Supplementary Material

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Crossfield SSR, *et al. RMD Open* 2021; 7:e001888. doi: 10.1136/rmdopen-2021-001888

Glossary of Terms

CPRD	The Clinical Research Practice Datalink
AS	Ankylosing spondylitis
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

Supplementary Methods

Supplementary Table S1. STROBE Checklist for cohort studies with reference to this study

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6, 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6, 7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7, 8
Bias	9	Describe any efforts to address potential sources of bias	7, 8
Study size	10	Explain how the study size was arrived at	6, 7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7, Sup. Material
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7, 8
		(*b*) Describe any methods used to examine subgroups and interactions	7, 8
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for	8, 9, Fig. 2

		eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	8, Fig. 2
		(c) Consider use of a flow diagram	8, 9 Fig. 2
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, 9, Sup. Table S5
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	8, 9, Sup. Table S6
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-11, Sup. Tables S6, S7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(*b*) Report category boundaries when continuous variables were categorized	8, Sup. Material
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14, 15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14, 15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

Supplementary Table S2. Read Codes used to confirm the initial AS diagnosis, in the sensitivity analysis

Code	Term Description
N100.	Ankylosing spondylitis
2377.	ankyl.spondyl.chest def.
388p.	BASDAI - Bath ankylosing spondylitis disease activity index
388p0	Bath Ankylosing Spondylitis Functional Index
38QL.	Bath Ankylosing Spondylitis Metrology Index

Supplementary Table S3. Read Codes used to determine back pain

Code	Term Description
N142.	Low back pain
16C9.	Chronic low back pain
16CA.	Mechanical low back pain
16C6.	Back pain without radiation NOS
N149.	Back stiffness
N10z.	Spondylitis NOS
16C7.	C/O - upper back ache
16C..	Backache symptom
16C2.	Backache
16C3.	Backache with radiation
16C8.	Exacerbation of backache
16CZ.	Backache symptom NOS
14G4.	H/O: back problem
N145.	Backache; unspecified
N141.	Pain in thoracic spine
16C5.	C/O - low back pain
N1460	Lumbosacral ankylosis
N1461	Sacroiliac ankylosis
N1462	Sacral ankylosis NOS
N1466	Sacroiliac disorder
N148.	Ankylosis/instability of cervical;thoracic or lumbar spine
N1486	Lumbar spine ankylosis
N14z.	Ankylosis of spine NOS

Supplementary Table S4. Read Codes used to indicate a rheumatology referral had occurred

Code	Term Description
66H9.	Rheumatology management plan given
67Ih.	Advice to GP from rheumatology service
8H2C.	Admit rheumatology emergency
8H3H.	Non-urgent rheumatology admisn
8H4B.	Referred to rheumatologist
8HJC.	Rheumatology self-referral
8HKA.	Rheumatology D.V. requested
8HLA.	Rheumatology D.V. done
8HMA.	Listed for Rheumatology admiss
8HTd.	Referral to rheumatology clinic
8HTP.	Referral to musculoskeletal clinic
8HVQ.	Private referral to rheumatologist

99HB.	Rheumatology disorder annual review
9N0w.	Seen in musculoskeletal clinic
9N1C0	Rheumatology service home visit
9N1O.	Seen in rheumatology clinic
9NIR.	Seen by rheumatology nurse specialist
9NNT.	Under care of rheumatologist
ZL18T	Under care of rheumatologist
ZL22G	Under care of rheumatology nurse specialist
ZL5AR	Referral to rheumatologist
ZL62G	Referral to rheumatology nurse specialist
ZL9AT	Seen by rheumatologist
ZLA2G	Seen by rheumatology nurse specialist
ZLD3T	Discharge by rheumatologist
ZLD7E	Discharge by rheumatology nurse specialist
ZLE6Q	Discharge from rheumatology service

Supplementary Results

Supplementary Table S5. Number of AS patients in the primary and sensitivity analysis, overall and diagnosed during follow-up, and median age at diagnosis, by sex and Index of Multiple Deprivation (2015) quintile

	AS in primary analysis		AS in sensitivity analysis	
	Full cohort	**Incident cohort**	**Full cohort**	**Incident cohort**
Patient count (%)	12,333	3,101	4,882	1,071
Women	3,209 (26.0)	953 (30.8)	1,095 (22.4)	299 (27.9)
Men	9,124 (74.0)	2,148 (69.2)	3,787 (77.6)	772 (72.1)
Median age at diagnosis (IQR)	36 (28-47)	43 (33-56)	34 (27-44)	40 (32-51)
Women	38 (30-50)	43 (33-55)	35 (28-46)	40 (33-51)
Men	35 (28-46)	43 (33-56)	34 (27-43)	40 (31-50)
Index of Multiple Deprivation quintile (%¥)	7,276	1,751	2,970	611
1 (least deprived)	1,789 (24.6)	429 (24.5)	723 (24.3)	163 (26.7)
2	1,715 (23.6)	395 (22.6)	699 (23.5)	121 (19.8)
3	1,553 (21.3)	368 (21.0)	644 (21.7)	119 (19.5)
4	1,243 (17.1)	300 (17.1)	512 (17.2)	114 (18.7)
5 (most deprived)	976 (13.4)	259 (14.8)	392 (13.2)	94 (15.4)

Note: AS = ankylosing spondylitis, IQR = interquartile range

¥Percentage calculated for participants with available data.

Supplementary Table S6. Incidence of AS by calendar year and stratified by sex, age-group and geographical area (N = 7,532,147)

	Number of events (person-years at risk / 10,000)		Incidence rate per 10,000 person-years (95% CI)	
	Main analysis	Sensitivity analysis	Main analysis	Sensitivity analysis
Overall	3,102 (5,753.9)	1,071 (5,585.9)	0.54 (±0.02)	0.19 (±0.01)
Year				
1998	106 (146.3)	50 (146.4)	0.72 (±0.14)	0.34 (±0.09)
1999	119 (166.9)	58 (167.0)	0.71 (±0.13)	0.35 (±0.09)
2000	125 (202.6)	61 (202.8)	0.62 (±0.11)	0.30 (±0.08)
2001	142 (246.3)	64 (246.5)	0.58 (±0.09)	0.26 (±0.06)
2002	145 (273.5)	61 (273.7)	0.53 (±0.09)	0.22 (±0.06)
2003	181 (307.7)	81 (308.0)	0.59 (±0.09)	0.26 (±0.06)
2004	202 (329.6)	62 (329.9)	0.61 (±0.08)	0.19 (±0.05)
2005	177 (351.6)	74 (351.9)	0.50 (±0.07)	0.21 (±0.05)
2006	186 (357.5)	79 (357.8)	0.52 (±0.07)	0.22 (±0.05)
2007	140 (359.3)	46 (359.6)	0.39 (±0.06)	0.13 (±0.04)
2008	183 (361.1)	73 (361.4)	0.51 (±0.07)	0.20 (±0.05)
2009	176 (361.6)	68 (362.0)	0.49 (±0.07)	0.19 (±0.04)
2010	183 (356.0)	60 (356.3)	0.51 (±0.07)	0.17 (±0.04)
2011	166 (346.7)	45 (347.0)	0.48 (±0.07)	0.13 (±0.04)
2012	167 (341.1)	54 (341.5)	0.49 (±0.07)	0.16 (±0.04)
2013	198 (323.9)	63 (324.2)	0.61 (±0.09)	0.19 (±0.05)
2014	158 (293.8)	31 (294.1)	0.54 (±0.08)	0.11 (±0.04)
2015	133 (253.2)	20 (253.5)	0.53 (±0.08)	0.08 (±0.03)
2016	117 (202.3)	21 (202.5)	0.58 (±0.10)	0.10 (±0.04)
2017	98 (172.9)		0.57 (±0.11)	
Sex				
Female	954 (2,919.6)	299 (2,833.3)	0.33 (±0.02)	0.09 (±0.01)
Male	2,148 (2,834.3)	772 (2,752.6)	0.76 (±0.03)	0.21 (±0.02)
Age-group				
18-19	31 (115.7)	11 (112.2)	0.27 (±0.09)	0.09 (±0.06)
20-29	476 (773.7)	186 (750.6)	0.62 (±0.06)	0.24 (±0.04)
30-39	792 (987.7)	318 (960.2)	0.80 (±0.06)	0.33 (±0.04)
40-49	704 (1,102.1)	264 (1,072.2)	0.64 (±0.05)	0.25 (±0.03)
50-59	507 (999.4)	183 (968.4)	0.51 (±0.04)	0.19 (±0.03)
60-69	333 (814.7)	68 (790.9)	0.41 (±0.04)	0.09 (±0.02)
70-79	188 (581.4)	32 (563.5)	0.32 (±0.05)	0.06 (±0.02)
80-89	67 (313.1)	9 (218.9)	0.21 (±0.05)	0.04 (±0.03)
90-99	≤5	≤5		
Geographical area				
North East	53 (91.1)	25 (91.2)	0.58 (±0.16)	0.27 (±0.11)
North West	385 (648.3)	155 (637.5)	0.59 (±0.06)	0.24 (±0.04)
Yorkshire & The Humber	101 (173.8)	43 (174.0)	0.56 (±0.11)	0.25 (±0.07)
East Midlands	82 (186.2)	25 (186.4)	0.44 (±0.10)	0.13 (±0.05)
West Midlands	260 (542.8)	98 (531.2)	0.48 (±0.06)	0.18 (±0.04)
East of England	275 (472.3)	92 (466.8)	0.58 (±0.07)	0.20 (±0.04)
South West	269 (485.1)	88 (478.0)	0.55 (±0.07)	0.18 (±0.04)
South Central	307 (596.3)	123 (586.6)	0.51 (±0.06)	0.21 (±0.04)
London	271 (541.2)	74 (524.2)	0.50 (±0.06)	0.14 (±0.03)
South East Coast	322 (552.6)	84 (533.7)	0.58 (±0.06)	0.16 (±0.03)
Northern Ireland	149 (196.7)	65 (186.5)	0.76 (±0.12)	0.35 (±0.08)
Scotland	312 (598.1)	92 (562.0)	0.52 (±0.06)	0.16 (±0.03)
Wales	308 (656.2)	107 (616.7)	0.47 (±0.05)	0.17 (±0.03)

