11 (11)	11 (10)	10 (10)
Co-morbid conditions	Alopecia areata	N (%)	20 (5.4%)	<5	12 (2.0%)	15 (4.5%)	75 (11.3%)	34 (5.2%)
	Axial spondylitis	N (%)	28 (7.6%)	<5	35 (5.8%)	7 (2.1%)	45 (6.8%)	29 (4.4%)
	Inflammatory bowel disease	N (%)	34 (9.2%)	22 (39.3%)	160 (26.5%)	9 (2.7%)	58 (8.7%)	44 (6.7%)
	Juvenile arthritis	N (%)	6 (1.6%)	8 (14.3%)	16 (2.6%)	0 (0.0%)	9 (1.4%)	25 (3.8%)
	Juvenile idiopathic arthritis	N (%)	5 (1.4%)	7 (12.5%)	15 (2.5%)	0 (0.0%)	8 (1.2%)	23 (3.5%)
	Psoriatic arthritis	N (%)	16 (4.3%)	<5	20 (3.3%)	8 (2.4%)	64 (9.6%)	50 (7.6%)
	Rheumatoid arthritis	N (%)	60 (16.3%)	6 (10.7%)	52 (8.6%)	16 (4.8%)	82 (12.3%)	54 (8.2%)
Upadacitinib - Axial spondylitis								
Number individuals	–	N	256	71	302	353	465	723
Age	–	Median [Q25 – Q75]	52 [43 – 59]	45 [38 – 53]	43 [34 – 53]	50 [41 – 59]	50 [43 – 57]	46 [36 – 56]
		Mean (SD)	51 (11)	47 (12)	44 (13)	50 (13)	49 (10)	46 (13)
		Range	18 to 82	23 to 77	17 to 76	21 to 88	19 to 75	17 to 85
Sex	Female	N (%)	169 (66.0%)	37 (52.1%)	148 (49.0%)	188 (53.3%)	257 (55.3%)	414 (57.3%)
Treatment duration (months)*	–	Median [Q25 – Q75]	9 [3 – 21]	–	17 [5 – 24]	6 [3 – 15]	7 [2 – 14]	6 [3 – 16]
		Mean (SD)	14 (14)	–	18 (14)	11 (13)	10 (9)	12 (13)
Co-morbid conditions	Alopecia areata	N (%)	7 (2.7%)	<5	<5	<5	40 (8.6%)	13 (1.8%)
	Atopic dermatitis	N (%)	28 (10.9%)	<5	35 (11.6%)	7 (2.0%)	45 (9.7%)	29 (4.0%)
	Inflammatory bowel disease	N (%)	53 (20.7%)	21 (29.6%)	106 (35.1%)	40 (11.3%)	110 (23.7%)	90 (12.4%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Juvenile arthritis	N (%)	8 (3.1%)	<5	15 (5.0%)	6 (1.7%)	13 (2.8%)	49 (6.8%)
	Juvenile idiopathic arthritis	N (%)	7 (2.7%)	<5	14 (4.6%)	6 (1.7%)	13 (2.8%)	47 (6.5%)
	Psoriatic arthritis	N (%)	28 (10.9%)	<5	17 (5.6%)	53 (15.0%)	71 (15.3%)	102 (14.1%)
	Rheumatoid arthritis	N (%)	108 (42.2%)	25 (35.2%)	80 (26.5%)	104 (29.5%)	134 (28.8%)	130 (18.0%)
Upadacitinib - Inflammatory bowel disease								
Number individuals	–	N	350	388	1,742	599	492	752
Age	–	Median [Q25 – Q75]	43 [30 – 55]	36 [27 – 49]	37 [27 – 47]	42 [33 – 54]	45 [35 – 53]	41 [30 – 53]
		Mean (SD)	43 (15)	38 (14)	38 (13)	44 (14)	44 (13)	42 (15)
		Range	18 to 76	11 to 81	13 to 80	15 to 87	13 to 73	10 to 82
Sex	Female	N (%)	177 (50.6%)	204 (52.6%)	692 (39.7%)	305 (50.9%)	255 (51.8%)	420 (55.9%)
Treatment duration (months)*	–	Median [Q25 – Q75]	7 [3 – 14]	–	12 [4 – 20]	7 [3 – 14]	6 [3 – 9]	6 [3 – 12]
		Mean (SD)	9 (8)	–	13 (9)	10 (9)	7 (7)	9 (9)
Co-morbid conditions	Alopecia areata	N (%)	13 (3.7%)	<5	11 (0.6%)	12 (2.0%)	46 (9.3%)	13 (1.7%)
	Atopic dermatitis	N (%)	34 (9.7%)	22 (5.7%)	160 (9.2%)	9 (1.5%)	58 (11.8%)	44 (5.9%)
	Axial spondylitis	N (%)	53 (15.1%)	21 (5.4%)	106 (6.1%)	40 (6.7%)	110 (22.4%)	90 (12.0%)
	Juvenile arthritis	N (%)	8 (2.3%)	11 (2.8%)	36 (2.1%)	<5	7 (1.4%)	31 (4.1%)
	Juvenile idiopathic arthritis	N (%)	5 (1.4%)	11 (2.8%)	31 (1.8%)	<5	7 (1.4%)	26 (3.5%)
	Psoriatic arthritis	N (%)	14 (4.0%)	12 (3.1%)	26 (1.5%)	16 (2.7%)	28 (5.7%)	64 (8.5%)
	Rheumatoid arthritis	N (%)	52 (14.9%)	56 (14.4%)	74 (4.2%)	56 (9.3%)	65 (13.2%)	71 (9.4%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Upadacitinib - Juvenile arthritis								
Number individuals	–	N	39	44	143	33	76	376
Age	–	Median [Q25 – Q75]	30 [24 – 42]	31 [23 – 40]	29 [24 – 38]	31 [26 – 45]	42 [31 – 49]	28 [22 – 39]
		Mean (SD)	34 (12)	33 (12)	32 (12)	35 (12)	40 (13)	32 (13)
		Range	18 to 68	18 to 59	14 to 66	16 to 61	14 to 70	9 to 78
Sex	Female	N (%)	23 (59.0%)	39 (88.6%)	106 (74.1%)	26 (78.8%)	59 (77.6%)	297 (79.0%)
Treatment duration (months)*	–	Median [Q25 – Q75]	8 [1 – 16]	–	19 [7 – 27]	6 [3 – 10]	8 [2 – 20]	8 [3 – 17]
		Mean (SD)	12 (13)	–	21 (16)	9 (10)	12 (12)	13 (13)
Co-morbid conditions	Alopecia areata	N (%)	<5	<5	0 (0.0%)	0 (0.0%)	5 (6.6%)	9 (2.4%)
	Atopic dermatitis	N (%)	6 (15.4%)	8 (18.2%)	16 (11.2%)	0 (0.0%)	9 (11.8%)	25 (6.6%)
	Axial spondylitis	N (%)	8 (20.5%)	<5	15 (10.5%)	6 (18.2%)	13 (17.1%)	49 (13.0%)
	Inflammatory bowel disease	N (%)	8 (20.5%)	11 (25.0%)	36 (25.2%)	<5	7 (9.2%)	31 (8.2%)
	Juvenile idiopathic arthritis	N (%)	35 (89.7%)	43 (97.7%)	132 (92.3%)	30 (90.9%)	74 (97.4%)	363 (96.5%)
	Psoriatic arthritis	N (%)	<5	9 (20.5%)	16 (11.2%)	6 (18.2%)	14 (18.4%)	59 (15.7%)
	Rheumatoid arthritis	N (%)	22 (56.4%)	32 (72.7%)	80 (55.9%)	18 (54.5%)	53 (69.7%)	148 (39.4%)
Upadacitinib - Juvenile idiopathic arthritis								
Number individuals	–	N	35	43	132	30	74	363
Age	–	Median [Q25 – Q75]	29 [23 – 42]	31 [23 – 40]	30 [24 – 38]	30 [25 – 45]	42 [31 – 49]	28 [22 – 39]
		Mean (SD)	33 (13)	34 (12)	32 (12)	35 (12)	40 (13)	31 (13)
		Range	18 to 68	18 to 59	14 to 66	16 to 61	14 to 70	9 to 78
Sex	Female	N (%)	23 (65.7%)	39 (90.7%)	97 (73.5%)	24 (80.0%)	58 (78.4%)	289 (79.6%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Treatment duration (months)*	–	Median [Q25 – Q75]	6 [1 – 15]	–	19 [7 – 27]	6 [2 – 10]	8 [2 – 20]	8 [3 – 17]
		Mean (SD)	11 (13)	–	21 (16)	8 (10)	12 (12)	13 (14)
Co-morbid conditions	Alopecia areata	N (%)	<5	<5	0 (0.0%)	0 (0.0%)	5 (6.8%)	9 (2.5%)
	Atopic dermatitis	N (%)	5 (14.3%)	7 (16.3%)	15 (11.4%)	0 (0.0%)	8 (10.8%)	23 (6.3%)
	Axial spondylitis	N (%)	7 (20.0%)	<5	14 (10.6%)	6 (20.0%)	13 (17.6%)	47 (12.9%)
	Inflammatory bowel disease	N (%)	5 (14.3%)	11 (25.6%)	31 (23.5%)	<5	7 (9.5%)	26 (7.2%)
	Juvenile arthritis	N (%)	35 (100.0%)	43 (100.0%)	132 (100.0%)	30 (100.0%)	74 (100.0%)	363 (100.0%)
	Psoriatic arthritis	N (%)	<5	8 (18.6%)	11 (8.3%)	<5	12 (16.2%)	50 (13.8%)
	Rheumatoid arthritis	N (%)	21 (60.0%)	32 (74.4%)	76 (57.6%)	16 (53.3%)	53 (71.6%)	147 (40.5%)
Upadacitinib - Psoriatic arthritis								
Number individuals	–	N	161	72	285	644	451	1,153
Age	–	Median [Q25 – Q75]	53 [44 – 59]	52 [42 – 60]	51 [42 – 59]	57 [49 – 63]	53 [45 – 59]	53 [45 – 61]
		Mean (SD)	52 (10)	51 (13)	50 (13)	56 (12)	52 (11)	52 (13)
		Range	25 to 77	19 to 78	19 to 82	23 to 88	14 to 83	9 to 87
Sex	Female	N (%)	121 (75.2%)	53 (73.6%)	189 (66.3%)	427 (66.3%)	300 (66.5%)	747 (64.8%)
Treatment duration (months)*	–	Median [Q25 – Q75]	9 [4 – 24]	–	22 [7 – 24]	6 [3 – 15]	7 [2 – 17]	7 [3 – 18]
		Mean (SD)	14 (14)	–	20 (14)	12 (13)	11 (10)	13 (14)
Co-morbid conditions	Alopecia areata	N (%)	8 (5.0%)	<5	<5	5 (0.8%)	41 (9.1%)	14 (1.2%)
	Atopic dermatitis	N (%)	16 (9.9%)	<5	20 (7.0%)	8 (1.2%)	64 (14.2%)	50 (4.3%)
	Axial spondylitis	N (%)	28 (17.4%)	<5	17 (6.0%)	53 (8.2%)	71 (15.7%)	102 (8.8%)

Variable name	Variable level	Estimate name	Data source					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
	Inflammatory bowel disease	N (%)	14 (8.7%)	12 (16.7%)	26 (9.1%)	16 (2.5%)	28 (6.2%)	64 (5.6%)
	Juvenile arthritis	N (%)	<5	9 (12.5%)	16 (5.6%)	6 (0.9%)	14 (3.1%)	59 (5.1%)
	Juvenile idiopathic arthritis	N (%)	<5	8 (11.1%)	11 (3.9%)	<5	12 (2.7%)	50 (4.3%)
	Rheumatoid arthritis	N (%)	83 (51.6%)	42 (58.3%)	119 (41.8%)	234 (36.3%)	139 (30.8%)	231 (20.0%)
Upadacitinib - Rheumatoid arthritis								
Number individuals	–	N	666	256	973	2,066	1,213	2,382
Age	–	Median [Q25 – Q75]	57 [49 – 62]	54 [44 – 63]	53 [42 – 62]	59 [51 – 66]	54 [46 – 61]	57 [47 – 66]
		Mean (SD)	55 (11)	53 (14)	52 (14)	59 (12)	53 (10)	56 (14)
		Range	18 to 80	20 to 84	18 to 85	15 to 95	17 to 88	17 to 90
Sex	Female	N (%)	558 (83.8%)	188 (73.4%)	750 (77.1%)	1,567 (75.8%)	952 (78.5%)	1,896 (79.6%)
Treatment duration (months)*	–	Median [Q25 – Q75]	12 [4 – 30]	–	24 [11 – 39]	9 [3 – 23]	10 [4 – 23]	10 [3 – 26]
		Mean (SD)	19 (18)	–	26 (17)	15 (16)	15 (13)	16 (16)
Co-morbid conditions	Alopecia areata	N (%)	15 (2.3%)	<5	5 (0.5%)	27 (1.3%)	117 (9.6%)	33 (1.4%)
	Atopic dermatitis	N (%)	60 (9.0%)	6 (2.3%)	52 (5.3%)	16 (0.8%)	82 (6.8%)	54 (2.3%)
	Axial spondylitis	N (%)	108 (16.2%)	25 (9.8%)	80 (8.2%)	104 (5.0%)	134 (11.0%)	130 (5.5%)
	Inflammatory bowel disease	N (%)	52 (7.8%)	56 (21.9%)	74 (7.6%)	56 (2.7%)	65 (5.4%)	71 (3.0%)
	Juvenile arthritis	N (%)	22 (3.3%)	32 (12.5%)	80 (8.2%)	18 (0.9%)	53 (4.4%)	148 (6.2%)
	Juvenile idiopathic arthritis	N (%)	21 (3.2%)	32 (12.5%)	76 (7.8%)	16 (0.8%)	53 (4.4%)	147 (6.2%)
	Psoriatic arthritis	N (%)	83 (12.5%)	42 (16.4%)	119 (12.2%)	234 (11.3%)	139 (11.5%)	231 (9.7%)

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; SD = Standard Deviation; Q25 = 25th Percentile; Q75 = 75th Percentile; JAKi = Janus kinase inhibitor/s.

– is used when data is not available.

*Treatment duration was available in all data sources, except DK-DHR, where treatment end date was unavailable in the majority of JAKi prescriptions.

9.3. Other analysis

Large-scale characterisation was conducted with no remarkable additional findings on JAKi indications. Full results are available in the Shiny app here: [EUPAS1000000998](https://eupas1000000998.shinyapps.io/).

