

Supplemental Material

to the article “The management of pregnancy in autoimmune rheumatic diseases: maternal disease course, gestational and neonatal outcomes, and use of medications in the prospective Italian P-RHEUM.it study”.

Study Protocol. Version 1.0 - 24.09.2017 - See attachment.

Supplemental Figure 1. Design and timeline of the P-RHEUM.it study. Additional visits due to disease flares could be recorded at each time point during pregnancy and in the 6 months after delivery.

	Baseline visit	1st trim visit (6-12 GW)	2nd trim visit (18-24 GW)	3rd trim visit (30-36 GW)	30-60 days post-delivery visit	6 months post-delivery visit	12 months after delivery	24 months after delivery
Informed consent	●							
Inclusion/exclusion criteria	●							
Socio-demographic data	●							
Lifestyle	●							
Clinical and obstetric history	●							
Clinical features	●	●	●	●		●		
Obstetric features	●	●	●	●				
Laboratory tests	●	●	●	●		●		
Disease-specific clinimetrics	●	●	●	●		●		
Questionnaires & PROs	●	●	●	●		●		
PGA	●	●	●	●		●		
Therapy	●	●	●	●		●		
Adverse events (if any)		●	●	●	●	●		
Disease flare (if any)		●	●	●	●	●		
Pregnancy outcome, Neonatal features					●			
EPDS					●	●	●	
Child questionnaire						●	●	●

Abbreviations: EPDS: Edinburgh Postpartum Depression Scale; GW: gestational week; PGA: Physician Global Assessment; PROs: Patient-reported outcomes; trim: trimester.

Supplemental Table 1. Disease-specific clinical measurement tools and patient-reported outcomes used in the study.

Rheumatoid Arthritis Juvenile Idiopathic Arthritis Undifferentiated arthritis
28 swollen joint count
28 tender joint count
Disease Activity Score-C-reactive protein (DAS28-PCR) ¹
Modified Health Assessment Questionnaire (HAQ-V2) ²
Psoriatic Arthritis Spondyloarthritis
68 tender joint count
68 swollen joint count
Ankylosing Spondylitis Disease Activity Score Questionnaire (ASDAS) ³
Bath Ankylosing Spondylitis Functional Index (BASFI) ⁴
Systemic Lupus Erythematosus
Systemic Lupus International Collaborating Clinics-Damage Index (SLICC-DI) ⁵
SLE Disease Activity Index adjusted for pregnancy (SLEPDAI) ⁶
Systemic Sclerosis
Modified Rodnan skin score ⁷
Scleroderma Health Assessment Questionnaire (SHAQ) ⁸

1. Prevoo ML, van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum.* 1995 Jan;38(1):44-8.
2. Wolfe F. Which HAQ is best? A comparison of the HAQ, MHAQ and RA-HAQ, a difficult 8 item HAQ (DHAQ), and a rescored 20 item HAQ (HAQ20): analyses in 2,491 rheumatoid arthritis patients following leflunomide initiation. *J Rheumatol.* 2001 May;28(5):982-9.
3. Machado P, Landewé R, Lie E, Kvien TK, Braun J, Baker D, van der Heijde D; Assessment of SpondyloArthritis international Society. Ankylosing Spondylitis Disease Activity Score (ASDAS): defining cut-off values for disease activity states and improvement scores. *Ann Rheum Dis.* 2011 Jan;70(1):47-53.
4. Calin A, Jones SD, Garrett SL, Kennedy LG. Bath Ankylosing Spondylitis Functional Index. *Br J Rheumatol.* 1995 Aug;34(8):793-4.
5. Gladman D, Ginzler E, Goldsmith C, Fortin P, Liang M, Urowitz M, et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. *Arthritis Rheum.* 1996;39:363-369.
6. Buyon JP, Kalunian KC, Ramsey-Goldman R, Petri MA, Lockshin MD, Ruiz-Irastorza G, Khamashta M. Assessing disease activity in SLE patients during pregnancy. *Lupus.* 1999;8(8):677-84.
7. Furst DE, Clements PJ, Steen VD, Medsger TA Jr, Masi AT, D'Angelo WA, Lachenbruch PA, Grau RG, Seibold JR. The modified Rodnan skin score is an accurate reflection of skin biopsy thickness in systemic sclerosis. *J Rheumatol.* 1998 Jan;25(1):84-8.
8. Steen VD, Medsger TA Jr. The value of the Health Assessment Questionnaire and special patient-generated scales to demonstrate change in systemic sclerosis patients over time. *Arthritis Rheum.* 1997 Nov;40(11):1984-91.

