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A systematic review of the impact of inflammatory arthritis on intimate relationships and sexual function

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ABSTRACT

Objective: To systematically review evidence of the impact of inflammatory arthritis (IA) on, or association of IA with, intimate relationships and sexual function.

Methods: Ovid Medline, Ovid PsycINFO, Ovid EMBASE and EBSCO CINAHL databases were searched. Two independent reviewers selected articles, extracted data and conducted manual searches of reference lists from included studies and previous reviews. The quality of evidence was assessed using standard risk of bias tools.

Results: Fifty-five eligible studies were reviewed. Of these, 49 (89%) were quantitative, five (7.2%) were qualitative and one (3.6%) used a mixed-method design. Few quantitative studies were rated as low risk of bias (n=7; 14%), many were rated as moderate (n=37; 74%) or high risk (n=6; 12%). Quantitative study sample sizes ranged from 10-1,272 participants with reported age range 32-63 years. Qualitative study sample sizes ranged from 8-57 participants with reported age range 20-69 years. In studies reporting the Female Sexual Function Index, all IA groups demonstrated mean scores $\leq$26.55 (range of mean (SD) scores: 14.2(7.8)-25.7(4.7)), indicating sexual dysfunction. In studies reporting the International Index of Erectile Function, all IA groups reported mean scores ≤25 (range of mean (SD) scores: 16.3(6.2)-24.5(6.0)), indicating erectile dysfunction. Key qualitative themes were impaired sexual function and compromised intimate relationships; prominent sub-themes included IA-related pain and fatigue, erectile dysfunction, diminished sexual desire, and sexual function fluctuations according to disease activity.

Conclusion: Sexual dysfunction appears highly prevalent amongst men and women with IA, and increased clinician awareness of this impairment may guide provision of tailored education and support.

Key words

relationship; intimacy; sexual function; inflammatory arthritis; impact

SIGNIFICANCE AND INNOVATIONS

- This is the first systematic review to consider the impact of all types of inflammatory arthritis (IA) on intimate relationships and sexual function in both genders based on evidence from qualitative and quantitative studies.
- Eligible studies were primarily quantitative in design and demonstrated a higher prevalence of sexual dysfunction amongst the IA population in comparison to healthy populations; however, the impact on intimate relationships was rarely explored.
- Qualitative studies revealed that sexual dysfunction was impaired in IA due to pain, reduced sexual desire, erectile dysfunction and fatigue, along with the same

stressors that affect the general population such as stress, education and other concerns.

The International Classification of Functioning, Disability and Health (ICF) considers sexual health as comprising two distinct constructs: “sexual function”, relating to body functions, and “intimate relationships”, relating to activity and participation.(1) Sexual function in people with inflammatory arthritis (IA) may be affected by disease activity (pain, functional limitations and fatigue); psychological distress related to the disease including reduced self-esteem and altered body image perception; and/or side effects from pharmacological treatments (fatigue, lowered mood, vaginal dryness and erectile dysfunction).(2-10) Intimate relationships may, in turn, be affected by these and other factors,(11,12) potentially contributing to relationship dissatisfaction and family breakdown.(2,13-15) The impact of IA on sexual health appears to be an issue worldwide as it has been identified in populations in Europe, America, Asia and Africa.(13,16-19)

Sexual health and family planning are important considerations not only for individuals living with IA but also for the health practitioners who treat them,(20) yet these issues are rarely comprehensively addressed in clinical practice.(4,8,9,16,18,19,21-24) Earlier research has shown that 36-70% of people with rheumatoid arthritis (RA) experience impaired sexual health associated with their disease,(5,7,13,16,19,21,22,25,26) however, the majority have not discussed this with a health professional.(27) Additionally, people with IA vary in their preference of health professional with whom to discuss these issues(27), suggesting *all* health professionals involved in a person’s care should gain an improved understanding of the potential impacts of IA on sexual function and intimate relationships,.

The impact of IA on sexual health has been investigated previously, however systematic reviews published to date have important limitations.(5,6,28,29) First, many have not assessed the impact of IA on both genders, as most have focused on female sexual function only.(29-39) Second, most reviews have been disease-specific,(6,28-34,36-51) limiting transferability of the findings to other IA conditions. Although some reviews have considered rheumatic conditions more broadly,(10,35,52,53) they do not include contemporary evidence.(3,10,21,22,54-102) Finally, earlier reviews have largely been restricted to Western populations.(6,28)

To overcome existing limitations, we aimed to undertake a systematic review of self-reported perceptions (concerns, thoughts, beliefs, opinions) concerning the impact of IA on,

or the association of IA with, intimate relationships and sexual function among people with IA.

MATERIALS AND METHODS

Study design

A systematic review of quantitative and qualitative studies was undertaken in 2018. The systematic review protocol was registered on the PROSPERO International Prospective Register of Systematic Reviews (registration number CRD42017074189). The review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (Supplementary file).

Eligibility for inclusion

Primary qualitative, quantitative and mixed-method design studies published in English in peer–reviewed journals were included. Relevant self-reported outcomes included concerns, thoughts, beliefs and opinions of people with IA, concerning the impact of their IA on, or the association of IA with, intimate relationships and sexual function and were drawn from quantitative studies (e.g. surveys) or qualitative studies (e.g. interviews, focus groups). Studies conducted in any care setting were included. Studies that included males or females with a diagnosis of IA (including but not limited to rheumatoid arthritis (RA), seronegative arthritis, systemic lupus erythematous (SLE), systemic scleroderma/sclerosis (SSc), ankylosing spondylitis (AS), psoriatic arthritis (PsA), connective tissue disease (CTD), vasculitis, Sjogren's Syndrome (SS), spondyloarthritis (SpA), auto-immune arthritis, and juvenile idiopathic arthritis (JIA)) were included. Patients aged ≥16 years were eligible for the inclusion. Studies where the outcomes were not directly reported by people who live with IA (e.g. where outcomes were only reported by spouses) were excluded. Abstracts and conference proceedings were also excluded.

Search strategy and selection of studies

Four electronic databases (Ovid Medline, Ovid PsycINFO, Ovid EMBASE and EBSCO CINAHL Plus) were searched systematically from 1st of January 1990 to 8th of May 2018. An initial

search for studies was conducted in Medline and EMBASE, and an analysis of text words and subject terms was then used to develop the search (LR). Subject classification systems for each database were also investigated (with input from INA, SVD and AMB). The final searches of all four electronic databases was executed using the appropriate specifications of each database (LR). The comprehensive search strategy used for each of the four databases is presented in the Supplementary file. Grey literature was not considered. Two reviewers (LJR and SRD) independently screened the titles and abstracts of the yield to determine each paper's eligibility for inclusion. Any discordance regarding eligibility was discussed and resolved through consensus with arbitration by a third reviewer (AMB), if required. The full texts of the potentially eligible papers were reviewed independently by two reviewers (LJR and SRD) to confirm eligibility. Any discordance in selection of full texts was resolved through consensus and arbitrated by a third reviewer (AMB), if required. The reference lists of all included full text studies and any systematic reviews identified were manually screened by the reviewers (LJR and SRD). Citation screening and selection was documented and summarized in a PRISMA-compliant flow chart (Figure 1).

Data extraction

Data extraction was undertaken by two reviewers independently (LJR and SRD) and a consensus dataset derived. A standardised data extraction template was developed using Microsoft Excel (Microsoft Corporation, Albuquerque, New Mexico, United States) and piloted on three eligible papers by LJR, SRD, INA, SVD and AMB. Data from quantitative and qualitative studies were extracted separately. The following data were extracted (where available) for each study: research question, study design, study population including diagnoses, geographic region, study setting, demographic characteristics (e.g. age, gender), primary and secondary outcome measures and results. For qualitative studies, the first order data (the quotes from the primary study participants) and the second order data (themes, sub-themes developed by authors of included papers) were extracted to preserve the links to the original quotes and the context from the primary study.

Quality and risk of bias appraisal

The methodologic quality of the included studies was appraised independently by two reviewers (LJR and SRD) and a consensus appraisal score derived. Quantitative studies were

appraised using the Hoy et al risk of bias tool,(103) while the Critical Appraisal Skills Program (CASP) tool was used for qualitative studies.(104) While there are several risks of bias assessment tools available for quantitative and qualitative studies, these tools were selected for ease of use and alignment with other patient-centred systematic reviews relevant to rheumatic diseases.(105-110). The tools were piloted on three eligible papers to ensure inter-rater consistency. Any discordance regarding critical appraisal was discussed and resolved through consensus with arbitration by a third reviewer (AMB), if required.

Data analysis and synthesis of results

Two reviewers (LJR and SRD) independently extracted and synthesised the data from the eligible studies. Descriptive and outcome data from quantitative studies were summarised and reported descriptively. The independent datasets relating to the quantitative studies were compared for consistencies, with any discrepancies resolved to create a composite dataset. The results of the qualitative studies were meta-synthesised using a staged approach of thematic analysis.(111-113) Independent data files were merged and compared with discrepancies resolved by consensus, and if necessary, arbitration. First, each reviewer read the full text paper multiple times highlighting relevant sections that related to the review to inductively develop initial categories or themes. These themes/categories were organised into an initial thematic framework, which was reviewed by other authors (AMB, INA, SVD) to consider construct validity and clinical meaningfulness. Second, the framework was populated with extracted data from the studies to ensure the inductively-derived themes and sub-themes were underpinned by primary data. Once populated, the framework was again revised and reviewed by the authors.

