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16-10-2024

## Temporal trends in adverse pregnancy outcomes in axial spondyloarthritis in Sweden: a cohort study.

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**Supplementary appendix**

Supplement to Morin M, Frisell T, Stephansson O, and Hellgren K. Adverse pregnancy outcomes in axial spondyloarthritis: temporal trends in a Swedish nationwide cohort study.

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## Supplementary methods

### Setting and data sources

Health care in Sweden is public and tax-funded, and maternal care during pregnancy is free of charge. Data regarding antenatal care, delivery, and foetal outcomes are prospectively collected in the Medical Birth Register (MBR), including over 98% of births since 1973.<sup>1</sup> The information in MBR can be linked with that in other national registers by the unique personal identification number given to all Swedish residents.<sup>2</sup> The National Patient Register (NPR) contains information on hospitalizations since 1964 (nationwide since 1987) and outpatient specialist visits since 2001,<sup>3</sup> with associated diagnosis codes according to the Swedish version of the International Classification of Disease (ICD). The Prescribed Drug Register (PDR), introduced in July 2005, contains complete information on prescription medicines collected from Swedish pharmacies.<sup>4</sup> Additional demographic data such as age, sex, educational level, and income are available from population registers held by Statistics Sweden: the Total Population Register and the Longitudinal Integrated Database for Health Insurance and Labour Market Studies (LISA).<sup>5,6</sup> Statistics Sweden also holds the Multi-Generation Register, containing the personal identification number of the parents of each individual, enabling the linkage of data from mothers and children across registers.<sup>7</sup> The Swedish Rheumatology Quality Register (SRQ) is a clinical register longitudinally collecting disease characteristics, disease activity, and anti-rheumatic treatment as registered by the treating rheumatologist,<sup>8</sup> and can also be linked to the other registers via the personal identification number.

## Supplementary tables

**Supplementary table 1.** Sources and definitions of variables

	Source	ATC and ICD-10 codes	Details/Definition
<b>Exposure</b>			
axSpA	NPR SRQ	ICD-10 M45.9, M08.1, M46.8, M46.9	2 visits, $\geq 1$ visit at specialist clinic of internal medicine or rheumatology, with a recorded diagnosis of either AS or uSpA in NPR, after 2001. Or registered in SRQ with AS or uSpA after 2001.
<b>Outcomes</b>			
Pre-eclampsia	MBR	ICD-10 O14, O15	According to the clinical definition of pre-eclampsia during the study period: Two blood pressure measurements of $\geq 140/90$ with at least 4h apart combined with proteinuria ( $\geq 0.3$ grams per 24 h or one or more on a urine dipstick on at least two subsequent occasions)
Gestational diabetes	MBR	ICD-10 O244	New onset diabetes during pregnancy
Gestational hypertension	MBR	ICD-10 O13	New onset hypertension after 20 gw of pregnancy
Stillbirth	MBR		Non-live birth $\geq 22+0$ gw since 1 July 2008, before that non-live birth $\geq 28+0$ gw
Preterm birth	MBR		Birth before gw 37+0
Moderately preterm birth	MBR		Birth between gw 32+0-36+6
Very preterm birth	MBR		Birth between gw 22+0-31+6
Spontaneous onset of preterm birth	MBR		Birth before gw 37+0 with spontaneous onset of labour or preterm premature rupture of membranes (PPROM)
Medically indicated onset of preterm birth	MBR		Birth before gw 37+0 with an onset of labour that was not spontaneous, i.e. induction or prelabour Caesarean delivery
Caesarean delivery (all)	MBR		Both elective and emergency Caesarean deliveries
Elective caesarean delivery	MBR		Planned caesarean delivery before start of labour
Emergency caesarean delivery	MBR		Not planned caesarean delivery

