Supplementary material

Supplementary data S1. Inclusion and exclusion criteria of both cohorts.

ESPOIR (Etude et Suivi des Polyarthrites Indifférenciées Récentes)
Inclusion criteria • Patients aged over 18 years and under 70 years • Clinical diagnosis of rheumatoid arthritis (certain or probable) • Clinical diagnosis of undifferentiated arthritis that can potentially become RA over follow-up • At least 2 inflammatory (swollen joints in two articular sites) joints since 6 weeks • Arthritis symptoms must have started since less than 6 months • DMARDS naive, corticoids naïve, (accepted if taken less than 2 weeks ago or except intra-articular injection taken less than 6 weeks prior to inclusion)
Non-inclusion criteria • Undifferentiated arthritis that do not have a chance to become RA • Presence of other inflammatory rheumatisms that are clearly defined
DESIR (DEvenir des Spondylarthropathies Indifférenciées Récentes)
Inclusion criteria • Patients aged over 18 years and under 50 years with recen • Recent onset Inflammatory back pain (lasting longer than 3 months and less than 3 years) - Pain in the lumbar spine or thoracic spine or buttock - Meeting the Calin or Berlin criteria or both • A probable diagnosis of spondyloarthritis according to the doctor (≥ 5 on a visual numerical scale of 0 to 10)
Exclusion criteria • Diagnosis of painful spine disorder, other than spondyloarthritis • Pregnant women • History of alcoholism, drug abuse, psychological disorders, severe co-morbidity • History of biotherapy treatment and notably anti-TNF therapy”

Supplementary data S2. Disease activity scores and its components in rheumatoid arthritis and spondyloarthritis.

Variables	Rheumatoid arthritis	Spondyloarthritis
Disease Activity Score (Composite score made of the objective and subjective components given below)	Disease Activity Score 28 (DAS28)	Ankylosing Spondylitis Disease Activity Score-C-reactive protein (ASDAS-CRP)
Objective components	- Erythrocyte sedimentation rate in mm/h (ESR) - Swollen Joint count (SJC) based on 28 joints	C- reactive protein (CRP) in mg/dl
Subjective components	- Tender joint count (TJC) based on 28 joints - Patient assessment of global health based on visual analogue scale ranging 0 (no impact of disease on health) to 100 (worst impact of disease on health)	- Back pain visual analogue scale (VAS) ranging 0 (no symptoms/ impact) to 10 (worse symptoms/ impact) - Articular pain VAS - Stiffness duration VAS - Patient assessment of global health VAS

Calculation of Rheumatic Disease Comorbidity Index (RDCI).
Rheumatic disease comorbidity index[1] (RDCI) is calculated based on following diseases: respiratory (bronchitis, emphysema, asthma, bronchiectasis, pneumoconiosis, asbestosis, pneumopathy, pulmonary fibrosis, pneumonitis, pleurisy, rheumatoid lung), cardiovascular (valvular diseases, ischemic heart diseases, cardiomyopathies, conduction disorders and arrythmias, heart failure, hypertension, and stroke), gastrointestinal (ulcer, haemorrhage, and perforation), depression, fracture (pathological and stress fractures of vertebra, femur, tibia, or fibula for ESPOIR cohort and those with a osteodensitometry score ≤ -2.0 that increased susceptibility to pathological fractures[7] for DESIR cohort), cancer, and diabetes.