Assessment of confidence profile

The GRADE-Confidence in the Evidence from Reviews of Qualitative research (GRADE-CERQual) method was used to assess confidence in the meta-synthesis findings across four domains: 1) methodological limitations, 2) coherence, 3) adequacy of data, and 4) relevance of all the individual primary research study findings contributing to the meta-synthesis,(114) with each domain assigned a level of concern (minor, moderate, substantial). The review team (SRD, LJR, AMB) evaluated the confidence profile through discussions and allocated an overall level of confidence (high, moderate, low and very low confidence) to each finding in the meta-synthesis.

RESULTS

Search results and description of included studies

The search strategy returned 2100 unique citations of which 55 (2.6%) (7-9,19,22,27,60-77,79-102,115-121) met the inclusion criteria (Figure 1). Descriptive characteristics of the 55 included studies are summarised in Table 1. Of the included studies, 50 (90.1%) were quantitative,(7,9,19,27,60-76,79,81,82,84-88,90-94,96-102,115-121) five (9.1%) were qualitative (77,80,83,89,95) and one (1.8%) used a mixed-method design.(8) Four of the qualitative studies used focus groups or semi-structured interviews,(80,83,89,95) while all the quantitative studies used patient-reported questionnaires.(7,9,19,22,27,60-76,79, 81,82,84-88,90-94,96-102,115-121)

Included studies were conducted, where reported, in the European Union (n=16; 29%),(8, 19,27,62,69,79,83,87,89,90,94-98,117) Middle East (n=14; 25.4%),(22,65,67,68,71,75,77,80, 84,86,91,100,118,121) North America (n=5; 9%),(60,63,97,115,116) Africa (n=3; 5.4%),(7,85,88) Oceania (n=1; 1.8%) (70) and in South America (n=2; 3.6%).(66,92) Controlled cohort study designs were adopted by 33 (69%) of the quantitative studies,(9,19,22,60,61,64-69,71,72,75,81,82,84-87,91,92,96-102,115,118,120) while 12 (30.9%) used single group designs.(7,62,63,70,74,76,88,93,94,116,117,119) Sixteen (29%) studies sampled people with RA only,(7,9,19,27,68,75,82-85,88,93,94,96,100,118) 16 (29%) with AS only,(22,61,62,64-66,71-74,80,81,92,119-121) nine (16.3%) with SS only,(63,69,76, 77,79,90,97,115,117) five (9%) with SLE only,(60,70,89,99,116) four (7.2%) with SS only,(87,91,101,102) and three (5.4%) with mixed inflammatory arthritis conditions.(74) Mean (SD) IA disease duration ranged from 3.3 (2.6) years to 19.0 (11.6), 52 (94.5%) studies reported participants had a disease duration of greater than five years.(7-9,19,27,60-70,72-77,79-82,84-102,115-121)

Participants were recruited from tertiary hospital outpatient rheumatology clinics in eight (14%) studies,(9,19,62,67,70,81,84,93,95) research hospital outpatient rheumatology clinics in four (7%) studies,(8,72,100,118) non-tertiary outpatient rheumatology clinics in six (10%) studies, (7,69,71,74,98,99) university hospitals in 15 (27%) studies (22,63,65,66,75-

77,80,85,87,88,91,92,122) and from research or disease databases/registries in seven (12%) studies.(60,89,96,97,115-117,121) Sample size ranged from 10-1,272 participants (reported age range: 32-63 years; proportion female: 0-100%) in quantitative studies (7,19,22,27,60-76,79,81,82,84-88,90-94,96-102,115-121) and 8-57 participants (reported age range: 20-69 years; proportion female: 30-53%) in qualitative and mixed-method studies.(8,77,80,83, 89,95)

Outcomes reported

Outcomes from quantitative studies highlighted that sexual dysfunction was more prevalent among people with IA for both men and women compared with controls (Table 2). The two most common instruments were the Female Sexual Function Index (FSFI) and the International Index for Erectile Function (IIEF).

FSFI scores were reported in 15 (30%) studies (Figure 2). All patient groups demonstrated a mean score lower than the FSFI threshold for sexual dysfunction of ≤26.55 (123), indicating the presence of sexual dysfunction.(22,68,69,71,72,76,82,86,87,90,91,98,99,101,102) Of these 15 studies, 13 (87%) compared an IA patient group with a control group, highlighting that most of the IA groups had lower FSFI mean scores than controls.(22,68,69,71,72,82,86,87,91,98,99,101,102) In two studies (13%), control groups demonstrated greater sexual dysfunction than the IA patient groups.(71,82) In five (38%) studies, control groups reported sexual dysfunction, based on the FSFI threshold, although their mean scores were still higher than IA patient groups.(68,69,71,82,101) Two studies (13%) did not utilise control groups, however, the mean scores reported for their IA groups on the FSFI appeared much lower than the mean scores of studies with control groups.(76,90) Comparing outcomes by disease, populations with SSc reported mean FSFI scores that tended to be the lowest,(69,76,90,98) although these studies were uncontrolled.(76,90)

Seven (14%) studies used the IIEF to assess the impact of IA on men's erectile function (64,67,75,81,90,120,121) (Figure 3). In all studies,(64,67,75,81,90,120,121) the mean IIEF scores were ≤25, indicating erectile dysfunction.(124) All but one study compared IIEF scores of IA patients to controls and found lower mean scores in the IA group.(64,67,75,81,120,121) Mean scores for most control groups suggested normal erectile

function except for two studies where the control group mean scores were on the threshold for erectile dysfunction, however these scores were not lower than the IA patients' mean scores.(64,81) One study did not involve comparison with a control group, although the mean IIEF score remained lower compared to mean scores of IA groups across other studies.(90) Comparing outcomes by disease, a population with SSc reported the lowest mean IIEF score, (90) followed by AS groups (64,67,81,120,121), while those with RA appeared to have the highest IIEF mean score.(75)

Twenty-six (52%) studies reported outcome measures that included other validated and reliable tools, shortened versions of existing tools, or customised tools for that specific study.(7-9,19,27,60-62,65,66,70,73,74,79,84,85,93,94,96,97,100,115-119) All identified sexual dysfunction amongst their IA groups, however few commented on the impact of IA on intimate relationships.(8,62) In those that did, only the prevalence of disrupted relationships was explored, which was reported by 38% of men with AS (62,96) and 25%-76% of males and females with RA.(8,96) Among the 12 (43%) studies that compared outcomes with control groups, impaired sexual function was more consistently reported by patients with IA, compared to controls.(9,19,61,65,66,74,84,92,97,100,115,118). Scope of sexual dysfunction measured in these studies involved the degree of sexual or erectile dysfunction;(7,9,27,60-62,65,85,95,96,100,117-119,125) prevalence of sexual dysfunction;(8,70,73,93,97) prevalence of patients engaging, initiating and avoiding intercourse and foreplay;(126) satisfaction with sexual life;(74) and individual domains of sexual function (including desire, masturbation, fantasies, frequency, fatigue, pain, sensation, lubrication, orgasm, intensity of orgasms and overall sexual satisfaction).(66,84,115)

Subject data collection,(7,9,19,22,27,60-65,67-69,71-76,79,81,82,84-86,88,90-94,98,99,101,115-121) acceptable case definition,(7,9,19,22,60-62,64-76,79,81,82,84-86,88,90-94,96-100,115-121) mode of data collection,(7-9,19,22,27,60-69,71-76,79,81,82,84-86,88,90-94,96-100,115-121) a short prevalence period,(9,19,22,60,62-65,67-69,71-76,79,82,84-86,88,90-93,96-100,118-121) and validity of measurement tools (7,9,19,22,60,62-65,67-69,71-73,75,79,81,82,84,86,88,90-92,96-100,117,119-121) were the most common shortfalls across included studies. Most (n=37, 74%) quantitative studies were assessed as having a moderate risk of bias(7,8,22,60,61,63,64,68-71,74-76,79,81,82, 84-

86,88,90,92-94,96-98,100,101,115-121). Only 7 (14%) of the studies were considered at low risk of bias,(62,65,67,72,87,91,99) while 6 (12%) were assessed as having a high risk of bias.(9,19,27,66,73,102) Risk of bias in these high risk studies was primarily related to internal validity considerations (mode of data collection, case definition, reliable and acceptable diagnosis, short period for determining prevalence).(9,19,27,66,102)

Meta-synthesis of qualitative data

Meta-synthesis outcomes for the six eligible qualitative studies are summarised in Table 3. Two key themes were identified, supported by several sub-themes.