Small for gestational age (SGA)	MBR		Birthweight below 2 standard deviations of sex-specific mean weight per gestational age
Large for gestational age (LGA)	MBR		Birthweight above 2 standard deviations of sex-specific mean weight per gestational age
5 min Apgar score <7	MBR		
Neonatal or severe infant infection within the first year of life in the offspring	NPR (main diagnosis) and MBR	ICD-10 A00-B99, G00, G01, G02, G04.2, G05, G06, G07, H66, H67, H70, J00, J01, J02, J03, J04, J05, J06, J09, J10, J11, J12, J13, J14, J15, J16, J17, J18, J20, J21, J22, J32, J34.0, J36, J38.3, J39.0, J39.1, K10.2, L00, L01, L02, L03, L04, L05, L08, M00, M01, M46.2, M46.3, M46.4, M46.5, M86, N10, N30	An ICD code of infection at birth or requiring hospitalization i.e in inpatient care within one year after birth
<b>Other covariates</b>			
Maternal age	MBR		In years. Modelled as third-grade polynomial.
Parity	MBR		Coded primiparous/parous
Maternal country of birth	Total Population Register		Coded Nordic/Non-Nordic
Annual disposable income	LISA		In year before pregnancy, in quartiles.
Level of formal education	LISA		In year before pregnancy, coded ≤9 years, 10-12 years, >12 years
Smoking	MBR		At first antenatal visit. Coded smoker/non-smoker
BMI	MBR		At first antenatal visit. Modelled as third-grade polynomial.
Height	MBR		At first antenatal visit. Modelled as third-grade polynomial.
Previous preterm birth	MBR		Birth before gw 37+0 in a previous pregnancy
<i>Medical history</i>			
Diabetes	NPR or PDR	ICD-10 E10-E14, O24.0 O24.1, O24.2, O24.3, O24.9 And/or dispensed prescription of ATC A10	Ever before pregnancy, but earliest 1997 for NPR (start of ICD10) and July 2005 for PDR (start of PDR)
Hypertension	NPR or MBR	ICD-10 I10, I11, I12, I13, I15.0 in NPR and/or checkbox in MBR and/or ICD-10 O10 in MBR	Ever before pregnancy, but earliest 1997 for NPR (start of ICD10)
Thyroid disease	NPR or PDR	ICD-10 E038, E039, E063, E050, E051, E052, E053, E058, E059, O905 and/or PDR: dispensed prescription of ATC H03AA01 or H03AA02  But not: Diagnosis of thyroid cancer (C739) in the Cancer register or NPR (main diagnosis), or dispensed prescription of ATC C01BD01, N05AN01, L03AB01/L03AB04/L03AB05	Ever before pregnancy, but earliest 1997 for NPR (start of ICD10) and July 2005 for PDR (start of PDR)
<i>Measures of disease activity/inflammation/functional status</i>			
Elevated CRP	SRQ		CRP >10 mg/litre in year before or during pregnancy
BASDAI	SRQ		In year before or during pregnancy, continuous
HAQ-DI	SRQ		In year before or during pregnancy, continuous
<i>Treatment</i>			
TNF $\alpha$	PDR or SRQ (for infliximab)	ATC L04AB01, L04AB02, L04AB04, L04AB05, or L04AB06	Dispensed prescription in year before pregnancy, dispensed prescription ever during pregnancy, or treatment registered in SRQ during these periods (for infliximab)
csDMARDs	PDR	ATC A07EC01, L01BA01/L04AX03, L04AX01, or P01BA	Dispensed prescription in year before pregnancy Dispensed prescription ever during pregnancy
NSAIDs	PDR	ATC M01A	Dispensed prescription in year before pregnancy Dispensed prescription ever during pregnancy
Corticosteroids	PDR	ATC H02AB	Dispensed prescription in year before pregnancy

Heavy treatment	Composed by multiple treatment variables		Dispensed prescription ever during pregnancy Dispensed prescriptions of at least 2 of TNFi, csDMARDs, or corticosteroids
<i>SpA manifestations</i>			
Anterior uveitis	NPR	ICD-10 H20, H22.1	≥2 visits, ≥1 at specialist clinic of ophthalmology, ever before delivery
Psoriatic arthritis	NPR or SRQ	ICD-10 L40.5, M07.3, M09.0	≥2 visits, ≥1 at specialist clinic of internal medicine, rheumatology or dermatology, or registered in SRQ, ever before delivery
Psoriasis	NPR or PDR	ICD-10 L40 (except L40.5) or dispensed prescription of ATC D05	≥2 visits, ≥1 visit at specialist clinic of dermatology, ever before delivery
Inflammatory Bowel Disease	NPR or SRQ	ICD-10 K50, M07.4, M09.1 K51, M07.5, M09.2	2 visits, ≥1 visit at specialist clinic of internal medicine, rheumatology or gastroenterology, or registered in SRQ, ever before delivery
<i>Other rheumatic diagnoses</i>			
Rheumatoid Arthritis	NPR or SRQ	ICD-10 M05, M06, M08.0, M08.3	≥2 visits, ≥1 visit at specialist clinic of internal medicine or rheumatology, or registered in SRQ, ever before pregnancy
Systemic Lupus Erythematosus	NPR or SRQ	ICD-10 M32, L93	≥2 visits, ≥1 visit at specialist clinic of internal medicine, rheumatology, or nephrology, or in SRQ, ever before pregnancy

NPR=National Patient Register. SRQ=Swedish Rheumatology Quality Register. MBR=Medical Birth Register. LISA=Longitudinal integrated database for health insurance and labour market studies. PDR=Prescribed Drug Register. gw=gestational week. CRP=C-reactive protein. BASDAI=Bath Ankylosing Spondylitis Disease Activity Index. HAQ-DI=Health Assessment Questionnaire–Disability Index. NSAIDs=non-steroidal anti-inflammatory drugs. csDMARDs=conventional systemic disease-modifying anti-rheumatic drugs. TNFi=tumour necrosis factor inhibitors. ATC=Anatomic Therapeutic Chemical. ICD-10=International Classification of Diseases, 10<sup>th</sup> revision.

**Supplementary table 2.** Relative risks of adverse pregnancy outcomes among births in Swedish women with axSpA (n=1580) and comparator births (n=15792; matched 1:10 on year of delivery, maternal age, and parity).