10. DISCUSSION

10.1. Key results

Among the 5 included JAKi ingredients, upadacitinib had the highest count of individuals initiating treatment across the data sources, ranging from 710 (DK-DHR) to 5,635 (HI-SPEED), with a total of 17,657 individuals across all data sources. Abrocitinib had the lowest count, with only 167 individuals from FinOMOP-THL and 94 from VID. In general, new use of JAKi as a class increased over the study period in most data sources. Baricitinib and tofacitinib showed the earliest rising trend, since these were the first JAKi therapies approved. An increase in use of filgotinib and upadacitinib were subsequently observed from 2020, which is in line with their approval in 2019 and 2020. At the same time, trends of baricitinib and tofacitinib either declined or plateaued in all data sources, indicating a preference for the newer JAKi. Abrocitinib was only observed from 2022 onwards, in line with its approval in 2021.

Among the 5 included JAKi ingredients, the median age of initiation was 41 – 60 years old. The exception is abrocitinib, with most individuals starting therapy before age 40.

Treatment duration was highly variable with median treatment duration ranging from 6 – 12 months for abrocitinib, 4 – 24 months for baricitinib, 6 – 24 months for filgotinib, 7 – 24 months for tofacitinib, and 7 – 15 months for upadacitinib. Additionally, duration varied significantly by potential indication; for example, the median treatment duration for baricitinib in NAJS varied from 6 months for individuals with inflammatory bowel disease to 22 months for individuals with rheumatoid arthritis. Similarly, the median treatment duration for filgotinib in FinOMOP-THL varied from 1 month for individuals with psoriatic arthritis to 24 months for atopic dermatitis, inflammatory bowel disease, juvenile arthritis, and rheumatoid arthritis.

The majority of individuals initiating JAKi had a history of rheumatoid arthritis as their likely indication, except for abrocitinib, where 99.4% of initiators in FinOMOP-THL and 92.6% in VID had a record of atopic dermatitis. After rheumatoid arthritis and (for abrocitinib) atopic dermatitis, other commonly recorded indications for JAKi included inflammatory bowel disease, psoriatic arthritis, and axial spondylitis. In general, at least 90% of new JAKi initiators in all data sources had a history of at least one potential indication. The exception to this was individuals initiating baricitinib in NAJS, where a third had an unknown indication. Demographic differences were found between indications. Atopic dermatitis and inflammatory bowel disease are typically found in younger individuals, and has a fairly balanced sex distribution, while rheumatoid arthritis and psoriatic arthritis are typically found in older, female individuals.

Time from potential indication diagnosis to JAKi initiation varied substantially by data source and indication, with median time varying from 60 – 104 months for abrocitinib, 18 – 183 months for baricitinib, 9 – 132 months for filgotinib, 18 – 175 months for tofacitinib, and 24 – 203 months for upadacitinib. Typically, time from diagnosis to initiation was shorter for individuals with alopecia areata and longer for individuals with juvenile arthritis.

10.2. Strengths and limitations of the research methods

General limitations

The study was informed by routinely collected health care data, and therefore, data quality must be considered. As with all drug use estimated based on prescription/dispensation data, there is no guarantee that the drug was actually used. In addition, assumptions around the duration of drug use are unavoidable

and might impact the estimate. However, validated methods were used for the estimation of treatment duration, based on the concatenation of prescriptions and accounting for refill gaps.[13]

The actual indication for prescription of the drugs of interest was only recorded in DK-DHR. For the remaining data sources, indication was assessed via a proxy, based on pre-defined conditions recorded on or before the date of therapy initiation. Therefore, recording of potential indication may be incomplete or misclassified when more than one potential indication was present.

Finally, the completeness of recording of comorbidities used for the individual-level characterisation of individuals initiating JAKi may vary across data sources, as they cover different healthcare settings and have different follow-up.

Due to these limitations, caution should be taken when interpreting the median time from indication diagnosis to JAKi initiation. Variation between data sources most likely reflects the variation in healthcare settings. Additionally, the first record of a potential indication for each individual may not be their initial diagnosis; therefore, this may not be a true reflection of the time between first diagnosis with an indication and treatment initiation. This is particularly relevant for individuals with prior history of juvenile arthritis or juvenile idiopathic arthritis.

Data source specific limitations

NAJS: Drug duration was imputed as 30 days as a default for prescriptions, and 1 day for drug administration records.

DK-DHR: It was not possible to estimate JAKi treatment duration in DK-DHR, as the treatment end date was not available.

FinOMOP-THL: Drug exposure duration was given as 30 days as a default for all prescription records in FinOMOP-THL, but multiple dispensations based on one prescription were allowed. The diagnostics results showed that the median number of days between dispensations of JAKi prescriptions was less than 60 days. Therefore, when taking the gap era of 90 days into consideration, it was expected that consecutive dispensation records were captured in the same treatment regimen.

IQVIA DA Germany: The observation period of the individuals in this data source is defined by their last interaction with the primary care system. This affects which individuals are considered “at risk” for initiating the medicines of interest (i.e. included in the denominator), particularly in the most recent months of data, where healthier or infrequent users may no longer appear active. As a result, denominators used to calculate incident JAKi use may show an artificial decrease while incident users remained constant, leading to the underestimation of incidence rates towards the end of data collection.

VID: Females born before 1953 were not included in the current version of the data source, which meant the results were not fully representative of the general population in Valencia.

HI-SPEED: Drug records in HI-SPEED were only available from 2018 onwards; therefore, for older data, it was not possible to confirm whether an individual’s first recorded JAKi use reflected their true treatment initiation. To address this, the study start date was 2019 for HI-SPEED to allow at least 365 days of prior history.

10.3. Interpretation

The motivation of the current drug utilisation study was to cover the gap in evidence around the safety of JAKi use among individuals with indications other than rheumatoid arthritis, and therefore, different risk profiles. Baricitinib and tofacitinib were the two earliest approved JAKi (2017) and were initially only used to treat rheumatoid arthritis. Since then, additional JAKi have been approved, and indications of use have since been extended to conditions, such as atopic dermatitis and inflammatory bowel disease. These conditions predominantly affect younger populations and have a more balanced sex distribution, in

contrast to rheumatoid arthritis, which primarily affects older females. The majority of safety studies evaluating JAKi use focus on individuals with rheumatoid arthritis and are therefore not representative of the broader population of individuals using JAKi therapies.

Incidence of new JAKi use over time and characteristics of individuals initiating JAKi were estimated to inform the feasibility of future safety studies on JAKi within the DARWIN EU® Network. Baricitinib and tofacitinib were observed as having increasing uptake in the early years of the study period, followed by either a decreased or stable trend towards the end of the study period. Upadacitinib, filgotinib, and abrocitinib received marketing authorisation in 2019, 2020, and 2021, respectively, and therefore, records for these drugs only appeared in the later years of this study, with the use of newer JAKi (in particular upadacitinib) increasing over the same time period. JAKi use in FinOMOP-THL, VID, and HI-SPEED was lower in 2020 compared to the years before and after, which may reflect the impact of the onset of the COVID-19 pandemic.

Prior history of at least one co-morbid indication was found in 90% of individuals initiating JAKi in all data sources, except for baricitinib in NAJS, where a third of individuals had an unknown indication. Rheumatoid arthritis remained as the most common indication recorded among individuals initiating JAKi of baricitinib, filgotinib, tofacitinib and upadacitinib. Individuals initiating these four JAKi ingredients were mostly female and aged 41 – 60, in line with the general demographics of individuals with rheumatoid arthritis.[14] Conversely, abrocitinib is only indicated in atopic dermatitis.

The sex distribution of JAKi initiators with atopic dermatitis and inflammatory bowel disease were more balanced, and they were typically younger. This was consistent across all individual JAKi and is in line with the epidemiology of these conditions.[15, 16]

The median treatment duration for all included JAKi ingredients was less than 1 year across all data sources with sufficient data quality, with exception of FinOMOP-THL, where the median treatment duration was between 12 – 24 months. This is not an uncommon finding. In a meta-analysis on the effectiveness of tofacitinib in individuals with ulcerative colitis, including 19 observational studies with median follow-up duration of 7 – 44 weeks, the treatment discontinuation rate was 12 – 56.1%.[17] The treatment duration from the current study was much shorter than that from the ORAL Surveillance study,[3] for which the median duration of tofacitinib use in individuals with rheumatoid arthritis was 44 months. Future JAKi safety studies should consider this during study design. Findings on treatment duration in DK-DHR were not informative due to data incompleteness, as stated in the above limitations. Additionally, treatment duration estimates for FinOMOP-THL may not be reliable since the duration of each prescription/dispensation was assumed to be 30 days (see above limitations). Therefore, the length of treatment could have been overestimated. Researchers should also be aware of the short treatment duration of JAKi in real-world settings and be cautious with the interpretation of results from future safety studies with regards to the treatment duration.

The median time between diagnosis of potential indication and JAKi initiation varied substantially by indication and data source, typically between 5 – 20 years. This is not an uncommon finding, with various studies finding that JAKi are commonly used in later lines of treatment. A drug utilisation study from Italy found that 31.1% of individuals initiated JAKi as second-line, 33.1% as third-line, and 27.8% as fourth-line treatment.[18] Time from diagnosis of alopecia areata to JAKi initiation was frequently shorter than for other indications, likely reflecting the acute onset and rapid progression of the condition, as well as its higher prevalence among younger individual.[19] However, much of the variation observed between data sources in the time from indication diagnosis to JAKi initiation may also be explained by differences in the healthcare settings covered by each data source. This should be taken into consideration when interpreting the findings of this study and any future drug utilisation studies.

Switching of JAKi was not uncommon. For example, 11 – 26% of individuals with rheumatoid arthritis initiating filgotinib had received baricitinib, 7 – 17% tofacitinib and 7 – 27% upadacitinib before the index

treatment initiation. Similarly, a considerable proportion of individuals with rheumatoid arthritis initiating upadacitinib had received baricitinib (3 – 24%) or tofacitinib (4 – 28%). However, the majority of individuals had no prior use of other JAKi recorded (between 62 – 96%). This information is important and must be considered when designing future JAKi safety studies.

There is a scarcity of literature on the utilisation of JAKi in Europe. One previous study reported on the use of JAKi in Canada from 2016 to 2022.[20] The study analysed pharmacy dispensing records in 10 Canadian provinces. Tofacitinib was the most dispensed JAKi, accounting for 76% of records, followed by upadacitinib at 7.9% and baricitinib at 1.1%. There are also US-based reports of the utilisation of tofacitinib in individuals with psoriatic arthritis and in individuals with ulcerative colitis.[21, 22] One drug utilisation study examined the use of tofacitinib or baricitinib in individuals with rheumatoid arthritis in Italy.[18] This highlights the importance of the current drug utilisation study to understand the patterns of use of JAKi in Europe.

10.4. Generalisability

This study included data sources from six European countries (Croatia, Denmark, Finland, Germany, Sweden, and Spain), covering different regions of Europe. This study also included data from diverse healthcare settings, including primary care and specialist care, secondary care, and hospital inpatient care. However, findings from this study only reflect the situation in the specific region, setting, and period covered by the respective data source, and should not be generalised to other countries or data sources.

11. CONCLUSION

Novel use of JAKi was shown to have increased over the study period. Among the 5 included JAKi ingredients, upadacitinib had the highest count of individuals initiating treatment across the data sources, whilst abrocitinib had the lowest count. Except for abrocitinib, most individuals initiating JAKi were aged 41 – 60 years at the time of initiation, and predominantly female. The most commonly recorded indication was rheumatoid arthritis, except for abrocitinib, where it was atopic dermatitis, and upadacitinib, where it was used commonly for both rheumatoid arthritis and inflammatory bowel disease. Average duration of the index JAKi treatment was generally less than a year, excluding FinOMOP-THL, where treatment duration was 12 – 24 months. Prior use of other JAKi before treatment initiation varied from 4 – 16% for tofacitinib to 20 – 38% for filgotinib, indicating a trend of switching from older to newer JAKi treatments.

The results of this study show that a comparative safety study on JAKi use among younger individuals with atopic dermatitis or inflammatory bowel disease might be feasible, depending on other feasibility considerations. Larger sample sizes may be achievable for baricitinib, tofacitinib, and upadacitinib; however, abrocitinib remains sparsely used and only in a few countries. Additionally, it appears that filgotinib is primarily used to treat rheumatoid arthritis and is therefore not commonly used in younger populations.

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13. ANNEXES

ANNEX I. Description of data sources

Croatia: National Public Health Information System (NAJS)

#	Section	Description
1	Data source identification and country	NAJS (Croatian National Public Health Information System) Croatia
2	Data partner information section	Croatian Institute of Public Health Department of Data Science and Analytics
3	Coverage and timespan	Data collection since: 1998 Extent: Nation-wide. Geographic coverage covers whole Croatia, with various levels of resolution for different registries. Current estimates for the population in Croatia will be available at: https://podaci.dzs.hr/hr/podaci/stanovnistvo/procjena-stanovnistva/ for each year. The total and active person count in the NAJS data is larger than the current population of Croatia. This explained by: a) the person table included deceased and all previously insured people and b) there is no information about insurance ending, c) healthcare is also used by people with dual citizenship from neighbouring countries It is known that a lot of people emigrated (300k-400k) and weren't included in the last population census but still are in the NAJS database. There is also an influx of immigrant workers that are insured and registered but weren't included in the census.
4	Healthcare setting / type of data	Primary care – General Practitioner, and secondary care – specialists (ambulatory or hospital outpatient care), and hospital inpatient care. Primary care – gps, and secondary care – specialists (ambulatory or hospital outpatient care), and hospital inpatient care. For both inpatient and outpatient setting diagnoses, medication, procedures, and measurements are captured. The year of availability of information depends on the setting • 2014-2025 for biochemical lab tests in primary care from EHR patients records (measurements with results) • 2015-2025 for primary care data from EHR patient records (conditions, procedures, and drug prescriptions) • 2015- 2024 for inpatient hospital data from EHR administrative records (conditions, procedures, measurements without results and drug administrations) • 2016-2025 for health risk assessment data entered by GPs (measurements with results - height, weight...) • 2016-2022 for secondary conciliatory care data from EHR administrative records (conditions, procedures, measurements without results and drug administrations) • 2016-2022 for emergency care data from EHR patient records (conditions) • 2017-2025 for hospital records from registry data (conditions and procedures) • 2020-2025 for vaccination data from EHR patient records
5	Data collection process	Inpatient hospital billing systems, and Other. Data is entered by clinicians at healthcare contact, then combined by CIPH into the NAJS database and integrated with registries for public health purposes.
6	General representativeness	The data is collected from the evidence of public health records collected for public health purposes, as the majority of health care in Croatia is public and under single health insurance provider. Personal details are collected to a better extent for insured individuals compared to uninsured patients, who are excluded in the ETL process.
7	Data content /source coding	Medication prescriptions are recorded with ATC codes with an additional 3 digit code denoting the package. Diagnoses with ICD10 codes (Australian modification). Procedures with local source codes. Lab results with local source codes.
8	Data Harmonisation	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. Records from 2017 include insured patients with reliable IDs. Uninsured patients do not have reliable IDs. For example, if a patient changed their status from insured to uninsured, or vice

