Women with systemic lupus erythematosus get pregnant more easily than women with rheumatoid arthritis.

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Abstract

Objectives: To examine possible differences in the ability to get pregnant and time to pregnancy (TTP) in women with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), and to study possible influencing factors.

Methods: Data from RevNatus, a Norwegian nationwide prospective observational register including women with inflammatory rheumatic diseases when planning pregnancy or after conception, was used. We compared rate of achieved pregnancy, the pregnancy outcomes live birth or pregnancy loss and time to pregnancy between women with SLE (n = 53) and women with RA (n = 180). Time to pregnancy was compared between the groups using Kaplan-Meier plots, and Cox proportional hazard regression was performed adjusting for maternal age, parity and medication use. RAND-36 assessed health-related quality of life (HRQoL) in women achieving and not achieving pregnancy.

Results: Women with SLE had a pregnancy ratio of 1.91 (CI 1.27 to 2.88, p = 0.002) compared to women with RA, and a substantially shorter median TTP (3.0 vs 7.0 months, p = 0.001). Higher maternal age, medication use and low HRQoL in the physical domains may influence on the ability to achieve pregnancy and prolong TTP in women with RA. Women with SLE not achieving pregnancy had lower HRQoL scores than SLE-women achieving pregnancy, while women with RA had generally low scores in physical domains whether or not achieving pregnancy, indicating poor HRQoL.

Conclusions: In the studied cohort, women with SLE got pregnant more easily than women with RA.

Keywords: SLE – RA - Fertility – Family planning – Health-related Quality of life

Key messages:

Women with SLE more often succeed in achieving pregnancy than women with RA.

Women with SLE have a shorter time to pregnancy than women with RA.

Maternal age, medication use and HRQoL are factors influencing on the ability to achieve pregnancy.

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INTRODUCTION

Fertility is the capacity to establish a clinical pregnancy, while fecundity is the capacity to have a live birth (1). Total fertility rate (TFR) is defined as the average number of live births per woman (1). Female fertility and fecundity may be compromised, resulting in increased time to establish pregnancy (TTP) and reduced total fertility rate (2). Total fertility rate in Norway has gradually declined from 3 children in 1964 to 1.7 in 2015 (3).

Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are auto inflammatory, systemic rheumatic diseases, affecting fertile women. SLE typically leads to manifestations of skin, joints and internal organs (4) and has a more serious prognosis compared to RA, which classically is more often limited to the musculoskeletal system (5). Previous studies have shown that women with SLE and RA have lower total fertility rate than the general obstetric population, although there has been an increasing number of children born to mothers with rheumatic diseases during the last decades (6, 7). Subfertility is defined as TTP > one year, and has increased in Norwegian women (8). A higher occurrence of 36 – 42% in RA-women (9-11), is perceived the main cause of reduced TFR in this group, although lower fecundity may also play a role (12). In women with SLE, compromised fecundity is considered the main reason (13), even though severe and active disease as well as medication use are also associated with reduced fertility (14, 15). Studies comparing fertility, fecundity, total fertility rate and influencing factors between SLE and RA patients are rare, although extended data should be of importance to patients as well as treating physicians.

In women with chronic rheumatic diseases the disease itself, the treatment and fear of complications may lower total fertility rate (10, 14, 16-19) due to ovulatory disturbances (9), reduced ovarian reserve (20-23) and impaired sexual function caused by decreased health-

related quality of life (HRQoL) (18, 24, 25). Earlier findings indicate lower HRQoL in rheumatic diseases compared to population controls (26, 27), and in RA especially in the physical domains (28). Acquiring a chronic disease in reproductive age may influence family planning. Clowse et al (10), found that women with SLE and RA reported fewer children than wished for, and that personal choice was one of the reasons.

The objective of this study was to examine possible differences in the ability to achieve pregnancy and time to pregnancy (TTP) among women with SLE and RA, and to study possible influencing factors including health-related quality of life (HRQoL).

PATIENTS AND METHODS

Study population

The study population was retrieved from RevNatus, a nationwide Norwegian multicenter, prospective observational register including women with inflammatory rheumatic diseases when planning pregnancy or after conception. The register was established in 2006, and all but two departments of Rheumatology contribute with eligible patients. According to national guidelines (29), pregnant women with rheumatic diseases should have follow-up by a specialist in Rheumatology. Women 18 years or older are recruited and followed-up in each trimester of pregnancy and at 6 weeks, 6 months and 12 months after birth. Disease characteristics, disease activity, HRQoL, use of medications, outcomes and complications in mother and child are recorded. Studied women were included before pregnancy and had follow-up during pregnancy and 6 weeks after birth or pregnancy loss, or at least one year if not achieving pregnancy. They were included in the period 2006 to 2016.