Theme 1: Impaired sexual function

Subtheme analysis demonstrated that sexual function was affected by pain, reduced sexual desire, erectile dysfunction and fatigue, along with the same stressors that affect the general population such as stress, education and other general life concerns.(8,80,95,122) People with IA reported that they typically changed the positions previously adopted during intercourse, assuming a more passive role to reduce pain.(80,95) Pain was associated with a fear of interrupted intercourse, or intercourse being postponed.(80,95) Level of sexual dysfunction often varied with flares in disease activity, but also with time of day, as pain and fatigue were more likely to affect sexual dysfunction during the evening.(95,122) Erectile dysfunction largely accounted for sexual dysfunction in males, which caused frustration, shock, stress and a sense of emasculation.(95,122) Negative body image, reduced desire for intercourse and erectile dysfunction all contributed to an altered sense of sexuality across both genders.(89,95,122)

Theme 2: Compromised intimate relationships

Intimate relationships tended to transition towards a more caring and less physical nature as the importance of sexual intercourse was reduced, particularly during disease flares.(95) Some partners had greater acceptance and understanding of the impact IA had on sexual function than others, assisting to strengthen relationships between partners.(8) Others found that their partners poorly understood the impact of IA on their ability to engage in

intercourse, creating tension and fear in relationships.(77,95,122) Despite the sexual dysfunction associated with IA, women often felt pressured to maintain a normal sex life to prevent relationships being compromised by IA.(8,95) Poor body image reduced sexual desire in both male and female populations and restricted people from finding partners.(95)

Quality assessment of the qualitative studies is summarised in the Supplementary file. Many of the qualitative studies were considered to have a risk of bias due to lack of consideration of the relationship between researcher and their participants,(8,77,80,89,95) ethical issues (95) or a failure to clearly state the research aims.(89)

Confidence in the meta-synthesis findings was evaluated based on the four domains of the GRADE-CERQual approach (Supplementary file). Overall, we identified 11 key findings based on the summary of results from primary studies (Table 3); two were associated with a high level of confidence that the review findings were a reasonable representation of the phenomenon of interest, while three were rated as moderate confidence and three were rated as very low confidence.

DISCUSSION

We identified consistent evidence (albeit of varying methodological quality) highlighting an association between IA and impacts on intimate relationships and sexual function for both genders. People living with IA consistently demonstrated a higher prevalence of sexual dysfunction compared to healthy peers, although these estimates tend to be crude and are not adjusted for potential confounders. For both genders, disease-related factors contributed to sexual dysfunction (including pain, fatigue and mobility restrictions) and reduced sexual desire, as well as non-disease-related factors that typically affect the general population. Erectile dysfunction and its emotional sequelae largely accounted for sexual dysfunction while females experienced pressured to continue intimate relationships despite their sexual dysfunction, causing stress in relationships.(8,95,122)

Our review demonstrated that studies have primarily assessed the impact of IA on sexual function utilising the FSFI and IIEF instruments. All studies using the FSFI demonstrated that IA populations had a mean score lower than the FSFI threshold of ≤26.55 (123) indicating the

prevalence of sexual dysfunction compared to healthy controls.(22,68,69,71,72,76,82, 86,87,90,91,98,99,101,102) Two studies found that healthy populations demonstrated greater sexual dysfunction than their matched IA populations.(71,82) Demir et al. (71) suggested this may be due to excluding psychiatric history and antidepressant use, which may have reduced the prevalence of mental health conditions and sexual dysfunction sequelae amongst the IA group. However, four other studies used these exclusion criteria and their IA populations had greater sexual dysfunction than controls and no statistically significant difference in depression between the IA group and healthy controls was observed.(22,68,86,91) Hari et al.(82) reported healthy controls had lower FSFI mean scores than the IA population with both groups falling into the sexual dysfunction category, but sexual dysfunction was highest amongst the IA group (76%) compared with healthy controls (47.5%).

Several included studies used the IIEF as an outcome measure and demonstrated mean scores of ≤25 indicating erectile dysfunction in IA populations.(43,64,67,75,81,90,120, 121,124) Two studies reported control group mean scores were on the threshold for erectile dysfunction, however these scores were not lower than the IA patients' mean scores.(64,81) Bal et al. (64) reported that these scores were not significantly different between groups, however due to a small sample size this study likely lacked adequate statistical power to observe meaningful difference. While mean scores of the control group in the study by Dhakad et al. (81) also suggested erectile dysfunction, IIEF mean scores of the IA group were significantly lower. As erectile dysfunction has a multifactorial aetiology, and numerous risk factors have been identified, this may also explain the prevalence of this condition amongst healthy controls.(127,128) However, on a background of other disease-related impacts in men (such as pain, mobility restrictions and fatigue), IA appears to be consistently related to impaired sexual function and a key contributor to compromised intimate relationships.

The synthesised qualitative data support the quantitative findings, providing further evidence about the impact of IA on sexual health and relationships. While clinical tools such as the FSFI and IIEF were useful in quantifying sexual dysfunction, data from the included qualitative studies provided more in-depth insights, particularly with respect to how intimate relationships were compromised. This appeared to differ across studies and samples and may also reflect the dynamics of individual relationships. For example, some

participants reported a decreased focus on sexual intercourse while others felt pressured to maintain intimate relationships despite their apparent sexual dysfunction.(8,95) This may also reflect varying levels of partners' understanding of the sexual dysfunction associated with IA. Partners with a greater understanding assisted to strengthen relationships while among those who poorly understood disease impacts, tension and fear were created within relationships.(8,77,95,122)

The strengths of this review included our comprehensive systematic review methods, which involved a specialist research librarian during search strategy development, and the involvement of at least two independent reviewers at every stage of the review process. Unlike previous reviews (29-39), both genders were considered, quantitative and qualitative study designs were included, and all types of IA were included, whereas previous reviews were mostly disease-specific.(6,28-34,36-51) The review also covered a broad range of geographic regions. Overall risk of bias for the qualitative studies was reasonably low, according to the CASP tool.(104) The GRADE-CERQual evaluation provides moderate confidence that the review findings can be used to appropriately answer our research question.

We also acknowledge the review limitations. We were unable to conduct a meta-analysis given heterogeneity of study populations and outcome measures, and some of the included quantitative studies were of poor methodological quality. Overall, 74% of the quantitative studies were considered to have a moderate risk of bias, suggesting that further research is likely to have an impact on our confidence of these findings. Nonetheless, the included studies represent the contemporary evidence base and provide consistent evidence of an association between IA and sexual dysfunction. While grey literature was not systematically searched, we are confident that the comprehensive nature of our search strategy identified the breadth of evidence relating to IA and sexual function and intimacy. Given the consistency identified in quantitative and qualitative data, we do not expect that unpublished work would change our overall findings. We observed a limited range of outcome measures reported in quantitative studies, which may introduce an outcomes bias when interpreting the available evidence. Due to the small number of eligible qualitative studies, meta-synthesis was limited as themes and sub-themes were drawn from only six studies.(8,77,80,89,95,122) Furthermore, most studies explored impact on sexual function

rather than intimate relationships. Finally, from the data available we are unable to speculate on the temporal nature of the association between disease and sexual dysfunction and compromised relationships (since most studies sampled people with a disease duration of IA of five years or more) and whether age, disease duration, management approaches or other health-related factors are likely to mediate the relationship. This represents an important area for future research. Based on the volume and quality of evidence reviewed, potential biases associated with cross-sectional studies and importance of the topic to patients, we suggest the impact of the findings is moderate.

Our review identified that many types of IA have substantial impacts on sexual function and intimate relationships. These issues are sensitive in nature and commonly addressed poorly in clinical practice as they may be embarrassing for the clinician and/or the patient to raise. (8,9,18,19,21-24,56,59,129) Our findings can be used to increase clinicians' awareness and thus encourage discussions with their patients from the early stages of management. While raising these issues in initial consultations may be difficult given competing disease priorities and the need to establish rapport and active disease management, our findings suggest that sexual health and relationships are important components of overall health and should therefore be components of routine IA management.

CONCLUSION

Sexual dysfunction is prevalent in female and male populations diagnosed with various forms of IA. Sexual dysfunction in IA is associated with pain, reduced sexual desire, erectile dysfunction, fatigue and mobility restrictions. As sexual health is an important component of wellbeing, raising clinician and patient awareness of sexual dysfunction associated with IA could facilitate the provision of more holistic care.

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Figure Legends

Figure 1: PRISMA flow chart of included studies.

Figure 2: Mean Female Sexual Function Index (FSFI) scores and standard deviations (error bars). Studies are grouped by type of IA. Sexual dysfunction is indicated by FSFI score $\leq$ 26.5 (123), indicated by the solid horizontal line on the graph.

Abbreviations: AS: Ankylosing Spondylosis; SS: Sjogren's Syndrome; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematous; SSc: Systemic Sclerosis

*van Nimwegen et al. (2015) (102) did not report standard deviations.

Figure 3: Mean International Index of Erectile Function (IIEF) scores and standard deviations (error bars). Studies are grouped by type of IA. Sexual dysfunction is indicated by IIEF score $\leq$ 25 (43, 124), indicated by the solid horizontal line on the graph.

Abbreviations: AS: Ankylosing Spondylosis; RA: Rheumatoid Arthritis; SSc: Systemic Sclerosis.

*As Rezvani et al. (2012) (67) did not report mean scores or standard deviations, median scores for this study are shown instead.

