Supplementary materials
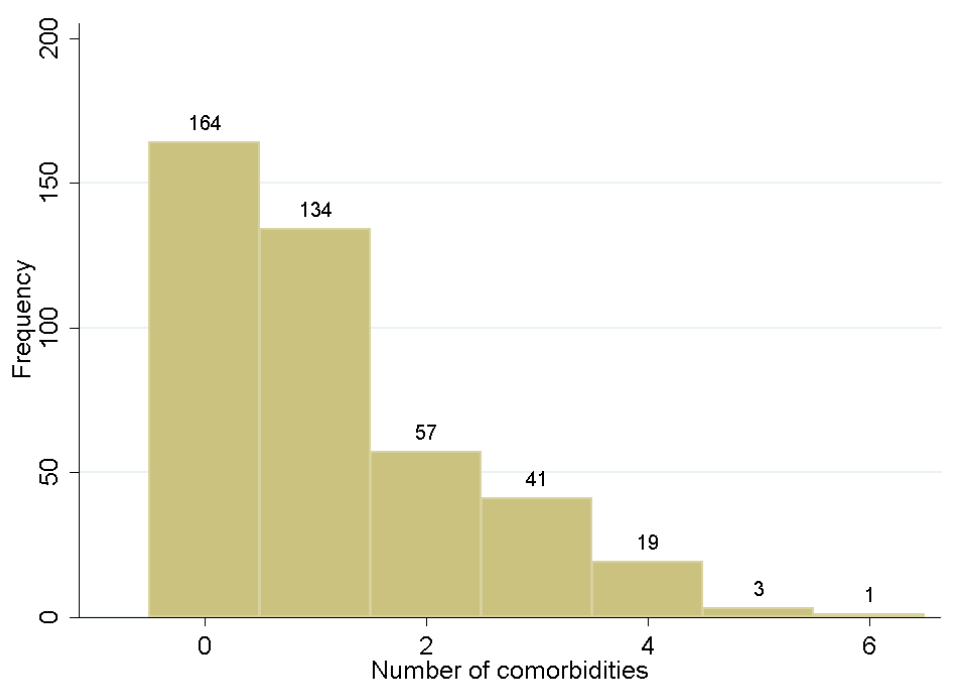
Supplementary table 1. Comorbidities assumed to be present if history and medications were suggestive.	
Hypertension	Prescribed anti-hypertensives in the absence of kidney or heart disease
Dyspepsia	Prescribed proton pump inhibitors or H2 blockers in the absence of glucocorticoids or NSAIDs
Coronary heart disease	Prescribed antianginals (eg. nitrates) or secondary prophylaxis combinations (eg. statin, antiplatelet and beta-blocker/ACE inhibitor) in the absence of other indications.
Diabetes	Prescribed oral hypoglycaemics or insulin.
Irritable bowel syndrome (IBS)	Prescribed mebeverine in the absence of other intestinal diseases
Constipation	Prescribed laxatives without gastroenteric diseases such as chronic liver disease or IBS.
Depression	Prescribed selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, or tricyclics in the absence of any neuropsychiatric conditions or chronic pain.
Fibromyalgia	Prescribed duloxetine, pregabalin or gabapentin in the absence of neuropsychiatric conditions or other neuropathic pain.
Other psychoactive substance misuse	Includes documented use of cannabis.
Alcohol problems	Includes documented weekly alcohol use of ≥50 units for men or ≥35 units for women. These thresholds are defined by UK government as high risk drinking [1].

Multiple imputation

Multiple imputation was performed using chained equations (-mi impute mice- command in Stata v13). All variables in each model were included in the respective imputation models, with 30 imputed datasets. Logistic (ordinal/multinomial) models were used for categorical variables and predictive mean matching for continuous variables, which accounts for their restricted range.

Supplementary figure 1. Frequency of the number of comorbidities in 419 patients with axial spondyloarthritis.