Ethics

The register RevNatus was approved by the regional committee for medical and health research ethics (REK Midt) in 2006. Eligible women signed written informed consent before inclusion in the register. The present study has been approved by REK Midt (2012/1905).

Variables

Background variables were obtained from data collected at the pre-conceptional visit and included background and disease specific characteristics, medication use, health-related quality of life (HRQoL) variables and information on earlier pregnancy outcomes. Disease activity was measured using scores validated for the respective disease: lupus activity index (LAI) in SLE (30) and disease activity score-CRP (DAS–CRP) in RA (31). The main outcome variables were achieving pregnancy (yes/no), time to pregnancy (TTP), live birth or pregnancy loss. These data were collected after birth or pregnancy loss, or at study closure.

Time to pregnancy

Time to pregnancy (TTP) was defined as the time in months between pregnancy-wish and the first day of the last menstrual period before pregnancy, or by subtracting 40 weeks from the expected date of delivery based on an ultrasound examination around 18 weeks of pregnancy. Women were censored at the end of the study period if they had been included in the register at least one year earlier without becoming pregnant.

Health-related quality of life

RAND-36 (32) is a composite measure of different aspects of health-related quality of life (HRQoL). It has eight domains: Physical Function, Role Physical, Bodily Pain, General Health, Vitality, Social Function, Role Emotional and Mental Health, each including 2 - 10 items and translating to a score of 0 – 100. A higher score indicates a better HRQoL. A change in score of ≥ 5 points is considered a minimal clinically important difference (MCID), with ≥ 5 and < 10

perceived a marginal change and ≥ 10 a clear change(33). It is a generic measure, useful for comparing HRQoL between diseases (34). RAND- 36 is validated for use in both RA (35) and SLE (36).

Statistics

Group comparisons were performed using independent samples t-test for continuous variables and the unconditional z-pooled test (37, 38) or the exact -Wilcoxon-Mann-Whitney test for categorical variables. Time to pregnancy was compared between the groups using Kaplan-Meier plots, the log rank test, and further using Cox proportional hazard regression, unadjusted as well as adjusted for maternal age, parity and use of disease modifying antirheumatic drugs (DMARDs). We use the term pregnancy ratio for hazard ratio in Cox regression. Two-sided p-values less than 0.05 were considered statistically significant, and 95% confidence intervals (CI) are reported where relevant. The statistical analyses were performed using SPSS 24 and StatXact11 (unconditional z-pooled test).

RESULTS

Patient characteristics

We included 53 women with SLE and 180 women with RA in the study. See supplemental Figure S1 for the selection process. Background characteristics are shown in Table 1. There were no statistically significant differences between the groups.

Table 1

Among women with SLE 12 (24.5%) had been pregnant before diagnosed with rheumatic disease. This applied to 55 (35.9%) women with RA. Data was not available in 4 SLE-women and 27 RA-women. After diagnosis but before the current follow-up, 24 (48.0%) SLE-women

and 61 (39.4%) RA-women had achieved pregnancy. No data was available in 3 and 25 women, respectively. The mean number of prior pregnancies per woman at inclusion was 1.3 for both disease groups. Table 2 describes and compares disease related characteristics among women with SLE and RA. Women with SLE were younger at diagnosis, had longer disease duration, a higher percentage had active disease, and the majority used ≥ 1 DMARD.

Table 2

During follow-up 47 (88.7%) SLE- women and 130 (72.2%) RA-women conceived. The Kaplan-Meier plot in figure 1 illustrates the higher success rate in achieving pregnancy among women with SLE compared to women with RA, as well as a shorter time to pregnancy with median 3.0 months (95% CI 1.36 to 4.64) in SLE and median 7.0 months (95% CI 5.29 to 8.71) in RA. The differences were statistically significant (Log rank test with Chi-sq 11.45, p = 0.001). Eight (15.1%) of 53 women with SLE and 65 (36.1%) of 180 women with RA had TTP exceeding one year (p = 0.005), indicating subfertility. Cox regression showed a pregnancy ratio of 1.72 (CI 1.23 to 2.41, p = 0.002) for women with SLE compared to women with RA. The pregnancy ratio increased to 1.91 (CI 1.27 to 2.88, p = 0.002) after adjusting for maternal age, parity and DMARDs-use.

Figure 1

The main outcomes are outlined in Table 3. In women achieving pregnancy during follow-up, assisted reproduction only occurred in women with RA and mean time to pregnancy was shorter in women with SLE than women with RA.

Table 3

Four of six women with SLE not achieving pregnancy (NAP) were nulliparous, a higher frequency smoked, had active disease or overweight compared to SLE-women achieving

pregnancy (AP). Women with RA not achieving pregnancy were older and had a history of preeclampsia more frequently than women with RA achieving pregnancy (Table 4).