	axSpA births n (%) events	Comparator births n (%) events	Risk ratio (95% CI)	Adj. risk ratio* (95% CI)
<b>Maternal outcomes</b>				
<b>Among all births</b>				
Pre-eclampsia	61 (3.9)	441 (2.8)	1.38 (1.04–1.84)	1.44 (1.08–1.92)
Gestational diabetes	33 (2.1)	320 (2.0)	1.03 (0.71–1.50)	1.23 (0.84–1.82)
Gestational hypertension	32 (2.0)	316 (2.0)	1.01 (0.70–1.46)	0.94 (0.64–1.38)
Stillbirth	0 (0.0)	64 (0.4)	..	..
<b>Among live births</b>				
Caesarean delivery	382 (24.2)	2760 (17.5)	1.38 (1.24–1.53)	1.39 (1.24–1.55)
Elective	236 (14.9)	1496 (9.5)	1.57 (1.36–1.81)	1.59 (1.37–1.84)
Emergency	146 (9.2)	1264 (8.0)	1.15 (0.97–1.37)	1.15 (0.96–1.37)
Preterm birth	99 (6.3)	682 (4.3)	1.44 (1.17–1.79)	1.43 (1.13–1.80)
Moderately preterm	92 (5.8)	575 (3.6)	1.59 (1.27–1.99)	1.55 (1.22–1.96)
Very preterm	7 (0.4)	107 (0.7)	0.65 (0.30–1.39)	0.64 (0.26–1.58)
Medically indicated preterm	30 (1.9)	206 (1.3)	1.45 (0.97–2.17)	1.44 (0.93–2.22)
Spontaneous preterm	69 (4.4)	472 (3.0)	1.45 (1.13–1.87)	1.44 (1.09–1.90)
<b>Infant outcomes (live births)</b>				
Apgar <7 at 5 min	20 (1.3)	287 (1.8)	0.69 (0.43–1.11)	0.69 (0.41–1.15)
Small for gestational age†	25 (1.6)	352 (2.2)	0.71 (0.48–1.04)	0.77 (0.51–1.16)
Large for gestational age†	61 (3.9)	582 (3.7)	1.04 (0.80–1.36)	1.02 (0.77–1.34)
Infant infection	105 (6.6)	795 (5.0)	1.31 (1.08–1.59)	1.29 (1.05–1.59)

Relative risks from modified Poisson regression. \*Adjusted for year of delivery, maternal age, parity, height, body-mass index, smoking, educational level, disposable income and country of birth. †1 axSpA birth and 13 comparator births were missing data for small- and large for gestational age.

**Supplementary table 3.** Risk differences of adverse pregnancy outcomes among births in Swedish women with axSpA (n=1580) and comparator births (n=15792; matched 1:10 on year of delivery, maternal age, and parity).

	axSpA births n (%) events	Comparator births n (%) events	Risk difference (95% CI)	Adj. risk difference* (95% CI)
<b>Maternal outcomes</b>				
<b>Among all births</b>				
Pre-eclampsia	61 (3·9)	441 (2·8)	1·07 (0·00–2·14)	1·27 (0·12–2·42)
Gestational diabetes	33 (2·1)	320 (2·0)	0·06 (-0·72–0·84)	0·41 (-0·41–1·23)
Gestational hypertension	32 (2·0)	316 (2·0)	0·02 (-0·72–0·77)	-0·14 (-0·94–0·65)
Stillbirth	0 (0·0)	64 (0·4)	..	..
<b>Among live births</b>				
Caesarean delivery	382 (24·2)	2760 (17·5)	6·63 (4·13–9·12)	6·79 (4·22–9·35)
Elective	236 (14·9)	1496 (9·5)	5·43 (3·40–7·45)	5·55 (3·46–7·64)
Emergency	146 (9·2)	1264 (8·0)	1·20 (-0·37–2·77)	1·24 (-0·40–2·87)
Preterm birth	99 (6·3)	682 (4·3)	1·93 (0·64–3·22)	1·75 (0·46–3·03)
Moderately preterm	92 (5·8)	575 (3·6)	2·17 (0·92–3·41)	1·94 (0·69–3·19)
Very preterm	7 (0·4)	107 (0·7)	-0·24 (-0·59–0·11)	-0·19 (-0·52–0·14)
Medically indicated preterm	30 (1·9)	206 (1·3)	0·59 (-0·15–1·33)	0·53 (-0·20–1·25)
Spontaneous preterm	69 (4·4)	472 (3·0)	1·37 (0·30–2·43)	1·25 (0·16–2·34)
<b>Infant outcomes (live births)</b>				
Apgar <7 at 5 min	20 (1·3)	287 (1·8)	-0·56 (-1·17–0·05)	-0·55 (-1·18–0·08)
Small for gestational age†	25 (1·6)	352 (2·2)	-0·66 (-1·29–0·02)	-0·49 (-1·18–0·19)
Large for gestational age†	61 (3·9)	582 (3·7)	0·16 (-0·87–1·19)	0·08 (-0·99–1·15)
Infant infection	105 (6·6)	795 (5·0)	1·59 (0·34–2·84)	1·53 (0·20–2·86)

Risk differences from linear regression with robust standard errors. \*Adjusted for year of delivery, maternal age, parity, height, body-mass index, smoking, educational level, disposable income and country of birth. †1 axSpA birth and 13 comparator births were missing data for small- and large for gestational age.

**Supplementary table 4.** Relative risks of preterm birth by level of inflammation, disease activity, treatment, and presence of SpA manifestations, in 1443 births by women with axSpA with complete data on background characteristics