	Supplementary table 2. Prevalence of 38 chronic diseases in 419 patients with axial spondyloarthritis.	
1	Hypertension	81 (19%)
2	Depression	66 (16%)
3	Anxiety and other neurotic disorders	15 (4%)
4	Schizophrenia or bipolar disorder	5 (1%)
5	Alcohol problems	18 (4%)
6	Other psychoactive substance misuse	18 (4%)
7	Chronic liver disease	3 (1%)
8	Viral hepatitis	4 (1%)
9	Migraine	8 (2%)
10	Epilepsy*	5 (1%)
11	Thyroid disorders	13 (3%)
12	Diabetes	21 (5%)
13	Atrial fibrillation	5 (1%)
14	Coronary heart disease	24 (6%)
15	Heart failure	3 (1%)
16	Stroke and TIA	6 (1%)
17	Peripheral vessel disease	1 (<1%)
18	COPD	13 (3%)
19	Asthma*	18 (4%)
20	Chronic sinusitis	2 (<1%)
21	Prostate disorders	5 (1%)
22	Fibromyalgia	19 (5%)
23	Irritable bowel syndrome	15 (4%)
24	Osteoporosis	24 (6%)
25	Diverticular disease	5 (1%)
26	Constipation*	4 (1%)
27	Cancer**	4 (1%)
28	Chronic kidney disease	10 (2%)
29	Dyspepsia*	48 (11%)
30	Glaucoma	1 (0.2%)
31	Learning disability	1 (0.2%)
32	Blindness or low vision	1 (0.2%)
33	Parkinson's disease	1 (0.2%)
34	Multiple sclerosis	1 (0.2%)
35	Anorexia or bulimia	0
36	Dementia	0
37	Hearing loss	0
38	Bronchiectasis	0
*Currently treated **New diagnosis in last 5 years		

Supplementary table 3. Sensitivity analysis using multiple imputation for outcome measures compared between each patient cluster.

Cluster	1	2	3 and 5	4	6	7	8	9	10	11 to 15
Disease(s)	Isolated axSpA	Dyspepsia	Anxiety and/or depression	Fibromyalgia and/or IBS	Hypertension and/or CHD	Alcohol problems and/or osteoporosis	Thyroid	Other substance misuse	Asthma	Other rare conditions
n	164	31	54	18	88	19	9	16	14	6
EQ5D	reference	-0.05 (-0.2, 0.09)	-0.23 (-0.35, -0.11)	-0.18 (-0.36, 0.01)	-0.02 (-0.14, 0.09)	0.08 (-0.11, 0.27)	0.17 (-0.09, 0.43)	-0.16 (-0.36, 0.04)	-0.10 (-0.3, 0.11)	-0.16 (-0.48, 0.15)
Global health	reference	0.3 (-0.6, 1.3)	0.9 (0.1, 1.7)	1.2 (0.03, 2.5)	0.4 (-0.4, 1.1)	-0.05 (-1.3, 1.2)	0.6 (-1.1, 2.3)	1.3 (0.002, 2.6)	0.7 (-0.6, 2.0)	0.9 (-1.2, 2.9)
Fatigue	reference	0.7 (-0.3, 1.8)	1.1 (0.2, 1.9)	1.4 (0.1, 2.7)	0.3 (-0.5, 1.1)	-0.7 (-2, 0.6)	-0.4 (-2.2, 1.4)	0.03 (-1.4, 1.5)	-0.2 (-1.7, 1.2)	0.6 (-1.6, 2.7)
BASDAI	reference	-0.2 (-1.2, 0.8)	0.9 (0.1, 1.7)	1.5 (0.3, 2.7)	0.4 (-0.4, 1.1)	-0.2 (-1.4, 1.0)	-0.3 (-1.9, 1.4)	1.0 (-0.2, 2.3)	1.0 (-0.3, 2.3)	1.7 (-0.4, 3.9)
Spinal pain	reference	0.1 (-1.0, 1.3)	1.1 (0.2, 2)	1.9 (0.5, 3.3)	0.3 (-0.6, 1.2)	-0.1 (-1.5, 1.4)	0.6 (-1.4, 2.5)	0.9 (-0.6, 2.4)	0.8 (-0.8, 2.4)	1.4 (-1.3, 4)
BASFI	reference	0.04 (-1.1, 1.2)	1.6 (0.8, 2.5)	1.9 (0.5, 3.2)	0.7 (-0.2, 1.5)	0.7 (-0.7, 2.0)	0.4 (-1.5, 2.3)	0.8 (-0.7, 2.2)	1.4 (-0.1, 3.0)	2.0 (-0.4, 4.3)
ESR*	reference	-0.10 (-0.53, 0.34)	0.11 (-0.24, 0.46)	-0.25 (-0.79, 0.3)	0.02 (-0.33, 0.37)	0.05 (-0.52, 0.62)	-0.09 (-0.85, 0.67)	0.47 (-0.11, 1.05)	-0.04 (-0.68, 0.6)	0.41 (-0.64, 1.45)
CRP*	reference	-0.44 (-0.97, 0.08)	0.10 (-0.32, 0.52)	0.04 (-0.62, 0.69)	-0.05 (-0.46, 0.37)	-0.27 (-0.96, 0.43)	-0.09 (-1.02, 0.83)	0.04 (-0.66, 0.74)	-0.23 (-1.01, 0.54)	0.38 (-0.82, 1.59)