Table 4

Medication at inclusion

Traditional non-steroidal anti-inflammatory drugs (NSAIDs) were used more often in women with RA and prednisolone more often in women with SLE (Table 2) before pregnancy. The most commonly used DMARD was hydroxychloroquine in SLE (80.8%) and sulfasalazine in RA (28.6%). One (1.9%) SLE-woman and twenty (11.4%) RA-women used methotrexate, while 3 (5.8%) SLE-women used mycophenolate-mofetil pre-conceptionally. Fifty-one (29.1%) RA-women used TNF-alpha-inhibitors at inclusion (see supplementary Table S1).

Health- related quality of life

There were no statistically significant differences comparing health-related quality of life (HRQoL) in women achieving (AP) and not achieving pregnancy (NAP) in the two groups. However, women with SLE not achieving pregnancy had lower mean scores than women with SLE achieving pregnancy, exceeding the minimal clinically important difference (MCID) in several domains (Diff score ≥ 5) (Table 5).

Table 5

DISCUSSION

In our study women with SLE had higher pregnancy ratio and shorter time to pregnancy (TTP) compared to women with RA. We found no differences in background characteristics to explain this finding, but there are differences in disease related characteristics that may be of relevance. Women with SLE were younger at diagnosis and had longer disease duration

at inclusion. It may be of advantage to have time to accept and adjust to a chronic disease before family planning is relevant, as opposed to acquiring a disease when the wish for and expectations about having children is already expressed. This is in accordance with earlier findings comparing women with juvenile arthritis and RA (39).

Previous studies have found that both disease groups have increased subfertility and reduced total fertility rates compared to population controls (8, 10, 14, 15, 39, 40). Generally, age is one of the main factors to determine subfertility (41). In our study, women with SLE had a mean age similar to the general obstetric population in Norway (42), with no significant difference between women achieving and not achieving pregnancy. Accordingly, age does not seem to influence on fertility in women with SLE, besides the general increase in maternal age at first birth (8). In contrast, women with RA had a substantially higher mean age, found to be statistically significantly higher in women not achieving pregnancy compared to women achieving pregnancy. Earlier studies have shown that women childless at diagnosis have lower parity than matched references (39). In both women with SLE and RA not achieving pregnancy, we found higher frequencies of nulliparity compared to in women achieving pregnancy, even though the small SLE-group demands caution in interpreting the results.

During follow-up, women with SLE and RA achieving pregnancy had pregnancy loss in 19.1% (9/47) and 20.0% (26/130), respectively, indicating no difference in fecundity. This is in contrast to earlier findings, reporting a higher frequency of pregnancy loss in women with SLE than women with RA (10). In the general population, the pregnancy loss rate is commonly reported to be lower, around 15% (43, 44). It is possible that early miscarriages were acknowledged and reported more often due to the tight follow up in the RevNatus

register. However, a higher occurrence of miscarriages in SLE after diagnosis compared to before diagnosis (45) is reported. Similarly, women with RA had a higher relative risk of miscarriage compared to reference women without inflammatory rheumatic disease in a recent Norwegian study (12). Positive antiphospholipid antibodies are associated with pregnancy loss, and this is well documented in SLE (46, 47). The SLE-women in our population that had a pregnancy loss did not have any positive antiphospholipid antibodies (missing data in 2 of 9 women). The biological and clinical meaning of antiphospholipid antibodies concerning fertility remains to be clarified (48). Due to high missing numbers in the registration of these antibodies, we cannot assess their impact in our population of women with SLE and RA.

In our study, only one miscarriage was reported associated to medication with teratogenic potential (methotrexate) used less than 3 months before pregnancy or in pregnancy. No other associations between medication and pregnancy loss were found.

Diminished ovarian reserve due to SLE and RA itself is discussed as a reason for lower TFR, though controversial (20-23). Unfortunately, neither AMH-levels nor antral follicle count to assess this, were registered in RevNatus. Prior cyclophosphamide (CYC) administration is a proven risk factor for ovarian failure and decreasing AMH-levels (49). In our study two women with SLE (with live births) had been treated with cyclophosphamide more than 5 years earlier, but none of the women not achieving pregnancy in either diagnosis group were treated with cyclophosphamide in the past or at inclusion. Accordingly, CYC does not affect the ability to achieve pregnancy in our cohort.

NSAID- use may cause ovulatory disturbances and transiently reduce fertility (49). None of the SLE-women not achieving pregnancy used NSAIDs, while 18.4% of RA-women not

achieving pregnancy did, potentially extending TTP and amplifying the age factor. Moreover, we found a substantially higher (though not statistically significant) use of NSAIDs in women with RA not achieving than achieving pregnancy, possibly strengthening this effect.