#	Section	Description
		versa, they could be counted several times, as could tracking records from before 2017 and after. By using the unique personal identifier for Croatian citizens, it can be checked and verified.
9	Quality control (data source specific)	There is a network of registry personnel (leaders, administrators, coders, sources) working on data coverage and other quality dimensions. An analytical team routinely checks for erroneous entries in hospital records, removing double entries, false dates, and overlapping stays. Entries without enough data or with obviously erroneous dates from primary care analysis are being excluded.
10	Linkage	The national death registry is updated yearly, with one year lag, but the fact of someone's death (just the date) is updated daily, without the cause of death or any other additional details. Primary care is updated weekly and hospital level care monthly. Specific registries are included in NAJS (e.g. diabetes registry), where inclusion criteria vary across these registries.
11	Vital status	NAJS is linked to the national death registry.
12	Limitations	Hospital data is available from 2017 onwards. This is often used as start of data collection, while laboratory and GP data is captured before that (since 2014 and 2015 respectively). Drug duration is often not available and set to 1 day for administration and 30 days for prescription. Hospital discharge summaries are currently not captured in NAJS. Hospital drug administration data is less reliable than prescription data from primary care, with some drugs (monoclonal antibodies / precision medicine drugs) that require additional approval not being recorded at all.
13	Main references	No main reference provided.
14	Link to HMA-EMA catalogue and data source webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111155 Website: https://www.hzjz.hr/nacionalni-javnozdravstveni-informacijski-sustav-najs/

Denmark: Danish Data Health Registries (DK-DHR)

#	Section	Description
1	Data source identification and country	DK-DHR (Danish Data Health Registries) Denmark
2	Data partner information section	Danish Medicines Agency (DKMA) Data Analytics Centre (DAC)
3	Coverage and timespan	Data collection since: 1995 Extent: Nation-wide. The data is representative of the entire Danish population.
4	Healthcare setting / type of data	Community pharmacists, and secondary care – specialists (ambulatory or hospital outpatient care), and hospital inpatient care. The following data elements are collected: diagnosis (including rare diseases and pregnancy data), hospital admissions, discharge and ICU data, Cause of death, Drug prescriptions, dispensing, vaccination and contraception, Procedures (surgical and non-surgical hospital), and Sociodemographic information (sex and age only).
5	Data collection process	Outpatient electronic health records, and Inpatient hospital electronic health records, and Registries, and Other. All causes of deaths, all retrieved drug prescriptions, all records of vaccinations, all hospital inpatient and outpatients contacts including disease diagnoses and hospital surgical and non-surgical procedures, histologically confirmed incident cancers, laboratory test results for the entire Danish population from 1/1/1995 onwards.
6	General representativeness	The data is representative of the entire Danish population. Healthcare is free in Denmark, so we do not expect any bias in data collection based on socio-economic status.

#	Section	Description
7	Data content /source coding	Diagnoses and causes of death are collected using the ICD-10 vocabulary. ATC and RxNorm are used for Drugs. SNOMED codes are used for Procedures.
8	Data Harmonisation	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. Patients have unique identifiers used to link datasets.
9	Quality control (data source specific)	The data we have received relating to nationwide Danish Health Data registries offer an opportunity for large-scale, population-based studies with several advantages 1) Their large size improves the precision of estimates and enables the study of rare exposures and outcomes with long-term latency, 2) Inclusion of nearly all individuals in the target population ensures that the data reflect routine clinical care and all clinical segments of the source population, 3) Data are collected independently of each research study, thus minimising certain types of bias, e.g. non-response, and the influence from attention to the research question on the diagnostic process. Before the source data is sent to us, the Danish Health Data Authority runs and does comprehensive checks of the registry table data validity of the variables, breaks in data, changes in variable coding, missingness, etc. We perform checks of missingness/completeness in relation to requested variables. In essence, we are receiving a dump of a mirror of the data that is controlled by the SDS. The documentation performed by SDS is available online, in Danish primarily https://www.esundhed.dk/Dokumentation (all variables), but also in English https://sundhedsdatastyrelsen.dk/da/english/health_data_and_registers/national_health_registers
10	Linkage	There is no linkage in this data source.
11	Vital status	The Cause of Death registry (DAR) is used, the cause of death is collected using ICD-10 codes.
12	Limitations	DK-DHR has the following limitations, which may be relevant confounders for certain complex DARWIN EU® studies: - We lack information on key socio-economic status (SES) factors, such as occupation, education, and income. These variables may be important for analysis in some studies. - We only have complete data on lifestyle factors (such as smoking status and weight) for pregnant women. - We have no information on patient contacts in primary care (visits to the GP). Consequently, the incidence of chronic diseases like Type 2 Diabetes (T2D) and asthma must be determined using drug prescriptions as a proxy. Stillborn children will not have any records in our CDM. This means that e.g. birth length of stillborns is not recorded.
13	Main references	Schmidt M, Schmidt SAJ, Adelborg K, Sundbøll J, Laugesen K, Ehrenstein V, Sørensen HT "The Danish health care system and epidemiological research: from health care contacts to database records." Clinical epidemiology (2019): 31372058
14	Link to HMA-EMA catalogue and data source webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111217 Website: https://sundhedsdatastyrelsen.dk/da/english/health_data_and_registers/healthdatadenmark

Finland: Finnish Care Register for Health Care (FinOMOP-THL)

#	Section	Description
1	Data source identification and country	FinOMOP-THL (Finnish Care Register for Health Care) Finland
2	Data partner information section	FinOMOP (FinOMOP) The Department of Data and Analytics, Finnish Institute for Health and Welfare
3	Coverage and timespan	Data collection since: 1998 Extent: Nation-wide. The current CDM population comprises all persons having been alive and residing in Finland since the beginning of 2015.

#	Section	Description
4	Healthcare setting / type of data	Primary care – General Practitioner, and primary care specialists (e.g. paediatricians), and secondary care – specialists (ambulatory or hospital outpatient care), and hospital inpatient care, and other (specify). THL maintains health registers that cover both public and private, primary, and specialised inpatient, urgent and outpatient health care encounters in Finland, starting from 2011. The entire public sector and private inpatient encounters have been included since 2011, while private outpatient encounters, including occupational care, are included since 2020. Since 1998, the Care Register for Health Care (TerveysHilmo) has covered both public outpatient and inpatient specialised care and private inpatient care. Since 2009, the Finnish National Vaccination Register has covered all vaccinations from the public sector and from a large part of private vaccination providers, with the data coverage from both sections being very good to complete from 2020 onwards. Since 2011, the Register of Primary Health Care Visits (AvoHilmo) has covered public primary care. Since 2020, the register has also covered private outpatient care and occupational care. In addition, the CDM also contains positive COVID-19 test results from the Finnish National Infectious Diseases Register. The register itself covers all laboratory confirmations for around 70 specific microbes from 1995 onwards, but only COVID-19 has currently been mapped to the CDM. The CDM also includes prescription records from multiple different sources. Both Care Register for Health Care and Register of Primary Health Care Visits contain very basic prescription data recorded during health care encounters that include just the ATC-code and trade name of medication. More comprehensive prescription data from Kanta Prescription Centre, maintained by Social Insurance Institution of Finland (Kela), has been integrated into the CDM since its 2024 release. The Kanta Prescription records are based electronic prescriptions, which were adopted by most public health care providers in 2010 and by most private providers by 2017.
5	Data collection process	Outpatient electronic health records, and Inpatient hospital electronic health records, and Registries. Data is entered by clinicians upon healthcare contact and processed by THL (Kela in the case of Kanta Prescription Centre).
6	General representativeness	The THL data has national coverage and is therefore well representative of the Finnish population. Using the complete population as a basis for the person table also serves to facilitate calculations on a population level, e.g. incidence rates.
7	Data content /source coding	The following coding systems have been OMOP-mapped, typically to a good level of completeness: ICD10fi Finnish Extension, ICPC-2, ATC, Toimenpideluokitus (procedure classification adapted from the Nordic Classification of Surgical Procedures (NCSP)), Terveystieteiden tutkimuskeskus (Hilmo specific provider speciality), Rokotustapa (AR/YDIN National classification for vaccine administration), Tupakointitilastus (AR/YDIN National classification for smoking status). Vaccinations are identified on product level based on batch number, trade name, vaccine title, and ATC-code. This is mapped on brand and type in the OMOP CDM.
8	Data Harmonisation	The data has been mapped to the OMOP CDM v5 and the OMOP standard vocabularies. The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. Each patient in THL has a unique identifier.
9	Quality control (data source specific)	The source data collection undergoes a structural and semantic validation before entry into the source database. Additionally, some coded variables undergo quality assessment against the respective code systems post entry into the database. The source registers are also assessed for completeness and coverage, with the aim of improving future collection in the areas where data is lacking.
10	Linkage	THL is already a linkage of multiple Finnish registries (see above).
11	Vital status	The National Population registry data forms the basis for forming the patient population. This ensures an up-to-date location (municipality of residence) of patients, as well as complete death occurrences (although not the cause of death).
12	Limitations	The current release of the CDM excludes primary care events falling under home care and telehealth. The former belongs mainly under social care and as such doesn't fall under to scope of the CDM. The later on the other hand are comparable to the regular primary care GP

#	Section	Description
		visitations, and will be added back in a later release. The lack of the primary health care telehealth reduces the interpretability for treatments being performed in primary care GP settings. The CDM does not currently have meaningful end dates or days of supply for drug exposure. This information is not available for Care Register for Health Care or Register of Primary Health Care Visits, and for Kanta Prescription Centre it is only available in unstructured, free-form format that has not been converted into OMOP CDM. The source system for prescription drug data is only available to the DP until Dec-2023, therefore drug_exposure records from this source are only available in that time range. Not all private health care records are covered for the CDM's entire follow-up time from 2011 onwards. For Register of Primary Health Care Visits and Finnish National Vaccination Register, records from private health care have been available from 2020 onwards. For Kanta Prescription Centre, the coverage of private health care records has been good from 2017 onwards. The inclusion of private health care mainly presents itself as an increase in the number of observations, meaning that it has to be accounted for when interpreting any time series data from the CDM.
13	Main references	Häkkinen, Pirjo; Mölläri, Kaisa; Saukkonen, Sanna-Mari; Väyrynen, Riikka; Mielikäinen, Lasse; Järvelin, Jutta "Hilmo - Sosiaali- ja terveydenhuollon hoitoilmoitus 2020 : Määrittelyt ja ohjeistus : Voimassa 1.1.2020 alkaen" Terveyden ja hyvinvoinnin laitos (2019):
14	Link to HMA-EMA catalogue and data source webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111187 ; https://catalogues.ema.europa.eu/data-source/1111191 Website: https://thl.fi/en/statistics-and-data/data-and-services/register-descriptions ; https://www.kanta.fi/en/research-and-knowledge-management

Germany: IQVIA Disease Analyzer (IQVIA DA Germany)

#	Section	Description
1	Data source identification and country	IQVIA DA Germany (IQVIA Disease Analyzer Germany) Germany
2	Data partner information section	IQVIA
3	Coverage and timespan	Data collection since: 1989 Extent: Nation-wide. GP and specialists in Germany using specific patient management software.
4	Healthcare setting / type of data	Primary care – General Practitioner, and primary care specialists (e.g. paediatricians). Diagnoses, medication, and procedures from an ambulatory setting. Medications are recorded as prescriptions of marketed products.
5	Data collection process	Outpatient electronic health records. By clinicians at healthcare contact.
6	General representativeness	No specific details on general representativeness given.
7	Data content /source coding	Prescription is on product code level (German PZN), ICD10, NFC, Local lab coding.
8	Data Harmonisation	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. There can be patients registered under different ID numbers, because there is no linkage between different GPs.
9	Quality control (data source specific)	Data is quality checked on plausibility.
10	Linkage	No.

#	Section	Description
11	Vital status	Death information is derived from medical events.
12	Limitations	No database-specific limitations documented. General limitations for the data type applicable.
13	Main references	No main reference provided.
14	Link to HMA-EMA catalogue and data source webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/104282 Website: https://www.iqvia.com/

Spain: Valencia Health System Integrated Dataset (VID)

#	Section	Description
1	Data source identification and country	VID (Valencia Health System Integrated Dataset) Comunitat Valenciana, Spain
2	Data partner information section	FISABIO Health Services Research & Pharmacoepidemiology Unit
3	Coverage and timespan	Data timespan: 2009-2024 Extent: Regional. The VID covers the general population of the Valencia region, comprising 10.7% of the Spanish population. The total active population is estimated to be around 5,300,000.
4	Healthcare setting / type of data	Primary care – GPs and paediatricians, and secondary care – specialists (ambulatory or hospital outpatient care), emergency department (ED) care and hospital inpatient care. Both primary and secondary care settings are covered, where visits, diagnoses, medications, measurements, and procedures are recorded. The population information system collects sociodemographic, health coverage, and mortality data. The Electronic prescription and dispensing system captures all information related to medication (active ingredient, strength, duration, indication, etc.). ED and hospital admissions are registered, providing information on dates, diagnoses, and procedures. Measurements are captured additionally from the vaccine information system and the Microbiological surveillance network. Mortality is also captured.
5	Data collection process	Outpatient electronic health records, and Inpatient hospital electronic health records, and Registries, and Other. Data extraction is performed by clinical IT personnel. Data is released by the health authorities on a project basis and can only be used for such purposes.
6	General representativeness	The population captured by the VID should represent the Valencia region well, as the VID contains data of the general population covered by the universal public health care system. About 97% of the population in this region is covered by public care.
7	Data content /source coding	Prescribed and dispensed medications are coded with the ATC system. The indications of each prescription, as well as procedures are coded using ICD9CM and ICD10ES.
8	Data Harmonisation	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network.
9	Quality control (data source specific)	The data is reviewed carefully with the IT personnel who perform the extraction of data and then by a senior researcher with expertise in RWD management in the HSRP unit. Several quality check scripts are run against the received data. Finally, a senior researcher with RWD and clinical expertise assesses the completeness, consistency, and quality of the data extraction. If any inconsistency or error is detected, the dataset is requested and extracted again.
10	Linkage	VID also contains hospital discharge records, emergency care discharge records, birth registry, congenital anomaly registry, perinatal mortality registry, cancer registry, pharmacy prescription and dispensing records, vaccine records, and microbiology records. Mother- and father-child linkage is also available. Most databases are updated daily, but certain registries, such as the congenital anomaly registry and perinatal mortality registries, are updated yearly.

