ONLINE SUPPLEMENTARY DATA

Supplementary Data 1. Detailed methods

Detailed Variables and data sources

Respondents could choose from a selection of conditions included in the questionnaire: diabetes, high blood pressure, coronary heart disease, congestive heart failure and peripheral arterial occlusive disease. Mucosal dryness, Sicca syndrome and/or Sjogren's syndrome were summarised in one question".

The CSFQ-14 is a short form of the 36-item based CSFQ questionnaire with five scales of sexual functioning: pleasure, desire/interest, desire/frequency, arousal, orgasm. Questions can be answered with „never – rarely – sometimes – often – every day", or with „no – little - some – much – great enjoyment or pleasure ". The CSFQ-14 ranges from 14 to 70. A total score at or below 41 is indicative of sexual dysfunction. We intentionally decided to use this specific questionnaire as it is a core instrument, widely used and studied in this field. We obtained permission to use the validated German version for the purpose of this study.

The BDI-FS is a self-report questionnaire containing seven psychological symptoms of depression: sadness, pessimism (hopelessness), sense of failure, loss of a sense of pleasure, loss of self-confidence, self-blame, and suicidal tendencies. The seven items are rated on a four-point scale (0-3) and assess frequency over the past two weeks. It excludes somatic symptoms such as fatigue or exhaustion, which are common in a number of chronic diseases. These can be recorded as symptoms of depression, although they could possibly be seen as the result of a somatic illness. The score ranges from 0 to 21, with higher scores indicating a more depressive symptomatology, and was validated for RA. The HAQ-DI consists of 20 questions, which cover 8 categories of daily life activities (dressing, getting up, eating, walking, hygiene, reaching, gripping and general activities). Questions can be answered with "possible without any difficulty (0 point)", "possible with some difficulty (1 point)", "possible with much difficulty

(2 points)" and "unable to do (3 points)". Use of any aids increases the score by 1 point. The worst score of each category is accepted as representative value for this activity. The total HAQ-DI score is equal to the mean value of all sub-scores.

Bias:

Given the sensitive topic in the present study we performed a very detailed explanation of the study to every single potential participant and stressed our efforts to ensure complete anonymity. Due to the design of our study, we were not able to link any data from the returned questionnaires to any study participant or study site. This resulted in a return rate of 235 of 319 (73.7%) questionnaires handed out to RA patients and 180 of 306 (58.8%) handed out to controls (total return rate: 415/625, 66.4%).

Study size:

From previous research [1], we estimated the difference in CSFQ-14 to be 13% between the two groups (previous research found a difference of approximately 18% difference in FSD with the use of a different score; accounting for this and the different setting, we decided to use a more conservative estimation (approximately 25% smaller difference in FSD for our sample size calculation)). Using an alpha of 0.05 and a beta of 0.2 (i.e., power of 80%) a study population of total n=462 (i.e., 231 per group, using a 1:1 ratio) would be required (two-sided test). Assuming at least 20% non-response in each group, the sample size needed to be increased by a factor of 1.25. This yielded a total study population of at least 578 (i.e., 289 per group). These considerations justified a minimum sample of 300 women per group

Statistical details:

Quantitative variables were used either as continuous variables (e.g. weight, height, etc.) or were transformed into ordered categorised variables. 10-year bands were used for age. HAQ was transformed into 3 categories: 0-0.5, >0.5-1.5 and >1.5. BDI was transformed into the following groups: 0-3 (minimal),