A lower frequency of women with SLE (7.7%) used DMARDs incompatible with pregnancy at inclusion compared to women with RA (11.4%). In SLE-women not achieving pregnancy mycophenolate mofetil was used in one woman at inclusion, while in RA-women not achieving pregnancy methotrexate was used in 14.3% at inclusion. Accordingly, the need to adjust medication and ensure clinically acceptable disease modifying effect before conception may be of more importance in increasing TTP and maternal age in RA-women than SLE-women. Nevertheless, in 13 women with RA achieving pregnancy there were 12 live births and one miscarriage. They were all exposed to methotrexate less than 3 months before pregnancy or in early pregnancy, illustrating that medication use does not always delay conception. There were no statistically significant differences concerning use of MTX in RA—women achieving and not achieving pregnancy, supporting recent studies demonstrating that MTX-use does not reduce ovarian function (9, 22).

Women with SLE more frequently had active disease, a known risk factor for reduced fertility and fecundity (14, 47), and in the small group of SLE-women not achieving pregnancy this was even more apparent. However, women with active SLE had mainly low disease activity (LAI < 0.5) with mean LAI 0.28 (0.063 – 0.79), while women with active RA had moderate disease activity (DAS CRP > 3.2) with mean DAS CRP 3.62 (2.80 – 6.39). We believe this can explain why disease activity does not interfere more with fertility and fecundity in the women with SLE in our cohort.

Women with SLE failing to conceive had poorer HRQoL than SLE-women achieving pregnancy. In the domains physical role, social function and role emotional we found a clear change (deterioration) and in the domains physical function, vitality and mental health a marginal change compared to the SLE-women achieving pregnancy. In this group reduced HRQoL in the domains social function, role emotional and mental health may impair sexual function, in line with earlier findings (10, 25). The low HRQoL scores in both SLE and RA concerning vitality and general health may impact TTP and the choice or ability to achieve pregnancy. Women with RA had similar but generally low scores whether achieving or not achieving pregnancy concerning physical role and bodily pain, implicating physical hindrance to sexual activity, while social functioning, role emotional and mental health domains were higher. Our results indicate that women with RA have a generally lower HRQoL than women with SLE, and that this is a probable risk factor for prolonged TTP and lower total fertility rate in these women.

A strength of this study is the prospective follow-up design, securing more accurate and unbiased registration of disease activity, medication use and HRQoL domains.

A possible weakness is that some of the women may not have a pregnancy wish at the time of inclusion in the register, but plan pregnancy in the future. Not excluding a patient when a pregnancy wish is no longer present is another potential bias. However, we excluded 22 women because pregnancy was no longer relevant due to changing social status or other life events, reducing this source of error. A selection bias may be that SLE is a potentially more serious disease than RA, and that women with severe SLE do not try to conceive, while this is rarely the case in women with RA. Another selection bias might be that women with mild disease, especially RA, are not recruited into RevNatus, biasing our population towards more

severe disease. However, pregnant women with rheumatic diseases should have preconceptional counselling and specialized health care follow-up (2, 19, 29, 46, 47), implying recruitment in RevNatus.

In our prospective study, women with SLE had less problems in achieving pregnancy than women with RA. There was a similar occurrence of pregnancy loss indicating reduced fecundity in both groups compared to references without rheumatic disease. In women with RA, higher maternal age, more use of NSAIDs and medication not compatible with pregnancy together with a lower HRQoL compared to women with SLE are factors influencing negatively on time to pregnancy and total fertility rate. These findings may be helpful in counselling women with rheumatic diseases who plan pregnancy. Focus on disease activity and medication needs continued attention, and maternal age must be acknowledged as an important risk factor for reduced fertility. Moreover, assessing HRQoL may identify factors contributing to not achieving pregnancy.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION

All authors have been participants in this study and assisted in patient recruitment, study design and/or data interpretation. All authors have reviewed and made comments on the drafts involved in the development of this manuscript, and have approved the final version.

ETHICS APPROVAL

The Regional committee for medical and health research ethics (REK Mid-Norway).