#	Section	Description
11	Vital status	Mortality dates and causes of death are available in the mortality registry and the perinatal mortality registry.
12	Limitations	A subgroup of women (born before 1953) is not mapped into OMOP CDM yet. General limitations for the data type applicable.
13	Main references	García-Sempere A, Orrico-Sánchez A, Muñoz-Quiles C, Hurtado I, Peiró S, Sanfélix-Gimeno G, Díez-Domingo J "Data Resource Profile: The Valencia Health System Integrated Database (VID)." International journal of epidemiology (2020): 31977043
14	Link to HMA-EMA catalogue and data source webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111174

Sweden: Health Impact - Swedish Population Evidence Enabling Data-linkage (HI-SPEED)

#	Section	Description
1	Data source identification and country	HI-SPEED (Health Impact - Swedish Population Evidence Enabling Data-linkage) Sweden
2	Data partner information section	SMPA-GU: - Pharmacoepidemiology and Analysis Department (FeA), Läkemedelsverket, Box 26, 751 03 Uppsala, Sweden - School of Public Health and Community Medicine, Institute of Medicine, University of Gothenburg, Box 469, 405 30 Gothenburg, Sweden
3	Coverage and timespan	Data collection since: 2015 Extent: Nation-wide. The catchment area includes the whole of Sweden, covering the full population of approximately 11.7 million.
4	Healthcare setting / type of data	Primary care – General Practitioner, and secondary care – specialists (ambulatory or hospital outpatient care), and hospital inpatient care. Primary care (GPs) is available only for the 2 largest regions (~40% of national population) The following data elements are collected: Socio-demographics, dispensed drug prescriptions, cause of death, diagnoses and procedures from secondary (specialist) care and inpatient visits or clinical events, as well as from primary care visits (40%pop only).
5	Data collection process	Registries. The data is acquired from the relevant Swedish national and regional registries, only once all legislative, GDPR and ethical approvals have been granted. Therefore only relevant data is passed on, which will then be entered and processed by the study team. The data are updated several times annually.
6	General representativeness	The coverage includes all patients of all sociodemographic characteristics. Therefore it should mirror the source population to a very good extent.
7	Data content /source coding	Medicines are coded with ATC and NPLID (National Product ID), ICD10-SE is used for diagnoses and the Swedish procedure coding system (KVA) is used for clinical procedures.
8	Data Harmonisation	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. Patients have a uniquely id across datasets.
9	Quality control (data source specific)	The source data are obtained from the relevant Swedish National and Regional Registers. The registers perform some regular quality controls on their data. After receiving the data, we perform additional checks and cleaning. We also run regular quality checks on the data we manage.

#	Section	Description
10	Linkage	Data on specialist care is acquired from the National Patient Register, mortality information is provided by the Cause-Of-Death Registry. Drug data is provided by the Patient Drug Register. And similarly for other registers. Data are linked very accurately using the national personal ID number, and pseudonymised before delivery to HI-SPEED. All data are updated 2-4 times per year.
11	Vital status	Data on death and underlying + contributing causes-of-death are extracted from the Cause-of-Death registry (i.e. based on death certificates).
12	Limitations	General limitations for the data type applicable. This is a research project where all studies require ethics approval. Data collection since: 2015 for most data, except prescribed drug register (from 2018), and some COVID-related data (tests, vaccination) from 2020 Primary care is only available for a subset.
13	Main references	Nyberg F, Franzén S, Lindh M, Vanfleteren L, Hammar N, Wettermark B, Sundström J, Santosa A, Björck S, Gisslén M "Swedish Covid-19 Investigation for Future Insights - A Population Epidemiology Approach Using Register Linkage (SCIFI-PEARL)." Clinical epidemiology (2021): 34354377
14	Link to HMA-EMA catalogue and data source webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/node/4463/ Website: https://www.gu.se/en/research/scifi-pearl

ANNEX II. Fitness for use assessment

Data source justification for inclusion and key characteristics

Table S1. Key data source characteristics.

Theme/Issue	Croatia (NAJS)	Denmark (DK-DHR)	Finland (FinOMOP-THL)	Germany (IQVIA DA Germany)	Spain (VID)	Sweden (HI-SPEED)
Care settings covered	Primary care GP, secondary care specialist, hospital inpatient care	Community pharmacists, secondary care specialist, hospital inpatient care	Primary care GP, primary care specialist, secondary care specialist, hospital inpatient care	Primary care GP, primary care specialist	Primary care GP, primary care specialist, secondary care specialist, hospital inpatient care, other	Primary care GP, secondary care specialist, hospital inpatient care
Feasibility (person-counts)	2800	3500	4800	11200	6300	12800
Data availability and follow-up	Sufficient (median follow-up: 3840 days)	Sufficient (median follow-up: 7920 days)	Sufficient (median follow-up: 5020 days)	Sufficient (median follow-up: 121 days)	Sufficient (median follow-up: 5840 days)	Sufficient (median follow-up: 3890 days)
Treatment duration	Available, based on assumptions (30 days for prescriptions, 1 day for in-hospital administrations)	Not available.	Available, based on assumptions (30 days for prescriptions and dispensations)	Available, with some assumptions used to impute missing values.	Available.	Available.
IRB timelines	Feasible (1 to 3 months)	Feasible (blanket approval)	Feasible (blanket approval)	Feasible (blanket approval)	Feasible (1 to 3 months)	Feasible (less than 1 month)

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset

National Public Health Information System (NAJS)

NAJS was included in this study because it is a population-based registry data source that provides relevant information on treatment of interest in the general population, as NAJS includes records of drugs prescribed/dispensed in specialist outpatient settings, which is the setting where JAKi are mainly prescribed.

Based on a preliminary feasibility assessment, the expected number of person-counts for JAKi initiation in NAJS was 2800. Moreover, data availability and follow-up in NAJS was sufficient, as data availability started in February 2014, and the date of the most recent data extraction was June 2025, which aligned with the study period. The median follow-up of the first observation period in NAJS was 3840 days (interquartile range (IQR): 3310 – 3930).

There were some study specific limitations present in NAJS. For example, drug records from primary care were only available from 2015 – 2025, while those from secondary conciliatory care were available from 2016 – 2024.

Actual end date of drug prescription and administration records were not available in NAJS; therefore, an assumption of 30-day exposure was applied to prescriptions, and an assumption of 1-day exposure was applied to drug administration records.

Lastly, Institutional Review Board approval for NAJS was estimated to take 1 – 3 months, which made the execution of this study feasible within the study timelines.

Danish Data Health Registries (DK-DHR)

DK-DHR was included in this study because it is a nationwide registry data source that provides relevant information on treatment of interest in the general population, as DK-DHR includes records of drugs prescribed/dispensed in specialist outpatient settings, which is the setting where JAKi are mainly prescribed.

Based on a preliminary feasibility assessment, the expected number of person-counts for JAKi initiation in DK-DHR were 3500. Moreover, data availability and follow-up in DK-DHR was sufficient, as data availability started in January 1995, and the date of the most recent data extraction was October 2025, which aligned with the study period. The median follow-up in DK-DHR was 7920 days (IQR: 2610 – 10900).

In DK-DHR, treatment duration was calculated as the amount prescribed divided by the DDD. However, this was only available for EHR dispensing records. End date was not available for drug records originating from the patient registry. Since a substantial proportion of JAKi initiations were recorded in the patient registry, it was not possible to estimate the duration of JAKi treatment for DK-DHR.

Lastly, DK-DHR have blanket IRB approval.

Finnish Care Register for Health Care (FinOMOP-THL)

FinOMOP-THL was included in this study because it is a nationwide registry data source that provides relevant information on treatment of interest in the general population, as FinOMOP-THL includes records of drugs prescribed/dispensed in primary and secondary healthcare settings, which is the setting where JAKi are mainly prescribed. FinOMOP-THL also includes both drug prescription and dispensing records.

Based on a preliminary feasibility assessment, the expected number of person-counts for JAKi initiation in FinOMOP-THL were 4800. However, this feasibility count was based on the data cut from the end of 2023. It was expected to have an update in mid-May 2026, with data up to early 2026. Together with data availability starting in January 2011, it was therefore expected that data availability and follow-up in FinOMOP-THL was sufficient for the study and aligned with the study period. The median follow-up in FinOMOP-THL was 5020 days (IQR: 4030 – 5020).

Actual end date of drug prescription and dispensing records were not available in FinOMOP-THL, and an assumption of 30-day exposure was applied to both prescription and dispensing records.

Lastly, FinOMOP-THL have blanket IRB approval.

IQVIA Disease Analyzer (IQVIA DA Germany)

IQVIA DA Germany was included in this study because it is a primary care data source that provides relevant information on the outcomes and exposures of interest in the general population.

Based on a preliminary feasibility assessment, the expected number of person-counts for JAKi initiation in IQVIA DA Germany was 11200. Moreover, data availability and follow-up in IQVIA DA Germany was sufficient, as data availability started in February 1992, and the date of the most recent data extraction was June 2025, which aligned with the study period. The median follow-up of the first observation period in IQVIA DA Germany was 121 days (IQR: 0 – 1570).

Additionally, IQVIA DA Germany included records of drugs prescribed/dispensed in specialist outpatient settings, which is the setting where JAKi are mainly prescribed.

There were some study specific limitations present in IQVIA DA Germany, namely: in IQVIA DA Germany, each individual's observation period is defined by their last interaction with the primary care system. This affected which individuals are considered "at risk" for the medicines of interest (i.e. included in the denominator), particularly in the most recent months of data, where healthier or infrequent users may no longer appear active. As a result, denominators used to calculate incident JAKi use may show an artificial decrease while incident users remain. This was considered when interpreting results.

Treatment duration in IQVIA DA Germany was calculated as the prescribed amount divided by the DDD. For drug records where DDD was missing, the most frequent daily dosage for the drug was used (oral solid forms) or the assumed average maintenance dose per day (other forms).

Lastly, IQVIA DA Germany has blanket IRB approval.

Valencia Health System Integrated Dataset (VID)

VID was included in this study because it is a registry data source that provides relevant information on the outcomes and exposures of interest in the general population.

Based on a preliminary feasibility assessment, the expected number of person-counts for JAKi initiation in VID was 6300. Moreover, data availability and follow-up in VID was sufficient, as data availability started in January 2009, and the date of the most recent data extraction was December 2024, which aligned with the study period. The median follow-up of the first observation period in VID was 5840 days (IQR: 4460 – 5840). Additionally, VID included records of drugs prescribed/dispensed in specialist outpatient settings, which is the setting where JAKi are mainly prescribed.

There were some study specific limitations present in VID, namely: VID is a regional data source, and complete coverage of the region was expected. However, in VID, females born before 1953 were not included in the current version of the data source, which means the results cannot fully represent the general population. However, considering the age range of individuals initiating JAKi (over 40 years), most JAKi initiations were expected to be captured when.

Actual end date of drug prescription and dispensing records were available in VID.

Lastly, IRB approval for VID was estimated to take 1 – 3 months, which made the execution of this study feasible within the current study timelines.

Health Impact - Swedish Population Evidence Enabling Data-linkage (HI-SPEED)

HI-SPEED was included in this study because it is a registry data source that provides relevant information on the outcomes and exposures of interest in the general population.

Based on a preliminary feasibility assessment, the expected number of person-counts for JAKi initiation in HI-SPEED was 12800. Moreover, data availability and follow-up in HI-SPEED was sufficient, as data availability started in January 2015, and the date of the most recent data extraction was August 2025, which aligned with the study period. The median follow-up of the first observation period in HI-SPEED was 3890 days (IQR: 3330 – 3890). Additionally, HI-SPEED included records of drugs prescribed/dispensed in specialist outpatient settings, which is the setting where JAKi are mainly prescribed.

There were some study specific limitations present in HI-SPEED, namely: primary care records had incomplete coverage (available for the two largest regions in Sweden, covering approximately 40% of the national population), but secondary care records were nationwide. As JAKi drugs are mainly prescribed in specialist outpatient settings though, most JAKi initiations should therefore be captured in HI-SPEED. A second limitation would be that, as drug records are only available from 2018 onwards, it was not possible to confirm whether a patient's first recorded JAKi use reflected their true treatment initiation. This was taken into consideration when interpreting the results.

Actual end date of drug dispensing records were available in HI-SPEED.

Lastly, IRB approval for HI-SPEED was estimated to take less than one month, which made the execution of this study feasible within the current study timelines.

ANNEX III. Operational and reporting considerations

DATA MANAGEMENT

Data management

All data sources previously mapped their data to the OMOP common data model. This enabled the use of standardised analytics and using DARWIN EU® tools across the network since the structure of the data and the terminology system was harmonised. The OMOP CDM was developed and maintained by the Observational Health Data Sciences and Informatics (OHDSI) initiative and is described in detail on the wiki page of the CDM: <https://ohdsi.github.io/CommonDataModel> and in The Book of OHDSI: <http://book.ohdsi.org>

The analytic code for this study was written in R and used standardised analytics wherever possible. Each data partner executed the study code against their data source containing individual data and then returned the results (csv files), which only contained aggregated data. The results from each of the contributing data sites were then combined in tables and figures for the study report.

Data storage and protection

For this study, personal data from individuals in various EU member states were processed, using information collected from national/regional electronic health record data sources. Due to the sensitive nature of this personal medical data, it is important to be fully aware of ethical and regulatory aspects and to strive to take all reasonable measures to ensure compliance with ethical and regulatory issues on privacy.

All data sources used in this study were already used for pharmaco-epidemiological research and have a well-developed mechanism to ensure that European and local regulations dealing with ethical use of the data and adequate privacy control were adhered to. In agreement with these regulations, rather than combining person level data and performing only a central analysis, local analyses were run, which generate non-identifiable aggregate summary results.

The output files are stored in the DARWIN EU® Digital Research Environment (DRE). These output files do not contain any data that allow identification of individuals included in the study. The DRE implements further security measures to ensure a high level of stored data protection to comply with the local implementation of the General Data Protection Regulation (GDPR) (EU) 679/2016 in the various member states.

QUALITY CONTROL

Data source quality control

When defining drug cohorts, non-systemic products were excluded from the list of included codes summarised on the ingredient level.

When defining cohorts for indications, a systematic search of possible codes for inclusion was identified using the *CodelistGenerator* R package (<https://github.com/darwin-eu/CodelistGenerator>). This package allows the user to define a search strategy and will use this to query the vocabulary tables of the OMOP common data model so as to find potentially relevant codes. In addition, the *PhenotypeR* (<https://github.com/OHDSI/PhenotypeR>) R package was run to assess the use of different codes across the data sources contributing to the study and identify any codes potentially omitted in error.

The study code was based on DARWIN EU® R packages: *IncidencePrevalence* to estimate yearly incidence, *DrugUtilisation* to characterise the drug use, and *CohortCharacteristics* to characterise the cohort by indication. These packages include numerous automated unit tests to ensure the validity of the codes, alongside software peer review and user testing. The study code is publicly available via GitHub.

ANNEX IV. Supplementary tables

Table S2. Incidence of new JAKi initiation among the individuals without prior exposure to any JAKi.