RDCI[1] (range 0–9): 2 X lung disease + [2 X (heart attack, other cardiovascular, OR stroke) OR 1 X hypertension] + fracture + depression + diabetes + cancer + gastrointestinal disease

Supplementary data S3. Details on mixed linear models used for examining evolution of pain by opioid-prescription trajectories.
To validate the identified opioid-prescription trajectories, evolution of SF-36 BP over follow-up by these trajectories were plotted using mixed linear models. Only indication for opioids is unresolved moderate to severe pain, thus evolution of pain scores would likely correspond to the temporal trends in the prescription of opioids. Time scale spanned annually from the first visit. Time, time^2, and time^3 (slope terms) were incorporated to model non-linear evolution of pain. Random effects for the intercept and time allowed individual differences in pain score at intercept and changes in pain over time. The models were adjusted for sociodemographic factors and their interaction with time, selected disease-related [symptom duration, clinical and inflammatory markers (ESR, SJC, TJC for RA and CRP, arthritis, enthesitis, and synovitis index for SpA), imaging and biological markers], treatment, lifestyle, and health factors.

Supplementary data S4. Adjustment for mixed models examining evolution of pain disease activity and its components.

Outcome	Adjustment for the complete model
SF-36 Bodily pain in RA	Intercept + slope (time + time^2 + time^3) + Sociodemographic factors + sociodemographic factors*slope + disease-related factors [symptom duration + symptom duration*slope + ESR + SJC + TJC + imaging marker + biological marker (RF positivity + ACPA positivity + ACPA positivity*slope)] + treatment (corticosteroids, NSAIDs, DMARDs) + lifestyle factors + health factors
SF-36 Bodily pain in SpA	Intercept + slope (time + time^2 + time^3) + Sociodemographic factors + sociodemographic factors*slope + disease-related factors [symptom duration + symptom duration*slope + CRP + arthritis index + enthesitis index + synovitis index + imaging marker + imaging marker*slope + biological marker + biological marker*slope] + treatment (corticosteroids, NSAIDs, DMARDs) + lifestyle factors + health factors
DAS28 in RA	Intercept + slope (time + time^2 + time^3) + Sociodemographic factors + sociodemographic factors*slope + disease-related factors [symptom duration + symptom duration*slope + imaging marker + biological marker (RF positivity + ACPA positivity + ACPA positivity*slope)] + treatment (corticosteroids, NSAIDs, DMARDs) + lifestyle factors + health factors
Subjective components (TJC & PAGH) in RA	Intercept + slope (time + time^2 + time^3) + Sociodemographic factors + sociodemographic factors*slope + disease-related factors [symptom duration + symptom duration*slope + ESR + SJC + imaging marker + biological marker (RF positivity + ACPA positivity + ACPA positivity*slope)] + treatment (corticosteroids, NSAIDs, DMARDs) + lifestyle factors + health factors
ASDAS-CRP in SpA	Intercept + slope (time + time^2 + time^3) + Sociodemographic factors + sociodemographic factors*slope + disease-related factors [symptom duration + symptom duration*slope + synovitis index + imaging marker + imaging marker*slope + biological marker + biological marker*slope] + treatment (corticosteroids, NSAIDs, DMARDs) + lifestyle factors + health factors
Subjective components (Back pain, articular pain, stiffness duration & PAGH) in SpA	Intercept + slope (time + time^2 + time^3) + Sociodemographic factors + sociodemographic factors*slope + disease-related factors [symptom duration + symptom duration*slope + CRP + synovitis index + imaging marker + imaging marker*slope + biological marker + biological marker*slope] + treatment (corticosteroids, NSAIDs, DMARDs) + lifestyle factors + health factors

Five models were proposed: Basic model including time terms, opioid-prescription trajectories and its interaction with time was adjusted additionally and sequentially for socio-demographic factors and their interaction with time (model 1), disease-related (model 2), treatment (model 3), lifestyle (model 4), and health factors (model 5). Depending on the outcome, adjusting for disease-related factors varied (see above table) : when outcome is disease activity adjustment was done for selected clinical and inflammatory markers (symptom duration in RA and symptom duration, and synovitis index in SpA), imaging and biological markers and when outcome is a subjective component of disease activity then adjustment was done for selected clinical and inflammatory markers (symptom duration, ESR, and SJC in RA and symptom duration, CRP, and synovitis index in SpA), imaging and biological markers.