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Table 1. Background characteristics at inclusion among women with SLE and RA

Characteristic	SLE	RA	P - value
	n = 53	n = 180	
Age, years, mean (SD)	30.2 (3.92)	31.1 (4.58)	0.22
≥ 35 years	8 (15.1%)	38 (21.1%)	
missing	0	0	
Parity			0.89[a, b]
0	28 (54.9%)	92 (53.8%)	
1	17 (33.3%)	57 (33.3%)	
2+	6 (11.8%)	22 (12.9%)	
missing	2	9	
Smoking	5 (10.6%)	12 (7.1%)	0.46[b]
missing	6	11	
Body mass index, mean (SD)	24.7 (5.6)	25.0 (4.8)	0.72
underweight (< 18.5)	0	8 (5.1)	
normalweight (18.5 – 24.9)	24 (61.5)	78 (49.7)	
overweight (≥ 25)	15 (38.5)	71 (45.2)	
missing	14	23	
Educational level			0.91[c]
low[d]	4 (7.5%)	4 (2.4%)	
intermediate[e]	10 (18.9%)	42 (24.7%)	
high[f]	39 (73.6%)	124 (72.9%)	
missing	0	10	
Prior pregnancy loss	15 (30.0%)	41 (27.9%)	0.92[b]
missing	3	33	
Prior preterm birth	1 (4.8%)	2 (3.0%)	0.83[b]
missing	2	12	
Prior preeclampsia	2 (12.5%)	7 (13.5%)	1.0[b]
missing	7	27	

SLE = systemic lupus erythematosus, RA = rheumatoid arthritis, [a] No children vs ≥ 1 child, [b]unconditional z-pooled test, [c]exact Wilcoxon-Mann-Whitney, [d]10 years, [e]12 – 13 years, [f]>15 years

Table 2. Disease related characteristics at inclusion among women with SLE and RA

Characteristic	SLE n = 53	RA n = 180	P-value
Age at diagnosis, mean (SD)	21.6 (6.1)	25.3 (5.9)	<0.001
missing	4	12	
ACR criteria fulfilled	34 (91.9%)	119 (84.4%)	0.25[a]
missing	16	39	
Disease duration years, mean (SD)	8.6 (6.1)	5.7 (4.8)	0.001
missing	4	12	
Active disease	24 (66.0%)	59 (38.8%)	0.002[a]
missing	17	28	
NSAID-use	4 (7.7%)	21 (12.0%)	0.41[a]
missing	1	5	
Prednisolone-use	22 (42.3%)	55 (31.4%)	0.15[a]
missing	1	5	
≥ 1 DMARD	40 (90.9%)	77 (44.0%)	<0.001
	9	5	

SLE = systemic lupus erythematosus, RA = rheumatoid arthritis, [a]unconditional z-pooled test

Figure 1. Kaplan Meier plot for time to pregnancy, comparing women with SLE and RA.