Note: results are not shown where the number of cases is ≤5

Supplementary Table S7. Percentage prevalence of AS by calendar year and stratified by sex, age-group and geographical area (N = 7,532,980)

	Percentage prevalence (95% CI)	
	Main analysis	Sensitivity analysis
Overall	0.15 (±0.003)	0.06 (±0.002)
Year		
1998	0.13 (±0.006)	0.07 (±0.004)
1999	0.14 (±0.006)	0.07 (±0.004)
2000	0.14 (±0.005)	0.07 (±0.004)
2001	0.14 (±0.005)	0.07 (±0.003)
2002	0.15 (±0.005)	0.07 (±0.003)
2003	0.15 (±0.004)	0.07 (±0.003)
2004	0.16 (±0.004)	0.07 (±0.003)
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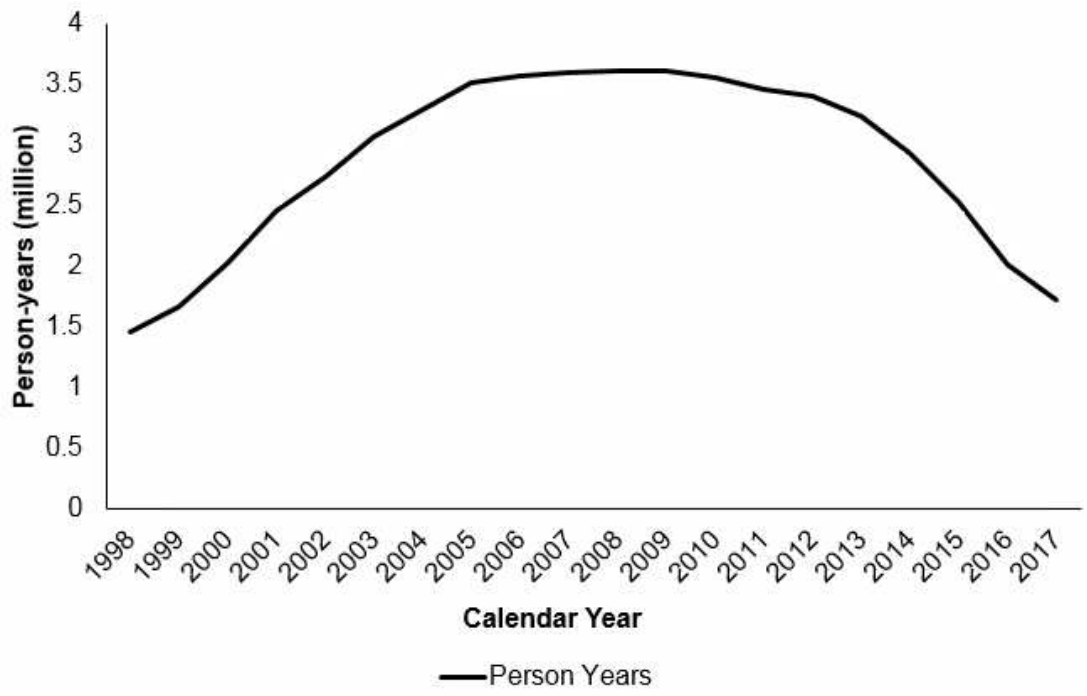
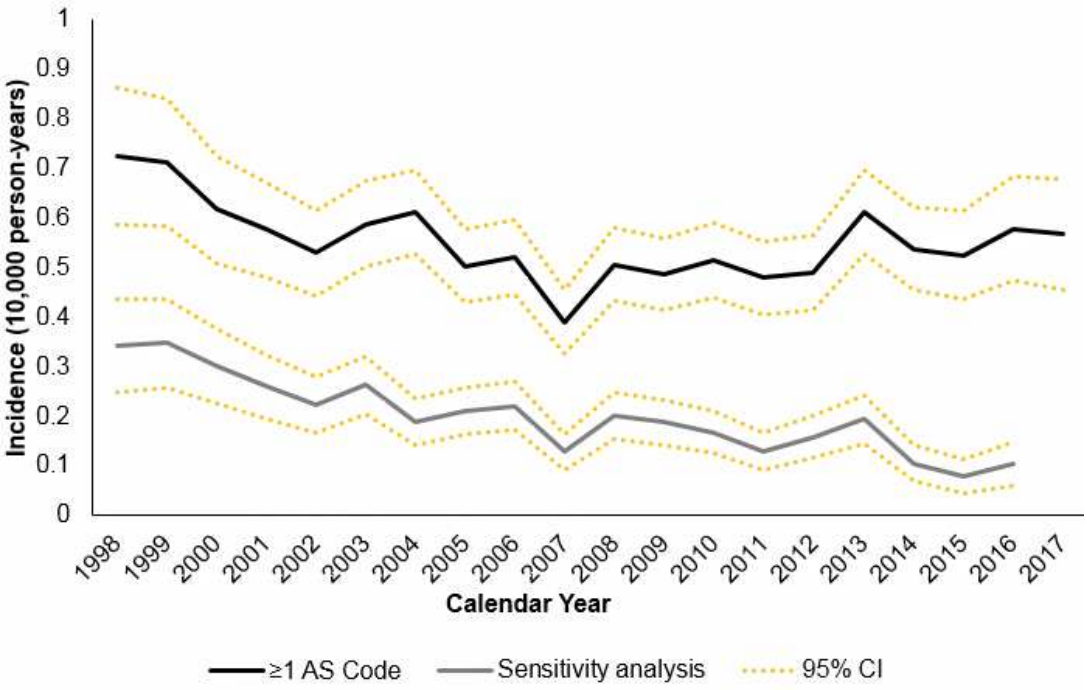
2007	0.16 (±0.004)	0.07 (±0.003)
2008	0.17 (±0.004)	0.07 (±0.003)
2009	0.17 (±0.004)	0.08 (±0.003)
2010	0.17 (±0.004)	0.08 (±0.003)
2011	0.17 (±0.004)	0.08 (±0.003)
2012	0.17 (±0.004)	0.08 (±0.003)
2013	0.17 (±0.005)	0.08 (±0.003)
2014	0.17 (±0.005)	0.08 (±0.003)
2015	0.18 (±0.005)	0.08 (±0.003)
2016	0.18 (±0.006)	0.08 (±0.003)
2017	0.18 (±0.006)	0.07 (±0.004)
Sex		
Female	0.08 (±0.003)	0.03 (±0.002)
Male	0.23 (±0.005)	0.10 (±0.003)
Age group		
18-19	0.001 (±0.001)	0.001 (±0.0003)
20-29	0.03 (±0.001)	0.016 (±0.001)
30-39	0.11 (±0.002)	0.06 (±0.002)
40-49	0.18 (±0.003)	0.09 (±0.002)
50-59	0.23 (±0.003)	0.11 (±0.002)
60-69	0.26 (±0.003)	0.11 (±0.002)
70-79	0.21 (±0.004)	0.07 (±0.002)
80-89	0.14 (±0.004)	0.03 (±0.002)
90-99	0.09 (±0.007)	0.01 (±0.003
Geographical area		
North East	0.16 (±0.02)	0.09 (±0.02)
North West	0.17 (±0.01)	0.07 (±0.01)
Yorkshire & The Humber	0.15 (±0.02)	0.07 (±0.01)
East Midlands	0.15 (±0.02)	0.06 (±0.01)
West Midlands	0.14 (±0.01)	0.06 (±0.01)
East of England	0.16 (±0.01)	0.07 (±0.01)
South West	0.17 (±0.01)	0.07 (±0.01)
South Central	0.16 (±0.01)	0.07 (±0.01)
London	0.11 (±0.01)	0.04 (±0.004)
South East Coast	0.17 (±0.01)	0.06 (±0.01)
Northern Ireland	0.18 (±0.02)	0.08 (±0.01)
Scotland	0.17 (±0.01)	0.05 (±0.01)
Wales	0.15 (±0.01)	0.06 (±0.01)