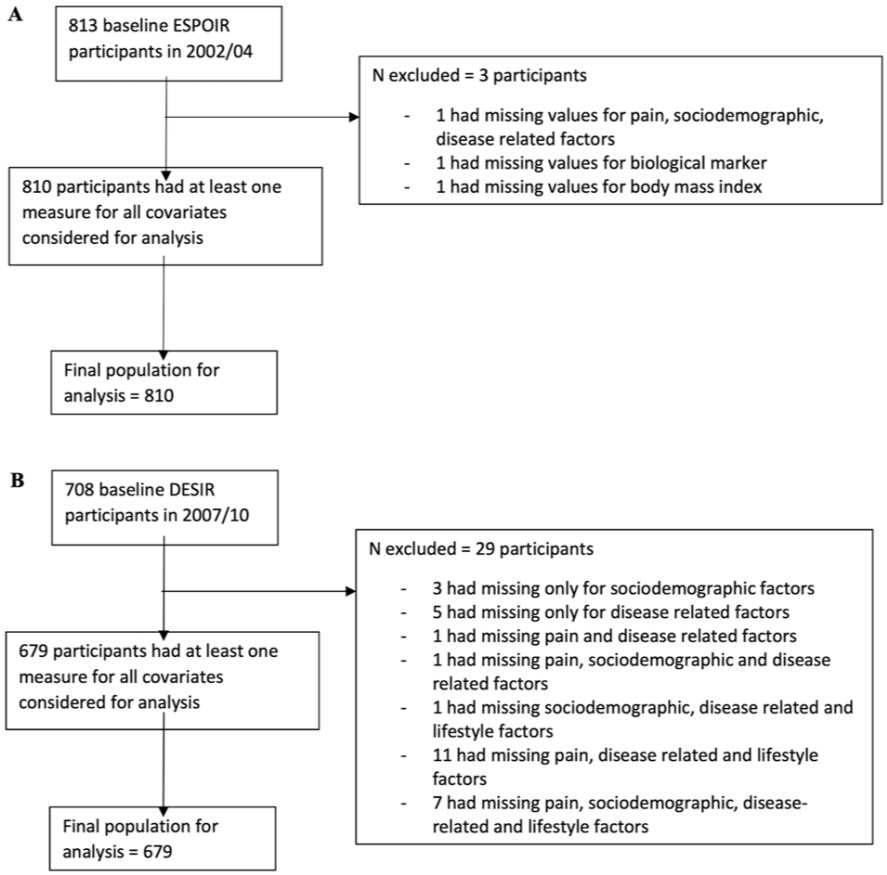
Supplementary Table S1. Choosing the number of groups for GBTM.

Number of groups, n (%)	BIC	AIC	Average posterior probability	Odds of correct classification	Entropy
Rheumatoid arthritis					
Order 3, 3	-	-	0.99	66.6	0.97
Group 1, 578 (71)	233	233	0.99	482.5	
Group 2, 235 (29)	99.8	58.4			
Order 3, 3, 3	-	-	0.99	50.9	0.95
Group 1, 504 (61)	208	207	0.98	155.0	
Group 2, 166 (20)	35.6	71.1	0.97	177.6	
Group 3, 143 (17)					
Order 3, 3, 3, 3	-	-	0.98	320.3	0.96
Group 1, 93 (12)	189	188	0.98	40.2	
Group 2, 498 (60)	54.9	67.4	0.98	252.5	
Group 3, 116 (15)			0.97	197.5	
Group 4, 106 (13)					
Order 3, 3, 3, 3, 3	-	-	0.96	213.2	0.95
Group 1, 92 (11)	178	177	0.99	38.5	
Group 2, 450 (55)	15.3	04.7	0.96	157.7	
Group 3, 105 (13)			0.98	394.3	
Group 4, 74 (9)			0.94	136.6	
Group 5, 92 (11)					
Spondyloarthritis					
Order 3, 3	-	-	1.00	263.9	0.99
Group 1, 485 (68)	150	150	0.99	498.4	
Group 2, 223 (31)	64.3	25.2			
Order 3, 3, 3	-	-	0.99	91.1	0.96
Group 1, 379 (53)	134	133	0.98	134.8	
Group 2, 165 (23)	30.7	69.9	0.99	419.0	
Group 3, 164 (23)					
Order 2, 3, 3, 3	-	-	0.99	79.3	0.95
Group 1, 387 (54)	124	123	0.97	257.0	
Group 2, 74 (11)	75.8	97.6	0.96	128.9	
Group 3, 112 (16)			0.98	239.1	
Group 4, 135 (19)					
Order 3, 3, 3, 3, 3	-	-	0.96	233.6	0.95
Group 1, 60 (8)	119	118	0.98	56.6	
Group 2, 317 (44)	36	31.7	0.99	291.4	
Group 3, 145 (21)			0.96	177.1	
Group 4, 84 (12)			0.97	201.8	
Group 5, 102 (14)					