Supplemental Table 2. Maternal features regarding family status, education level, lifestyle habits, comorbidities, and associated autoimmune diseases. For women with more than one pregnancy enrolled in the study, the information related to the first enrolled pregnancy was considered. Categorical variables are expressed as numbers (percentages) and continuous variables as median (interquartile range).

	All patients	RA	PsA	axSpA	JIA	UA	SLE	PAPS – aPL carriers	UCTD	pSS	SSc	IIM	SV	Anti-Ro/SSA carriers
Number of pregnancies	851	121	67	47	30	11	167	130	135	40	28	20	37	18
Family Status														
Single	6 (0.7%)	0 (0%)	0 (0%)	0 (0%)	1 (3.3%)	0 (0%)	1 (0.6%)	3 (2.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)	0 (0%)
Non cohabitant partner	34 (4%)	9 (7.4%)	3 (4.5%)	2 (4.3%)	1 (3.3%)	0 (0%)	2 (1.2%)	5 (3.8%)	4 (3%)	1 (2.5%)	4 (14.3%)	0 (0%)	3 (8.1%)	0 (0%)
Married/living with partner	672 (79%)	95 (78.5%)	53 (79.1%)	38 (80.9%)	22 (73.3%)	10 (90.9%)	133 (79.6%)	102 (78.5%)	105 (77.8%)	35 (87.5%)	17 (60.7%)	17 (85%)	32 (86.5%)	13 (72.2%)
Separated/Divorced	3 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	1 (0.8%)	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Widow	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	136 (16%)	17 (14%)	11 (16.4%)	7 (14.9%)	6 (20%)	1 (9.1%)	30 (18%)	19 (14.6%)	25 (18.5%)	4 (10%)	7 (25%)	3 (15%)	1 (2.7%)	5 (27.8%)
Education level														
Primary school	59 (6.9%)	7 (5.8%)	2 (3%)	6 (12.8%)	2 (6.7%)	0 (0%)	13 (7.8%)	9 (6.9%)	7 (5.2%)	4 (10%)	2 (7.1%)	1 (5%)	6 (16.2%)	0 (0%)
Secondary school	253 (29.7%)	41 (33.9%)	21 (31.3%)	11 (23.4%)	9 (30%)	4 (36.4%)	46 (27.5%)	40 (30.8%)	35 (25.9%)	10 (25%)	11 (39.3%)	6 (30%)	13 (35.1%)	6 (33.3%)
University degree	270 (31.7%)	32 (26.4%)	24 (35.8%)	16 (34%)	7 (23.3%)	3 (27.3%)	46 (27.5%)	47 (36.2%)	52 (38.5%)	14 (35%)	9 (32.1%)	4 (20%)	10 (27%)	6 (33.3%)
Missing	269 (31.6%)	41 (33.9%)	20 (29.9%)	14 (29.8%)	12 (40%)	4 (36.4%)	62 (37.1%)	34 (26.2%)	41 (30.4%)	12 (30%)	6 (21.4%)	9 (45%)	8 (21.6%)	6 (33.3%)
Cigarette Smoking														
Never	738 (72.5%)	100 (71.4%)	53 (66.2%)	35 (67.3%)	26 (68.4%)	15 (83.3%)	143 (73.7%)	112 (70.9%)	126 (75.9%)	43 (84.3%)	22 (71%)	14 (66.7%)	31 (68.9%)	18 (75%)
Occasionally	49 (4.8%)	6 (4.3%)	6 (7.5%)	5 (9.6%)	0 (0%)	1 (5.6%)	12 (6.2%)	7 (4.4%)	10 (6%)	0 (0%)	1 (3.2%)	0 (0%)	1 (2.2%)	0 (0%)
Regularly	11 (1.1%)	4 (2.9%)	2 (2.5%)	1 (1.9%)	0 (0%)	0 (0%)	2 (1%)	2 (1.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Past smoker	177 (17.4%)	20 (14.3%)	17 (21.2%)	9 (17.3%)	11 (28.9%)	2 (11.1%)	34 (17.5%)	29 (18.4%)	21 (12.7%)	5 (9.8%)	6 (19.4%)	7 (33.3%)	13 (28.9%)	3 (12.5%)
Missing	43 (4.2%)	10 (7.1%)	2 (2.5%)	2 (3.8%)	1 (2.6%)	0 (0%)	3 (1.5%)	8 (5.1%)	9 (5.4%)	3 (5.9%)	2 (6.5%)	0 (0%)	0 (0%)	3 (12.5%)
Alcohol consumption														
Never	476 (55.9%)	66 (54.5%)	43 (64.2%)	30 (63.8%)	17 (56.7%)	4 (36.4%)	85 (50.9%)	72 (55.4%)	82 (60.7%)	25 (62.5%)	11 (39.3%)	8 (40%)	20 (54.1%)	13 (72.2%)
Occasionally	345 (40.5%)	49 (40.5%)	22 (32.8%)	15 (31.9%)	12 (40%)	7 (63.6%)	77 (46.1%)	53 (40.8%)	50 (37%)	15 (37.5%)	14 (50%)	11 (55%)	16 (43.2%)	4 (22.2%)
Regularly	3 (0.4%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	27 (3.2%)	5 (4.1%)	2 (3%)	2 (4.3%)	1 (3.3%)	0 (0%)	4 (2.4%)	4 (3.1%)	3 (2.2%)	0 (0%)	3 (10.7%)	1 (5%)	1 (2.7%)	1 (5.6%)