	Births with risk factor	Births without risk factor	Risk ratio (95% CI)	Adj. risk ratio* (95% CI)
<b>Disease activity &amp; functional status before or during pregnancy</b>				
BASDAI†	4.1 (2.5)	..	0.98 (0.84–1.15)	0.90 (0.69–1.17)
HAQ-DI†	0.6 (0.6)	..	1.26 (0.64–2.50)	1.54 (0.49–4.78)
CRP >10 mg/l	6/94 (6.4)	21/319 (6.6)	1.01 (0.43–2.42)	0.94 (0.36–2.43)
<b>Treatment before pregnancy</b>				
No treatment	23/449 (5.1)	61/994 (6.1)	0.83 (0.52–1.33)	0.83 (0.47–1.44)
NSAIDs	44/668 (6.6)	40/775 (5.2)	1.28 (0.84–1.94)	1.31 (0.81–2.12)
csDMARDs	15/262 (5.7)	69/1181 (5.8)	0.98 (0.57–1.68)	1.14 (0.56–2.30)
Corticosteroids	24/371 (6.5)	60/1072 (5.6)	1.16 (0.73–1.82)	1.10 (0.52–2.33)
TNFi	23/383 (6.0)	61/1060 (5.8)	1.04 (0.65–1.67)	1.08 (0.53–2.20)
Heavy treatment‡	17/261 (6.5)	67/1182 (5.7)	1.15 (0.69–1.91)	1.23 (0.58–2.60)
<b>Treatment during pregnancy</b>				
No treatment	52/927 (5.6)	32/516 (6.2)	0.90 (0.59–1.40)	1.09 (0.60–1.98)
NSAIDs	8/152 (5.3)	76/1291 (5.9)	0.89 (0.44–1.81)	0.66 (0.30–1.48)
csDMARDs	6/135 (4.4)	78/1308 (6.0)	0.75 (0.33–1.66)	0.62 (0.21–1.79)
Corticosteroids	16/238 (6.7)	68/1205 (5.6)	1.19 (0.70–2.02)	1.09 (0.45–2.61)
TNFi	13/202 (6.4)	71/1241 (5.7)	1.12 (0.63–2.00)	0.95 (0.41–2.20)
Heavy treatment‡	8/120 (6.7)	76/1323 (5.7)	1.16 (0.58–2.31)	0.93 (0.38–2.31)
<b>SpA manifestations before delivery</b>				
Anterior uveitis	13/267 (4.9)	71/1176 (6.0)	0.81 (0.45–1.43)	0.82 (0.44–1.52)
Psoriatic arthritis	3/76 (3.9)	81/1367 (5.9)	0.67 (0.22–2.05)	0.80 (0.23–2.71)
Psoriasis	1/45 (2.2)	83/1398 (5.9)	0.37 (0.05–2.65)	0.43 (0.07–2.49)
Inflammatory bowel disease	5/79 (6.3)	79/1364 (5.8)	1.09 (0.46–2.62)	1.14 (0.44–2.93)

Data are mean (SD) for continuous variables or n events/N pregnancies (%) for dichotomous variables. Relative risks from modified Poisson regression, on 50 multiply imputed datasets, by increasing disease activity or in births with vs. without disease-related factors. BASDAI=Bath Ankylosing Spondylitis Disease Activity Index. HAQ-DI=Health Assessment Questionnaire–Disability Index. NSAIDs=non-steroidal anti-inflammatory drugs. csDMARDs=conventional systemic disease-modifying anti-rheumatic drugs. TNFi=tumour necrosis factor inhibitors. \*Adjusted for the other covariates in the table (i.e. disease activity, treatment before and during pregnancy, presence of SpA manifestations), plus year of delivery, maternal age, parity, height, body-mass index, smoking, educational level, disposable income and country of birth. †Analysed as continuous variables. ‡At least two of TNFi, csDMARDs or corticosteroids.



**Supplementary table 5.** Relative risks of infant infection by level of inflammation, disease activity, treatment, and presence of SpA manifestations, in 1443 births by women with axSpA with complete data on background characteristics

	Births with risk factor	Births without risk factor	Risk ratio (95% CI)	Adj. risk ratio* (95% CI)
<b>Disease activity &amp; functional status before or during pregnancy</b>				
BASDAI†	4·1 (2·5)	..	1·04 (0·89–1·23)	1·07 (0·80–1·43)
HAQ-DI†	0·6 (0·6)	..	1·02 (0·56–1·87)	0·75 (0·23–2·46)
CRP >10 mg/l	6/94 (6·4)	21/319 (6·6)	1·12 (0·51–2·49)	0·98 (0·39–2·46)
<b>Treatment before pregnancy</b>				
No treatment	25/449 (5·6)	71/994 (7·1)	0·78 (0·51–1·20)	0·81 (0·49–1·35)
NSAIDs	48/668 (7·2)	48/775 (6·2)	1·16 (0·80–1·69)	1·14 (0·73–1·77)
csDMARDs	18/262 (6·9)	78/1181 (6·6)	1·04 (0·64–1·70)	0·79 (0·40–1·55)
Corticosteroids	32/371 (8·6)	64/1072 (6·0)	1·44 (0·97–2·16)	1·41 (0·80–2·51)
TNFi	26/383 (6·8)	70/1060 (6·6)	1·03 (0·67–1·59)	1·08 (0·56–2·06)
Heavy treatment‡	19/261 (7·3)	77/1182 (6·5)	1·12 (0·69–1·81)	0·89 (0·45–1·77)
<b>Treatment during pregnancy</b>				
No treatment	57/927 (6·1)	39/516 (7·6)	0·81 (0·55–1·20)	0·86 (0·54–1·39)
NSAIDs	11/152 (7·2)	85/1291 (6·6)	1·10 (0·61–1·99)	1·05 (0·55–2·00)
csDMARDs	10/135 (7·4)	86/1308 (6·6)	1·13 (0·60–2·10)	1·24 (0·52–2·95)
Corticosteroids	19/238 (8·0)	77/1205 (6·4)	1·25 (0·77–2·02)	0·90 (0·46–1·78)
TNFi	15/202 (7·4)	81/1241 (6·5)	1·14 (0·67–1·93)	1·24 (0·57–2·70)
Heavy treatment‡	8/120 (6·7)	88/1323 (6·7)	1·00 (0·50–2·01)	0·81 (0·35–1·87)
<b>SpA manifestations before delivery</b>				
Anterior uveitis	17/267 (6·4)	79/1176 (6·7)	0·95 (0·58–1·56)	0·84 (0·50–1·41)
Psoriatic arthritis	2/76 (2·6)	94/1367 (6·9)	0·38 (0·10–1·51)	0·27 (0·07–1·01)
Psoriasis	5/45 (11·1)	91/1398 (6·5)	1·71 (0·73–3·99)	2·61 (1·24–5·47)
Inflammatory bowel disease	8/79 (10·1)	88/1364 (6·5)	1·57 (0·79–3·10)	1·69 (0·78–3·65)