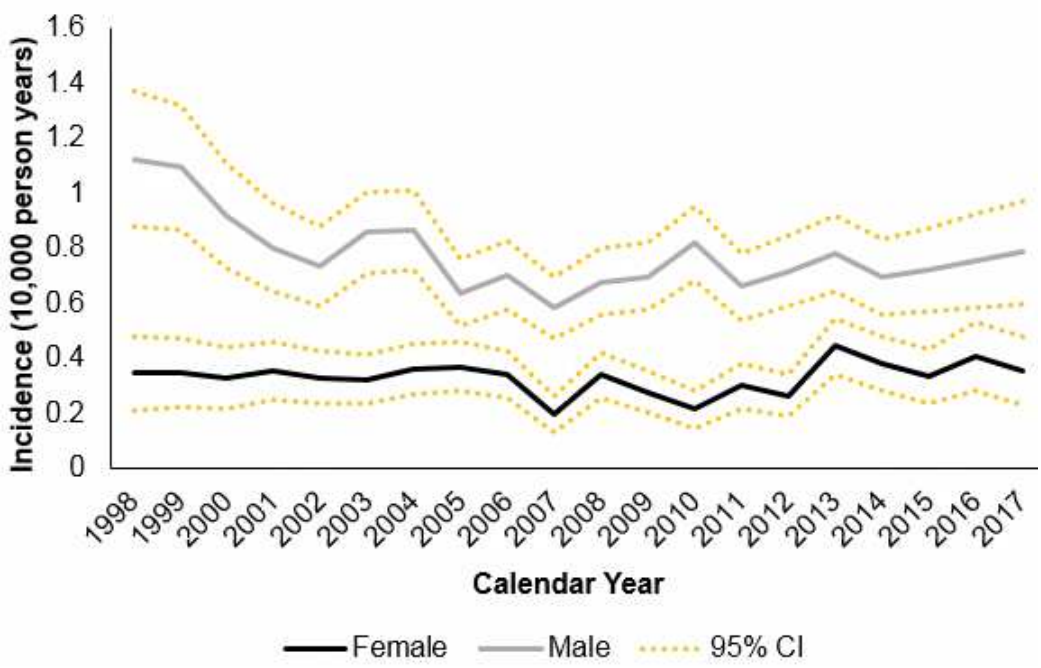
Supplementary Figure S1. Person-years (million) in the incidence 'at-risk' cohort per year, 1998-2017 (N = 8,052,546)



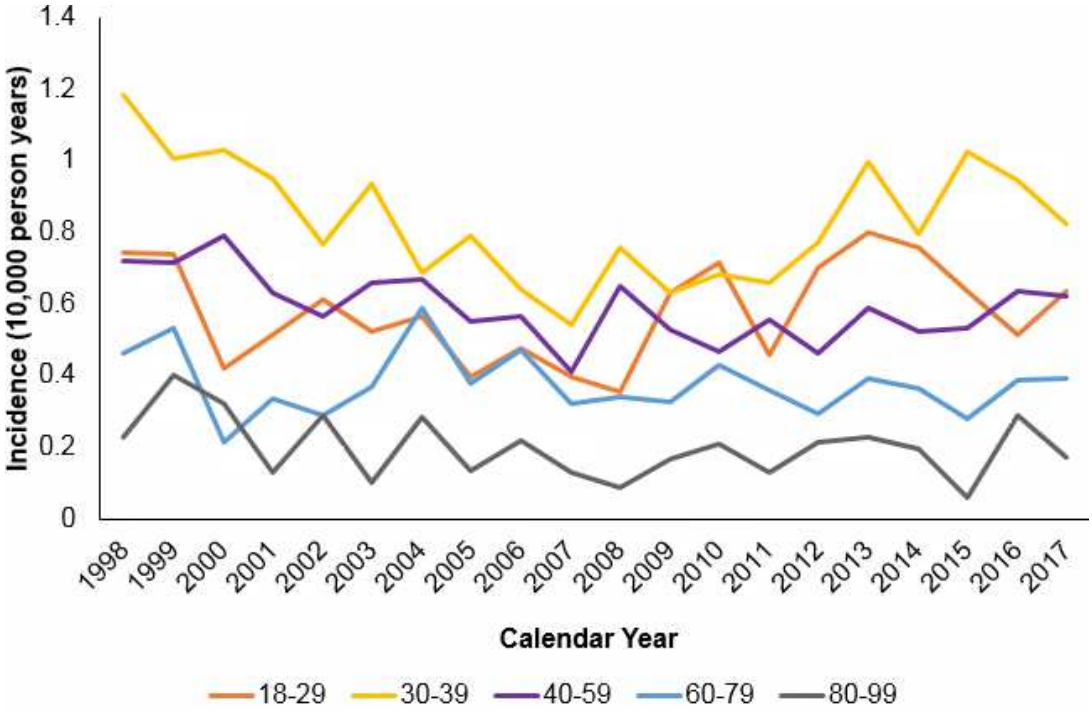
Supplementary Figure S2. Annual incidence rate of AS defined as having ≥1 AS diagnostic code, 1998-2017 (N = 8,052,546), and in the sensitivity analysis, 1998-2016 (N = 7,919,770)



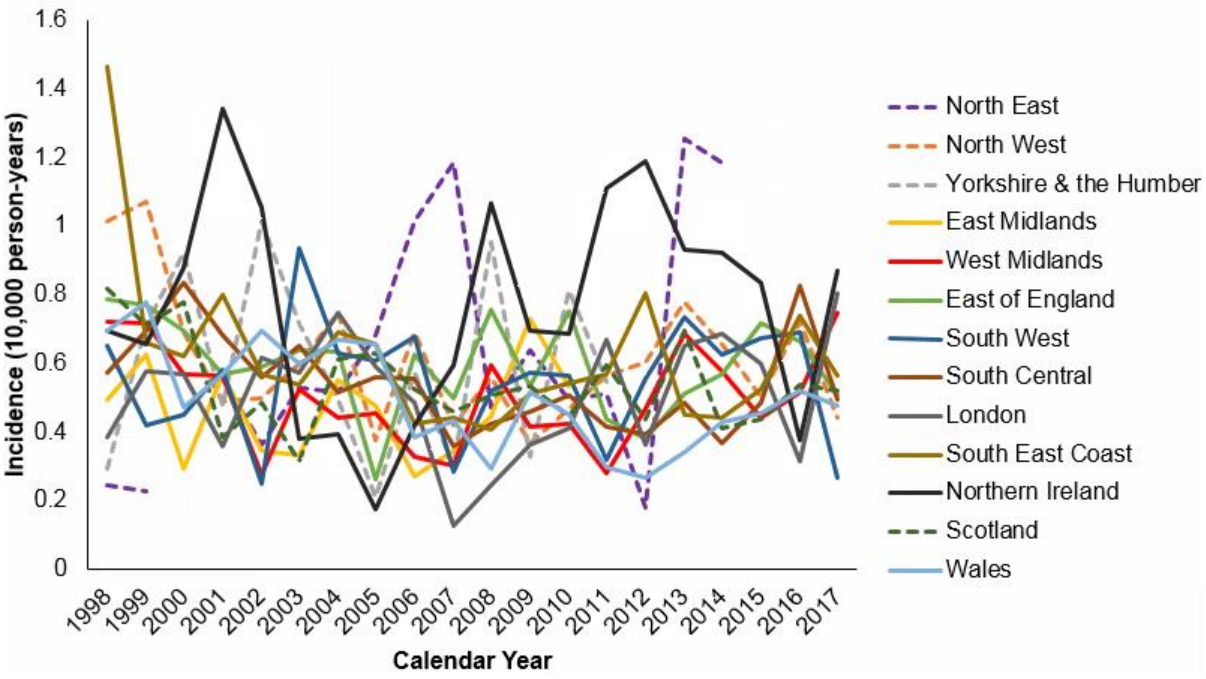
Supplementary Figure S3. Annual incidence rate of AS in women and men, 1998-2017 (N = 8,052,546)