	All patients	RA	PsA	axSpA	JIA	UA	SLE	PAPS – aPL carriers	UCTD	pSS	SSc	IIM	SV	Anti- Ro/SSA carriers
Comorbidities														
Arterial hypertension	18 (2.1%)	1 (0.8%)	1 (1.5%)	1 (2.1%)	0 (0%)	0 (0%)	7 (4.2%)	5 (3.8%)	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)	1 (5.6%)
Diabetes mellitus type 2	5 (0.6%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.2%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)	0 (0%)
Previous thromboembolic events	45 (5.3%)	2 (1.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	7 (4.2%)	30 (23.1%)	1 (0.7%)	2 (5%)	0 (0%)	1 (5%)	2 (5.4%)	0 (0%)
Associated autoimmune diseases														
Diabetes Mellitus type 1	3 (0.4%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)	0 (0%)
Celiac disease	16 (1.9%)	1 (0.8%)	1 (1.5%)	0 (0%)	0 (0%)	1 (9.1%)	2 (1.2%)	2 (1.5%)	5 (3.7%)	3 (7.5%)	0 (0%)	0 (0%)	0 (0%)	1 (5.6%)
Autoimmune atrophic gastritis	2 (0.2%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)	0 (0%)
Ulcerative colitis	6 (0.7%)	0 (0%)	1 (1.5%)	3 (6.4%)	0 (0%)	0 (0%)	2 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Crohn's disease	5 (0.6%)	1 (0.8%)	0 (0%)	2 (4.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)	0 (0%)
Autoimmune hyperthyroidism	4 (0.5%)	0 (0%)	1 (1.5%)	1 (2.1%)	0 (0%)	0 (0%)	2 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Autoimmune thyroiditis	116 (13.6%)	11 (9.1%)	7 (10.4%)	4 (8.5%)	4 (13.3%)	1 (9.1%)	21 (12.6%)	16 (12.3%)	25 (18.5%)	7 (17.5%)	3 (10.7%)	4 (20%)	6 (16.2%)	7 (38.9%)
Autoimmune hepatitis	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Autoimmune thrombocytopenia	7 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.8%)	5 (3.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (5.6%)

Abbreviations: aPL: antiphospholipid antibodies; SpA: Spondyloarthritis; IIM: Idiopathic Inflammatory Myopathies; JIA: Juvenile Idiopathic Arthritis; PAPS: Primary Antiphospholipid Syndrome; PGA: Physician Global Assessment; PsA: Psoriatic Arthritis; pSS: Primary Sjögren's Syndrome; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; SSc: Systemic Sclerosis; SV: Systemic Vasculitis; UA: Undifferentiated Arthritis; UCTD: Undifferentiated Connective Tissue Disease

Supplemental Table 3. Frequency of positive disease-specific/disease-associated autoantibody/laboratory markers. Percentages were calculated on available data in each disease group.