Data are mean (SD) for continuous variables or n events/N pregnancies (%) for dichotomous variables. Relative risks from modified Poisson regression, on 50 multiply imputed datasets, by increasing disease activity or in births with vs. without disease-related factors. BASDAI=Bath Ankylosing Spondylitis Disease Activity Index. HAQ-DI=Health Assessment Questionnaire–Disability Index. NSAIDs=non-steroidal anti-inflammatory drugs. csDMARDs=conventional systemic disease-modifying anti-rheumatic drugs. TNFi=tumour necrosis factor inhibitors. \*Adjusted for the other covariates in the table (i.e. disease activity, treatment before and during pregnancy, presence of SpA manifestations), plus year of delivery, maternal age, parity, height, body-mass index, smoking, educational level, disposable income and country of birth. †Analysed as continuous variables. ‡At least two of TNFi, csDMARDs or corticosteroids.

**Supplementary table 6.** Relative risks of pre-eclampsia by level of inflammation, disease activity, treatment, and presence of SpA manifestations, in 1443 births by women with axSpA with complete data on background characteristics

	Births with risk factor	Births without risk factor	Risk ratio (95% CI)	Adj. risk ratio* (95% CI)
<b>Disease activity &amp; functional status before or during pregnancy</b>				
BASDAI†	4·1 (2·5)	..	1·26 (1·03–1·54)	1·50 (1·06–2·13)
HAQ-DI†	0·6 (0·6)	..	1·20 (0·52–2·80)	0·41 (0·09–1·91)
CRP >10 mg/l	4/94 (4·3)	13/319 (4·1)	1·00 (0·40–2·51)	0·93 (0·31–2·78)
<b>Treatment before pregnancy</b>				
No treatment	15/449 (3·3)	45/994 (4·5)	0·74 (0·41–1·33)	0·69 (0·33–1·45)
NSAIDs	25/668 (3·7)	35/775 (4·5)	0·83 (0·49–1·39)	0·79 (0·42–1·47)
csDMARDs	15/262 (5·7)	45/1181 (3·8)	1·50 (0·82–2·77)	1·35 (0·58–3·13)
Corticosteroids	17/371 (4·6)	43/1072 (4·0)	1·14 (0·63–2·07)	1·23 (0·47–3·27)
TNFi	12/383 (3·1)	48/1060 (4·5)	0·69 (0·38–1·28)	0·69 (0·30–1·59)
Heavy treatment‡	12/261 (4·6)	48/1182 (4·1)	1·13 (0·57–2·26)	0·96 (0·37–2·51)
<b>Treatment during pregnancy</b>				
No treatment	37/927 (4·0)	23/516 (4·5)	0·90 (0·54–1·49)	0·97 (0·44–2·12)
NSAIDs	7/152 (4·6)	53/1291 (4·1)	1·12 (0·53–2·38)	1·30 (0·62–2·73)
csDMARDs	8/135 (5·9)	52/1308 (4·0)	1·49 (0·72–3·08)	1·02 (0·33–3·13)
Corticosteroids	10/238 (4·2)	50/1205 (4·1)	1·01 (0·49–2·09)	1·06 (0·35–3·24)
TNFi	5/202 (2·5)	55/1241 (4·4)	0·56 (0·23–1·37)	0·67 (0·22–1·98)
Heavy treatment‡	4/120 (3·3)	56/1323 (4·2)	0·79 (0·29–2·12)	0·88 (0·28–2·76)
<b>SpA manifestations before delivery</b>				
Anterior uveitis	7/267 (2·6)	53/1176 (4·5)	0·58 (0·26–1·28)	0·67 (0·29–1·53)
Psoriatic arthritis	4/76 (5·3)	56/1367 (4·1)	1·28 (0·48–3·42)	1·21 (0·41–3·56)
Psoriasis	3/45 (6·7)	57/1398 (4·1)	1·64 (0·52–5·12)	1·40 (0·39–5·05)
Inflammatory bowel disease	5/79 (6·3)	55/1364 (4·0)	1·57 (0·64–3·83)	2·30 (0·87–6·11)