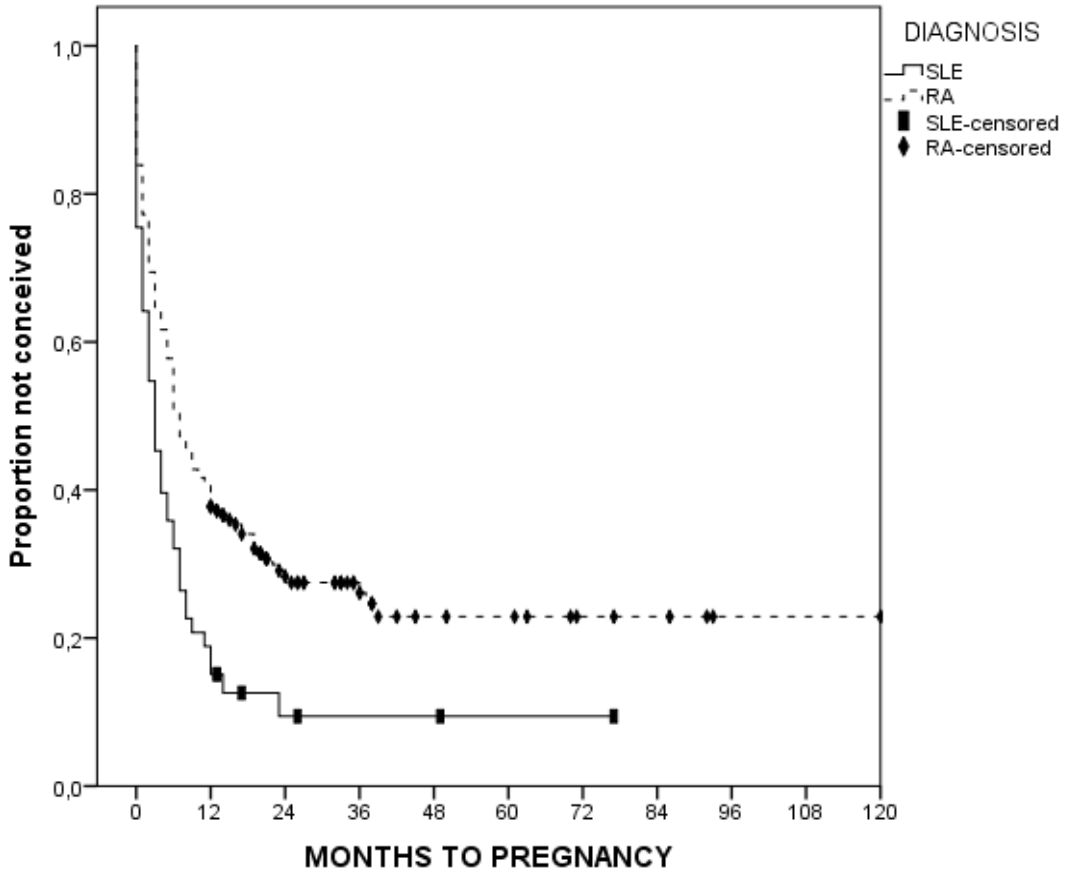


Table 3. Pregnancy related outcomes among women with SLE and RA

	SLE n = 53	RA n = 180	p-value
Achieved pregnancy	47 (88.7%)	130 (72.2%)	0.014[a]
missing	0	0	
Outcome			0.031[b]
Live birth	38 (71.7%)	104 (57.8%)	
Pregnancy loss	9 (17.0%)	26 (14.4%)	
Not pregnant	6 (11.3%)	50 (27.8%)	
missing	0	0	
Assisted reproduction[c]	0	12 (11.1%)	0.02[a]
missing	7	22	
Months to pregnancy, mean (SD)[c]	3.9 (4.7)	6.2 (7.7)	0.017
missing	0	0	
TTP > 1 year[c]	2 (4.3%)	18 (13.8%)	0.11[a]
missing	0	0	

SLE = systemic lupus erythematosus, RA = rheumatoid arthritis, [a]unconditional z-pooled test, [b]exact Wilcoxon-Mann-Whitney, [c] Outcomes in women achieving pregnancy during follow-up

Table 4. Background and clinical characteristics in women with SLE and RA achieving pregnancy (AP) and not achieving pregnancy (NAP).

Characteristic	SLE AP (n = 47)	SLE NAP (n = 6)	P - value	RA AP (n = 130)	RA NAP (n = 50)	P - value
Maternal age, mean (SD)	30.2 (4.0)	30.7 (3.8)	0.76	30.4 (4.4)	32.9 (4.7)	0.001
missing	0	0		-	-	
Parity			0.29[a,b]			0.28[a,b]
0	24 (52.2%)	4 (80.0%)		63 (51.2%)	29 (60.4%)	
1	17 (37.0%)	0		44 (35.8%)	13 (27.1%)	
2+	5 (10.8%)	1 (20.0%)		16 (13.0%)	6 (12.5%)	
missing	1	1		7	2	
Smoking	4 (9.8%)	1 (16.7%)	0.84[b]	9 (7.6%)	3 (6.0%)	0.75[b]
missing	6	0		11	0	
BMI, mean (SD)	24.5 (5.4%)	28.0(6.5%)	0.16	24.9 (4.6%)	25.5(5.2%)	0.64
missing	13	1		23	0	
Educational level			0.61[c]			0.60[c]
low[d]	3 (6.4%)	1 (16.7%)		3 (2.5%)	1 (2.0%)	
intermediate[e]	9 (19.1%)	1 (16.7%)		28 (23.3%)	14 (28.0%)	
high[f]	35 (74.5%)	4 (66.7%)		89 (74.2%)	35 (70.0%)	
missing	0	0		10	0	
Age at diagnosis, mean (SD)	21.4 (6.1)	23.3(5.8)	0.47	25.1 (6.0)	26.0 (5.5)	0.35
missing	4	0		9	3	
ACR criteria fulfilled[g]	31 (91.2%)	3(100.0%)	0.86[b]	87 (84.5%)	32 (84.2%)	0.99[b]
missing	13	3		27	12	
Disease duration, mean (SD)	8.8 (6.2)	7.3 (5.8)	0.60	5.3 (4.9)	6.7 (4.7)	0.088
missing	4	0		9	3	
Active disease	21 (63.6%)	3(100.0%)	0.27[b]	45 (41.7%)	14 (31.8%)	0.27[b]
missing	14	3		22	6	
Prior pregnancy loss	14 (31.1%)	1 (20.0%)	0.81[b]	30 (28.3%)	11 (26.8%)	0.95[b]
missing	2	1		24	9	
Prior preterm birth	1 (5.0%)	0	1.0[b]	2 (3.9%)	0	0.82[b]
missing	2	0		9	3	
Prior preeclampsia	2 (13.3%)	0	1.0[b]	3 (7.3%)	4 (36.4%)	0.018[b]
missing	7	0		19	8	

SLE = systemic lupus erythematosus, RA = rheumatoid arthritis, AP = achieving pregnancy, NAP = not achieving pregnancy
[a] No children vs ≥ 1 child, [b]the unconditional z-pooled test, [c]exact Wilcoxon-Mann-Whitney, [d]10 years, [e]12 – 13 years, [f]>15 years, [g]According to diagnosis