Abbreviations: ANA: anti-nuclear antibodies; ANCA: anti-neutrophil cytoplasmic antibodies; anti-dsDNA: anti-double-stranded DNA; anti-MPO: anti-myeloperoxidase antibodies; anti-PR3: anti-proteinase 3 antibodies; aPL: antiphospholipid antibodies; C3-C4: complement fraction C3-C4; HLA: Human Leukocyte Antigen; PAPS: primary antiphospholipid syndrome; SLE: Systemic Lupus Erythematosus; UCTD: Undifferentiated Connective Tissue Disorders.

Rheumatoid Factor Anti-citrullinated proteins antibodies
49/101 (48.5%) 58/102 (56.7%) out of 121 patients with Rheumatoid Arthritis
4/28 (14.3%) 4/28 (14.3%) out of 30 patients with Juvenile Idiopathic Arthritis
1/10 (10%) 0/10 (0%) out of 11 patients with Undifferentiated Arthritis
Anti-dsDNA antibodies Low levels of C3 and/or C4
77/127 (60.6%) 55/135 (40.7%) out of 167 patients with SLE
Single Double Triple aPL positivity
48% 32% 20% of 44 patients positive for aPL out of 167 with SLE
43% 33% 24% of 130 with PAPS/aPL carriers
Anti-Ro/SSA antibodies
4.6% of 107 patients out of 121 with Rheumatoid Arthritis
3.1% of 65 patients out of 67 with Psoriatic Arthritis
2.3% of 44 patients out of 47 with Spondyloarthritis
3.4% of 29 patients out of 30 with Juvenile Idiopathic Arthritis
23.8% of 158 patients out of 167 with SLE
6.2% of 130 patients out of 130 with PAPS/aPL carriers
35.2% of 128 patients out of 135 with UCTD
97.5% of 40 patients out of 40 with Primary Sjögren's Syndrome
7.7% of 26 patients out of 28 with Systemic Sclerosis
21.1% of 19 patients out of 20 with Idiopathic Inflammatory Myopathies
Anti-Scl70 antibodies anti-centromere antibodies
11/28 (39%) 9/28 (32%) out of 28 patients with Systemic Sclerosis [3 patients with positive anti-U1RNP; 2 patients with isolated positive ANA at high titre; 1 patient with positive ANA 1:640 nucleolar pattern and positive anti-PL12; 1 patient with positive anti-Th/To; 1 patient with positive anti-Ku]
Anti-Jo1 antibodies
1/12 (8%) out of 20 Idiopathic Inflammatory Myopathies
ANCA anti-PR3 ANCA anti-MPO
1/5 (20%) 1/5 (20%) out of 5 patients with ANCA-associated vasculitis
HLA-B27
2/30 (7%) out of 67 patients with Psoriatic Arthritis
30/44 (68%) out of 47 patients with Spondyloarthritis
1/22 (4%) out of 30 patients with Juvenile Idiopathic Arthritis
HLA-B51
10/23 (43.5%) out of 23 patients with Behçet's Disease

Supplemental Table 4. Maternal features: patient- and physician-reported outcomes. For women with more than one pregnancy enrolled in the study, the information related to the first enrolled pregnancy was considered. Categorical variables are expressed as numbers (percentages) and continuous variables as median (interquartile range). Categorical variables are expressed as numbers (percentages) and continuous variables as median (interquartile range).