Table 1: Summary of included studies

Study	Country where data collected	Study Design	Setting	IA group N, gender (%), mean (SD) age in years unless stated otherwise	Type of IA N (%)	IA disease duration, mean (SD) years unless stated otherwise	Control group N, gender (%), mean (SD) age in years unless stated otherwise
Abda et al., 2016 (85)	Egypt	Quantitative cross-sectional controlled cohort survey	Department of rheumatology and rehabilitation, university hospital	200, female (100), 44.2 (9.1)	RA: 200 (100)	5.8 (4.1)	100, female (100), 42.5 (6.3)
Aguiar et al., 2014 (74)	Not stated	Quantitative cross-sectional single group survey	Outpatient rheumatology clinic in private hospital setting	76, female (50), 46.1 (12.1)	PsA: 31 (41); AS: 30 (39); undifferentiated SpA: 9 (12); IBD: 6 (8)	12.2 (10.3)	N/A
Akkurt et al., 2016 (86)	Turkey	Quantitative cross-sectional controlled cohort survey	Not stated	54, female (100), 39.3 (8.6)	IA: 100 (100)	8.5 (5.1)	56, female (100), 37.6 (9.6)
Aras et al., 2013 (68)	Turkey	Quantitative cross-sectional controlled cohort survey	Department of physical medicine and rehabilitation in a tertiary hospital setting	104, female (100), 48.6 (8.6)	RA: 104 (100)	9.3 (SD not reported)	82, female (100), 46.7 (7.6)
Bagcivan et al., 2015 (80)	Turkey	Qualitative study (semi – structured interviews)	Rheumatology outpatient clinic, university hospital	23, female (30), 29.6 (6.0)	AS: 23 (100)	5.4 (3.5)	N/A
Bal et al., 2011 (64)	Not stated	Quantitative cross-sectional controlled cohort survey	Not stated	37, male (100), 42.8 (10.8)	AS: 37 (100)	10 (9)	67, male (100), 43.6 (5.9)
Bhadauria et al., 1995 (115)	United States of America	Quantitative cross-sectional controlled cohort survey	Private practice of rheumatologist in private hospital setting	60, female (100), 50.5 (12.0)	SSc: 60 (100)	10.9 (7.6)	23, female (100), 46.0 (12.3)

Bongi et al., 2013 (69)	Italy	Quantitative cross-sectional controlled cohort survey	Outpatient clinic and day hospital for the division of rheumatology	46, female (100), 56.1 (12.4)	SSc: 46 (100)	10 (6)	46, female (100), 52.0 (9.0)
Coskun et al., 2014 (75)	Turkey	Quantitative cross-sectional controlled cohort survey	Outpatient department of rheumatology clinic, Uludag university hospital	32, female (100), 38.4 (6.9)	RA: 32 (100)	Not stated	20, female (100), 39.3 (5.5)
Daleboudt et al., 2013 (70)	New Zealand	Quantitative cross-sectional single group survey	Outpatient clinic, City hospital	106, female (94.3), 43.3 (14.9)	SLE: 106 (100)	10.2 (9.1)	Not stated
Demir et al., 2013 (71)	Turkey	Quantitative cross-sectional controlled cohort survey	Outpatient rheumatology clinic, Bezmialem Vakif university	3, female (100), 39.3 (6.3)	AS: 23 (100)	3.3 (2.6)	27, female (100), 37.6 (9.6)
Dhakad et al., 2015 (81)	India	Quantitative longitudinal controlled cohort survey	Rheumatology department of a tertiary hospital with data collected at baseline	100, male (100), 32.4 (9.8)	AS:100 (100)	5.1 (0.1)	100, male (100), 30.1 (6.2)
Dincer et al., 2007 (61)	Not stated	Quantitative cross-sectional controlled cohort survey	Not stated	68, male (100), 32.9 (11.0)	AS: 68 (100)	Not stated	45, male (100), 30.1 (6.24)
Dorner et al., 2018 (93)	Not stated	Quantitative cross-sectional single group survey	Outpatient clinic of a non-tertiary hospital	54, female (61), 47.8 (10.6)	RA: 54 (100)	5 (2-8) *median (IQR)	N/A
Druley et al., 1997 (116)	United States of America	Quantitative cross-sectional single group survey	Chapters of the Lupus Foundation of America, community setting	74, female (100), 42.8 (12.9)	SLE: 74 (100)	Not stated	N/A
El Miedany et al., 2012 (7)	Egypt	Quantitative cross-sectional single group survey	Rheumatology outpatient clinic in private hospital setting	231, female (44.7), 47.9 (10.4)	RA: 231 (100)	Not stated	N/A
Foocharoen et al., 2012 (117)	Switzerland	Quantitative longitudinal single group survey	Multinational database of EUSTAR (European League Against Rheumatism Scleroderma Trial and Research group) centres with data	130, male (100), median (IQR) age: 52.3 (45.1-61.5)	SSc: 130 (100)	7.0 (3.7 to 11.9) *median (IQR)	N/A

			collected at baseline				
Frikha et al., 2014 (76)	Tunisia	Quantitative longitudinal single group survey	Department of internal medicine in Sfax-Tunisia university hospital with data collected at baseline	10, female (100), 52.4 (8.2)	SSc: 10 (100)	7.7 (7.7)	N/A
Gallinaro et al., 2012 (66)	Brazil	Quantitative cross-sectional controlled cohort survey	Outpatient SpA clinic, university hospital	32, female (12.5), 47.4 (19.3)	AS: 32 (100)	13.7 (9.7)	32, male (87.5), 38.4 (14.3)
Garcia et al., 2013 (72)	Spain	Quantitative cross-sectional controlled cohort survey	Systemic autoimmune diseases unit of Hospital of San Cecilio of Granada	65, female (100), 9.0 (10.8)	AS: 65 (100)	7.2 (7.4)	55, female (100), 35.7 (11.3)
Hari et al., 2015 (82)	Not stated	Quantitative cross-sectional controlled cohort survey	Not stated	60, female (100), 49.9 (9.3)	RA: 60 (100)	6 (3-10) *median (IQR)	40, female (100), 45.0 (9.2)
Healey et al., 2009 (62)	UK	Quantitative cross-sectional single group survey	Ten site specific NHS (National Health Services) trust hospitals	612, female (28.4), 50.8 (12.2)	AS: 612 (100)	17.3 (11.7)	N/A
Helland et al., 2008 (94)	Norway	Quantitative cross-sectional single group survey	Postal questionnaires to patients in ORAR (Oslo Rheumatoid Arthritis Register)	830, female (74), 58.5 (14.2)	RA: 830 (100)	13.4 (10.3)	N/A
Helland et al., 2011 (95)	Norway	Qualitative study (interviews and focus groups)	Rheumatology clinic, tertiary hospital	23, female (43) 44.2 (10.5)	RA: 11 (48); AS: 7 (30); PsA: 4 (17); JIA: 1 (4)	13.6 (10.2)	N/A
Hill et al., 2003 (8)	United Kingdom	Mixed study (quantitative, cross-sectional single group survey and free text questionnaires	Two consecutive rheumatology outpatient clinics at a large teaching hospital	57, female (82), 58, age range: 36-75	RA: 57 (100)	Female: 1.5 (3.0-6.3) Male: 5 (3.2-6.3) *median (IQR)	N/A
Impens et al., 2009 (63)	America	Quantitative cross-sectional single group survey	Outpatient clinic of the scleroderma program of a university hospital	101, female (100), 47.5 (no range/SD/IQR)	SSc: 101 (100)	Not stated	N/A

Isik et al., 2017 (91)	Turkey	Quantitative cross-sectional controlled cohort survey	State university hospital	46, female (100), 40.4 (5.1)	SSc: 46 (100)	5.3 (3-8) *median (range)	47, female (100), 39.8 (3.2)
Josefsson et al., 2012 (27)	Sweden	Quantitative cross-sectional single group survey	Two rehabilitation clinics in non-tertiary hospital	150, female (81), 56, age range: (19-77)	RA: 150 (100)	Female: 15 (2-50) Male: 10 (1-20) *median (range)	N/A
Khnaba et al., 2016 (88)	Morocco	Quantitative, cross-sectional single group survey	Ei Ayachi university hospital	60, female (100), 45.2 (8.8)	RA: 60 (100)	5.7 (3.1-10.6) *median (percentile)	Not stated
Kobelt et al., 2012 (96)	France	Quantitative cross-sectional controlled cohort survey	French patient association (Association Nationale de Défense contre l'Arthrite Rhumatoïde, ANDAR).	1272, female (84), 63.8 (12.4)	RA: 1272 (100)	19.0 (11.6)	70, female (77), 59.6 (11.7)
Levis et al., 2012 (97)	Canada and France	Quantitative cross-sectional controlled cohort survey	Database of women from CSRG (Canadian Scleroderma Research Group) Registry and general population sample from the Adult Twins UK registry	730, female (100), 57.0 (11.3)	SSc: 730 (100)	12.8 (9.7)	1498, female (100), 55.4 (11.5)
Majerovitz et al., 1994(9)	Not stated	Quantitative cross-sectional controlled cohort survey	Practices of 11 rheumatologists affiliated with a major metropolitan tertiary hospital	113, Female (72.6), 57.0 (no range/SD/IQR)	RA: 90 (79.6); Polymyalgia rheumatic, temporal arteritis, vasculitis, polymyositis, dermatomyositis, SSc, and	Not stated	74, female (50), 53.6 (no range/SD/IQR)