Table 5. Health related quality of life in women with SLE and RA achieving pregnancy (AP) and not achieving pregnancy (NAP), reported as mean (SD)

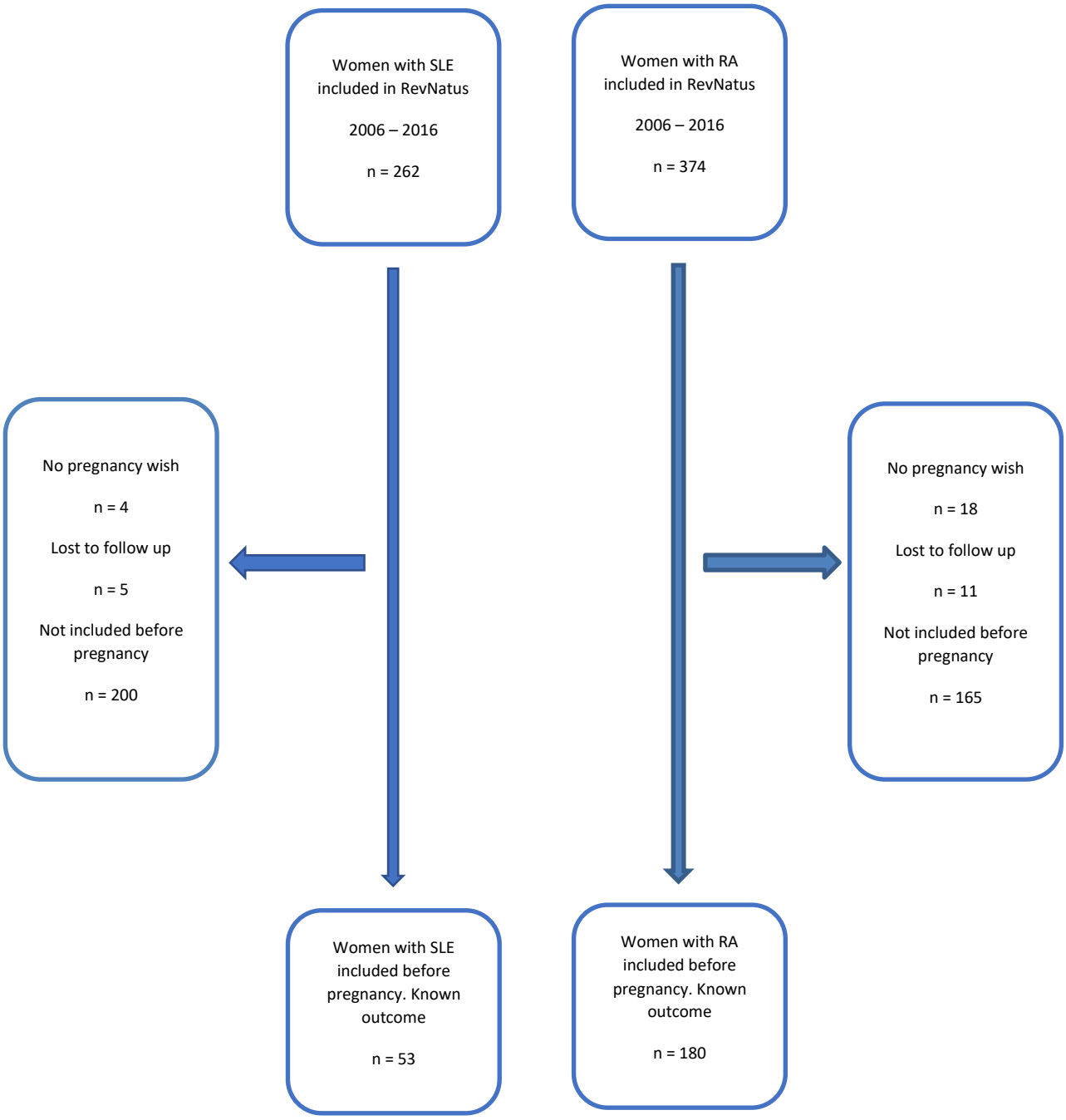
Domain	SLE AP n = 47	SLE NAP n = 6	P-value	Diff score	RA AP n = 130	RA NAP n = 50	P-value	Diff score
Physical function	90.2 (13.5)	80.8 (21.1)	0.33	- 9.4	80.1 (19.8)	78.9 (22.1)	0.74	- 1.2
missing	5	0			19	6		
Physical Role	65.2 (40.7)	45.8 (40.1)	0.28	- 19.4	58.9 (40.4)	57.4 (45.0)	0.85	- 1.5
missing	5	0			19	6		
Bodily Pain	72.5 (23.6)	79.0 (31.6)	0.55	+ 6.5	61.8 (24.0)	65.4 (25.4)	0.42	+ 3.6
missing	5	0			19	6		
General Health	60.3 (26.1)	56.0 (13.9)	0.55	- 4.3	57.5 (21.9)	57.0 (24.1)	0.90	- 0.5
missing	5	0			20	6		
Vitality	50.7 (22.4)	42.5 (27.2)	0.42	- 8.2	48.0 (19.9)	50.1 (21.0)	0.56	+ 2.1
missing	5	0			19	7		
Social function	75.0 (24.4)	64.6 (27.9)	0.34	- 10.4	80.6 (22.8)	80.4 (21.3)	0.95	- 0.2
missing	5	0			19	6		
Role emotional	79.4 (36.8)	50.0 (46.0)	0.082	- 29.4	81.7 (32.3)	77.3 (35.1)	0.46	- 4.4
missing	5	0			19	6		
Mental health	74.9 (14.7)	68.7 (12.8)	0.53	- 6.2	77.7 (13.7)	80.2 (15.4)	0.33	+ 2.5
missing	5	0			19	7		