	All patients	RA	PsA	SpA	JIA	UA	SLE	PAPS – aPL carriers	UCTD	pSS	SSc	IIM	SV	Anti-Ro/SSA carriers
Number of women	851	121	67	47	30	11	167	130	135	40	28	20	37	18
Physician reported flares in the 12 months prior to conception	180 (21.2%)	39 (32.2%)	23 (34.3%)	19 (40.4%)	8 (26.7%)	6 (54.5%)	33 (19.8%)	11 (8.5%)	14 (10.4%)	7 (17.5%)	3 (10.7%)	6 (30%)	11 (29.7%)	0 (0%)
Missing	31 (3.6%)	4 (3.3%)	1 (1.5%)	2 (4.3%)	2 (6.7%)	0 (0%)	7 (4.2%)	4 (3.1%)	8 (5.9%)	0 (0%)	0 (0%)	1 (5%)	1 (2.7%)	1 (5.6%)
PGH in the 12 months prior to conception (PGH-VAS 0-100)	95 (80 - 100)	90 (69.8 - 100)	89 (65.8 - 99.2)	90 (61 - 100)	96 (85.8 - 100)	90 (67 - 95)	95 (80 - 100)	100 (90.2 - 100)	98 (90 - 100)	99.5 (87.5 - 100)	90 (81.5 - 96.5)	90.5 (78 - 100)	94 (80 - 100)	100 (99 - 100)
Missing	61 (7.2%)	9 (7.4%)	3 (4.5%)	6 (12.8%)	2 (6.7%)	0 (0%)	11 (6.6%)	8 (6.2%)	13 (9.6%)	4 (10%)	1 (3.6%)	0 (0%)	3 (8.1%)	1 (5.6%)
PGA at enrolment (PGA-VAS 0-100)	4 (0 - 13.5)	5 (0 - 20)	10 (0 - 23.8)	7 (0 - 22)	2 (0 - 10)	15 (6.2 - 43.8)	5 (0 - 10)	0 (0 - 10)	0 (0 - 5.5)	1.5 (0 - 18.5)	6 (0 - 11)	4 (0 - 9.5)	7 (0 - 17.5)	1 (0 - 2)
Missing	64 (7.5%)	14 (11.6%)	1 (1.5%)	6 (12.8%)	5 (16.7%)	1 (9.1%)	10 (6%)	3 (2.3%)	16 (11.9%)	2 (5%)	3 (10.7%)	1 (5%)	2 (5.4%)	0 (0%)
PGH at enrolment (PGH-VAS 0-100)	80 (70 - 90)	81 (70 - 91)	76 (60.5 - 90)	80 (70 - 90)	90 (80 - 95)	58.5 (42.5 - 85)	85 (75 - 92)	80 (70 - 93)	80 (67 - 90.5)	71 (50 - 80)	81 (71.2 - 92.2)	80 (73 - 90)	80 (70 - 90)	89 (76.2 - 94.2)
Missing	64 (7.5%)	14 (11.6%)	0 (0%)	5 (10.6%)	5 (16.7%)	1 (9.1%)	10 (6%)	3 (2.3%)	16 (11.9%)	3 (7.5%)	4 (14.3%)	1 (5%)	2 (5.4%)	0 (0%)
EQ-5D-3L at enrolment	1 (0.8 - 1)	0.8 (0.8 - 1)	0.8 (0.8 - 1)	1 (0.8 - 1)	1 (0.8 - 1)	1 (0.8 - 1)	1 (0.8 - 1)	1 (0.8 - 1)	1 (0.8 - 1)	1 (0.8 - 1)	1 (0.8 - 1)	1 (1 - 1)	1 (0.8 - 1)	1 (1 - 1)
Missing	66 (7.8%)	14 (11.6%)	0 (0%)	6 (12.8%)	5 (16.7%)	1 (9.1%)	12 (7.2%)	3 (2.3%)	17 (12.6%)	3 (7.5%)	3 (10.7%)	1 (5%)	1 (2.7%)	0 (0%)