					mixed connective tissue disease: 23 (20.4)		
Oksel et al., 2014 (77)	Turkey	Qualitative study (semi structured interviews)	Rheumatology polyclinic, university hospital	20, female (100), 50.9 (10.0)	SSc: 20 (100)	8.8 (7.6)	N/A
Onem et al., 2014 (118)	Turkey	Quantitative cross-sectional controlled cohort survey	Rheumatology outpatient unit at a Sisli Etfal training and research hospital	47, female (100), 37.4(7.2)	RA: 47 (100)	4.8 (4.6)	45, female (100), 37.4 (6.1)
Ostlund et al., 2015 (83)	Sweden	Qualitative study (semi structured interviews)	Informants' home or workplace, or the hospital or university	45, female (53), age range: (20-63)	RA: 45(100)	Not stated	N/A
Ozgul et al., 2006 (119)	Not stated	Quantitative, cross-sectional single group survey	Not stated	167, male (100), 23.9 (3.0)	AS: 167 (100)	37.7% had for 0-5 years 36.6% had for 6-10 years 15.8% had for 11-15 years 9.9% had for >15 years	N/A
Ozkorumak et al., 2011 (65)	Turkey	Quantitative cross-sectional controlled cohort survey	Physical medicine and rehabilitation department, Karadeniz Technical university	43, male (100), 36.3 (8.8)	AS: 43 (100)	Not stated	43, male (100), 36.5 (6.5)
Pendeke et al., 2016 (89)	Scotland, England and Wales	Qualitative study (semi structured interviews)	Various community hospital locations in Scotland, England and Wales with the help of Lupus UK	8, male (100), age range: (20-69)	SLE: 8 (100)	11.5 (SD not stated)	N/A
Pirildar et al., 2004 (120)	Not stated	Quantitative cross-sectional controlled cohort survey	Not stated	65, male (100), 36 (8.1)	AS: 65 (100)	12.2 (6.4)	65, male (100), 37 (5.2)

Priori et al., 2015 (87)	Italy	Quantitative cross-sectional controlled cohort survey	Systemic sclerosis clinic, university hospital	24, female (100), 50.4 (12.0)	SS:24 (100)	Not stated	24, female (100), 47.0 (13.3)
Rezvani et al., 2012 (67)	Turkey	Quantitative cross-sectional controlled cohort survey	Rheumatology outpatient clinic of a tertiary care centre	39, male (100), 38, age range: (27-52)	AS: 39 (100)	4.4 (1.9-26)	27, male (100), 30, age range: (23-45)
Rosato et al., 2014 (79)	Italy	Quantitative cross-sectional single group survey	Scleroderma Centre of Clinical Immunology and Rheumatology clinic, tertiary hospital	102, female (100), 51 (13)	SSc: 102 (100)	8 (6)	N/A
Rostom et al., 2013 (73)	Not stated	Quantitative cross-sectional single group survey	Not stated	110, male (100), 38.9 (12.5)	AS: 110 (100)	9 (0-40) *median (IQR)	N/A
Saadat et al., 2015 (84)	Iran	Quantitative cross-sectional controlled cohort survey	Rheumatologic ward, Baquiyatallah tertiary hospital	90, female (100), 40.1 (4.1)	RA: 90 (100)	Not stated	110, female (100), 37.5 (2.1)
Sanchez et al., 2016 (90)	France	Quantitative cross-sectional single group survey	Department of internal medicine, Cochin hospital	292, female (82.2), 55.9 (14)	SS: 292 (100)	8.6 (7.7)	N/A
Santana et al., 2017 (92)	Brazil	Quantitative cross-sectional controlled cohort survey	Rheumatology unit, university hospital	40, male (100), 45.8 (11.4)	AS: 40 (100)	18 (8.2-20.0) *median (IQR)	40, male (100), 46.0 (11.1)
Sariyildiz et al., 2013 (121)	Turkey	Quantitative cross-sectional controlled cohort survey	Two centres of physical medicine and rehabilitation at university hospitals	70, male (100), 36.4 (7.4)	AS: 70 (100)	9.9 (6.9)	60, male (100), 35.2 (7.7)
Sariyildiz et al., 2013 (22)	Turkey	Quantitative cross-sectional controlled cohort survey	Two centres of physical medicine and rehabilitation at university hospitals	37, female (100), 34.1 (7.0)	AS: 37 (100)	8.6 (7.4)	33, female (100), 33.5 (6.2)
Schouffoer et al., 2009 (98)	Netherlands	Quantitative cross-sectional controlled cohort survey	Two academic rheumatology outpatient university hospitals	37, female (100), 45.6 (9.5)	SSc: 37 (100)	6.5 (8.8)	37, female (100), 43.3 (8.0)
Seawell et al., 2005 (60)	United States of America	Quantitative cross-sectional controlled cohort survey	Postal questionnaire to women listed in database of NENYLFA (North East New York Lupus Foundation of America	54, female (100), 47.4, age range: (22 – 75)	SLE: 54 (100)	Not stated	29, female (100), 44.7, age range: (22-67)

Tseng et al., 2011 (99)	Taiwan	Quantitative cross-sectional controlled cohort survey	Rheumatology outpatient clinic, general hospital	279, female (100), 37.5 (10.2)	SLE: 279 (100)	9.5 (6.4)	1580, female (100), 34.8 (8.5)
Ugurlu et al., 2014 (101)	Not stated	Quantitative cross-sectional controlled cohort survey	Not stated	64, female (100), 40.1 (7.5)	SS:64 (100)	Not stated	32, female (100), 37.4 (7.0)
van Berlo et al., 2007 (19)	Netherlands	Quantitative cross-sectional controlled cohort survey	Departments of rheumatology in three hospitals (large regional hospital, university hospital and a small hospital serving mainly a rural area)	213, female (63.8), 52.7 (11.8)	RA: 231 (100)	13.1 (9.8)	107, female (49), 49.4 (10.8)
van Nimwegen et al., 2015 (102)	Not stated	Quantitative cross-sectional controlled cohort survey	Postal questionnaire to patients in general practitioner`s office	46, female (100), 46.3 (10.5)	SS:46 (100)	7 (4-14) *median (IQR)	43, female (100), 44.4 (11.3)
Yilmaz et al., 2012 (100)	Turkey	Quantitative cross-sectional controlled cohort survey	Department of physical medicine and rehabilitation in research hospital	203, female (100), 40.9 (7.3)	RA: 203 (100)	5.9 (5.0)	108, female (100), 40.1 (8.1)

Abbreviations: IA: Inflammatory Arthritis, AS: Ankylosing Spondylitis, SS: Sjogren`s Syndrome, RA: Rheumatoid Arthritis, SLE: Systemic Lupus Erythematous, SSc: Systemic Scleroderma/ Systemic Sclerosis, IBD: Irritable Bowel Disease, PsA: Psoriatic Arthritis, SpA: spondyloarthitis

Table 2: Summary of outcome* and risk of bias assessment from quantitative studies. The two most common outcomes are presented (FSFI and IIEF), as well as other outcome measures reported in the included studies.

Study	Female Sexual Function Index (FSFI) mean (SD)		International Index of Erectile Function (IIEF) mean (SD)		Other outcome measures			
	IA Group	Control Group	IA Group	Control Group	Other outcome measure(s); scale (range); interpretation	IA Group (mean (SD), unless stated otherwise)	Control Group (mean (SD), unless stated otherwise)	Overall Risk of Bias: Total score 10 (Category) ◊
Abda et al., 2016 (85)					Sexual disability and satisfaction questionnaire derived from Health Assessment Questionnaire (HAQ) Disability Index. Data presented as N (%) by grade (grade range: 0-3), where lower grades indicate better sexual function Grade 0: able Grade 1: mild Grade 2: moderate Grade 3: completely unable	Grade 0: 42 (21) Grade 1: 90 (45) Grade 2: 34 (17) Grade 3: 34 (17)		5 (Moderate)
Aguiar et al., 2014 (74)					Custom questionnaire; continuous scale (0-100), presented as mean (SD). Higher score associated with higher satisfaction with sexual life.	52.3 (31.0)	57.6 (29.9)	6 (Moderate)