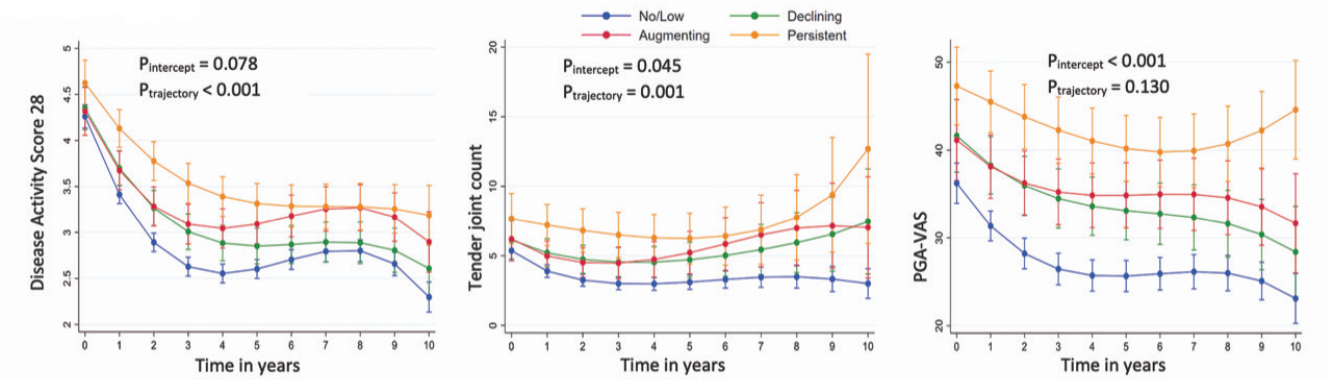
Increasing the number of groups beyond 4 did improve fit statistics, however they were not as distinct as the 4 group trajectories (no/low, declining, augmenting and persistent) and represented only the sub-groups of the 4 distinct groups. For instance, in both RA and SpA the 5 group trajectories were no/low, early declining, late declining, augmenting and persistent. However, while examining the evolution of pain by these trajectories we found that: in RA the evolution of pain in the no/low trajectory were not different from that of early declining; and in SpA the evolution of pain in early declining was not different from that of late declining. As the aim of this study was to identify clinically relevant distinct trajectories, we decided to keep the 4-group model as the final model.

Reference

ENGLAND BR, SAYLES H, MIKULS TR *et al*.: Validation of the Rheumatic Disease Comorbidity Index. *Arthritis Care Res* (Hoboken) 2015; 67(6): 865-72. doi: 10.1002/acr.22456



Supplementary Fig. S1. Flow chart describing selection of analytic sample from **A**) ESPOIR and **B**) DESIR cohorts.
The analytic population for both evolution of pain by opioid prescription trajectories and evolution for disease activity and its subjective components by opioid prescription trajectories were the same. Whenever pain variable was missing, disease related factors were also missing thus constituting the same analytic sample. However, the number of observations per participant varied in both analyses.