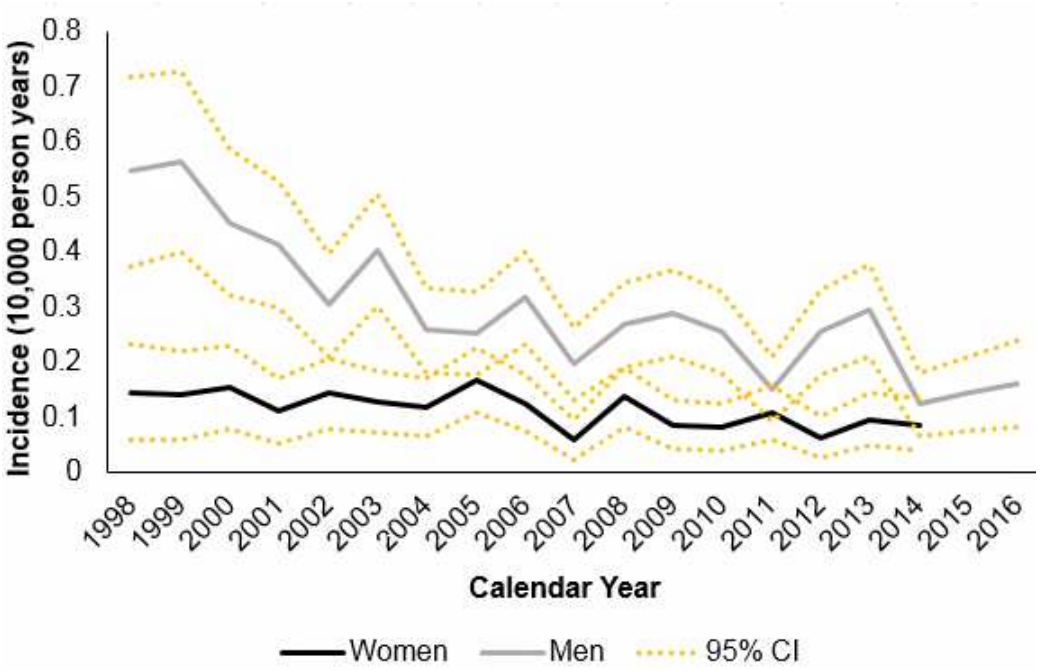
Supplementary Figure S4. Annual incidence rate of AS by age-group, 1998-2017 (N = 8,051,097)



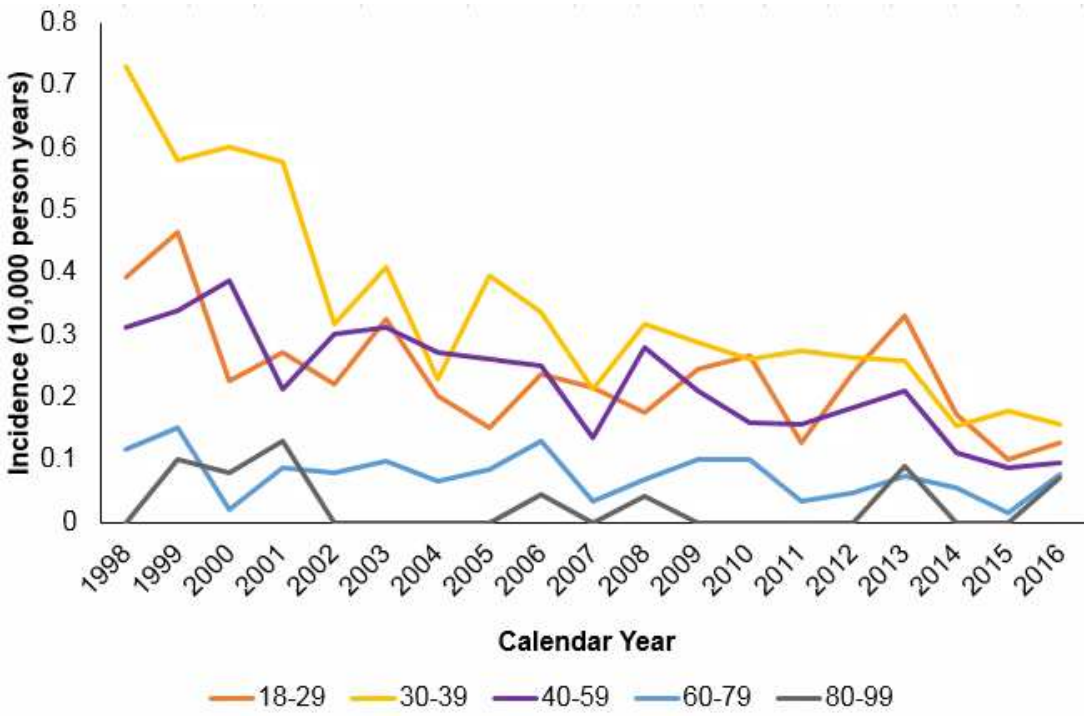
Supplementary Figure S5. Annual incidence rate of AS by geographic region, 1998-2017 (N = 8,044,388)



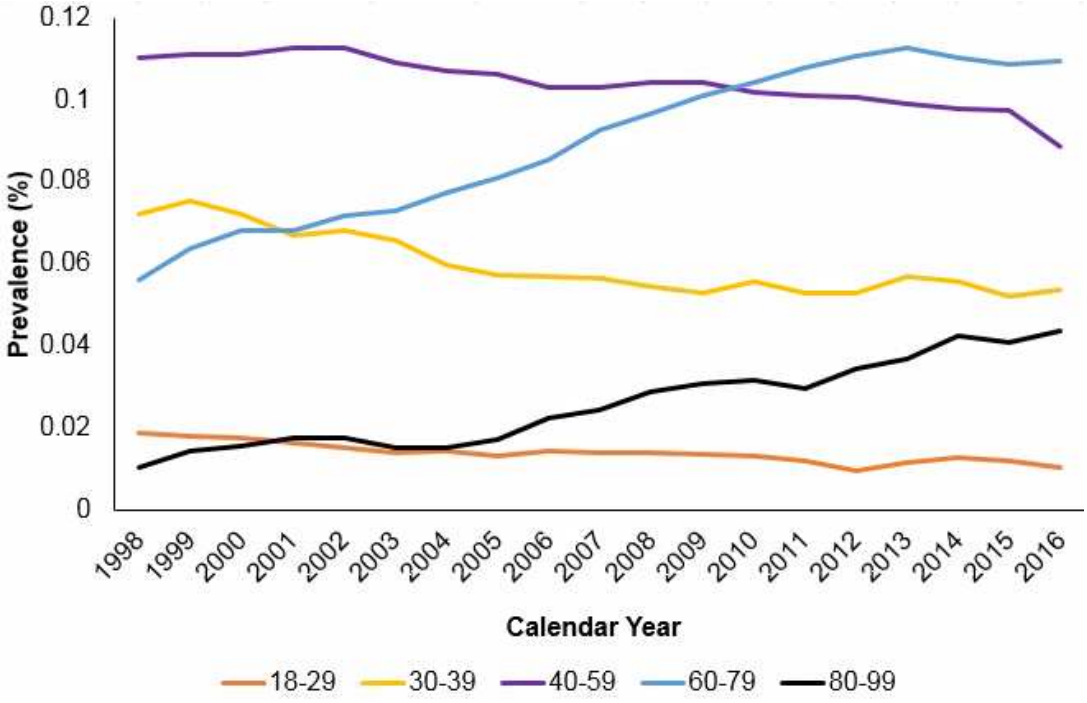
Supplementary Figure S6. Annual incidence rate of AS in women and men in the sensitivity analysis, 1998-2017 (N = 7,919,770)