Akkurt et al., 2016 (86)	22.1 (5.5) *	31.4 (3.0) *						5 (Moderate)
Aras et al., 2013 (68)	19.1 (4.7) *	24.6 (4.2) *						4 (Moderate)
Bal et al., 2011 (64)			23.8 (7)	25.1 (6.6)				5 (Moderate)
Bhadauria et al., 1995 (115)					Sexual function and semi-quantitative sexual satisfaction index. Data presented as N (%) patients reporting: Decreased desire: Decreased frequency of intercourse: Decreased orgasms: Decreased intensity of orgasms:	39.6 (66) 43.8 (73) 31.2 (52) * 31.8 (53) *	13.8 (60) 16.8 (73) 3.9 (17) * 2.3 (10) *	6 (Moderate)
Bongi et al., 2013 (69)	18.0 (12.3)	21.2 (11.5)						4 (Moderate)
Coskun et al., 2014 (75)			24.5 (6.0) *	32.3 (3.5) *				4 (Moderate)
Daleboudt et al., 2013 (70)					PDSBE and MIS-SFQ; N (%) of patients reporting negative influence			5

					on sexual functioning:		(Moderate)
						52.5 (49.1)	
Demir et al., 2013 (71)	23.7 (5.6)	23.1 (5.9)					4 (Moderate)
Dhakad et al., 2015 (81)			20.5 (7.1) *	24.9 (3.8) *			5 (Moderate)
Dincer et al., 2007 (61)					BMSFI; Total score: 0-44; Lower scores indicate poor sexual function; no threshold score provided	28.9 (8.4) *	33.3 (7.6) *	6 (Moderate)
Dorner et al., 2018 (93)					Custom questionnaire; N (%) reported having some difficulty with intercourse	31.2 (57.7)		6 (Moderate)
Druley et al., 1997 (116)					QMI and a self-administered questionnaire designed for study; Sexual intercourse: N (%) reporting engaged N (%) reporting initiated N (%) reporting avoided Foreplay: N (%) reporting engaged N (%) reporting initiated N (%) reporting avoided	54.8 (74) 34.8 (47) 41.4 (56) 51.1 (69) 40.0 (54) 39.2 (53)		4 (Moderate)

El Miedany et al., 2012 (7)	23.2 (6.4)				5 (Moderate)
Foocharoen et al., 2012 (117)	SHIM; N (%) of patients reporting: Mild erectile dysfunction: Mild to moderate dysfunction: Moderate erectile dysfunction: Severe erectile dysfunction: EIIF; N (%) of patients reporting: No erectile dysfunction: Mild erectile dysfunction: Mild-moderate erectile dysfunction: Moderate erectile dysfunction: Severe erectile dysfunction:	18 (36.7) 16 (32.7) 13 (26.5) 2 (4.1) 23 (17.7) 25 (19.2) 26 (20.0) 14 (10.8) 40 (30.8)			4 (Moderate)
Frikha et al., 2014 (76)	14.2 (7.8)				6 (Moderate)
Gallinaro et al., 2012 (66)	Sexual activity questionnaire; N (%) reporting: Frequency of intercourse ≥ 2 x a week: Pain after sexual relationship: Sexual relationship interrupted due to Pain: Fatigue: Orgasm: Sexual satisfaction: Complete sexual act: Duration of sexual intercourse (minutes):	 21.3 (66.7) ^ 19.8 (61.9) ^ 3 (9.5) ^ 10.6 (33.3) ^ 22.8 (71.4) ^ 27.5 (85.8) ^ 22.8 (71.4) ^ 6.1 (19.2) ^	 24 (85.7) ^ 3 (10.7) ^ 0 (0) ^ 8 (28.6) ^ 21 (75.0) ^ 26 (92.9) ^ 25 (89.3) ^ 9.6 (34.2) ^		7 (High)
Garcia et al., 2013 (72)	24.5 (8.0) *	27.6 (7.7) *			1 (Low)

Hari et al., 2015 (82)	24.5 (7.8) *	18.3 (9.1) *			5 (Moderate)
Healey et al., 2009 (62)			Custom questionnaire; Extent AS affected intimate/sexual relationships: N (%) reporting not at all or a little bit: N (%) reporting moderately to extremely:	 342 (62) 210 (38)	2 (Low)
Helland et al., 2008 (94)			Item 15 of the 15D generic/ standardized HRQoL instrument; N (%) reporting impact on sexual activity: No effect: Slight effect: Considerable effect: Almost impossible: Impossible:	 257.3 (31) 315.4 (38) 174.3 (21) 24.9 (3) 58.1 (7)	5 (Moderate)
Hill et al., 2003 (8)			Questionnaire previously developed for patients with arthritis (130); N (%) reporting impact of RA on relationship: Not applicable: No change: Changed:	 14 (25) 23 (56) 18 (44)	4 (Moderate)
Impens et al., 2009 (63)	24.9 (6.7) *	30.5(5.3) *			5 (Moderate)
Isik et al., 2017 (91)	17.2 (SD not reported) *	27.4 (SD not reported) *			3

				(Low)
Josefsson et al., 2012 (27)	Questionnaire developed by authors; N (%) reporting: Good or very good sexual well-being: RA had negatively affected sexual health: Reduction in sexual desire due to RA: Continuing experience of decreased sexual desire: Decreased sexual satisfaction due to RA: Weak or no sexual satisfaction:	 55.5 (37) 55.5 (37) 93 (62) 81 (54) 64.5 (43) 28.5 (19)		8 (High)
Khnaba et al., 2016 (88)	18.3 (9.1)			4 (Moderate)
Kobelt et al., 2012 (96)	Self-assessed impact of RA on sexual activity questionnaire developed for study; N (%) reporting: RA an obstacle for intimate relationship: RA an obstacle for sexual relationships: RA to be a major obstacle for intimate relationships: RA to be a major obstacle for sexual relationships:	 864.3 (68) 966.0 (76) 368.6 (29) 419.4 (33)		6 (Moderate)
Levis et al., 2012 (97)	9-item abbreviated version of 19-item FSFI; N (%) reporting: Sexually active: Sexually impaired:	 296 (41) 181 (61)	 956 (64) 420 (44)	6 (Moderate)

Majerovitz et al., 1994 (9)	SDS; Scale (5-25); Higher scores indicating greater sexual dissatisfaction	M: 11.2 (4.4) ^ F: 13.9 (4.8) ^	M: 10.8 (3.6) ^ F: 13.1 (4.3) ^	8 (High)
Onem et al., 2014 (118)	GRISS; Scale (0-96); Higher scores indicating greater sexual dissatisfaction	36.7 (15.6)	34.2 (14.2)	6 (Moderate)
Ozgul et al., 2006 (119)	SF-36; N (%) reporting: *Sexual intercourse* had troubles: a little: somewhat: moderately: very: *Sexual satisfaction* had troubles: a little: somewhat: moderately: very: *Sexual desire* had troubles: a little:	 88 (52.7) 40.4 (24.2) 36.7 (22.1) 8.9 (5.3) 1.8 (1.1) 89 (53.3) 47.3 (28.3) 29.1 (17.4) 9 (5.4) 3.3 (2.2) 78.5 (47.0) 46.1 (27.6)		6 (Moderate)

				somewhat: moderately: very:	23.9 (14.3) 8.5 (5.1) 0		
Ozkorumak et al., 2011 (65)				GRISS; Scale (0-96); Higher scores indicating greater sexual dissatisfaction	5.1 (1.6) *	4.0 (1.7) *	3 (Low)
Pirildar et al., 2004 (120)			23.1 (7.5) *	27.1 (6.3) *			4 (Moderate)
Priori et al., 2015 (87)	23.1 (7.5) *	27.1 (6.3) *					2 (Low)
Rezvani et al., 2012 (67)			19.1 (7.3)	26.1 (8.8)			3 (Low)
Rosato et al., 2014 (79)	18.5 (9.8)				FSDS-R; Scale (0-30); FSDS-R score ≥11 indicates sexual distress;	10.2 (10)	4 (Moderate)
Rostom et al., 2013 (73)					MSSCQ; N (%) reporting: Unsatisfied with sexual activity: Erectile dysfunction: Orgasmic trouble:	32 (44) 30 (41) 28 (38.4)	7 (High)

Saadat et al., 2015 (84)				MSSCQ; Range not stated; Mean (SD); Lower scores indicative of poorer sexual function; Desire: Sensation: Lubrication: Cognition: Orgasm: Pain: Enjoyment: Partner related:	17.6 (5.5) 12.2 (4.5) * 6.2 (2.1) * 6.2 (2.0) 9.5 (3.3) * 10.9 (1.9) * 21.3 (7.5) * 7.7 (2.4) *	17.9 (3.8) 13.7 (4.5) * 6.9 (2.1) * 6.3 (1.7) 10.4 (2.9) * 10.1 (2.3) * 23.8 (5.9) * 8.5 (1.8) *	5 (Moderate)
Sanchez et al., 2016 (90)	16.3 (6.2)		16 (5.3)				5 (Moderate)
Santana et al., 2017 (92)			22.0 * (median, SD not reported)	29.0 * (median, SD not reported)			4 (Moderate)
Sariyildiz et al., 2013 (121)			23.8 (5.3) *	27.0 (2.1) *			4 (Moderate)
Sariyildiz et al., 2013 (22)	23.8 (4.1) *	28.3 (4.7) *					4 (Moderate)
Schouffoer et al., 2009 (98)	20.6 (9.4) *	27.6 (6.2) *					4