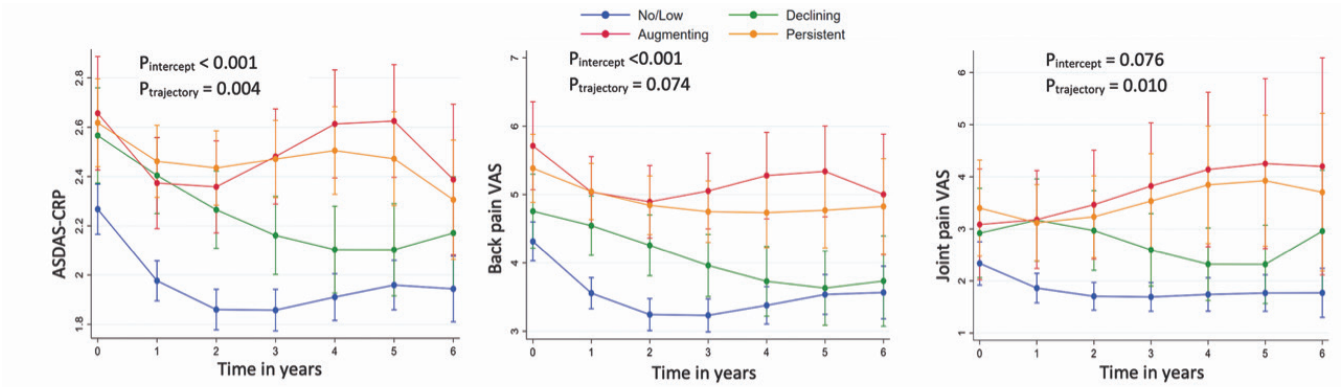


Year	Declining vs No/Low	Augmenting vs No/Low	Persistent vs No/Low
0	0.1 (-0.2 ; 0.3)	0.1 (-0.2 ; 0.3)	**0.4 (0.1 ; 0.6)**
1	**0.3 (0.1 ; 0.5)**	**0.3 (0.0 ; 0.5)**	**0.7 (0.5 ; 0.9)**
2	**0.4 (0.2 ; 0.6)**	**0.4 (0.2 ; 0.6)**	**0.9 (0.7 ; 1.1)**
3	**0.4 (0.2 ; 0.6)**	**0.5 (0.2 ; 0.7)**	**0.9 (0.7 ; 1.1)**
4	**0.3 (0.1 ; 0.5)**	**0.5 (0.3 ; 0.7)**	**0.8 (0.6 ; 1.1)**
5	**0.2 (0.0 ; 0.5)**	**0.5 (0.2 ; 0.7)**	**0.7 (0.5 ; 1.0)**
6	0.2 (-0.1 ; 0.4)	**0.5 (0.2 ; 0.7)**	**0.6 (0.3 ; 0.8)**
7	0.1 (-0.1 ; 0.3)	**0.5 (0.2 ; 0.7)**	**0.5 (0.2 ; 0.8)**
8	0.1 (-0.2 ; 0.3)	**0.5 (0.2 ; 0.7)**	**0.5 (0.2 ; 0.8)**
9	0.1 (-0.1 ; 0.4)	**0.5 (0.2 ; 0.8)**	**0.6 (0.3 ; 0.9)**
10	0.3 (0.0 ; 0.7)	**0.6 (0.2 ; 1.0)**	**0.9 (0.5 ; 1.3)**