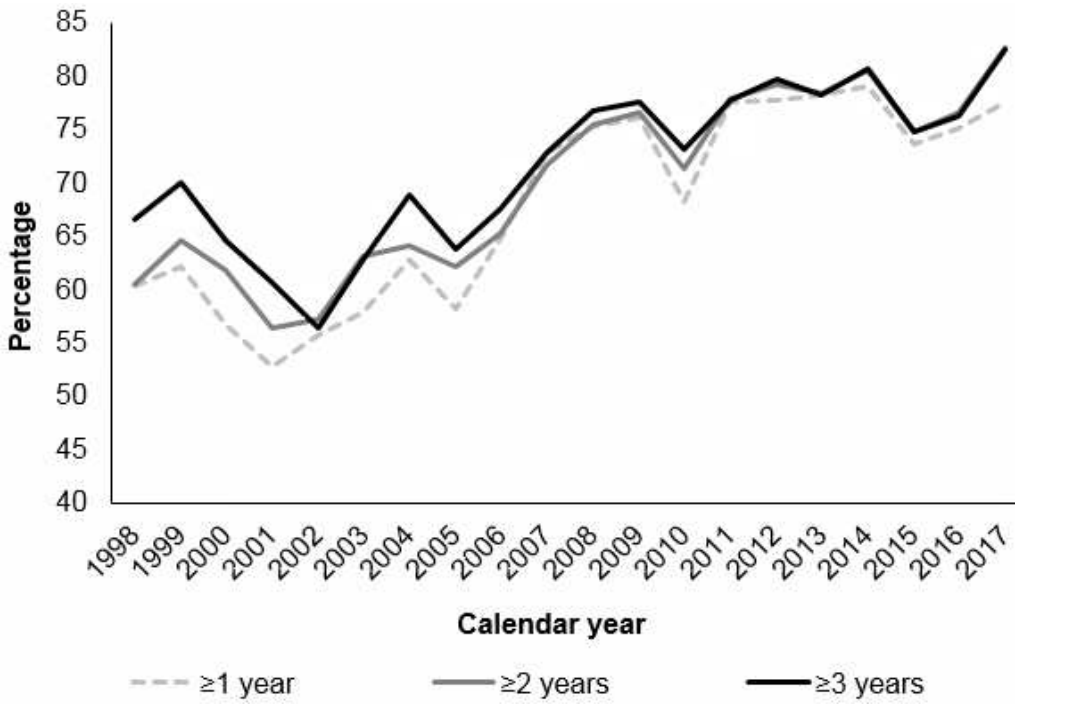
Supplementary Figure S7. Annual incidence rate of AS in the sensitivity analysis by age-group, 1998-2017 (N = 7,918,339)



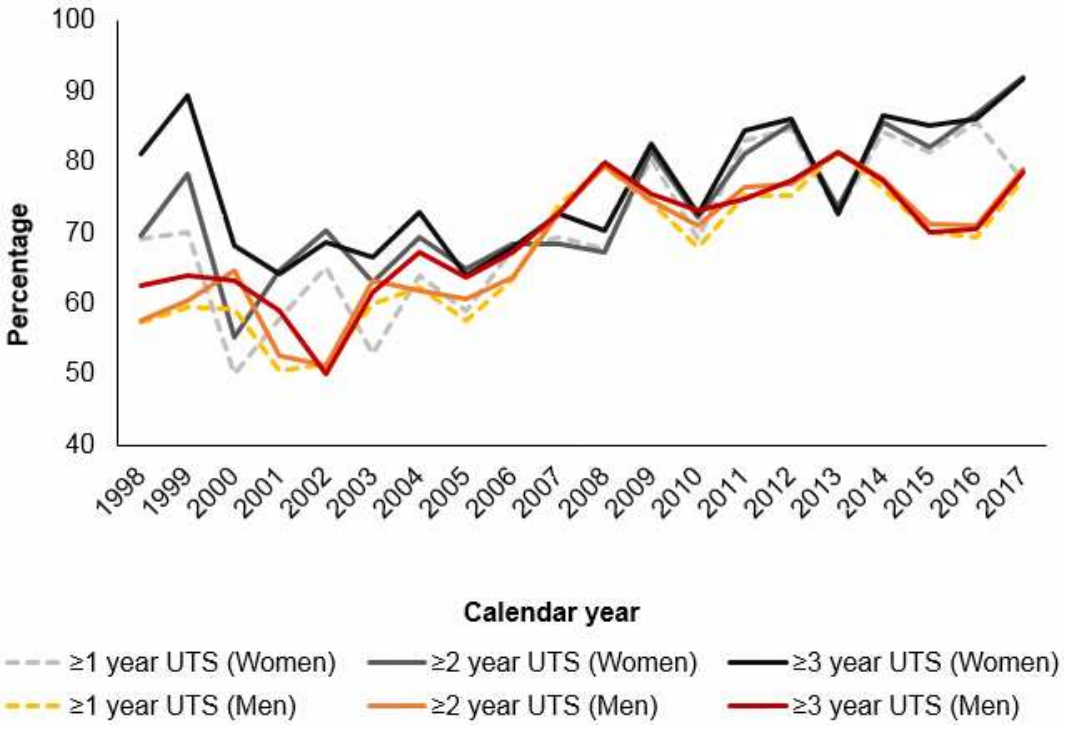
Supplementary Figure S8. Annual percentage prevalence of AS per age-group among patients aged 18-99 in the sensitivity analysis, 1997-2016 (N = 7,506,959)



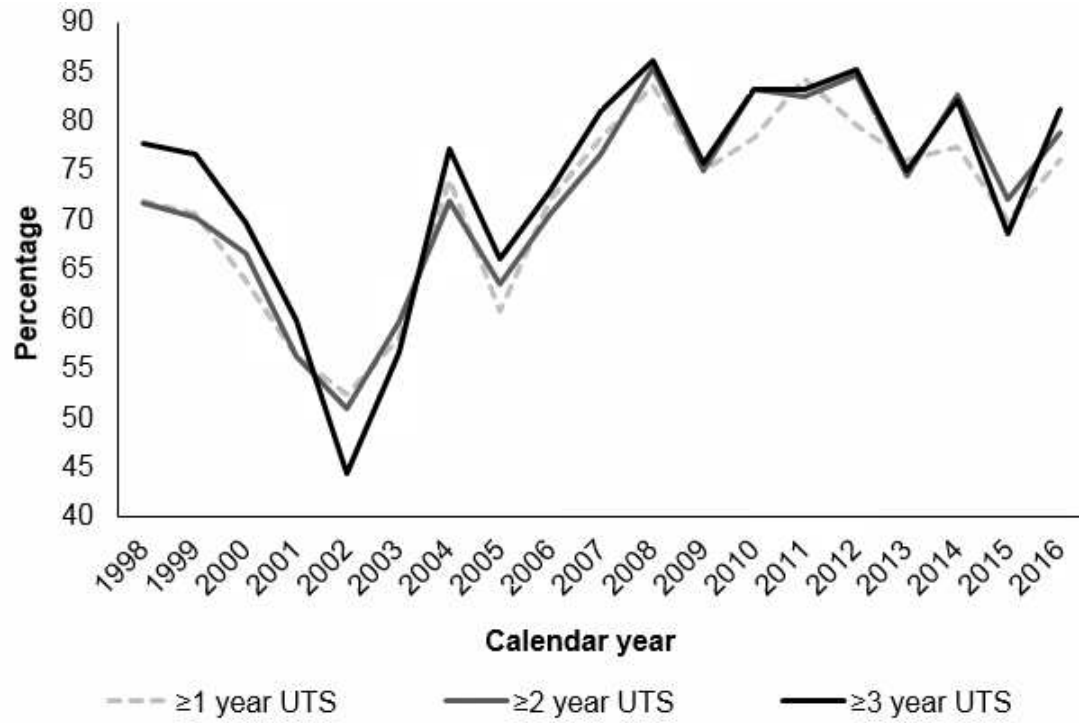
Supplementary Figure S9. Annual percentage of patients diagnosed with AS (having ≥1, ≥2 and ≥3 years of prior UTS registration) that had a prior back-pain symptom code, 1998-2017 (N = 3,101; N = 2,734; N = 2,417)



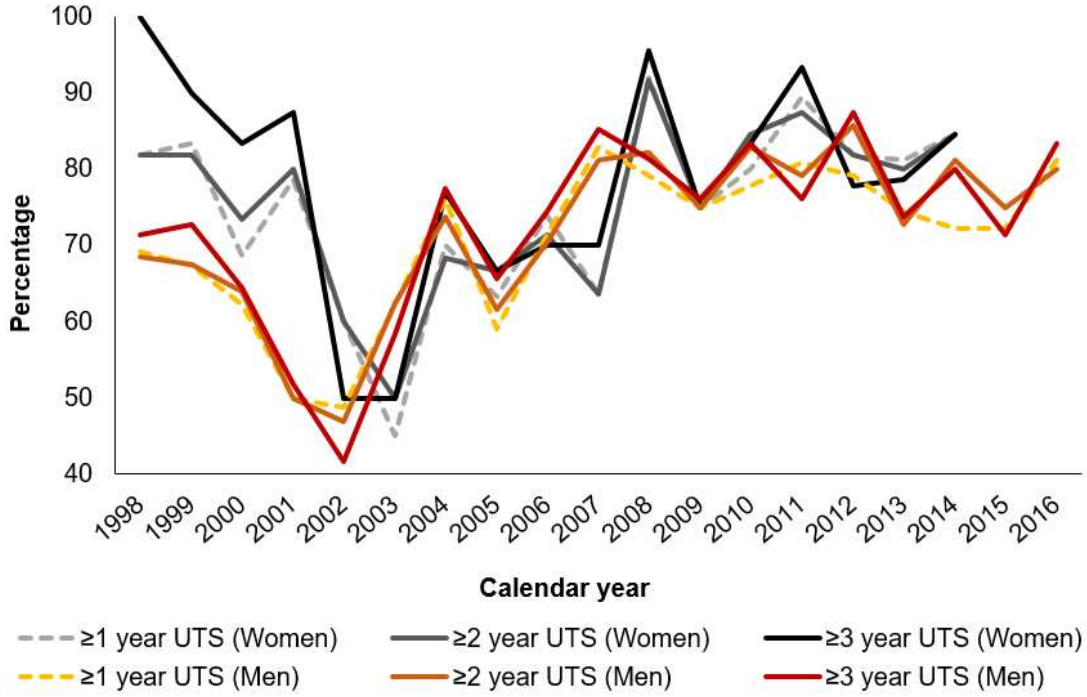
Supplementary Figure S10. Annual percentage of patients diagnosed with AS (having ≥1, ≥2 and ≥3 prior years of UTS) that had a prior back-pain symptom code, for women and men 1998-2017 (N = 3,101; N = 2,734; N = 2,417)