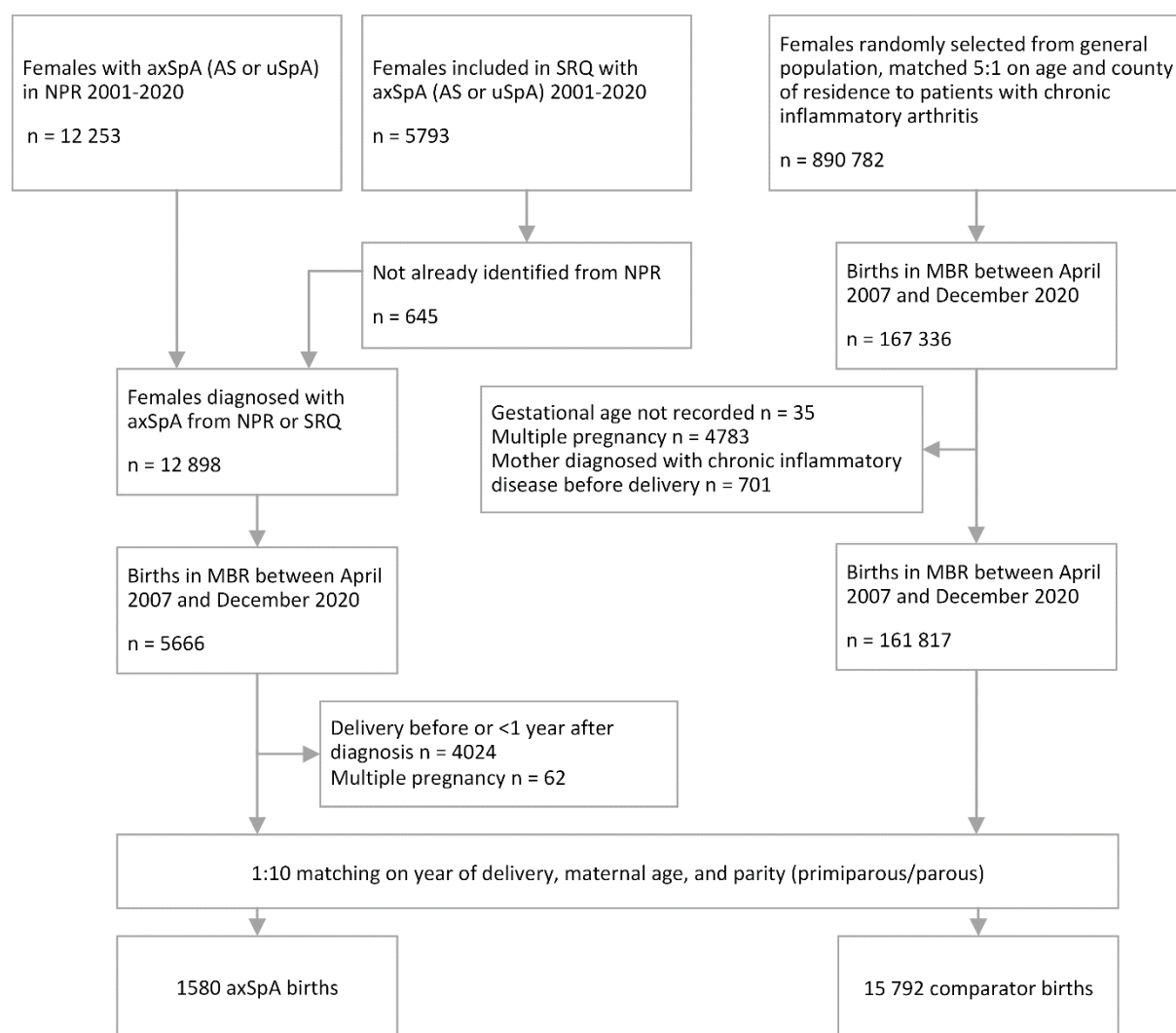
Data are mean (SD) for continuous variables or n events/N pregnancies (%) for dichotomous variables. Relative risks from modified Poisson regression, on 50 multiply imputed datasets, by increasing disease activity or in births with vs. without disease-related factors. BASDAI=Bath Ankylosing Spondylitis Disease Activity Index. HAQ-DI=Health Assessment Questionnaire–Disability Index. NSAIDs=non-steroidal anti-inflammatory drugs. csDMARDs=conventional systemic disease-modifying anti-rheumatic drugs. TNFi=tumour necrosis factor inhibitors. \*Adjusted for the other covariates in the table (i.e. disease activity, treatment before and during pregnancy, presence of SpA manifestations), plus year of delivery, maternal age, parity, height, body-mass index, smoking, educational level, disposable income and country of birth. †Analysed as continuous variables. ‡At least two of TNFi, csDMARDs or corticosteroids.