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Abrocitinib								
Overall	Overall	Denominator (N)	4,619,076	6,175,427	6,536,568	14,357,543	5,772,345	11,372,272
		Person-years	33,490,546.80	42,341,160.78	47,353,105.31	53,277,152.12	36,885,882.40	68,481,538.03
		Outcome (N)	0	0	135	0	61	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.01)	0.00 (0.00 – 0.01)	0.28 (0.24 – 0.34)	0.00 (0.00 – 0.01)	0.16 (0.13 – 0.21)	0.00 (0.00 – 0.00)
2018-01-01	2018-12-31	Denominator (N)	4,082,585	5,435,604	5,915,292	8,371,258	5,108,028	–
		Person-years	3,998,185.92	5,334,103.93	5,839,738.69	7,526,697.68	5,067,259.27	–
		Outcome (N)	0	0	0	0	0	–
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,514	5,446,906	5,932,029	8,499,225	5,223,572	10,263,741
		Person-years	4,052,717.20	5,348,017.58	5,858,397.39	7,673,476.13	5,184,750.82	10,078,121.44
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2020-01-01	2020-12-31	Denominator (N)	4,154,031	5,456,170	5,951,126	8,762,797	5,305,928	10,360,854
		Person-years	4,098,359.05	5,374,996.36	5,891,911.23	7,813,250.52	5,254,606.38	10,208,733.74
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
2021-01-01	2021-12-31	Denominator (N)	4,168,356	5,466,547	5,968,779	8,933,100	5,319,769	10,414,194
		Person-years	4,102,626.30	5,372,700.37	5,894,163.20	7,913,378.03	5,281,097.43	10,247,027.46
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2022-01-01	2022-12-31	Denominator (N)	4,200,653	5,485,853	5,994,426	9,059,750	5,327,080	10,481,267
		Person-years	4,122,720.76	5,383,594.06	5,911,821.02	7,739,312.40	5,288,684.26	10,308,043.94
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2023-01-01	2023-12-31	Denominator (N)	4,210,027	5,526,179	6,021,437	8,576,078	5,382,730	10,541,505
		Person-years	4,149,839.95	5,414,085.86	5,935,711.60	7,245,761.25	5,346,159.45	10,364,083.83
		Outcome (N)	0	0	48	0	26	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.81 (0.60 – 1.07)	0.00 (0.00 – 0.05)	0.49 (0.32 – 0.71)	0.00 (0.00 – 0.04)
2024-01-01	2024-12-31	Denominator (N)	4,225,158	5,546,895	6,073,636	7,317,959	5,568,132	10,570,120
		Person-years	4,176,667.76	5,457,854.55	5,991,980.11	5,721,821.41	5,463,324.78	10,412,689.61
		Outcome (N)	0	0	53	0	35	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.88 (0.66 – 1.16)	0.00 (0.00 – 0.06)	0.64 (0.45 – 0.89)	0.00 (0.00 – 0.04)
2025-01-01	2025-12-31	Denominator (N)	4,242,511	–	6,118,263	–	–	10,524,026
		Person-years	4,180,048.30	–	6,029,382.06	–	–	6,862,838.02
		Outcome (N)	0	–	34	–	–	0

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	–	0.56 (0.39 – 0.79)	–	–	0.00 (0.00 – 0.05)
Baricitinib								
Overall	Overall	Denominator (N)	4,619,053	6,175,207	6,536,472	14,357,379	5,772,200	11,372,076
		Person-years	33,490,467.89	42,340,711.49	47,353,044.13	53,276,827.29	36,885,540.98	68,480,991.72
		Outcome (N)	957	945	1,111	1,531	1,718	2,451
		Incidence 100,000 person-years [95% CI]	2.86 (2.68 – 3.04)	2.23 (2.09 – 2.38)	2.35 (2.21 – 2.49)	2.87 (2.73 – 3.02)	4.66 (4.44 – 4.88)	3.58 (3.44 – 3.72)
2018-01-01	2018-12-31	Denominator (N)	4,082,562	5,435,384	5,915,196	8,371,128	5,107,883	–
		Person-years	3,998,163.25	5,333,899.53	5,839,690.52	7,526,593.78	5,067,135.75	–
		Outcome (N)	12	114	336	184	203	–
		Incidence 100,000 person-years [95% CI]	0.30 (0.16 – 0.52)	2.14 (1.76 – 2.57)	5.75 (5.16 – 6.40)	2.44 (2.10 – 2.83)	4.01 (3.47 – 4.60)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,493	5,446,717	5,932,002	8,499,127	5,223,467	10,263,546
		Person-years	4,052,696.38	5,347,883.16	5,858,381.79	7,673,397.03	5,184,667.54	10,077,939.29
		Outcome (N)	171	43	233	358	192	934
		Incidence 100,000 person-years [95% CI]	4.22 (3.61 – 4.90)	0.80 (0.58 – 1.08)	3.98 (3.48 – 4.52)	4.66 (4.20 – 5.18)	3.70 (3.20 – 4.27)	9.27 (8.68 – 9.88)
2020-01-01	2020-12-31	Denominator (N)	4,154,013	5,456,082	5,951,118	8,762,721	5,305,858	10,360,684
		Person-years	4,098,344.35	5,374,941.32	5,891,906.16	7,813,193.31	5,254,545.48	10,208,572.61
		Outcome (N)	102	46	142	209	189	621

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	2.49 (2.03 – 3.02)	0.86 (0.63 – 1.14)	2.41 (2.03 – 2.84)	2.67 (2.33 – 3.06)	3.60 (3.10 – 4.15)	6.08 (5.61 – 6.58)
2021-01-01	2021-12-31	Denominator (N)	4,168,345	5,466,511	5,968,778	8,933,044	5,319,718	10,414,053
		Person-years	4,102,616.13	5,372,674.15	5,894,166.51	7,913,337.96	5,281,056.07	10,246,915.87
		Outcome (N)	280	129	106	242	274	292
		Incidence 100,000 person-years [95% CI]	6.82 (6.05 – 7.67)	2.40 (2.00 – 2.85)	1.80 (1.47 – 2.17)	3.06 (2.68 – 3.47)	5.19 (4.59 – 5.84)	2.85 (2.53 – 3.20)
2022-01-01	2022-12-31	Denominator (N)	4,200,644	5,485,832	5,994,433	9,059,713	5,327,051	10,481,187
		Person-years	4,122,713.98	5,383,578.66	5,911,825.19	7,739,287.79	5,288,666.51	10,307,985.36
		Outcome (N)	240	269	108	229	278	216
		Incidence 100,000 person-years [95% CI]	5.82 (5.11 – 6.61)	5.00 (4.42 – 5.63)	1.83 (1.50 – 2.21)	2.96 (2.59 – 3.37)	5.26 (4.66 – 5.91)	2.10 (1.82 – 2.39)
2023-01-01	2023-12-31	Denominator (N)	4,210,022	5,526,169	6,021,438	8,576,057	5,382,714	10,541,465
		Person-years	4,149,836.53	5,414,076.95	5,935,711.07	7,245,746.08	5,346,148.18	10,364,059.69
		Outcome (N)	65	93	46	127	285	142
		Incidence 100,000 person-years [95% CI]	1.57 (1.21 – 2.00)	1.72 (1.39 – 2.10)	0.78 (0.57 – 1.03)	1.75 (1.46 – 2.08)	5.33 (4.73 – 5.99)	1.37 (1.15 – 1.61)
2024-01-01	2024-12-31	Denominator (N)	4,225,157	5,546,890	6,073,633	7,317,950	5,568,125	10,570,107
		Person-years	4,176,667.39	5,457,850.52	5,991,980.46	5,721,817.05	5,463,321.45	10,412,682.67
		Outcome (N)	50	161	56	133	297	149

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	1.20 (0.89 – 1.58)	2.95 (2.51 – 3.44)	0.94 (0.71 – 1.21)	2.32 (1.95 – 2.76)	5.44 (4.84 – 6.09)	1.43 (1.21 – 1.68)
2025-01-01	2025-12-31	Denominator (N)	4,242,511	–	6,118,264	–	–	10,524,021
		Person-years	4,180,048.30	–	6,029,382.43	–	–	6,862,836.23
		Outcome (N)	37	–	84	–	–	97
		Incidence 100,000 person-years [95% CI]	0.88 (0.62 – 1.22)	–	1.39 (1.11 – 1.73)	–	–	1.41 (1.15 – 1.72)
Filgotinib								
Overall	Overall	Denominator (N)	4,619,030	6,175,420	6,536,536	14,357,254	5,772,245	11,371,904
		Person-years	33,490,405.84	42,341,132.10	47,353,098.47	53,276,585.77	36,885,675.80	68,480,486.57
		Outcome (N)	160	28	136	807	219	897
		Incidence 100,000 person-years [95% CI]	0.48 (0.41 – 0.56)	0.07 (0.04 – 0.10)	0.29 (0.24 – 0.34)	1.51 (1.41 – 1.62)	0.59 (0.52 – 0.68)	1.31 (1.23 – 1.40)
2018-01-01	2018-12-31	Denominator (N)	4,082,539	5,435,597	5,915,260	8,371,054	5,107,928	–
		Person-years	3,998,141.08	5,334,096.94	5,839,714.67	7,526,514.44	5,067,173.04	–
		Outcome (N)	0	0	0	0	0	–
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,471	5,446,899	5,932,011	8,499,031	5,223,498	10,263,376
		Person-years	4,052,675.95	5,348,011.58	5,858,387.30	7,673,333.09	5,184,693.38	10,077,778.64
		Outcome (N)	0	0	0	0	0	0

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2020-01-01	2020-12-31	Denominator (N)	4,154,002	5,456,164	5,951,123	8,762,643	5,305,881	10,360,530
		Person-years	4,098,335.81	5,374,990.54	5,891,912.53	7,813,145.52	5,254,571.87	10,208,442.02
		Outcome (N)	0	0	0	9	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.12 (0.05 – 0.22)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2021-01-01	2021-12-31	Denominator (N)	4,168,338	5,466,542	5,968,785	8,932,992	5,319,741	10,413,945
		Person-years	4,102,611.07	5,372,695.37	5,894,174.17	7,913,309.60	5,281,079.42	10,246,818.33
		Outcome (N)	0	0	14	135	<5	<5
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.24 (0.13 – 0.40)	1.71 (1.43 – 2.02)	-	-
2022-01-01	2022-12-31	Denominator (N)	4,200,639	5,485,848	5,994,440	9,059,697	5,327,071	10,481,099
		Person-years	4,122,711.20	5,383,589.93	5,911,831.64	7,739,274.34	5,288,679.88	10,307,922.85
		Outcome (N)	0	0	34	282	97	98
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.58 (0.40 – 0.80)	3.64 (3.23 – 4.10)	1.83 (1.49 – 2.24)	0.95 (0.77 – 1.16)
2023-01-01	2023-12-31	Denominator (N)	4,210,022	5,526,178	6,021,442	8,576,051	5,382,724	10,541,418
		Person-years	4,149,835.43	5,414,085.11	5,935,714.44	7,245,740.76	5,346,154.54	10,364,020.31
		Outcome (N)	9	<5	61	122	68	214

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	0.22 (0.10 – 0.41)	-	1.03 (0.79 – 1.32)	1.68 (1.40 – 2.01)	1.27 (0.99 – 1.61)	2.06 (1.80 – 2.36)
2024-01-01	2024-12-31	Denominator (N)	4,225,154	5,546,895	6,073,637	7,317,946	5,568,129	10,570,078
		Person-years	4,176,665.65	5,457,854.55	5,991,981.08	5,721,813.70	5,463,323.68	10,412,668.05
		Outcome (N)	42	22	18	171	52	337
		Incidence 100,000 person-years [95% CI]	1.01 (0.72 – 1.36)	0.40 (0.25 – 0.61)	0.30 (0.18 – 0.48)	2.99 (2.56 – 3.47)	0.95 (0.71 – 1.25)	3.24 (2.90 – 3.60)
2025-01-01	2025-12-31	Denominator (N)	4,242,510	–	6,118,264	–	–	10,524,019
		Person-years	4,180,048.08	–	6,029,382.65	–	–	6,862,836.36
		Outcome (N)	109	–	9	–	–	244
		Incidence 100,000 person-years [95% CI]	2.61 (2.14 – 3.15)	–	0.15 (0.07 – 0.28)	–	–	3.56 (3.12 – 4.03)
Tofacitinib								
Overall	Overall	Denominator (N)	4,619,053	6,175,346	6,536,526	14,357,454	5,772,278	11,371,995
		Person-years	33,490,454.26	42,340,956.71	47,353,090.58	53,276,961.58	36,885,723.55	68,480,840.19
		Outcome (N)	548	1,744	2,112	1,365	1,170	2,154
		Incidence 100,000 person-years [95% CI]	1.64 (1.50 – 1.78)	4.12 (3.93 – 4.32)	4.46 (4.27 – 4.65)	2.56 (2.43 – 2.70)	3.17 (2.99 – 3.36)	3.14 (3.01 – 3.28)
2018-01-01	2018-12-31	Denominator (N)	4,082,562	5,435,524	5,915,251	8,371,193	5,107,962	–
		Person-years	3,998,163.22	5,334,039.50	5,839,714.33	7,526,643.67	5,067,206.83	–
		Outcome (N)	17	110	437	292	226	–

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	0.42 (0.25 – 0.68)	2.06 (1.70 – 2.49)	7.48 (6.80 – 8.22)	3.88 (3.45 – 4.35)	4.46 (3.90 – 5.08)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,492	5,446,859	5,932,017	8,499,177	5,223,531	10,263,465
		Person-years	4,052,695.64	5,347,979.09	5,858,389.32	7,673,439.58	5,184,716.94	10,077,892.06
		Outcome (N)	121	509	469	414	245	561
		Incidence 100,000 person-years [95% CI]	2.99 (2.48 – 3.57)	9.52 (8.71 – 10.38)	8.01 (7.30 – 8.76)	5.39 (4.89 – 5.94)	4.72 (4.15 – 5.36)	5.57 (5.12 – 6.05)
2020-01-01	2020-12-31	Denominator (N)	4,154,012	5,456,133	5,951,120	8,762,760	5,305,900	10,360,657
		Person-years	4,098,341.37	5,374,961.42	5,891,909.62	7,813,217.48	5,254,580.98	10,208,553.54
		Outcome (N)	146	357	290	334	187	473
		Incidence 100,000 person-years [95% CI]	3.56 (3.01 – 4.19)	6.64 (5.97 – 7.37)	4.92 (4.37 – 5.52)	4.28 (3.83 – 4.76)	3.56 (3.07 – 4.11)	4.63 (4.22 – 5.07)
2021-01-01	2021-12-31	Denominator (N)	4,168,342	5,466,515	5,968,781	8,933,066	5,319,744	10,414,027
		Person-years	4,102,613.07	5,372,670.18	5,894,169.38	7,913,351.60	5,281,076.14	10,246,893.39
		Outcome (N)	63	136	330	141	144	354
		Incidence 100,000 person-years [95% CI]	1.54 (1.18 – 1.97)	2.53 (2.12 – 2.99)	5.60 (5.01 – 6.24)	1.78 (1.50 – 2.10)	2.73 (2.30 – 3.21)	3.46 (3.10 – 3.83)
2022-01-01	2022-12-31	Denominator (N)	4,200,643	5,485,826	5,994,435	9,059,722	5,327,063	10,481,158
		Person-years	4,122,712.07	5,383,571.35	5,911,828.38	7,739,292.40	5,288,671.22	10,307,955.52
		Outcome (N)	70	194	293	60	101	310