Supplementary Figure S11. Annual percentage of patients with in the sensitivity analysis, having ≥1, ≥2 and ≥3 prior years of UTS, who had a prior back-pain symptom code, 1998-2016 (N = 1,071; N = 957; N = 821)

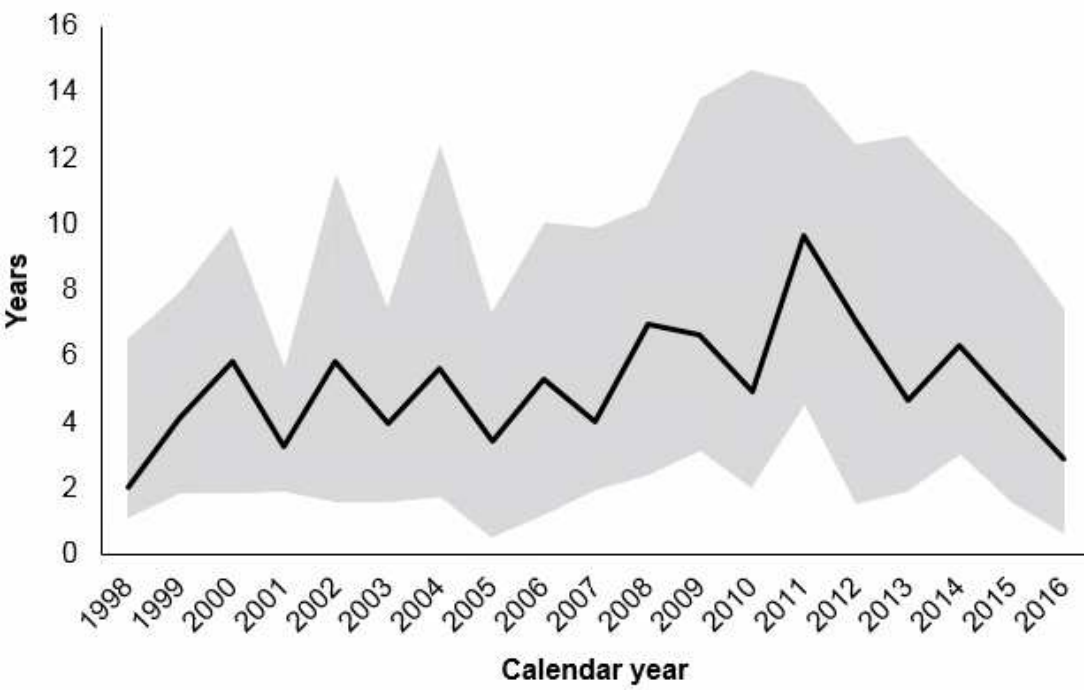


Supplementary Figure S12. Annual percentage of patients in the sensitivity analysis, having ≥1, ≥2 and ≥3 prior years of UTS, who had a prior back-pain symptom code, for women and men, 1998-2016 (N = 1,071; N = 957; N = 821)

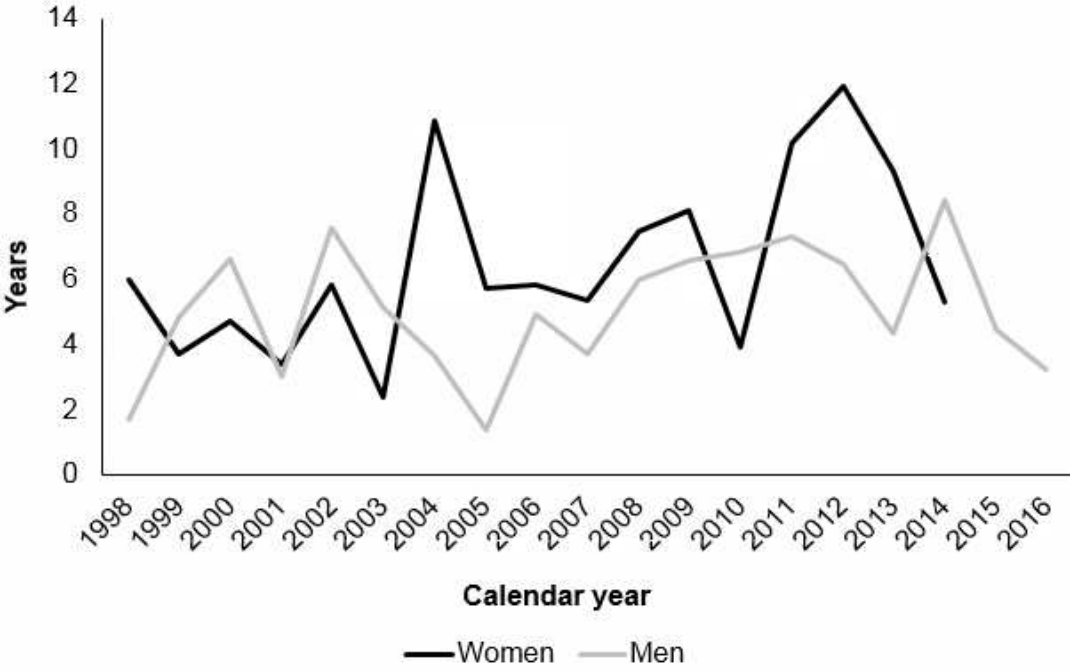


Note: data suppressed where there are ≤5 cases

Supplementary Figure S13. Median time in years from first recorded symptom to first diagnosis in the sensitivity analysis, 1998-2016 (N = 757)

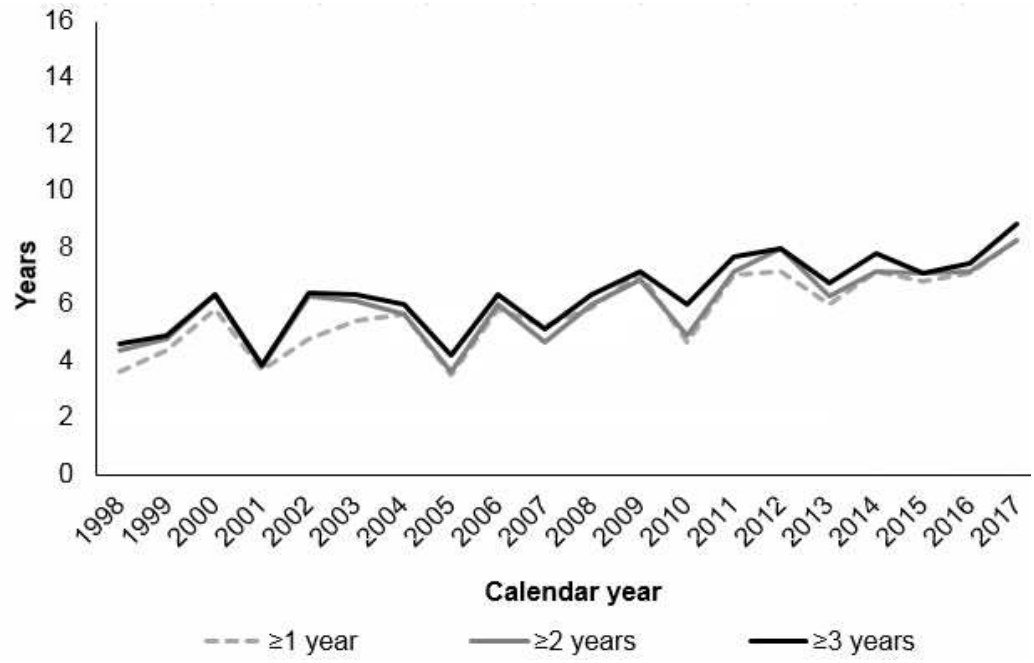


Supplementary Figure S14. Median time in years from first recorded symptom to first diagnosis in the sensitivity analysis, for women and men, 1998-2016 (N = 757)