**Supplementary table 7.** Characteristics of the cohort by year of delivery, in three strata

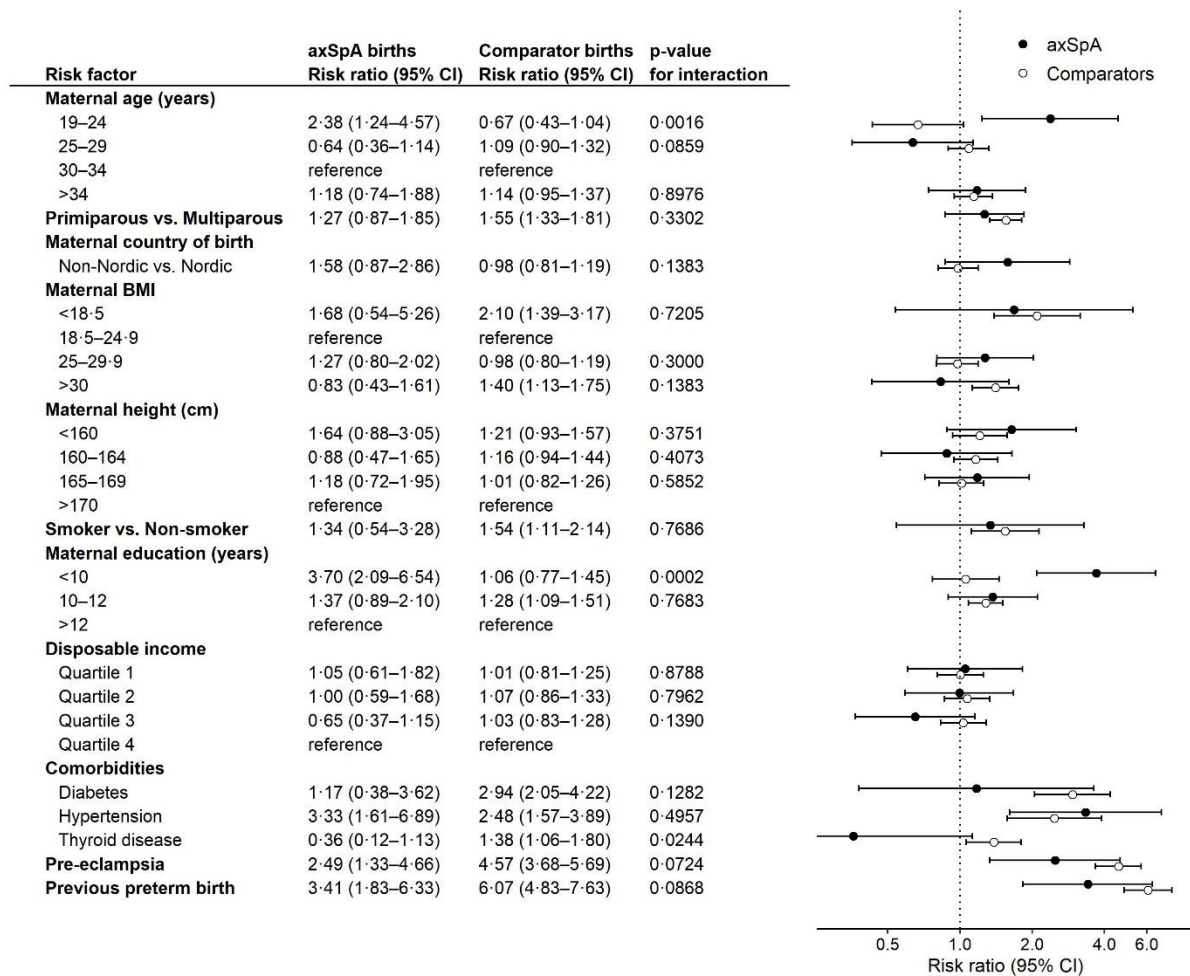
	Year of delivery		Year of delivery		Year of delivery	
	2007–2011		2012–2016		2017–2020	
	axSpA	Comparators	axSpA	Comparators	axSpA	Comparators
N	338	3380	609	6089	633	338
Ankylosing spondylitis diagnosis	165 (48·8)	..	301 (49·4)	..	304 (48·0)	..
<b>Maternal age, years</b>						
19–24	18 (5·3)	180 (5·3)	39 (6·4)	390 (6·4)	19 (3·0)	190 (3·0)
25–29	70 (20·7)	700 (20·7)	154 (25·3)	1540 (25·3)	163 (25·8)	1630 (25·8)
30–34	137 (40·5)	1370 (40·5)	256 (42·0)	2560 (42·0)	264 (41·7)	2640 (41·8)
≥35	113 (33·4)	1130 (33·4)	160 (26·3)	1599 (26·3)	187 (29·5)	1863 (29·5)
<b>Maternal BMI (early pregnancy)</b>						
<18·5	7 (2·1)	62 (1·8)	11 (1·8)	118 (1·9)	14 (2·2)	120 (1·9)
18·5–24·9	193 (57·1)	1949 (57·7)	324 (53·2)	3467 (56·9)	362 (57·2)	3283 (51·9)
25–29·9	66 (19·5)	780 (23·1)	148 (24·3)	1423 (23·4)	138 (21·8)	1648 (26·1)
≥30	41 (12·1)	373 (11·0)	88 (14·4)	735 (12·1)	87 (13·7)	897 (14·2)
Missing	31 (9·2)	216 (6·4)	38 (6·2)	346 (5·7)	32 (5·1)	375 (5·9)
<b>Smoking (early pregnancy)</b>						
Smoker	14 (4·1)	177 (5·2)	40 (6·6)	271 (4·5)	23 (3·6)	207 (3·3)
Non-smoker	305 (90·2)	3100 (91·7)	543 (89·2)	5514 (90·6)	575 (90·8)	5720 (90·5)
Missing	19 (5·6)	103 (3·0)	26 (4·3)	304 (5·0)	35 (5·5)	396 (6·3)
<b>Comorbidities*</b>						
Diabetes	6 (1·8)	46 (1·4)	15 (2·5)	74 (1·2)	20 (3·2)	114 (1·8)
Hypertension	6 (1·8)	40 (1·2)	15 (2·5)	61 (1·0)	9 (1·4)	81 (1·3)
Thyroid disease	11 (3·3)	135 (4·0)	45 (7·4)	395 (6·5)	70 (11·1)	514 (8·1)
<b>SpA manifestations†</b>						
Anterior uveitis	61 (18·0)	..	113 (18·6)	..	115 (18·2)	..
Psoriatic arthritis	19 (5·6)	..	25 (4·1)	..	42 (6·6)	..
Psoriasis	4 (1·2)	..	19 (3·1)	..	30 (4·7)	..
Inflammatory bowel disease	14 (4·1)	..	34 (5·6)	..	39 (6·2)	..
<b>Other rheumatic diagnoses*</b>						
Rheumatoid arthritis	27 (8·0)	..	62 (10·2)	..	46 (7·3)	..
Systemic lupus erythematosus	2 (0·6)	..	3 (0·5)	..	1 (0·2)	..