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	1.70 (1.32 – 2.14)	3.60 (3.11 – 4.15)	4.96 (4.40 – 5.56)	0.78 (0.59 – 1.00)	1.91 (1.56 – 2.32)	3.01 (2.68 – 3.36)
2023-01-01	2023-12-31	Denominator (N)	4,210,021	5,526,165	6,021,440	8,576,053	5,382,712	10,541,440
		Person-years	4,149,834.24	5,414,077.48	5,935,714.93	7,245,745.84	5,346,148.36	10,364,036.36
		Outcome (N)	51	173	143	54	125	195
		Incidence 100,000 person-years [95% CI]	1.23 (0.92 – 1.62)	3.19 (2.74 – 3.71)	2.41 (2.03 – 2.84)	0.74 (0.56 – 0.97)	2.34 (1.95 – 2.79)	1.88 (1.63 – 2.16)
2024-01-01	2024-12-31	Denominator (N)	4,225,153	5,546,890	6,073,636	7,317,948	5,568,128	10,570,090
		Person-years	4,176,665.23	5,457,850.42	5,991,982.09	5,721,816.38	5,463,323.06	10,412,672.87
		Outcome (N)	37	153	83	47	142	149
		Incidence 100,000 person-years [95% CI]	0.89 (0.62 – 1.22)	2.80 (2.38 – 3.28)	1.39 (1.10 – 1.72)	0.82 (0.60 – 1.09)	2.60 (2.19 – 3.06)	1.43 (1.21 – 1.68)
2025-01-01	2025-12-31	Denominator (N)	4,242,509	–	6,118,264	–	–	10,524,021
		Person-years	4,180,047.88	–	6,029,382.54	–	–	6,862,836.46
		Outcome (N)	43	–	67	–	–	112
		Incidence 100,000 person-years [95% CI]	1.03 (0.74 – 1.39)	–	1.11 (0.86 – 1.41)	–	–	1.63 (1.34 – 1.96)
Upadacitinib								
Overall	Overall	Denominator (N)	4,618,969	6,175,264	6,536,141	14,356,979	5,771,871	11,371,595
		Person-years	33,490,135.59	42,340,556.74	47,351,969.60	53,275,980.33	36,884,633.97	68,480,265.16
		Outcome (N)	1,342	544	2,863	2,863	2,309	4,661

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	4.01 (3.80 – 4.23)	1.28 (1.18 – 1.40)	6.05 (5.83 – 6.27)	5.37 (5.18 – 5.57)	6.26 (6.01 – 6.52)	6.81 (6.61 – 7.00)
2018-01-01	2018-12-31	Denominator (N)	4,082,479	5,435,441	5,914,865	8,370,824	5,107,561	–
		Person-years	3,998,081.20	5,333,952.65	5,839,359.40	7,526,315.54	5,066,852.87	–
		Outcome (N)	0	0	0	0	0	–
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,410	5,446,766	5,931,696	8,498,831	5,223,213	10,263,064
		Person-years	4,052,615.19	5,347,888.15	5,858,110.44	7,673,178.41	5,184,436.70	10,077,559.42
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2020-01-01	2020-12-31	Denominator (N)	4,153,943	5,456,051	5,950,875	8,762,521	5,305,656	10,360,410
		Person-years	4,098,284.27	5,374,886.45	5,891,695.04	7,813,051.45	5,254,376.31	10,208,401.94
		Outcome (N)	64	0	58	249	<5	146
		Incidence 100,000 person-years [95% CI]	1.56 (1.20 – 1.99)	0.00 (0.00 – 0.07)	0.98 (0.75 – 1.27)	3.19 (2.80 – 3.61)	-	1.43 (1.21 – 1.68)
2021-01-01	2021-12-31	Denominator (N)	4,168,289	5,466,449	5,968,597	8,932,915	5,319,587	10,413,975
		Person-years	4,102,564.74	5,372,607.26	5,894,023.39	7,913,242.34	5,280,949.22	10,246,853.11
		Outcome (N)	198	<5	207	441	226	1,036

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	4.83 (4.18 – 5.55)	-	3.51 (3.05 – 4.02)	5.57 (5.07 – 6.12)	4.28 (3.74 – 4.88)	10.11 (9.50 – 10.74)
2022-01-01	2022-12-31	Denominator (N)	4,200,600	5,485,766	5,994,320	9,059,621	5,326,960	10,481,131
		Person-years	4,122,684.52	5,383,523.81	5,911,743.81	7,739,226.08	5,288,585.43	10,307,931.04
		Outcome (N)	235	23	211	658	488	1,069
		Incidence 100,000 person-years [95% CI]	5.70 (5.00 – 6.48)	0.43 (0.27 – 0.64)	3.57 (3.10 – 4.08)	8.50 (7.86 – 9.18)	9.23 (8.43 – 10.08)	10.37 (9.76 – 11.01)
2023-01-01	2023-12-31	Denominator (N)	4,210,002	5,526,128	6,021,387	8,576,007	5,382,655	10,541,420
		Person-years	4,149,820.36	5,414,048.70	5,935,683.16	7,245,712.99	5,346,115.54	10,364,017.19
		Outcome (N)	163	51	513	569	608	833
		Incidence 100,000 person-years [95% CI]	3.93 (3.35 – 4.58)	0.94 (0.70 – 1.24)	8.64 (7.91 – 9.42)	7.85 (7.22 – 8.53)	11.37 (10.49 – 12.31)	8.04 (7.50 – 8.60)
2024-01-01	2024-12-31	Denominator (N)	4,225,141	5,546,873	6,073,618	7,317,922	5,568,113	10,570,074
		Person-years	4,176,656.39	5,457,842.47	5,991,971.98	5,721,799.63	5,463,317.89	10,412,665.77
		Outcome (N)	336	241	872	587	986	925
		Incidence 100,000 person-years [95% CI]	8.04 (7.21 – 8.95)	4.42 (3.88 – 5.01)	14.55 (13.60 – 15.55)	10.26 (9.45 – 11.12)	18.05 (16.94 – 19.21)	8.88 (8.32 – 9.47)
2025-01-01	2025-12-31	Denominator (N)	4,242,505	–	6,118,261	–	–	10,524,019
		Person-years	4,180,047.35	–	6,029,382.38	–	–	6,862,836.68
		Outcome (N)	346	–	1,002	–	–	652

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	8.28 (7.43 – 9.20)	–	16.62 (15.61 – 17.68)	–	–	9.50 (8.79 – 10.26)
Any JAKi								
Overall	Overall	Denominator (N)	4,619,076	6,175,427	6,536,600	14,357,543	5,772,378	11,372,272
		Person-years	33,490,546.80	42,341,160.78	47,353,273.34	53,277,152.12	36,886,034.34	68,481,538.03
		Outcome (N)	3,007	3,259	6,353	6,562	5,475	10,163
		Incidence 100,000 person-years [95% CI]	8.98 (8.66 – 9.30)	7.70 (7.43 – 7.97)	13.42 (13.09 – 13.75)	12.32 (12.02 – 12.62)	14.84 (14.45 – 15.24)	14.84 (14.55 – 15.13)
2018-01-01	2018-12-31	Denominator (N)	4,082,585	5,435,604	5,915,324	8,371,258	5,108,061	–
		Person-years	3,998,185.92	5,334,103.93	5,839,770.67	7,526,697.68	5,067,292.25	–
		Outcome (N)	29	224	773	476	428	–
		Incidence 100,000 person-years [95% CI]	0.72 (0.49 – 1.04)	4.20 (3.67 – 4.79)	13.24 (12.32 – 14.20)	6.32 (5.77 – 6.92)	8.45 (7.66 – 9.29)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,514	5,446,906	5,932,061	8,499,225	5,223,605	10,263,741
		Person-years	4,052,717.20	5,348,017.58	5,858,429.37	7,673,476.13	5,184,783.80	10,078,121.44
		Outcome (N)	292	552	702	772	437	1,495
		Incidence 100,000 person-years [95% CI]	7.20 (6.40 – 8.08)	10.32 (9.48 – 11.22)	11.98 (11.11 – 12.90)	10.06 (9.36 – 10.80)	8.43 (7.66 – 9.26)	14.83 (14.09 – 15.61)
2020-01-01	2020-12-31	Denominator (N)	4,154,031	5,456,170	5,951,158	8,762,797	5,305,961	10,360,854
		Person-years	4,098,359.05	5,374,996.36	5,891,943.29	7,813,250.52	5,254,639.44	10,208,733.74
		Outcome (N)	312	403	489	800	377	1,240

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	7.61 (6.79 – 8.51)	7.50 (6.78 – 8.27)	8.30 (7.58 – 9.07)	10.24 (9.54 – 10.97)	7.18 (6.47 – 7.94)	12.15 (11.48 – 12.84)
2021-01-01	2021-12-31	Denominator (N)	4,168,356	5,466,547	5,968,811	8,933,100	5,319,801	10,414,194
		Person-years	4,102,626.30	5,372,700.37	5,894,194.40	7,913,378.03	5,281,126.80	10,247,027.46
		Outcome (N)	541	269	654	959	646	1,686
		Incidence 100,000 person-years [95% CI]	13.19 (12.10 – 14.35)	5.01 (4.43 – 5.64)	11.10 (10.26 – 11.98)	12.12 (11.36 – 12.91)	12.23 (11.31 – 13.21)	16.45 (15.68 – 17.26)
2022-01-01	2022-12-31	Denominator (N)	4,200,653	5,485,853	5,994,455	9,059,750	5,327,105	10,481,267
		Person-years	4,122,720.76	5,383,594.06	5,911,844.71	7,739,312.40	5,288,702.75	10,308,043.94
		Outcome (N)	545	486	646	1,229	964	1,693
		Incidence 100,000 person-years [95% CI]	13.22 (12.13 – 14.38)	9.03 (8.24 – 9.87)	10.93 (10.10 – 11.80)	15.88 (15.00 – 16.79)	18.23 (17.09 – 19.41)	16.42 (15.65 – 17.23)
2023-01-01	2023-12-31	Denominator (N)	4,210,027	5,526,179	6,021,453	8,576,078	5,382,738	10,541,505
		Person-years	4,149,839.95	5,414,085.86	5,935,722.58	7,245,761.25	5,346,164.04	10,364,083.83
		Outcome (N)	288	317	811	871	1,112	1,384
		Incidence 100,000 person-years [95% CI]	6.94 (6.16 – 7.79)	5.86 (5.23 – 6.54)	13.66 (12.74 – 14.64)	12.02 (11.24 – 12.85)	20.80 (19.59 – 22.06)	13.35 (12.66 – 14.08)
2024-01-01	2024-12-31	Denominator (N)	4,225,158	5,546,895	6,073,643	7,317,959	5,568,135	10,570,120
		Person-years	4,176,667.76	5,457,854.55	5,991,985.14	5,721,821.41	5,463,325.26	10,412,689.61
		Outcome (N)	465	576	1,082	936	1,511	1,560

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	11.13 (10.14 – 12.19)	10.55 (9.71 – 11.45)	18.06 (17.00 – 19.17)	16.36 (15.33 – 17.44)	27.66 (26.28 – 29.09)	14.98 (14.25 – 15.74)
2025-01-01	2025-12-31	Denominator (N)	4,242,511	–	6,118,266	–	–	10,524,026
		Person-years	4,180,048.30	–	6,029,383.18	–	–	6,862,838.02
		Outcome (N)	535	–	1,196	–	–	1,105
		Incidence 100,000 person-years [95% CI]	12.80 (11.74 – 13.93)	–	19.84 (18.73 – 20.99)	–	–	16.10 (15.17 – 17.08)

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; CI = Confidence Interval; JAKi = Janus kinase inhibitor/s.

– is used when data is not available / too small for reporting (<5).

Table S3. Incidence of new JAKi initiation among the individuals without prior exposure to the same JAKi ingredient.

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
Abrocitinib								
Overall	Overall	Denominator (N)	4,619,092	6,175,458	6,536,791	14,359,869	5,772,446	11,373,943
		Person-years	33,500,307.17	42,352,707.77	47,376,366.84	53,303,162.76	36,899,969.25	68,523,985.50
		Outcome (N)	0	0	167	0	94	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.01)	0.00 (0.00 – 0.01)	0.35 (0.30 – 0.41)	0.00 (0.00 – 0.01)	0.26 (0.21 – 0.31)	0.00 (0.00 – 0.00)
2018-01-01	2018-12-31	Denominator (N)	4,082,585	5,435,619	5,915,499	8,371,682	5,108,105	–

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Person-years	3,998,198.08	5,334,206.37	5,840,333.21	7,527,305.00	5,067,549.32	–
		Outcome (N)	0	0	0	0	0	–
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,543	5,447,145	5,933,000	8,500,204	5,224,074	10,265,373
		Person-years	4,052,795.37	5,348,541.04	5,859,757.68	7,674,771.61	5,185,489.78	10,080,513.31
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2020-01-01	2020-12-31	Denominator (N)	4,154,354	5,456,957	5,952,788	8,764,761	5,306,866	10,363,950
		Person-years	4,098,852.29	5,375,999.23	5,893,805.74	7,815,354.18	5,255,725.88	10,212,383.60
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2021-01-01	2021-12-31	Denominator (N)	4,168,982	5,467,728	5,970,905	8,936,070	5,321,072	10,418,465
		Person-years	4,103,430.03	5,374,006.61	5,896,608.68	7,916,611.27	5,282,704.73	10,252,110.10
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
2022-01-01	2022-12-31	Denominator (N)	4,201,800	5,487,289	5,997,184	9,063,818	5,329,006	10,487,158
		Person-years	4,124,154.15	5,385,238.27	5,914,883.28	7,743,692.16	5,291,043.66	10,314,677.97
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2023-01-01	2023-12-31	Denominator (N)	4,211,679	5,528,075	6,024,793	8,581,322	5,385,568	10,548,978
		Person-years	4,151,618.90	5,416,123.97	5,939,403.67	7,251,123.10	5,349,517.17	10,372,202.54
		Outcome (N)	0	0	53	0	37	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.89 (0.67 – 1.17)	0.00 (0.00 – 0.05)	0.69 (0.49 – 0.95)	0.00 (0.00 – 0.04)
2024-01-01	2024-12-31	Denominator (N)	4,227,067	5,549,083	6,077,714	7,324,082	5,572,034	10,578,876
		Person-years	4,178,803.83	5,460,316.06	5,996,554.64	5,727,885.48	5,467,938.69	10,422,173.59
		Outcome (N)	0	0	65	0	57	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	1.08 (0.84 – 1.38)	0.00 (0.00 – 0.06)	1.04 (0.79 – 1.35)	0.00 (0.00 – 0.04)
2025-01-01	2025-12-31	Denominator (N)	4,244,871	–	6,123,331	–	–	10,534,241
		Person-years	4,182,657.09	–	6,035,019.93	–	–	6,869,924.38
		Outcome (N)	0	–	49	–	–	0