Declining vs No/Low	Augmenting vs No/Low	Persistent vs No/Low
0.8 (-0.7 ; 2.2)	0.8 (-0.8 ; 2.5)	**2.3 (0.5 ; 4.2)**
1.3 (0.3 ; 2.4)	1.1 (0.0 ; 2.2)	**3.3 (1.8 ; 4.8)**
1.5 (0.5 ; 2.5)	**1.3 (0.2 ; 2.4)**	**3.6 (2.0 ; 5.1)**
1.5 (0.5 ; 2.6)	**1.5 (0.3 ; 2.6)**	**3.5 (1.9 ; 5.1)**
1.6 (0.4 ; 2.7)	**1.8 (0.5 ; 3.0)**	**3.3 (1.6 ; 5.0)**
1.6 (0.3 ; 2.9)	**2.1 (0.6 ; 3.6)**	**3.1 (1.3 ; 4.9)**
1.7 (0.2 ; 3.2)	**2.6 (0.7 ; 4.4)**	**3.1 (1.1 ; 5.2)**
2.0 (0.2 ; 3.8)	**3.0 (0.8 ; 5.3)**	**3.4 (1.0 ; 5.9)**
2.5 (0.4 ; 4.5)	**3.5 (0.9 ; 6.1)**	**4.3 (1.3 ; 7.3)**
3.2 (0.7 ; 5.7)	**3.8 (0.9 ; 6.8)**	**6.1 (2.1 ; 10.0)**
4.5 (0.9 ; 8.0)	**4.0 (0.5 ; 7.6)**	**9.7 (3.1 ; 16.2)**

Declining vs No/Low	Augmenting vs No/Low	Persistent vs No/Low
5.4 (0.9 ; 9.9)	4.9 (-0.1 ; 9.9)	**11.1 (6.2 ; 15.9)**
6.9 (3.3 ; 10.6)	**6.8 (2.8 ; 10.8)**	**14.1 (10.2 ; 18.1)**
7.8 (4.0 ; 11.5)	**8.0 (3.9 ; 12.1)**	**15.6 (11.5 ; 19.7)**
8.0 (4.2 ; 11.9)	**8.8 (4.6 ; 12.9)**	**15.8 (11.7 ; 20.0)**
7.9 (4.2 ; 11.6)	**9.1 (5.1 ; 13.2)**	**15.3 (11.2 ; 19.5)**
7.5 (3.7 ; 11.2)	**9.2 (5.1 ; 13.3)**	**14.5 (10.4 ; 18.7)**
6.8 (2.9 ; 10.8)	**9.1 (4.7 ; 13.4)**	**13.9 (9.5 ; 18.2)**
6.2 (2.0 ; 10.4)	**8.8 (4.3 ; 13.4)**	**13.8 (9.2 ; 18.4)**
5.6 (1.3 ; 9.9)	**8.6 (3.9 ; 13.3)**	**14.7 (10.0 ; 19.5)**
5.3 (0.8 ; 9.8)	**8.5 (3.6 ; 13.4)**	**17.2 (12.2 ; 22.1)**
5.3 (-0.6 ; 11.2)	**8.6 (2.3 ; 14.9)**	**21.5 (15.2 ; 27.8)**