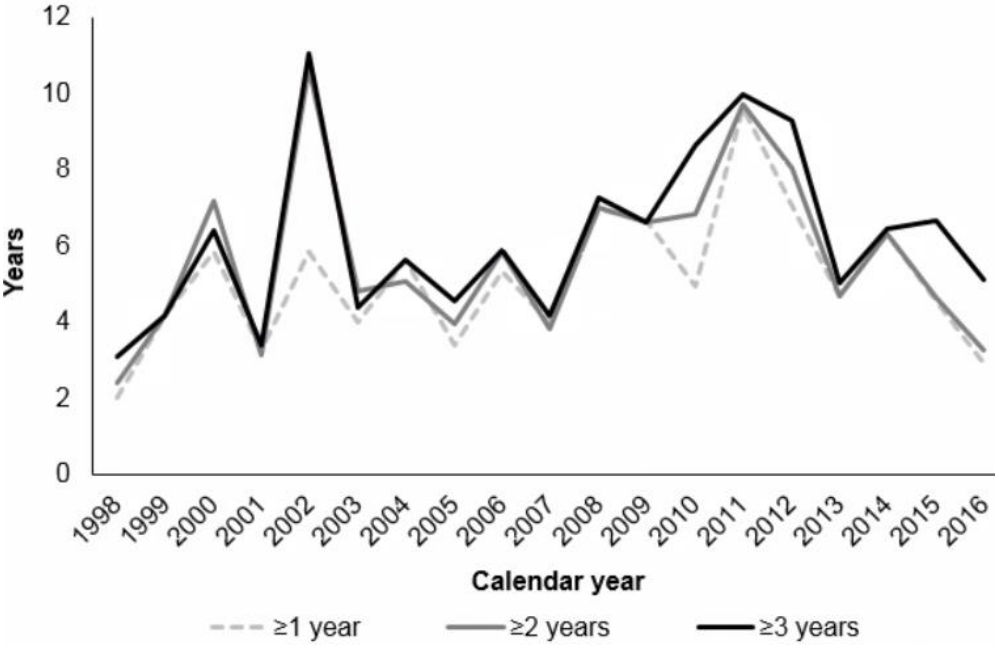


Note: data suppressed where there are ≤5 cases

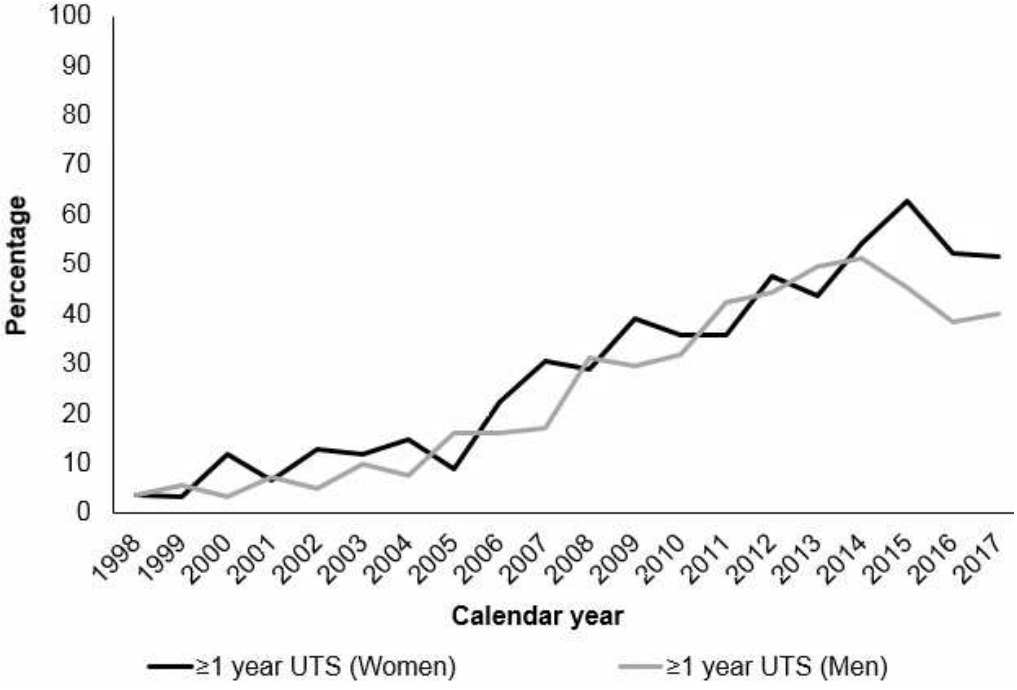
Supplementary Figure S15. Median time in years from symptom to diagnosis, for patients with ≥1, ≥2 and ≥3 years prior UTS registration, 1998-2017 (N = 2,120; N = 1,929; N = 1,750)



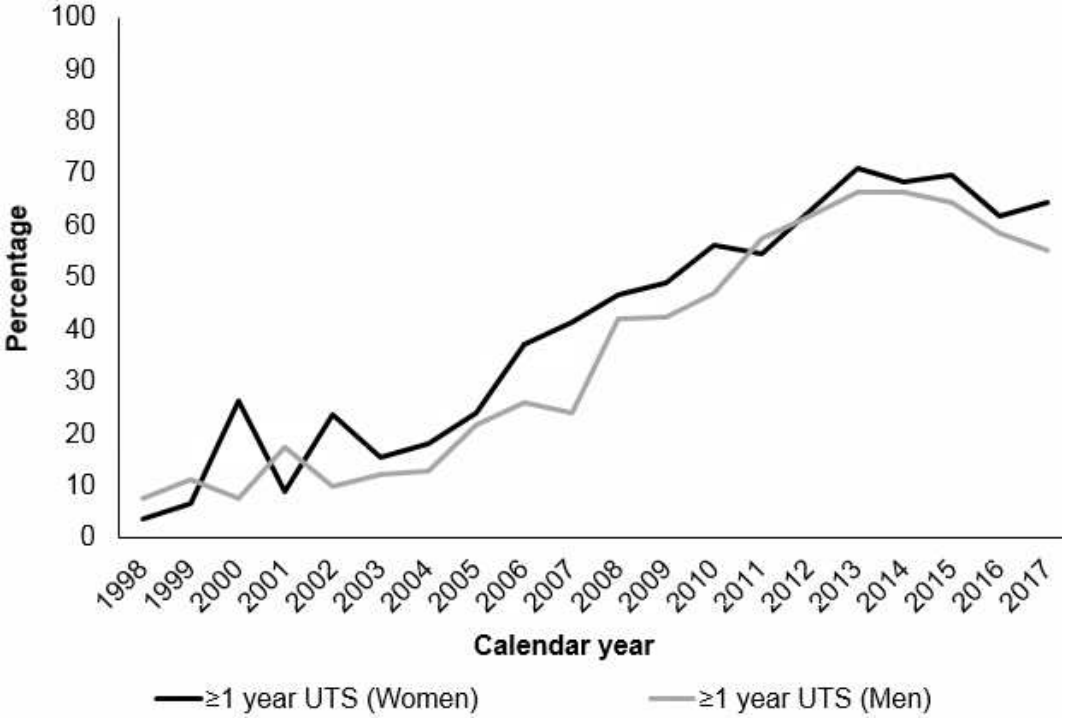
Supplementary Figure S16. Median time in years from symptom to diagnosis, for patients with ≥1, ≥2 and ≥3 years prior UTS registration in the sensitivity analysis, 1998-2016 (N = 757; N = 688; N = 606)