SLE = systemic lupus erythematosus, RA = rheumatoid arthritis, AP = achieving pregnancy, NAP = not achieving pregnancy

SUPPLEMENTARY FIGURE S1. FLOW CHART.

Women with SLE and RA included in RevNatus before pregnancy

2006 - 2016



Supplementary Table S1. Medication use before pregnancy in women with SLE and RA. Frequency (percentage)

Medication	SLE n = 53	RA n = 180	SLE (AP) n = 47	RA (AP) n = 130	SLE (NAP) n = 6	RA (NAP) n = 50	SLE (AD) n = 24	RA (AD) n = 59
NSAIDs	4/52 (7.7)	21/175 (12.0)	4/46 (8.7)	12/126 (9.5)	0/6 -	9/49 (18.4)	3/24 (12.5)	8/59 (13.6)
Prednisolone	22/52 (42.3)	55/175 (31.4)	19/46 (41.3)	43/126 (34.1)	3/6 (50.0)	12/49 (24.5)	8/24 (33.3)	24/59 (40.7)
≥ 7.5 mg daily	7/22 (31.8)	16/50 (32.0)	7/19 (36.8)	13/40 (32.5)	0/3 -	3/10 (30.0)	2/8 (25.0)	9/21 (42.9)
DMARDs	40/44 (90.9)	77/175 (44.0)	34/38 (89.5)	52/126 (41.3)	6/6 (100.0)	25/49 (51.0)	17/18 (94.4)	31/59 (52.5)
azathioprine	17/52 (32.7)	1/175 (0.6)	15/46 (32.6)	1/126 (0.8)	2/6 (33.3)	0/149 -	8/24 (33.3)	1/59 (1.7)
HCQ	42/52 (80.8)	10/175 (5.7)	36/46 (78.3)	9/126 (7.1)	6/6 (100.0)	1/49 (2.0)	19/24 (79.2)	4/59 (6.8)
sulfasalazine	0/52 -	50/175 (28.6)	0/46 -	32/126 (25.4)	0/6 -	18/49 (36.7)	0/24 -	24/59 (40.7)
methotrexate	1/52 (1.9)	20/175 (11.4)	1/46 (2.2)	13/126 (10.3)	0/6 -	7/49 (14.3)	1/24 (4.2)	4/59 (6.8)
MMF	3/52 (5.8)	0/176 -	2/46 (4.3)	0/127 -	1/6 (16.7)	0/49 -	1/24 (4.2)	0/59 -
Biologics	0/52 -	52/175 (29.8)	0/46 -	37/126 (29.4)	0/6 -	15/49 (30.6)	0/24 -	8/59 (13.6)
TNF-alfpha-inh	-	51/175 (29.1)	-	36/126 (28.6)	-	15/49 (30.6)	-	8/59 (13.6)
adalimumab	-	3/175 (1.7)	-	2/126 (1.6)	-	1/49 (2.0)	-	0/59
certolizumab	-	21/175 (12.0)	-	15/126 (11.9)	-	6/49 (12.2)	-	5/59 (8.5)
etanercept	-	25/175 (14.3)	-	17/126 (13.5)	-	8/49 (16.3)	-	2/59 (3.4)
rituximab	-	1/175 (0.6)	-	1/126 (0.8)	-	0/49	-	-

SLE = systemic lupus erythematosus, RA = rheumatoid arthritis, AP = achieving pregnancy, NAP = not achieving pregnancy, AD = active disease, DMARDs = disease modifying antirheumatic drugs, HCQ = hydroxychloroquine, MMF = mycophenolate mofetil