Data shown as regression coefficients (95% confidence interval). For EuroQol, higher values indicate better quality of life. For all other outcomes, higher values indicate more severe disease.

Coefficients derived from models using each outcome measure as independent variable, and cluster as a dummy variable with isolated axSpA as the reference group.

Models adjusted for age, gender, symptom duration, deprivation, current NSAID-use and smoking status.

Global health and fatigue were measured by single-item questions with 0 as best/no fatigue and 10 as worst.

*ESR and CRP were log-transformed using Ln(ESR) and Ln(CRP+1).

EuroQoL, 5-domain quality of life measure; BASDAI, Bath AS disease activity index; BASFI, Bath AS Functional index; IBS, irritable bowel syndrome; CHD, coronary heart disease.

Supplementary table 4. Sensitivity analysis using 28 morbidities that were prevalent in at least 2 patients.

Cluster	1	2	3	4	5	6	7	8	9	10	11
Number of patients	167	40	82	35	5	177	46	12	21	20	21
Hypertension			1 (2)	3 (17)		**72 (88)**	4 (25)	1 (11)			
Depression		3 (10)	**42 (86)**	4 (22)		10 (12)	5 (31)		1 (6)		1 (7)
Anxiety and other neuroses		2 (6)	**7 (14)**		**4 (100)**						
Schizophrenia or bipolar						3 (4)			1 (6)		1 (7)
Osteoporosis		1 (3)	5 (10)			10 (12)	3 (19)			**4 (40)**	1 (7)
Alcohol problems		1 (3)	1 (2)	1 (6)		5 (6)	1 (6)		**9 (90)**		
Other psychoactive substance misuse							1 (6)	**16 (100)**	1 (10)		
Chronic liver disease				1 (6)		1 (1)			1 (10)		
Viral hepatitis			1 (2)			1 (1)	1 (6)		1 (6)		
Migraine			6 (12)					1 (11)			1 (7)
Epilepsy*		1 (3)	3 (6)								1 (7)
Thyroid disorders			1 (2)			1 (1)		**9 (100)**			
Diabetes			3 (6)			15 (18)	2 (13)			3 (30)	
Atrial fibrillation						2 (2)	1 (6)				
Coronary heart disease			1 (2)			13 (16)	**9 (56)**				1 (7)
Heart failure						3 (4)					
Stroke and TIA			1 (2)			3 (4)	1 (6)			1 (10)	
COPD			3 (6)				**12 (75)**			1 (10)	
Asthma*						4 (5)					14 (100)
Chronic sinusitis						1 (1)					
Prostate disorders						5 (6)					
Fibromyalgia			2 (4)	**13 (72)**	1 (25)		2 (15)	1 (11)			
Irritable bowel syndrome			1 (2)	**10 (56)**		3 (4)					1 (7)
Diverticular disease			1 (2)			4 (5)					
Constipation*			1 (2)			2 (2)	1 (6)				
Cancer**			4 (8)								
Chronic kidney disease		3 (10)				6 (7)	1 (6)				
Dyspepsia*		**29 (94)**	1 (2)	3 (17)		11 (13)	2 (13)		2 (13)		

*Currently treated. **Cancer diagnoses in the past 5 years. Cells with zero prevalence were left empty for clarity. Bold text highlights dominant morbidities in each cluster. Clusters 12 (2 patients with AF) and 13 (1 with sinusitis) were omitted.

TIA, transient ischaemic attack; COPD, chronic obstructive pulmonary diseases.

References

1. Health & Social Care Information Centre. Statistics on Alcohol. 2015.Available from: https://www.gov.uk/government/statistics/statistics-on-alcohol-england-2015 [accessed: Oct 2018]