Data are n (%). BMI=body-mass index. \*Before pregnancy. †Before delivery.

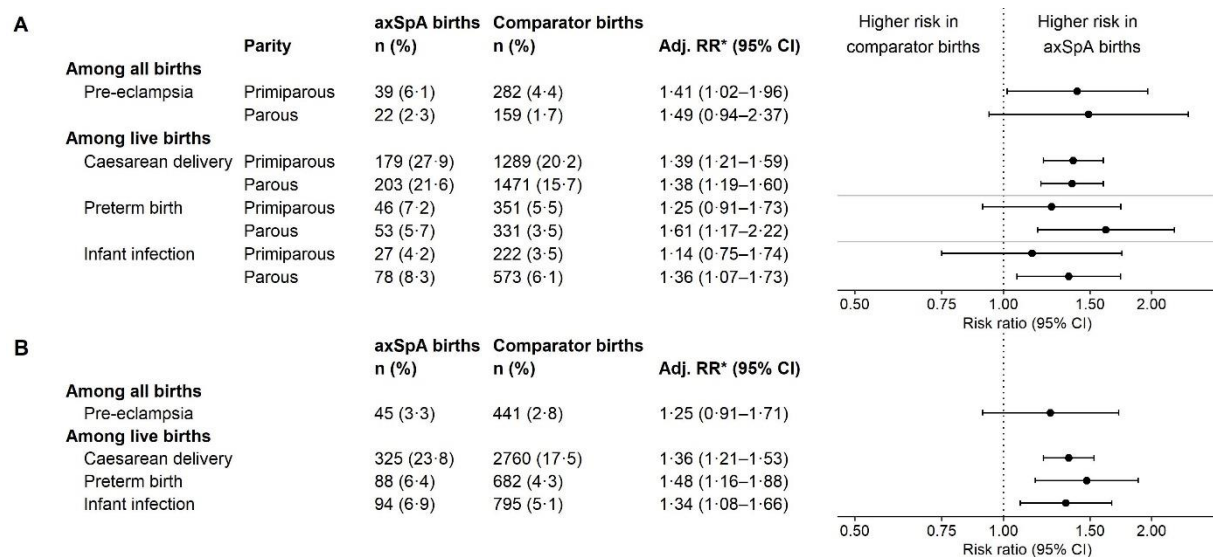
## Supplementary figures



**Supplementary figure 1. Flow diagram of selection of study participants.** AS=ankylosing spondylitis. uSpA=undifferentiated spondyloarthritis. NPR=National Patient Register. SRQ=Swedish Rheumatology Quality register. MBR=Medical Birth Register.



**Supplementary figure 2.** Effect modification of established risk factors of preterm birth by axSpA compared to general population comparators. Risk ratios from univariate modified Poisson regression. BMI=body-mass index.



**Supplementary figure 3.** Sensitivity analyses for outcomes with significantly increased risks in the axSpA population: A) Stratified by parity (first or subsequent births), and B) After exclusion of women in the axSpA cohort who were also diagnosed with rheumatoid arthritis, psoriatic arthritis, or systemic lupus erythematosus (n=135, 86, and 6, respectively) in the National Patient Register before start of pregnancy. Relative risks from modified Poisson regression. Comparators are all comparator births (n=15792). \*Adjusted for year of delivery, maternal age, parity (except in A), height, body-mass index, smoking, educational level, disposable income, and country of birth.

## References

- 1 Cnattingius S, Ericson A, Gunnarskog J, Källén B. A Quality Study of a Medical Birth Registry. *Scand J Soc Med* 1990; **18**: 143–48.
- 2 Ludvigsson JF, Otterblad-Olausson P, Pettersson BU, Ekbom A. The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. *Eur J Epidemiol* 2009; **24**: 659–67.
- 3 Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health* 2011; **11**: 450.
- 4 Wettermark B, Hammar N, Fored CM, et al. The new Swedish Prescribed Drug Register--opportunities for pharmacoepidemiological research and experience from the first six months. *Pharmacoepidemiol Drug Saf* 2007; **16**: 726–35.
- 5 Ludvigsson JF, Almqvist C, Bonamy AK, et al. Registers of the Swedish total population and their use in medical research. *Eur J Epidemiol* 2016; **31**: 125–36.
- 6 Ludvigsson JF, Svedberg P, Olén O, Bruze G, Neovius M. The longitudinal integrated database for health insurance and labour market studies (LISA) and its use in medical research. *Eur J Epidemiol* 2019; **34**: 423–37.
- 7 Ekbom A. The Swedish Multi-generation Register. *Methods Mol Biol* 2011; **675**: 215–20.
- 8 Eriksson JK, Askling J, Arkema EV. The Swedish Rheumatology Quality Register: optimisation of rheumatic disease assessments using register-enriched data. *Clin Exp Rheumatol* 2014; **32**: S-147–49.