Abbreviations: aPL: antiphospholipid antibodies; EQ-5D-3L: EuroQoL questionnaire (score range: -1.6: poorest quality of life; 1: excellent quality of life); IIM: Idiopathic Inflammatory Myopathies; JIA: Juvenile Idiopathic Arthritis; PAPS: Primary Antiphospholipid Syndrome; PGA: Physician Global Assessment; PsA: Psoriatic Arthritis; pSS: Primary Sjögren's Syndrome; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; SpA: Spondyloarthritis; SSc: Systemic Sclerosis; SV: Systemic Vasculitis; UA: Undifferentiated Arthritis; UCTD: Undifferentiated Connective Tissue Disease; PGA-VAS: Physician Global Assessment - Visual Analogic Scale (0-100; 0 no activity – 100 highest activity); PGH-VAS: Patient Global Health - Visual Analogic Scale (0-100; 0 poorest health – 100 full health).

Supplemental Table 5. Maternal and fetal complications (more than 1 complication may have occurred during the same pregnancy).

	All pregnancies	RA	PsA	SpA	JIA	UA	SLE	PAPS – aPL carriers	UCTD	pSS	SSc	IIM	SV	Anti-Ro/SSA carriers
Number of pregnancies	866	122	69	47	31	12	169	135	136	41	28	20	38	18
Complicated pregnancies (≥1 complication)	261 (30.1%)	38 (31.1%)	13 (18.8%)	12 (25.5%)	4 (12.9%)	4 (33.3%)	64 (37.9%)	47 (34.8%)	39 (28.7%)	8 (19.5%)	7 (25%)	4 (20%)	14 (36.8%)	7 (38.9%)
Gestational hypertension	31 (3.6%)	3 (2.5%)	5 (7.2%)	1 (2.1%)	0 (0%)	0 (0%)	11 (6.5%)	6 (4.4%)	1 (0.7%)	1 (2.4%)	1 (3.6%)	0 (0%)	2 (5.3%)	0 (0%)
Preeclampsia	20 (2.3%)	0 (0%)	3 (4.3%)	0 (0%)	1 (3.2%)	0 (0%)	7 (4.1%)	4 (3%)	2 (1.5%)	0 (0%)	1 (3.6%)	0 (0%)	0 (0%)	2 (11.1%)
Eclampsia	2 (0.2%)	0 (0%)	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HELLP syndrome	3 (0.3%)	0 (0%)	0 (0%)	1 (2.1%)	0 (0%)	0 (0%)	0 (0%)	2 (1.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gestational diabetes	61 (7%)	10 (8.2%)	4 (5.8%)	4 (8.5%)	0 (0%)	3 (25%)	8 (4.7%)	15 (11.1%)	7 (5.1%)	1 (2.4%)	1 (3.6%)	1 (5%)	4 (10.5%)	3 (16.7%)
Intrahepatic cholestasis of pregnancy	19 (2.2%)	3 (2.5%)	0 (0%)	2 (4.2%)	0 (0%)	0 (0%)	4 (2.4%)	6 (4.4%)	3 (2.2%)	0 (0%)	0 (0%)	0 (0%)	1 (2.6%)	0 (0%)
Gestational hypothyroidism	35 (4%)	2 (1.6%)	2 (2.9%)	1 (2.1%)	1 (3.2%)	1 (8.3%)	11 (6.5%)	4 (3%)	5 (3.7%)	3 (7.3%)	1 (3.6%)	1 (5%)	3 (7.9%)	0 (0%)
Thromboembolic events	3 (0.3%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
FGR	69 (8%)	13 (10.7%)	0 (0%)	1 (2.1%)	1 (3.2%)	0 (0%)	19 (11.2%)	16 (11.8%)	10 (7.3%)	2 (4.8%)	0 (0%)	1 (5%)	4 (10.5%)	2 (11.1%)
Placental abruption	18 (2.1%)	2 (1.6%)	0 (0%)	1 (2.1%)	0 (0%)	0 (0%)	5 (3%)	5 (3.7%)	2 (1.5%)	1 (2.4%)	1 (3.6%)	0 (0%)	1 (2.6%)	0 (0%)
Placental hematoma	5 (0.6%)	0 (0%)	0 (0%)	1 (2.1%)	0 (0%)	0 (0%)	0 (0%)	2 (1.5%)	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)	1 (2.6%)	0 (0%)
PPROM	14 (1.6%)	1 (0.8%)	2 (2.9%)	0 (0%)	1 (3.2%)	1 (8.3%)	1 (0.6%)	2 (1.5%)	4 (3%)	0 (0%)	2 (7.2%)	0 (0%)	0 (0%)	0 (0%)
PROM at term	47 (5.4%)	6 (4.9%)	3 (4.3%)	3 (6.3%)	0	1 (8.3%)	10 (5.9%)	4 (3%)	12 (8.8%)	2 (4.8%)	1 (3.6%)	1 (5%)	3 (7.9%)	1 (5.5%)