					(Moderate)
Seawell et al., 2005 (60)			SDS; Scale (5-25); Mean (SD); Higher scores indicated greater dissatisfaction	14.2 (5.4)	13.6 (3.2)	5 (Moderate)
Tseng et al., 2011 (99)	25.7 (4.7) *	26.8 (4.5) *				3 (Low)
Ugurlu et al., 2014 (101)	16.6 (7.9) *	23.3 (5.9) *				5 (Moderate)
van Berlo et al., 2007 (19)			QSD; Mean (SD); Higher scores = greater intercourse frequency and sexual satisfaction			7 (High)
			Frequency sexual daydreams/fantasies (1-7);	M: 2.4 (1.5) F: 1.4 (0.9) *	M: 3.1 (1.5) F: 1.9 (1.3) *	
			Frequency desire for sexual contact with partner (1-7)	M: 3.2 (1.6) * F: 2.9 (1.4)	M: 4.1 (1.4) * F: 3.4 (1.3)	
			Frequency sexual contact (1-7)	M: 2.8 (1.5) F: 3.2 (1.5)	M: 3.5 (1.3) F: 2.7 (1.4)	
			Frequency masturbation (1-7)	M: 1.8 (1.3) F: 1.2 (0.8) *	M: 2.4 (1.5) F: 1.8 (0.9) *	
			Frequency sexual contact against will (1-7)	M: 1.0 (0.0) F: 1.2 (0.6)	M: 1.0 (0.0) F: 1.1 (0.4)	
			Sexual satisfaction (1-5);	M: 3.6 (0.9) F: 2.7 (0.8)	M: 3.6 (0.8) F: 3.7 (0.9)	

van Nimwegen et al., 2015 (102)	20.6 (SD not reported) *	30.3 (SD not reported) *				6 (High)
Yilmaz et al., 2012 (100)			IFSI; Scale (5-45); Mean (SD); Higher scores indicate better sexual function	22.8 (9.0) *	34.6 (8.3) *	5 (Moderate)

◊Based on Hoy et al (2012) risk of bias tool

Low risk of bias: 0-3; Moderate risk of bias: 4-6 High risk of bias: 7-9, scored out of 10.

* indicates a statistically significant difference ($p<0.05$) reported between groups in the study

^ indicates groups were not compared using statistical analysis

Abbreviations:

ASES: The Arizona Sexual Experiences Scale

BMSFI: The Brief Male Sexual Function Inventory

FSDS-R: Female Sexual Distress Scale Revised

FSFI: Female Sexual Function Index, Score Range: 2-36, Scoring Direction: Sexual dysfunction indicated by score $\leq$ 26.5 (123)

FSFI15: Female Sexual function in Scleroderma pilot questionnaire developed by the Robert Wood Johnson Scleroderma Program

GRSSS: Glombok–Rust Sexual Satisfaction Scale; HAQ

Health Assessment Questionnaire; IFSI: Index of Female Sexual Function

IIEF: International Index of Erectile Function scoring system, Score Range: 0-30, Scoring Direction: Sexual dysfunction indicated by score $\leq$25 (43, 124)

MIS-SFQ: Medical Impact Scale of the Sexual Functioning Questionnaire

MSSCQ: Multidimensional Sexual Self-Concept Questionnaire

DSS: Sexual Dissatisfaction scale

PDSBE: Physical Disability and Sexual and Body Esteem Scale

QMI: Quality of Marriage Index

QSD: Questionnaire for screening sexual dysfunctions

SDS: Sexual dissatisfaction scale

SF-36: 36-item Short Form Health Survey

SHIM: Sexual Health Inventory for Men

Table 3: Meta-synthesis of qualitative data

Theme and sub-themes and meta-synthesis summary	Summary of results findings from primary study	Supporting excerpts
1.1 Pain (80, 95, 122) Sexual function was affected by pain, reduced sexual desire, erectile dysfunction and fatigue, along with the same stressors that affect general population such as stress, education and concerns. People with IA had typically changed the positions they previously adopted during intercourse, such as assuming a more passive role to reduce pain caused by movement and positions.	• Pain limited positions and movements during sexual intercourse, resulting in interrupted or postponed sexual intercourse.	"My sex life has been very affected. Because of the very severe pain, I cannot have sex. I cannot adapt myself to sex because of the pain I feel. In fact, to lie down in bed, even for a very short time, increases my pain" (male). (80)
	• Pain easily interrupted sexual intercourse for people with IA. This then instilled fear in people with IA that they would let their partner down.	"I encounter difficulty with sex because I cannot move my thighs very much because of pain. For that reason, I prefer easy position in bed" (female). (80)
	• Some women with IA needed to be in control during intercourse to reduce pain, while others reported playing a more passive role to reduce pain.	"I have been forced to interrupt sex sometimes. (. . .) It's always in the back of my mind; will I be able to carry it through? I worry that it will hurt his feelings or make me feel bad, because I have initiated something that I couldn't follow through on" (female). (95)
	• Men were frustrated with having to play a passive role during intercourse to reduce pain.	
	• Sexual activity varied depending on pain, as pain often restricted positions used, and time of day people with IA could be sexually active.	"If I am in a lot of pain, its better that I am in control, that I take the lead. Then we do different things or use different positions, which might mean that I am on top or that I make sure I don't get hit or bumped. It is important that I have control over the movements" (female). (95)
		"My experience is that you really want to be active, but you end up with being passive, and that's not very exciting, is it? It does something with your self-esteem

or the sense of being attractive. . .” (Female). (95)

“It’s irritating (being passive). Feeling that you can’t do exactly what you want for yourself or to make it best for both of us” (male). (95)

“In other words I have a lot of pain … you don’t think about being intimate then, not that day anyway … except I think it’s important, on the other hand I think it’s important with closeness, hugs, in other words that you, eh, that you kiss and hug but it can stop there, you don’t have to go further … sure, I can have pain then, when I go to bed I can have pain even then, so I mean sure, it limits me … it’s probably not the first thing you think about when you have sex with someone, if you have pain I mean” (female) (122)

“ [sex life] is limited sometimes … sometimes it works well and sometimes it doesn’t work at all, when I have pain it doesn’t work and then, unfortunately, that’s what’s a bit annoying with it, she thinks [the wife] then, amongst other things” (male) (122)

“ … she knows I have pain in my hands so that she can’t have... can’t take at any rate, you know … Especially if you’re lying and hugging, then your hands can get squeezed, you know. And that can really hurt. I’m more sore at night than … because I’ve been busy and maybe worked, so maybe I’m more sensitive than in the mornings” (male) (122)

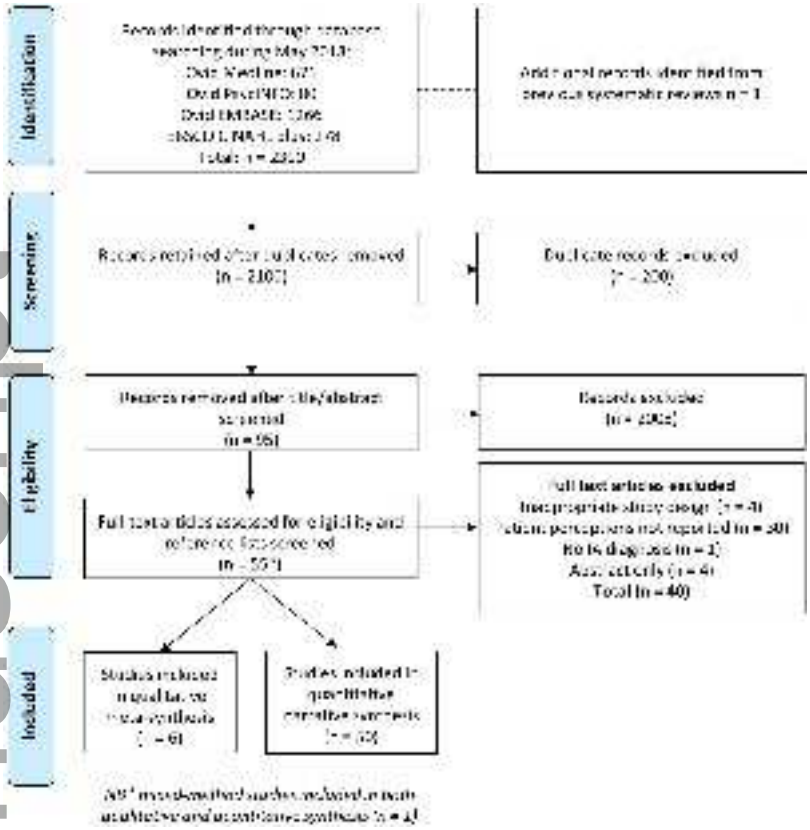
1.2 Erectile dysfunction (89, 95, 122) Erectile dysfunction largely contributed to male sexual dysfunction, which caused frustration, shock, stress and emasculation. Negative body image, reduced desire for intercourse, and erectile dysfunction all contributed to an altered sense of sexuality in men.	• Men were particularly frustrated and stressed with the impact their disease had on erections and how to explain this to partners. • Men were often shocked by the occurrence of erectile dysfunction and its threat to their masculinity.	"Getting an erection – everyone knows it's a really touchy area for men. I didn't think I would care about it so much, but I did. I would not have been so upset if it had been because my hip was so bad or my arm was like that" (male). (95) "I met a girl last year … and I didn't damn well know how I was going to bring it up because I knew he wasn't working as well as he had before 'John Thomas' … but it petered out ... because I explained to her that I had a bit of a problem with erections … he's not dead... it works of course but … dammit" (male) (122) "Sexual relations with my wife have suffered immensely.... As a husband I'm frustrated because it's taken away my ability to perform for the wife sexually. I did not see this coming at all. It's depressing, being a man on paper not one defined by their ability." (male) (89) "Where it matters most as a husband I have failed her. I have not been able to make love to my wife owing to erectile dysfunction caused by this condition. She probably sees me as half a man, if at all." (male) (89)
1.3 Fatigue and stressors (8, 95, 122) Fatigue reduced sexual desire and consequently the	• Fatigue reduced sexual desire and consequently the frequency of sexual intercourse. This was not an issue for some couples in long-term relationships	"Sometimes I am so tired and in pain that sex is the last thing I think about. A cuddle is just as nice." (female) (8)