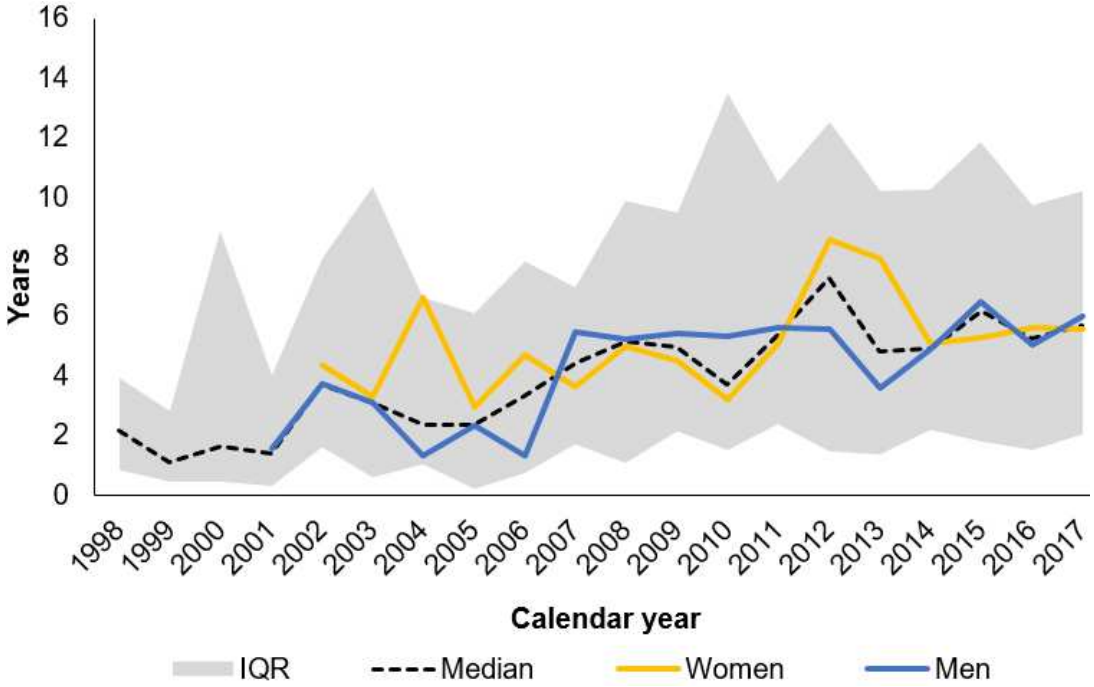
Supplementary Figure S17. Annual percentage of patients diagnosed with AS that had prior back pain and rheumatology referral, for women and men 1998-2017 (N = 3,101)



Supplementary Figure S18. Annual percentage of patients diagnosed with AS that had a prior rheumatology referral, for women and men 1998-2017 (N = 3,101)

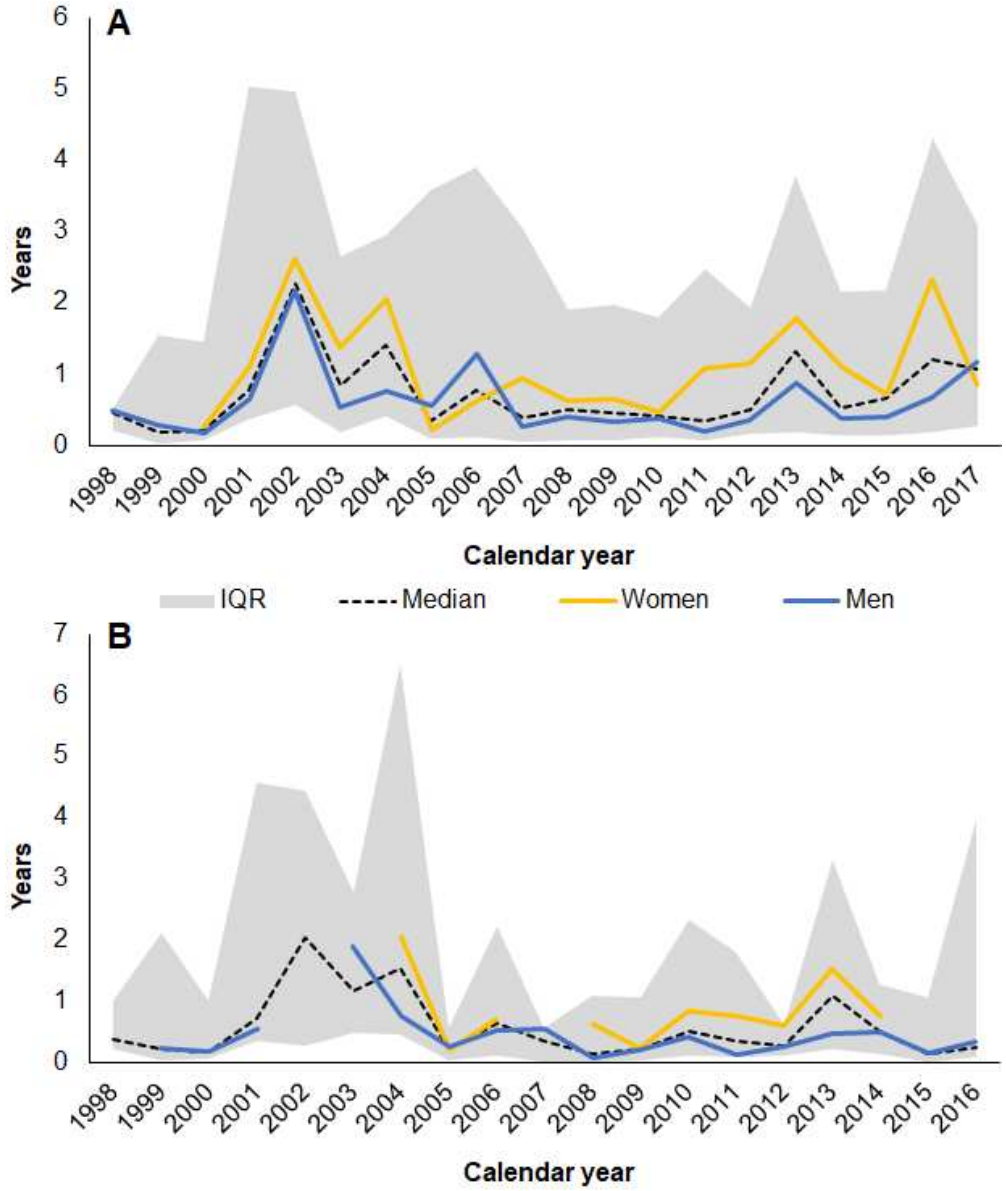


Supplementary Figure S19. Annual median time in years from first recorded back pain to rheumatology referral, for men and women, 1998-2017 (N = 819)



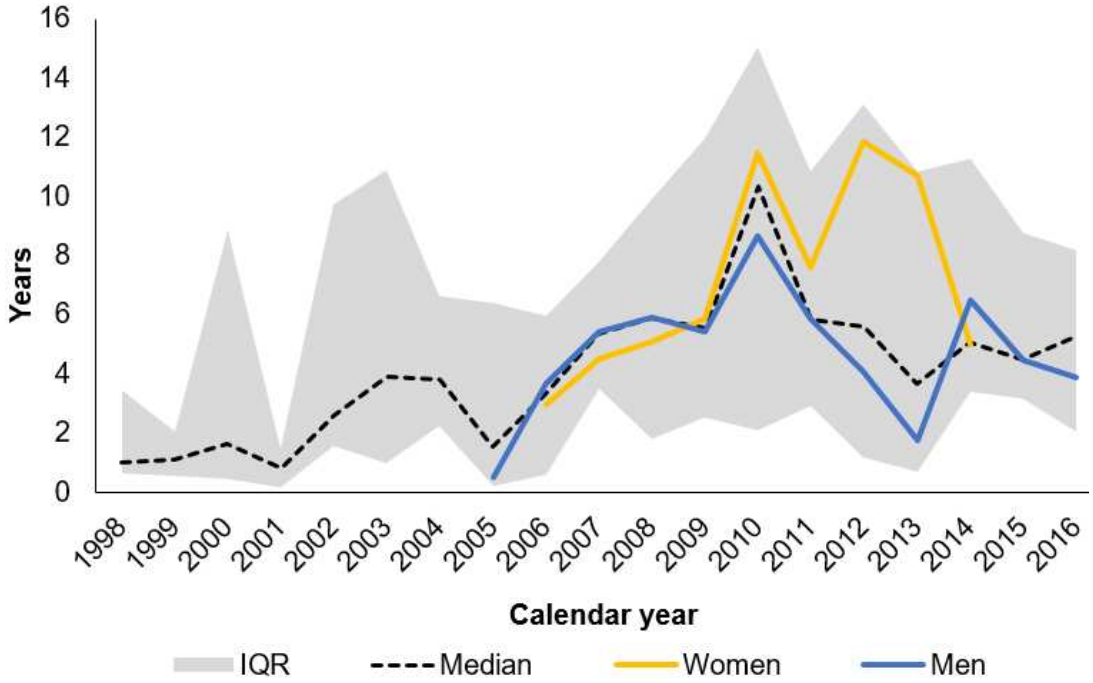
Note: data suppressed where there are ≤5 cases

Supplementary Figure S20. Annual median time in years from first rheumatology referral to diagnosis, for women and men: A) primary analysis, 1998-2017 (N = 1,167); B: sensitivity analysis, 1998-2016 (N = 399)



Note: data suppressed where there are ≤5 cases

Supplementary Figure S21. Annual median time in years from first recorded back pain symptom to rheumatology referral, for men and women in the sensitivity analysis, 1998-2016 (N = 279)



Note: data suppressed where there are ≤5 cases