Abbreviations: HELLP: Hemolysis, Elevated Liver enzymes, Low Platelets; GW: gestational week; IIM: Idiopathic Inflammatory Myopathies; FGR: fetal growth restriction; JIA: Juvenile Idiopathic Arthritis; PAPS: Primary Antiphospholipid Syndrome; PsA: Psoriatic Arthritis; PPRM: preterm premature rupture of membranes; PROM: premature rupture of membranes; pSS: Primary Sjögren's Syndrome; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; SpA: Spondyloarthritis; SSc: Systemic Sclerosis; SV: Systemic Vasculitis; UA: Undifferentiated Arthritis; UCTD: Undifferentiated Connective Tissue Disease.

Supplemental Table 6. Use of csDMARDs and bDMARDs during pregnancy (at least one reported use in any trimester). Categorical variables are expressed as numbers (percentages) and continuous variables as median (interquartile range).

	All pregnancies	RA	PsA	SpA	JIA	UA	SLE	PAPS – aPL carriers	UCTD	pSS	SSc	IIM	SV	Anti-Ro/SSA carriers
Number of pregnancies	866	122	69	47	31	12	169	135	136	41	28	20	38	18
csDMARDs	85 (9.8%)	4 (3.3%)	5 (5.8%)	1 (2.1%)	1 (3.2%)	0 (0%)	46 (27.2%)	4 (3%)	3 (2.2%)	0 (0%)	4 (14.3%)	10 (50%)	7 (18.4%)	0 (0%)
Azathioprine	62 (7.2%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	38 (22.5%)	4 (3%)	2 (1.5%)	0 (0%)	4 (14.3%)	6 (30%)	7 (18.4%)	0 (0%)
Cyclosporine-A	14 (1.6%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (4.7%)	0 (0%)	1 (0.7%)	0 (0%)	0 (0%)	4 (20%)	0 (0%)	0 (0%)
Sulfasalazine	9 (1%)	2 (1.6%)	5 (7.2%)	1 (2.1%)	1 (3.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cyclophosphamide	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Leflunomide	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Methotrexate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mycophenolate mofetil	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
bDMARDs	122 (14.1%)	46 (37.7%)	27 (39.1%)	17 (36.2%)	12 (38.7%)	5 (41.7%)	7 (4.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (5%)	7 (18.4%)	0 (0%)
Abatacept	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adalimumab	14 (1.6%)	3 (2.5%)	1 (1.4%)	4 (8.5%)	1 (3.2%)	2 (16.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (7.9%)	0 (0%)
Belimumab	5 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (2.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)
Certolizumab pegol	82 (9.5%)	39 (32%)	21 (30.4%)	11 (23.4%)	6 (19.4%)	3 (25%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.6%)	0 (0%)
Etanercept	17 (2%)	4 (3.3%)	5 (7.5%)	2 (4.3%)	5 (17.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)	0 (0%)
Golimumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infliximab	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.9%)	0 (0%)
Rituximab	3 (0.4%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.8%)	0 (0%)
Tocilizumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Others	1 (0.1%)*	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)*	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

*Ustekinumab used for ulcerative colitis in a patient with SLE

Abbreviations: DMARDs: Disease-modifying anti-rheumatic drugs; bDMARDs: biologic DMARDs; csDMARDs: conventional synthetic DMARDs; tsDMARDs: targeted synthetic DMARDs; IIM: Idiopathic Inflammatory Myopathies; JIA: Juvenile Idiopathic Arthritis; PAPS: Primary Antiphospholipid Syndrome; PsA: Psoriatic Arthritis; pSS: Primary Sjögren's Syndrome; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; SpA: Spondyloarthritis; SSc: Systemic Sclerosis; SV: Systemic Vasculitis; UA: Undifferentiated Arthritis; UCTD: Undifferentiated Connective Tissue Disease.