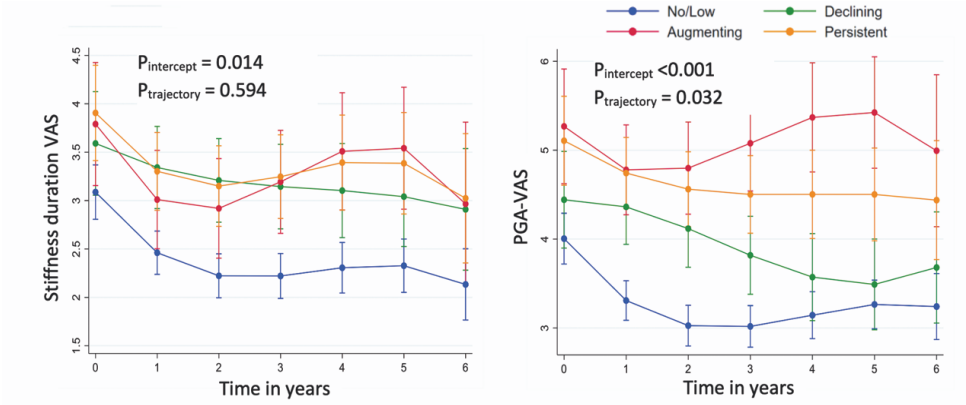
Supplementary Fig. S2. Evolution of disease activity and its subjective components by opioid-prescription trajectories in those fulfilling ACR criteria (ESPOIR).
PGA-VAS, patient assessment of global activity of disease on health-visual analogue scale.
The table beneath each graph, shows the evolution of differences in respective outcome (disease activity and subjective components) for each year over the follow-up.
Model for disease activity are adjusted for sociodemographic, disease-related (symptom duration, imaging and biological marker), treatment, lifestyle, and health factors.
Models for subjective outcomes are adjusted for sociodemographic, disease-related (symptom duration, ESR, SJC, imaging and biological marker), treatment, lifestyle, and health factors.
$P_{intercept}$ is *p*-value for difference in trajectories at year 0 and $P_{trajectory}$ is *p*-value for interaction of trajectories and time (trajectories*time, trajectories*time^2 and trajectories*time^3)
Those with $p<0.05$ are highlighted.



Year	Declining vs No/Low	Augmenting vs No/Low	Persistent vs No/Low
0	**0.3 (0.1 ; 0.5)**	**0.4 (0.1 ; 0.6)**	**0.4 (0.1 ; 0.6)**
1	**0.4 (0.3 ; 0.6)**	**0.4 (0.2 ; 0.6)**	**0.5 (0.3 ; 0.7)**
2	**0.4 (0.2 ; 0.6)**	**0.5 (0.3 ; 0.7)**	**0.6 (0.4 ; 0.7)**
3	**0.3 (0.1 ; 0.5)**	**0.6 (0.4 ; 0.8)**	**0.6 (0.4 ; 0.8)**
4	0.2 (0.0 ; 0.4)	**0.7 (0.5 ; 0.9)**	**0.6 (0.4 ; 0.8)**
5	0.1 (-0.1 ; 0.4)	**0.7 (0.4 ; 0.9)**	**0.5 (0.3 ; 0.7)**
6	0.2 (0.0 ; 0.5)	**0.4 (0.1 ; 0.8)**	**0.4 (0.1 ; 0.6)**

Declining vs No/Low	Augmenting vs No/Low	Persistent vs No/Low
0.4 (-0.2 ; 1.1)	**1.4 (0.7 ; 2.1)**	**1.1 (0.5 ; 1.6)**
1.0 (0.5 ; 1.5)	**1.5 (0.9 ; 2.1)**	**1.5 (1.0 ; 2.0)**
1.0 (0.5 ; 1.5)	**1.7 (1.1 ; 2.2)**	**1.6 (1.1 ; 2.1)**
0.7 (0.2 ; 1.3)	**1.8 (1.2 ; 2.4)**	**1.5 (1.0 ; 2.0)**
0.4 (-0.2 ; 0.9)	**1.9 (1.2 ; 2.6)**	**1.4 (0.8 ; 1.9)**
0.1 (-0.5 ; 0.7)	**1.8 (1.1 ; 2.5)**	**1.2 (0.6 ; 1.9)**
0.2 (-0.6 ; 0.9)	**1.4 (0.5 ; 2.4)**	**1.3 (0.5 ; 2.1)**