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	–	0.81 (0.60 – 1.07)	–	–	0.00 (0.00 – 0.05)
Baricitinib								
Overall	Overall	Denominator (N)	4,619,085	6,175,445	6,536,703	14,358,999	5,772,410	11,372,658
		Person-years	33,496,442.42	42,348,587.31	47,369,577.87	53,293,883.19	36,894,004.03	68,504,483.86
		Outcome (N)	980	1,170	1,264	1,753	1,900	2,691
		Incidence 100,000 person-years [95% CI]	2.93 (2.74 – 3.12)	2.76 (2.61 – 2.93)	2.67 (2.52 – 2.82)	3.29 (3.14 – 3.45)	5.15 (4.92 – 5.39)	3.93 (3.78 – 4.08)
2018-01-01	2018-12-31	Denominator (N)	4,082,585	5,435,610	5,915,413	8,371,412	5,108,075	–
		Person-years	3,998,193.31	5,334,148.14	5,840,061.16	7,526,958.08	5,067,415.16	–
		Outcome (N)	12	121	376	192	214	–
		Incidence 100,000 person-years [95% CI]	0.30 (0.16 – 0.52)	2.27 (1.88 – 2.71)	6.44 (5.80 – 7.12)	2.55 (2.20 – 2.94)	4.22 (3.68 – 4.83)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,532	5,447,017	5,932,543	8,499,709	5,223,830	10,264,099
		Person-years	4,052,754.37	5,348,377.89	5,859,167.57	7,674,106.17	5,185,133.83	10,078,754.86
		Outcome (N)	171	64	260	383	214	967
		Incidence 100,000 person-years [95% CI]	4.22 (3.61 – 4.90)	1.20 (0.92 – 1.53)	4.44 (3.91 – 5.01)	4.99 (4.50 – 5.52)	4.13 (3.59 – 4.72)	9.59 (9.00 – 10.22)

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
2020-01-01	2020-12-31	Denominator (N)	4,154,172	5,456,767	5,952,077	8,763,776	5,306,408	10,361,739
		Person-years	4,098,601.44	5,375,778.56	5,893,005.81	7,814,365.34	5,255,170.29	10,209,850.74
		Outcome (N)	104	91	162	234	205	647
		Incidence 100,000 person-years [95% CI]	2.54 (2.07 – 3.08)	1.69 (1.36 – 2.08)	2.75 (2.34 – 3.21)	2.99 (2.62 – 3.40)	3.90 (3.38 – 4.47)	6.34 (5.86 – 6.84)
2021-01-01	2021-12-31	Denominator (N)	4,168,703	5,467,451	5,970,047	8,934,802	5,320,413	10,415,655
		Person-years	4,103,095.21	5,373,633.64	5,895,696.29	7,915,272.53	5,281,896.38	10,249,160.61
		Outcome (N)	282	199	123	285	304	320
		Incidence 100,000 person-years [95% CI]	6.87 (6.09 – 7.72)	3.70 (3.21 – 4.26)	2.09 (1.73 – 2.49)	3.60 (3.19 – 4.04)	5.76 (5.13 – 6.44)	3.12 (2.79 – 3.48)
2022-01-01	2022-12-31	Denominator (N)	4,201,257	5,486,815	5,996,214	9,062,263	5,328,051	10,484,082
		Person-years	4,123,472.20	5,384,619.70	5,913,856.23	7,742,110.20	5,289,950.48	10,311,516.89
		Outcome (N)	246	309	124	271	301	266
		Incidence 100,000 person-years [95% CI]	5.97 (5.24 – 6.76)	5.74 (5.12 – 6.42)	2.10 (1.74 – 2.50)	3.50 (3.10 – 3.94)	5.69 (5.07 – 6.37)	2.58 (2.28 – 2.91)
2023-01-01	2023-12-31	Denominator (N)	4,210,929	5,527,303	6,023,719	8,579,543	5,384,340	10,545,721
		Person-years	4,150,851.65	5,415,292.82	5,938,332.86	7,249,381.16	5,348,141.14	10,368,881.78

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Outcome (N)	68	107	58	147	325	183
		Incidence 100,000 person-years [95% CI]	1.64 (1.27 – 2.08)	1.98 (1.62 – 2.39)	0.98 (0.74 – 1.26)	2.03 (1.71 – 2.38)	6.08 (5.43 – 6.78)	1.76 (1.52 – 2.04)
2024-01-01	2024-12-31	Denominator (N)	4,226,273	5,548,213	6,076,655	7,322,209	5,570,527	10,575,508
		Person-years	4,177,985.31	5,459,361.18	5,995,509.13	5,726,085.54	5,466,296.75	10,418,731.45
		Outcome (N)	53	179	67	170	337	185
		Incidence 100,000 person-years [95% CI]	1.27 (0.95 – 1.66)	3.28 (2.82 – 3.80)	1.12 (0.87 – 1.42)	2.97 (2.54 – 3.45)	6.16 (5.52 – 6.86)	1.78 (1.53 – 2.05)
2025-01-01	2025-12-31	Denominator (N)	4,244,037	–	6,122,275	–	–	10,530,745
		Person-years	4,181,816.00	–	6,033,948.82	–	–	6,867,587.53
		Outcome (N)	44	–	94	–	–	123
		Incidence 100,000 person-years [95% CI]	1.05 (0.76 – 1.41)	–	1.56 (1.26 – 1.91)	–	–	1.79 (1.49 – 2.14)
Filgotinib								
Overall	Overall	Denominator (N)	4,619,091	6,175,458	6,536,789	14,359,660	5,772,444	11,373,941
		Person-years	33,500,084.52	42,352,661.86	47,376,085.11	53,300,277.22	36,899,455.16	68,521,984.00
		Outcome (N)	206	35	208	1,228	355	1,357

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	0.62 (0.53 – 0.70)	0.08 (0.06 – 0.12)	0.44 (0.38 – 0.50)	2.30 (2.18 – 2.44)	0.96 (0.86 – 1.07)	1.98 (1.88 – 2.09)
2018-01-01	2018-12-31	Denominator (N)	4,082,585	5,435,619	5,915,499	8,371,682	5,108,105	–
		Person-years	3,998,198.08	5,334,206.37	5,840,333.21	7,527,305.00	5,067,549.32	–
		Outcome (N)	0	0	0	0	0	–
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,543	5,447,145	5,933,000	8,500,204	5,224,074	10,265,373
		Person-years	4,052,795.37	5,348,541.04	5,859,757.68	7,674,771.61	5,185,489.78	10,080,513.31
		Outcome (N)	0	0	0	0	0	0
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)
2020-01-01	2020-12-31	Denominator (N)	4,154,354	5,456,957	5,952,788	8,764,761	5,306,866	10,363,950
		Person-years	4,098,852.29	5,375,999.23	5,893,805.74	7,815,352.84	5,255,725.88	10,212,383.60
		Outcome (N)	0	0	0	15	0	0
		Incidence 100,000	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.19 (0.11 – 0.32)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.04)

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		person-years [95% CI]						
2021-01-01	2021-12-31	Denominator (N)	4,168,982	5,467,728	5,970,905	8,936,036	5,321,072	10,418,465
		Person-years	4,103,430.03	5,374,006.61	5,896,605.29	7,916,496.53	5,282,704.58	10,252,105.79
		Outcome (N)	0	0	22	217	<5	19
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.37 (0.23 – 0.56)	2.74 (2.39 – 3.13)	-	0.18 (0.11 – 0.29)
2022-01-01	2022-12-31	Denominator (N)	4,201,800	5,487,289	5,997,162	9,063,524	5,329,002	10,487,139
		Person-years	4,124,154.15	5,385,238.27	5,914,843.86	7,743,206.77	5,290,973.82	10,314,595.69
		Outcome (N)	0	0	53	413	155	180
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.90 (0.67 – 1.17)	5.33 (4.83 – 5.87)	2.93 (2.49 – 3.43)	1.75 (1.50 – 2.02)
2023-01-01	2023-12-31	Denominator (N)	4,211,679	5,528,075	6,024,718	8,580,609	5,385,408	10,548,777
		Person-years	4,151,614.29	5,416,123.84	5,939,303.01	7,250,355.62	5,349,307.86	10,371,837.89
		Outcome (N)	16	<5	81	196	107	346
		Incidence 100,000 person-years [95% CI]	0.38 (0.22 – 0.63)	-	1.36 (1.08 – 1.70)	2.70 (2.34 – 3.11)	2.00 (1.64 – 2.42)	3.34 (2.99 – 3.71)

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
2024-01-01	2024-12-31	Denominator (N)	4,227,051	5,549,080	6,077,610	7,323,145	5,571,803	10,578,335
		Person-years	4,178,758.61	5,460,297.69	5,996,472.22	5,726,899.73	5,467,703.91	10,421,406.97
		Outcome (N)	60	26	33	256	89	484
		Incidence 100,000 person-years [95% CI]	1.44 (1.10 – 1.85)	0.48 (0.31 – 0.70)	0.55 (0.38 – 0.77)	4.47 (3.94 – 5.05)	1.63 (1.31 – 2.00)	4.64 (4.24 – 5.08)
2025-01-01	2025-12-31	Denominator (N)	4,244,794	–	6,123,259	–	–	10,533,222
		Person-years	4,182,514.31	–	6,034,964.11	–	–	6,869,140.75
		Outcome (N)	130	–	19	–	–	328
		Incidence 100,000 person-years [95% CI]	3.11 (2.60 – 3.69)	–	0.32 (0.19 – 0.49)	–	–	4.78 (4.27 – 5.32)
Tofacitinib								
Overall	Overall	Denominator (N)	4,619,086	6,175,440	6,536,696	14,359,278	5,772,425	11,373,484
		Person-years	33,497,766.41	42,344,724.46	47,364,809.57	53,294,333.06	36,895,106.01	68,510,911.18
		Outcome (N)	571	1,828	2,199	1,512	1,274	2,555
		Incidence 100,000 person-years [95% CI]	1.71 (1.57 – 1.85)	4.32 (4.12 – 4.52)	4.64 (4.45 – 4.84)	2.84 (2.70 – 2.98)	3.45 (3.27 – 3.65)	3.73 (3.59 – 3.88)
2018-01-01	2018-12-31	Denominator (N)	4,082,585	5,435,611	5,915,410	8,371,520	5,108,091	–

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Person-years	3,998,190.69	5,334,158.20	5,840,017.89	7,527,018.80	5,067,418.07	–
		Outcome (N)	17	114	455	321	233	–
		Incidence 100,000 person-years [95% CI]	0.42 (0.25 – 0.68)	2.14 (1.76 – 2.57)	7.79 (7.09 – 8.54)	4.26 (3.81 – 4.76)	4.60 (4.03 – 5.23)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,525	5,447,021	5,932,461	8,499,672	5,223,830	10,264,930
		Person-years	4,052,757.89	5,348,147.93	5,858,936.40	7,674,073.54	5,185,104.70	10,079,736.31
		Outcome (N)	122	530	490	448	259	650
		Incidence 100,000 person-years [95% CI]	3.01 (2.50 – 3.59)	9.91 (9.08 – 10.79)	8.36 (7.64 – 9.14)	5.84 (5.31 – 6.40)	5.00 (4.40 – 5.64)	6.45 (5.96 – 6.96)
2020-01-01	2020-12-31	Denominator (N)	4,154,212	5,456,305	5,951,764	8,763,691	5,306,364	10,362,859
		Person-years	4,098,621.84	5,375,137.66	5,892,637.44	7,814,216.62	5,255,125.51	10,211,024.99
		Outcome (N)	147	367	296	352	200	553
		Incidence 100,000 person-years [95% CI]	3.59 (3.03 – 4.22)	6.83 (6.15 – 7.56)	5.02 (4.47 – 5.63)	4.50 (4.05 – 5.00)	3.81 (3.30 – 4.37)	5.42 (4.97 – 5.89)
2021-01-01	2021-12-31	Denominator (N)	4,168,696	5,466,715	5,969,598	8,934,608	5,320,377	10,416,840
		Person-years	4,103,115.25	5,372,925.35	5,895,127.69	7,915,140.56	5,281,930.46	10,250,292.29
		Outcome (N)	63	145	337	146	152	384

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Incidence 100,000 person-years [95% CI]	1.53 (1.18 – 1.96)	2.70 (2.28 – 3.17)	5.72 (5.12 – 6.36)	1.84 (1.56 – 2.17)	2.88 (2.44 – 3.37)	3.75 (3.38 – 4.14)
2022-01-01	2022-12-31	Denominator (N)	4,201,453	5,486,144	5,995,551	9,062,241	5,328,167	10,485,165
		Person-years	4,123,769.72	5,384,017.11	5,913,106.76	7,742,159.20	5,290,157.57	10,312,529.15
		Outcome (N)	73	199	298	74	106	357
		Incidence 100,000 person-years [95% CI]	1.77 (1.39 – 2.23)	3.70 (3.20 – 4.25)	5.04 (4.48 – 5.65)	0.96 (0.75 – 1.20)	2.00 (1.64 – 2.42)	3.46 (3.11 – 3.84)
2023-01-01	2023-12-31	Denominator (N)	4,211,258	5,526,753	6,022,878	8,579,763	5,384,629	10,546,650
		Person-years	4,151,173.17	5,414,729.12	5,937,440.20	7,249,584.69	5,348,527.58	10,369,754.05
		Outcome (N)	54	184	158	59	144	255
		Incidence 100,000 person-years [95% CI]	1.30 (0.98 – 1.70)	3.40 (2.92 – 3.93)	2.66 (2.26 – 3.11)	0.81 (0.62 – 1.05)	2.69 (2.27 – 3.17)	2.46 (2.17 – 2.78)
2024-01-01	2024-12-31	Denominator (N)	4,226,593	5,547,594	6,075,706	7,322,525	5,570,992	10,576,311
		Person-years	4,178,305.34	5,458,757.64	5,994,543.64	5,726,392.25	5,466,842.14	10,419,507.96
		Outcome (N)	44	163	89	73	180	209
		Incidence 100,000	1.05 (0.76 – 1.41)	2.99 (2.54 – 3.48)	1.49 (1.19 – 1.83)	1.27 (1.00 – 1.60)	3.29 (2.83 – 3.81)	2.01 (1.74 – 2.30)