Supplemental Table 7. Frequency of outcomes collected in the present study about pregnant women with autoimmune rheumatic diseases (ARD) which were also available in the Italian general obstetric population (official data from the Ministry of Health or published literature).

(a) median age at enrolment in the study; (b) mean age at delivery; (c) estimates of incidence and uncertainty range related to the European region (no Italian data available); (d) small-for-gestational-age babies (birthweight less than the 10th percentile for the gestational age); (e) birth weight <2500 gr; (f) first month after delivery; (g) 2-3 months after delivery. Abbreviations: GW: gestational week.

	Present study (866 pregnancies in 851 women with ARD)	Italian general obstetric population	Source
Mothers with previous 1-2 miscarriages	56.9%	17.5%	Certificato di assistenza al parto (CeDAP). Analisi dell'evento nascita - Anno 2022; https://www.salute.gov.it , last access 17 11 2023
Maternal age	34 years (a)	32.4 years (b)	Rapporto ISTAT 2022; https://www.istat.it/it/archivio/289772 , last access 17 11 2023
Assisted Reproduction Techniques	6.1%	3.7%	Certificato di assistenza al parto (CeDAP). Analisi dell'evento nascita - Anno 2022; https://www.salute.gov.it , last access 17 11 2023
Spontaneous miscarriage	7%	11%	Annuario Statistico Italiano 2022; https://www.istat.it/storage/ASI/2022/capitoli/C04.pdf , last access 17 11 2023
Preeclampsia	2.3%	5.3% (1.8–9.3) (c)	Abalos E, et al. Global and regional estimates of preeclampsia and eclampsia: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2013;170(1):1-7
Eclampsia	0.2%	0.015%	Maraschini A, et al.; ItOSS-Regional Working Group. Eclampsia in Italy: A prospective population-based study (2017-2020). Pregnancy Hypertens. 2022;30:204-209.
Preterm delivery (overall, <37 GW)	13.5%	6.3%	Certificato di assistenza al parto (CeDAP). Analisi dell'evento nascita - Anno 2022; https://www.salute.gov.it , last access 17 11 2023
Severe preterm delivery (<33 GW)	3.2%	1.6%	Certificato di assistenza al parto (CeDAP). Analisi dell'evento nascita - Anno 2022; https://www.salute.gov.it , last access 17 11 2023
Spontaneous vaginal delivery	31.2%	63.1%	European Perinatal Health Report 2015-2019; https://www.europeristat.com/index.php/reports/ephr-2019.html , last access 17 11 2023 (Italian data)
Elective cesarean section	22.2%	20.7%	European Perinatal Health Report 2015-2019; https://www.europeristat.com/index.php/reports/ephr-2019.html , last access 17 11 2023 (Italian data)
Emergent cesarean section	13.9%	12.3%	European Perinatal Health Report 2015-2019; https://www.europeristat.com/index.php/reports/ephr-2019.html , last access 17 11 2023 (Italian data)
Perinatal death	0.5%	0.2%	European Perinatal Health Report 2015-2019; https://www.europeristat.com/index.php/reports/ephr-2019.html , last access 17 11 2023 (Italian data)
Low birth weight	3.9% (d)	7.5% (e)	European Perinatal Health Report 2015-2019; https://www.europeristat.com/index.php/reports/ephr-2019.html , last access 17 11 2023 (Italian data)
Congenital malformations	2%	1.1%	Certificato di assistenza al parto (CeDAP). Analisi dell'evento nascita - Anno 2022; https://www.salute.gov.it , last access 17 11 2023
Exclusive maternal breastfeeding	46.7% (f)	47% (g)	Risultati "Sistema di Sorveglianza 0-2 anni sui principali determinanti di salute del bambino" 2022 ISS; https://www.epicentro.iss.it/sorveglianza02anni/indagine-2022 , last access 17 11 2023