Declining vs No/Low	Augmenting vs No/Low	Persistent vs No/Low
0.6 (-0.3 ; 1.5)	0.7 (-0.4 ; 1.9)	**1.1 (0.1 ; 2.0)**
1.3 (0.5 ; 2.1)	**1.3 (0.4 ; 2.3)**	**1.3 (0.5 ; 2.0)**
1.3 (0.5 ; 2.1)	**1.8 (0.7 ; 2.8)**	**1.5 (0.7 ; 2.3)**
0.9 (0.2 ; 1.6)	**2.1 (0.9 ; 3.3)**	**1.8 (0.9 ; 2.8)**
0.6 (-0.2 ; 1.3)	**2.4 (0.9 ; 3.9)**	**2.1 (1.0 ; 3.2)**
0.6 (-0.2 ; 1.3)	**2.5 (0.9 ; 4.1)**	**2.2 (0.9 ; 3.4)**
1.2 (0.0 ; 2.4)	**2.4 (0.3 ; 4.5)**	**1.9 (0.4 ; 3.5)**



Year	Declining vs No/Low	Augmenting vs No/Low	Persistent vs No/Low
0	0.5 (-0.1 ; 1.1)	**0.7 (0.0 ; 1.4)**	**0.8 (0.3 ; 1.4)**
1	**0.9 (0.4 ; 1.4)**	0.5 (0.0 ; 1.1)	**0.8 (0.4 ; 1.3)**
2	**1.0 (0.5 ; 1.5)**	**0.7 (0.1 ; 1.3)**	**0.9 (0.4 ; 1.4)**
3	**0.9 (0.4 ; 1.4)**	**1.0 (0.4 ; 1.6)**	**1.0 (0.5 ; 1.5)**
4	**0.8 (0.2 ; 1.4)**	**1.2 (0.5 ; 1.9)**	**1.1 (0.5 ; 1.6)**
5	**0.7 (0.1 ; 1.3)**	**1.2 (0.5 ; 1.9)**	**1.1 (0.5 ; 1.7)**
6	**0.8 (0.0 ; 1.5)**	0.8 (-0.1 ; 1.8)	**0.9 (0.1 ; 1.7)**

Declining vs No/Low	Augmenting vs No/Low	Persistent vs No/Low
0.4 (-0.2 ; 1.1)	**1.3 (0.6 ; 2.0)**	**1.1 (0.5 ; 1.7)**
1.1 (0.6 ; 1.5)	**1.5 (0.9 ; 2.0)**	**1.4 (1.0 ; 1.9)**
1.1 (0.6 ; 1.6)	**1.8 (1.2 ; 2.3)**	**1.5 (1.1 ; 2.0)**
0.8 (0.3 ; 1.3)	**2.1 (1.5 ; 2.7)**	**1.5 (1.0 ; 2.0)**
0.4 (-0.1 ; 1.0)	**2.2 (1.6 ; 2.9)**	**1.4 (0.8 ; 1.9)**
0.2 (-0.4 ; 0.8)	**2.2 (1.5 ; 2.9)**	**1.2 (0.6 ; 1.8)**
0.4 (-0.3 ; 1.2)	**1.8 (0.8 ; 2.7)**	**1.2 (0.4 ; 2.0)**

Supplementary Fig. S3. Evolution of disease activity and its subjective components by opioid-prescription trajectories in those fulfilling ASAS criteria (DESIR).

ASDAS-CRP, Ankylosing spondylitis disease activity score-C-reactive protein; VAS, visual analogue scale; PGA-VAS, patient assessment of global activity of disease on health-visual analogue scale.

The table beneath each graph, shows the evolution of differences in respective outcome (disease activity and subjective components) for each year over the follow-up.

Model for disease activity is adjusted for sociodemographic, disease-related (symptom duration, synovitis index, imaging and biological marker), treatment, lifestyle, and health factors.

Models for subjective outcomes are adjusted for sociodemographic, disease-related (symptom duration, CRP, synovitis index, imaging and biological marker), treatment, lifestyle, and health factors.

$P_{intercept}$ is *p*-value for difference in trajectories at year 0 and $P_{trajectory}$ is *p*-value for interaction of trajectories and time (trajectories*time, trajectories*time^2 and trajectories*time^3)

Those with $p<0.05$ are highlighted.