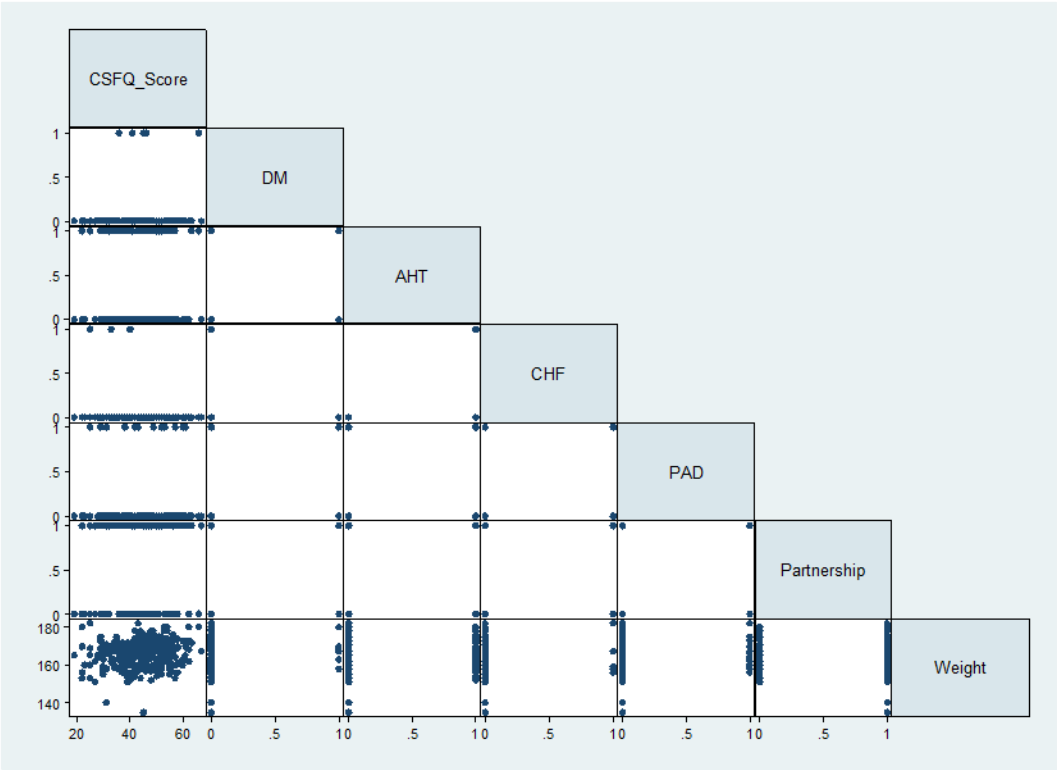
4-8 (mild), 9-12 (moderate) and >12 (severe). CDAI was transformed into the following groups: ≤ 2.8 (remission), >2.8 - <=10 (low disease activity), >10 - <=22 (moderate disease activity) and >22 (high disease activity).

RA is associated with depression (i.e., BDI). In addition, there is evidence that RA may cause – at least in part – depression [2,3]. Going further, depression is associated with and may cause FSD. Given these considerations, depression may be seen as being on the causal pathway between RA and FSD. That said, adjusting the association between RA and FSD for depression may be inappropriate and might underestimate the strength of association between exposure and outcome. Therefore, our main analysis did not include BDI as a confounder. However, in a sensitivity analysis we also adjusted for BDI. For the analyses of disease characteristics like CDAI and HAQ score we investigated the subgroup of RA patients separately (as these variables were not obtained in controls). The association of FSD with CDAI and HAQ is presented in its original form, as well as adjusted for potential confounders.

References:

1. Khnaba D, Rostom S, Lahlou R, Bahiri R, Abouqal R, Hajjaj-Hassouni N. Sexual dysfunction and its determinants in Moroccan women with rheumatoid arthritis. Pan Afr Med J 2016;6;24:16. (see ref. 9 in the main manuscript)
2. Atlantis E, Sullivan T. Bidirectional association between depression and sexual dysfunction: a systematic review and meta-analysis. J Sex Med 2012; 9:1497-1507. (see ref. 23 in the main manuscript)
3. Clayton AH, El Haddad S, Iluonakhamhe JP, Ponce Martinez C, Schuck AE. Sexual dysfunction associated with major depressive disorder and antidepressant treatment. Expert Opin Drug Saf 2014;13:1361-1374. (see ref. 24 in the main manuscript)

Supplementary Figure 1. Correlation matrix for FSD and comorbidities/selected variables



FSD: female sexual dysfunction, CSFQ: Sexual Functioning Questionnaire-short form, ATH: arterial hypertension, CHF: congestive heart failure, PAD: peripheral arterial occlusive disease

Supplementary Table 1. Association of disability (HAQ-DI) and disease activity (CDAI) with FSD in an unadjusted and adjusted analysis.

HAQ-DI category	n (%)	Unadjusted OR (95%CI) for FSD	Adjusted OR (95%CI) for FSD
0-0,5 (no - mild disability)	134 (59.8%)	1 .00 (ref)	1 .00 (ref)
0,51-1,5 (moderate disability)	66 (29.4%)	1.59 (0.83-3.06)	2.11 (0.55-8.11)
1,51-3 (severe disability)	24 (10.7%)	3.38 (1.26-9.08) *	0.67 (0.02-18.06)**
total	224 (100.0%)		
CDAI category			
≤ 2.8 (remission)	65 (29.3%)	1 .00 (ref)	1 .00 (ref)
>2.8 -≤10 (low disease activity)	100 (45.1%)	1.38 (0.70-2.71)	1.11 (0.22-5.58)
<10 - ≤ 22 (moderate disease activity)	42 (18.9%)	1.12 (0.48-2.58)	2.00 (0.38-10.58)
> 22 (high disease activity)	15 (6.8%)	0.83 (0.24-2.86) **	not computable **
total	222 (100.0%)		

HAQ-DI; Health Assessment Questionnaire Disability Index CDAI, Clinical Disease Activity Index, ref; Reference level, * Test for trend of odds: p= 0.007; ** Test for trend of odds: p>0.05