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		person-years [95% CI]						
2025-01-01	2025-12-31	Denominator (N)	4,244,356	–	6,121,315	–	–	10,531,488
		Person-years	4,182,116.77	–	6,032,999.54	–	–	6,868,066.42
		Outcome (N)	51	–	76	–	–	147
		Incidence 100,000 person-years [95% CI]	1.22 (0.91 – 1.60)	–	1.26 (0.99 – 1.58)	–	–	2.14 (1.81 – 2.52)
Upadacitinib								
Overall	Overall	Denominator (N)	4,619,090	6,175,456	6,536,785	14,359,126	5,772,439	11,373,484
		Person-years	33,496,751.12	42,351,836.91	47,370,328.20	53,293,708.17	36,895,649.34	68,510,911.18
		Outcome (N)	1,449	710	3,353	3,675	2,835	2,555
		Incidence 100,000 person-years [95% CI]	4.33 (4.11 – 4.55)	1.68 (1.55 – 1.80)	7.08 (6.84 – 7.32)	6.90 (6.68 – 7.12)	7.68 (7.40 – 7.97)	3.73 (3.59 – 3.88)
2018-01-01	2018-12-31	Denominator (N)	4,082,585	5,435,619	5,915,499	8,371,682	5,108,105	–
		Person-years	3,998,198.08	5,334,206.37	5,840,333.21	7,527,305.00	5,067,549.32	–
		Outcome (N)	0	0	0	0	0	–
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	–

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
2019-01-01	2019-12-31	Denominator (N)	4,123,543	5,447,145	5,933,000	8,500,204	5,224,074	10,264,930
		Person-years	4,052,795.37	5,348,541.04	5,859,757.68	7,674,771.61	5,185,489.78	10,079,736.31
		Outcome (N)	0	0	0	0	0	650
		Incidence 100,000 person-years [95% CI]	0.00 (0.00 – 0.09)	0.00 (0.00 – 0.07)	0.00 (0.00 – 0.06)	0.00 (0.00 – 0.05)	0.00 (0.00 – 0.07)	6.45 (5.96 – 6.96)
2020-01-01	2020-12-31	Denominator (N)	4,154,354	5,456,957	5,952,788	8,764,737	5,306,866	10,362,859
		Person-years	4,098,837.66	5,375,999.14	5,893,783.73	7,815,188.11	5,255,725.79	10,211,024.99
		Outcome (N)	69	<5	94	391	<5	553
		Incidence 100,000 person-years [95% CI]	1.68 (1.31 – 2.13)	-	1.59 (1.29 – 1.95)	5.00 (4.52 – 5.52)	-	5.42 (4.97 – 5.89)
2021-01-01	2021-12-31	Denominator (N)	4,168,912	5,467,727	5,970,811	8,935,546	5,321,068	10,416,840
		Person-years	4,103,259.16	5,374,001.60	5,896,375.83	7,915,834.63	5,282,542.43	10,250,292.29
		Outcome (N)	214	10	286	651	359	384
		Incidence 100,000 person-years [95% CI]	5.22 (4.54 – 5.96)	0.19 (0.09 – 0.34)	4.85 (4.30 – 5.45)	8.22 (7.60 – 8.88)	6.80 (6.11 – 7.54)	3.75 (3.38 – 4.14)
2022-01-01	2022-12-31	Denominator (N)	4,201,516	5,487,278	5,996,803	9,062,529	5,328,645	10,485,165
		Person-years	4,123,747.10	5,385,217.73	5,914,348.71	7,742,102.77	5,290,391.10	10,312,529.15

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Outcome (N)	249	35	297	829	624	357
		Incidence 100,000 person-years [95% CI]	6.04 (5.31 – 6.84)	0.65 (0.45 – 0.90)	5.02 (4.47 – 5.63)	10.71 (9.99 – 11.46)	11.80 (10.89 – 12.76)	3.46 (3.11 – 3.84)
2023-01-01	2023-12-31	Denominator (N)	4,211,148	5,528,028	6,024,117	8,579,159	5,384,587	10,546,650
		Person-years	4,150,990.75	5,416,043.09	5,938,493.43	7,248,762.18	5,348,198.74	10,369,754.05
		Outcome (N)	184	73	616	687	716	255
		Incidence 100,000 person-years [95% CI]	4.43 (3.82 – 5.12)	1.35 (1.06 – 1.70)	10.37 (9.57 – 11.22)	9.48 (8.78 – 10.21)	13.39 (12.43 – 14.40)	2.46 (2.17 – 2.78)
2024-01-01	2024-12-31	Denominator (N)	4,226,359	5,548,963	6,076,477	7,321,185	5,570,373	10,576,311
		Person-years	4,177,921.58	5,460,031.41	5,994,887.62	5,724,894.03	5,465,752.18	10,419,507.96
		Outcome (N)	358	323	964	695	1,132	209
		Incidence 100,000 person-years [95% CI]	8.57 (7.70 – 9.50)	5.92 (5.29 – 6.60)	16.08 (15.08 – 17.13)	12.14 (11.25 – 13.08)	20.71 (19.52 – 21.95)	2.01 (1.74 – 2.30)
2025-01-01	2025-12-31	Denominator (N)	4,243,808	–	6,121,197	–	–	10,531,488
		Person-years	4,181,411.49	–	6,032,347.99	–	–	6,868,066.42
		Outcome (N)	375	–	1,096	–	–	147
		Incidence 100,000	8.97 (8.08 – 9.92)	–	18.17 (17.11 – 19.28)	–	–	2.14 (1.81 – 2.52)

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		person-years [95% CI]						
Any JAKi								
Overall	Overall	Denominator (N)	4,619,076	6,175,427	6,536,600	14,357,543	5,772,378	11,372,272
		Person-years	33,490,546.80	42,341,160.78	47,353,273.34	53,277,152.12	36,886,034.34	68,481,538.03
		Outcome (N)	3,007	3,259	6,353	6,562	5,475	10,163
		Incidence 100,000 person-years [95% CI]	8.98 (8.66 – 9.30)	7.70 (7.43 – 7.97)	13.42 (13.09 – 13.75)	12.32 (12.02 – 12.62)	14.84 (14.45 – 15.24)	14.84 (14.55 – 15.13)
2018-01-01	2018-12-31	Denominator (N)	4,082,585	5,435,604	5,915,324	8,371,258	5,108,061	–
		Person-years	3,998,185.92	5,334,103.93	5,839,770.67	7,526,697.68	5,067,292.25	–
		Outcome (N)	29	224	773	476	428	–
		Incidence 100,000 person-years [95% CI]	0.72 (0.49 – 1.04)	4.20 (3.67 – 4.79)	13.24 (12.32 – 14.20)	6.32 (5.77 – 6.92)	8.45 (7.66 – 9.29)	–
2019-01-01	2019-12-31	Denominator (N)	4,123,514	5,446,906	5,932,061	8,499,225	5,223,605	10,263,741
		Person-years	4,052,717.20	5,348,017.58	5,858,429.37	7,673,476.13	5,184,783.80	10,078,121.44
		Outcome (N)	292	552	702	772	437	1,495
		Incidence 100,000 person-years [95% CI]	7.20 (6.40 – 8.08)	10.32 (9.48 – 11.22)	11.98 (11.11 – 12.90)	10.06 (9.36 – 10.80)	8.43 (7.66 – 9.26)	14.83 (14.09 – 15.61)

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
2020-01-01	2020-12-31	Denominator (N)	4,154,031	5,456,170	5,951,158	8,762,797	5,305,961	10,360,854
		Person-years	4,098,359.05	5,374,996.36	5,891,943.29	7,813,250.52	5,254,639.44	10,208,733.74
		Outcome (N)	312	403	489	800	377	1,240
		Incidence 100,000 person-years [95% CI]	7.61 (6.79 – 8.51)	7.50 (6.78 – 8.27)	8.30 (7.58 – 9.07)	10.24 (9.54 – 10.97)	7.18 (6.47 – 7.94)	12.15 (11.48 – 12.84)
2021-01-01	2021-12-31	Denominator (N)	4,168,356	5,466,547	5,968,811	8,933,100	5,319,801	10,414,194
		Person-years	4,102,626.30	5,372,700.37	5,894,194.40	7,913,378.03	5,281,126.80	10,247,027.46
		Outcome (N)	541	269	654	959	646	1,686
		Incidence 100,000 person-years [95% CI]	13.19 (12.10 – 14.35)	5.01 (4.43 – 5.64)	11.10 (10.26 – 11.98)	12.12 (11.36 – 12.91)	12.23 (11.31 – 13.21)	16.45 (15.68 – 17.26)
2022-01-01	2022-12-31	Denominator (N)	4,200,653	5,485,853	5,994,455	9,059,750	5,327,105	10,481,267
		Person-years	4,122,720.76	5,383,594.06	5,911,844.71	7,739,312.40	5,288,702.75	10,308,043.94
		Outcome (N)	545	486	646	1,229	964	1,693
		Incidence 100,000 person-years [95% CI]	13.22 (12.13 – 14.38)	9.03 (8.24 – 9.87)	10.93 (10.10 – 11.80)	15.88 (15.00 – 16.79)	18.23 (17.09 – 19.41)	16.42 (15.65 – 17.23)
2023-01-01	2023-12-31	Denominator (N)	4,210,027	5,526,179	6,021,453	8,576,078	5,382,738	10,541,505
		Person-years	4,149,839.95	5,414,085.86	5,935,722.58	7,245,761.25	5,346,164.04	10,364,083.83

Incidence start date	Incidence end date	Estimate name	Data source name					
			NAJS	DK-DHR	FinOMOP-THL	IQVIA DA Germany	VID	HI-SPEED
		Outcome (N)	288	317	811	871	1,112	1,384
		Incidence 100,000 person-years [95% CI]	6.94 (6.16 – 7.79)	5.86 (5.23 – 6.54)	13.66 (12.74 – 14.64)	12.02 (11.24 – 12.85)	20.80 (19.59 – 22.06)	13.35 (12.66 – 14.08)
2024-01-01	2024-12-31	Denominator (N)	4,225,158	5,546,895	6,073,643	7,317,959	5,568,135	10,570,120
		Person-years	4,176,667.76	5,457,854.55	5,991,985.14	5,721,821.41	5,463,325.26	10,412,689.61
		Outcome (N)	465	576	1,082	936	1,511	1,560
		Incidence 100,000 person-years [95% CI]	11.13 (10.14 – 12.19)	10.55 (9.71 – 11.45)	18.06 (17.00 – 19.17)	16.36 (15.33 – 17.44)	27.66 (26.28 – 29.09)	14.98 (14.25 – 15.74)
2025-01-01	2025-12-31	Denominator (N)	4,242,511	–	6,118,266	–	–	10,524,026
		Person-years	4,180,048.30	–	6,029,383.18	–	–	6,862,838.02
		Outcome (N)	535	–	1,196	–	–	1,105
		Incidence 100,000 person-years [95% CI]	12.80 (11.74 – 13.93)	–	19.84 (18.73 – 20.99)	–	–	16.10 (15.17 – 17.08)

DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; HI-SPEED = Health Impact - Swedish Population Evidence Enabling Data-linkage; IQVIA DA Germany = IQVIA Disease Analyzer Germany; NAJS = Croatian National Public Health Information System; VID = Valencia Health System Integrated Dataset; CI = Confidence Interval; JAKi = Janus kinase inhibitor/s.

– is used when data is not available / too small for reporting (<5).

ANNEX V. Glossary

Additional definitions are available in the EMA Glossary of terms <https://www.ema.europa.eu/en/about-us/glossaries>.

Aggregated Data

Data collected and combined from multiple sources to generate summary information, typically anonymised.

Benefit-Risk Assessment

Evaluation of the positive therapeutic effects of a medicine compared to its risks (e.g. side effects).

Common Data Model (CDM)

A standardised data structure that enables data from multiple sources to be harmonised, making analysis consistent and reproducible. DARWIN EU® utilises the OMOP CDM maintained by the OHDSI community.

Complex Studies (C3)

Studies requiring the development or customisation of specific study designs, protocols, and Statistical Analysis Plans (SAPs), with extensive collection or extraction of data. Examples include etiological studies measuring the strength and determinants of an association between an exposure and the occurrence of a health outcome in a defined population considering sources of bias, potential confounding factors, and effect modifiers.

Coordination Centre (CC)

The central hub responsible for managing and overseeing the activities within DARWIN EU®. It is based at Erasmus University Medical Center in Rotterdam, the Netherlands.

Data Access

The process of obtaining permission to use specific datasets for regulatory or scientific studies.

Data Quality Framework

A set of standards and procedures to ensure accuracy, completeness, timeliness, and consistency of data used in DARWIN EU®.

Data Source

A database or repository of structured health-related data, such as electronic health records (EHRs), insurance claims, or registries.

DARWIN EU®

The European Medicines Agency's (EMA) federated network of real-world data sources designed to generate evidence to support regulatory decision-making.

EMA (European Medicines Agency)

The regulatory body responsible for the evaluation and supervision of medicinal products in the EU, overseeing DARWIN EU®.

Evidence Generation

The process of analysing real-world data to produce scientific information that can inform healthcare or regulatory decisions.

Federated Network

A data infrastructure where data remain at their original location but can be analysed in a harmonised way across multiple partners using a common model and tools.

GDPR (General Data Protection Regulation)

The EU regulation governing the protection of personal data and privacy, crucial to how DARWIN EU® handles health data.

Health Technology Assessment (HTA)

A systematic evaluation of properties and impacts of health technology, often using DARWIN EU® data to support assessments.

Metadata

Descriptive information about a data source (e.g. its content, quality, and structure), essential for identifying relevant databases in DARWIN EU® studies.

Off-the-Shelf Studies (OTS)

Studies for which a standard protocol per study/analysis type and standardised analytics may be developed and applied or adapted, typically relating to a descriptive research question. This includes studies on disease epidemiology, for example, the estimation of the prevalence or incidence of health outcomes in defined time periods and population groups, or drug utilisation studies at the population or patient level.

OHDSI (Observational Health Data Sciences and Informatics)

An open-science collaborative community that develops tools and standards (including the OMOP CDM) to enable large-scale analytics of observational health data. OHDSI provides the technical and scientific foundation for DARWIN EU®'s analytical ecosystem.

Patient-Level Data

Data related to individuals, de-identified, used for longitudinal or detailed analyses.

OMOP (Observational Medical Outcomes Partnership)

A common data model (CDM) that standardises the structure and content of observational healthcare data, enabling systematic analysis across disparate datasets. DARWIN EU® uses the OMOP CDM to ensure interoperability and consistency in real-world evidence generation.

Real-World Data (RWD)

Data relating to individual health status or healthcare delivery that is collected from routine clinical practice rather than from randomised controlled trials.

Real-World Evidence (RWE)

Clinical evidence derived from the analysis of RWD, used to inform decisions by regulators, payers, or clinicians.

Regulatory Decision-Making

The process by which authorities like EMA assess data to authorise, monitor, or modify the use of medicines in the EU.

Routine Repeated Studies (RR)

Studies that are either Off-the-Shelf or Complex studies repeated on a regular basis, following the same protocol and study code, but with updated data and/or different data partners.

Study Protocol

A detailed plan describing how a specific real-world study will be conducted, including objectives, design, data sources, and analyses.

Very Complex Studies (C4)

Studies which cannot rely only on electronic health care databases, or which would require complex methodological work, for example, due to the occurrence of events that cannot be defined by existing diagnosis codes, including events that do not yet have a diagnosis code, where it may be necessary to combine a diagnosis code with other data such as results of laboratory investigations. These studies might require the collection of data prospectively, or the inclusion of new (not previously onboarded) data sources.