frequency of sexual intercourse, but this wasn't an issue for some couples in long-term relationships.	• Sex life was not affected by IA alone, but also by the same stressors that affect the general population.	"I believe that you possibly do get more tired and need to go to bed early at night and you might choose to get a good night's sleep instead (of having sex). Well, several of my medicines do list this as a side-effect saying that it can affect sexual desire, but that's hard to judge, I don't really know, I can't say, well, yes it is tiredness that affects me most... but I don't think my husband thinks like that, like he needs to take my illness into consideration, so it is the same thing there, because I don't feel that I am suffering from an illness he doesn't either need to treat me as being ill." (female) (122)
		"Sexual life is so incredibly susceptible to everything, it's so much in life that affects; stress, education, and concerns. So my experience is that many are concerned that they do not want too much put on the disease. There is so much in life in general that affect sexuality – okay, there are some drawbacks with it (the disease), but we experience many of the same stressors as healthy people do" (female) (95)
1.4 Sexual desire (8, 95) Poor body image reduced the sexual desire in both male and female people with IA and restricted people with IA from finding partners in the first place.	• IA reduced desire for intercourse causing substantial guilt for some people	"The disease has had a huge impact on my sex life. Not in terms of physical problems, but sex drive. It's really reduced" (male) (95)
	• A loss of desire for intercourse led to a sense of impaired masculinity.	"To some extent. The problem is on my side really. Feel guilty about not being able to pull my weight etc." (male) (8)
	• Body image, particularly for females, reduced desire for physical intimacy due to not feeling attractive.	"The disease has had a huge impact on my sex life. Not in terms of physical problems, but sex drive. It's really reduced" (male) (95)
		"In bad periods with a lot of activity, I feel rotten inside and then sex is not foremost in my mind. I feel very unattractive and tend to say no thanks" (female)

		(95)
1.5 Fluctuations of sexual function with disease activity/flares (95) Disease-related pain was associated with a fear of interrupted intercourse, or intercourse being postponed. The level of sexual dysfunction often varied with flares in disease activity as well as the time of the day of intercourse. For example, by the end of the day people with IA were often fatigued and experiencing pain.	• Sexual ability fluctuated depending on symptoms associated with IA disease activity. Intercourse was most often interrupted during disease flares. • Sexual intercourse was not considered important for people with IA, particularly during disease flares.	"Fluctuations in the disease and symptoms restrict my sex life. Sometimes it poses a problem, very often it doesn't. It's very up and down – there's no pattern" (female) (95) "When you can hardly move, and you have pain in your entire body, sex isn't exactly what's on your mind" (female) (95)
2.1 Reduced frequency of sexual activity (95) Intimate relationships tended to transition towards a caring and less physical nature as the importance of sexual intercourse was reduced, particularly during disease flares.	• Reduced importance of sexual life was highlighted. A greater need for caring relationships was identified. • People with IA were concerned that their partners would not accept them.	"The only thing I needed was a shoulder to cry on and an arm that cared and didn't mind. Our exciting sex life turned into more of a deeply caring relationship, which was really great" (female) (95) "Especially I think mentally … and you can feel really bad and you think yeah but, think if this continues, that I'm going to … feel like this and I'm going to look like

2.2 Embarrassment and frustration (122) People with IA were concerned that their partners would not accept them.		this, is he going to accept me then because sex is a big part of a relationship … I think it, eh, affects it a lot, and as I said, then it's how you feel on and off too … yes, it's [fear] that he's going to leave me and then I'll be sad and have low self-esteem also then, it leaves a mark, now I haven't been in a situation where it really has been a disaster, luckily, because I think it really would be, something that would sit emotionally for both of us I think, that the other one would maybe be, yeah but as my boyfriend then he'd be a little like this, a-ha, how is this actually going to work, will she be able to have sex with me in two years … that's how I feel … odd." (female) (122)
2.3 Altered self-image and/or sense of confidence in sexuality (77, 95, 122) People with IA felt that partners did not understand the impact IA had on their loved one`s ability to have intercourse. Reduce closeness and intimacy since IA diagnosis due to the perception of poor body image.	• People felt that partners did not understand the impact IA had on their loved one's ability to have intercourse • People with IA reported a reduced closeness and intimacy since their diagnosis due to the perception of poor body image • A negative body image perceived by people with IA impaired their sexuality • The impact IA had on body image restricted people from finding partners.	"… and I get tired and difficult when I'm with her … you have to try and be considerate all the same, show that … but she always looks at me when I'm in pain … but then she thinks I'm not enough maybe, all the time … if we're sitting and hugging and feeling good, then I don't want to do it, then I'd rather pull … away or, more accurately, push her away, unfortunately … I'm a failure. That's why I think she doesn't always accept the disease, but it's just how it is … I think that's the hardest thing right now, that you can't validate your wife when she maybe needs it, … but that's always something you have to work on … as long as you have rheumatism anyway." (male) (122) "It had a huge impact on our sex life that he never seemed to understand that I was exhausted or in pain until I couldn't sit down, go to the toilet or walk. Then he understood, and that hurt my feelings" (female) (95) ''My husband has become estranged from me since the diagnosis'' (female) (77)

		‘‘[It is] as if my husband does not consider me a woman (female) (95)
		“I can feel very, what shall I say, unsexy, when I can barely even walk, eh, and my hands especially, aren’t particularly beautiful, because they have bumps and I can’t move them so well back and forth” (female) (122)
		“It’s not easy to find a man (. . .) I often think that nobody could love me the way I look now, because I look awful, don’t I?” (female) (95)
2.4 Altered relationship with partner (8, 80, 89, 95) Despite the sexual dysfunction associated with IA, women often felt pressured to maintain a normal sex life to prevent relationships being affected by the disease. Some partners had greater acceptance and understanding of the impact IA had on sexual function than others, assisting to strengthen relationships between partners. Conversely, others experienced that their partners poorly understood the impact of IA on their ability to engage in intercourse, creating tension and fear of relationship instability.	• Some women felt they had to push themselves to have intercourse despite reduced desire and fatigue, as they feared partners would leave them or didn’t want their sexual relationships to be affected by the disease. • Some women felt the need to maintain a normal sex life for their partners despite the presence of sexual dysfunction • Some partners had greater acceptance and understanding of the impact IA had on sexual function than others, assisting to strengthen relationships. Conversely, others experienced that their partners poorly understood the impact of IA on their ability to engage in intercourse, creating tension and fear of relationship instability.	“I have pushed myself. Even if I was exhausted, I have made a really big effort. I don’t want all the reasons he is with me to disappear” (female) (95) "My husband and I have been married for 30 years and we have always had a loving sexual relationship. He is not over demanding which is most probably a good thing, but I do believe it is important, with all my problems to still have a normal sex life." (female) (8)



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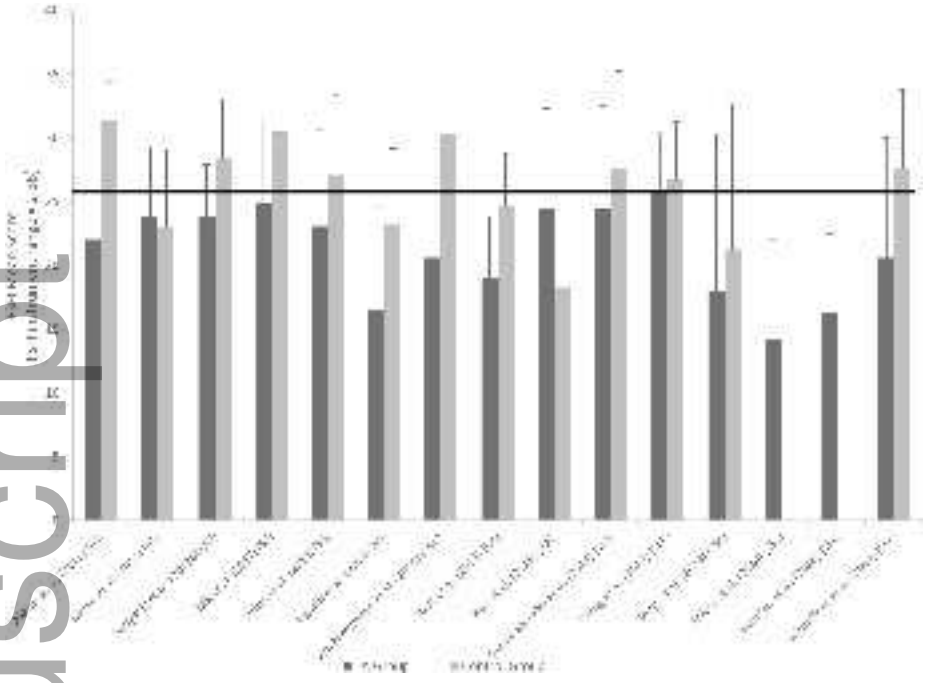

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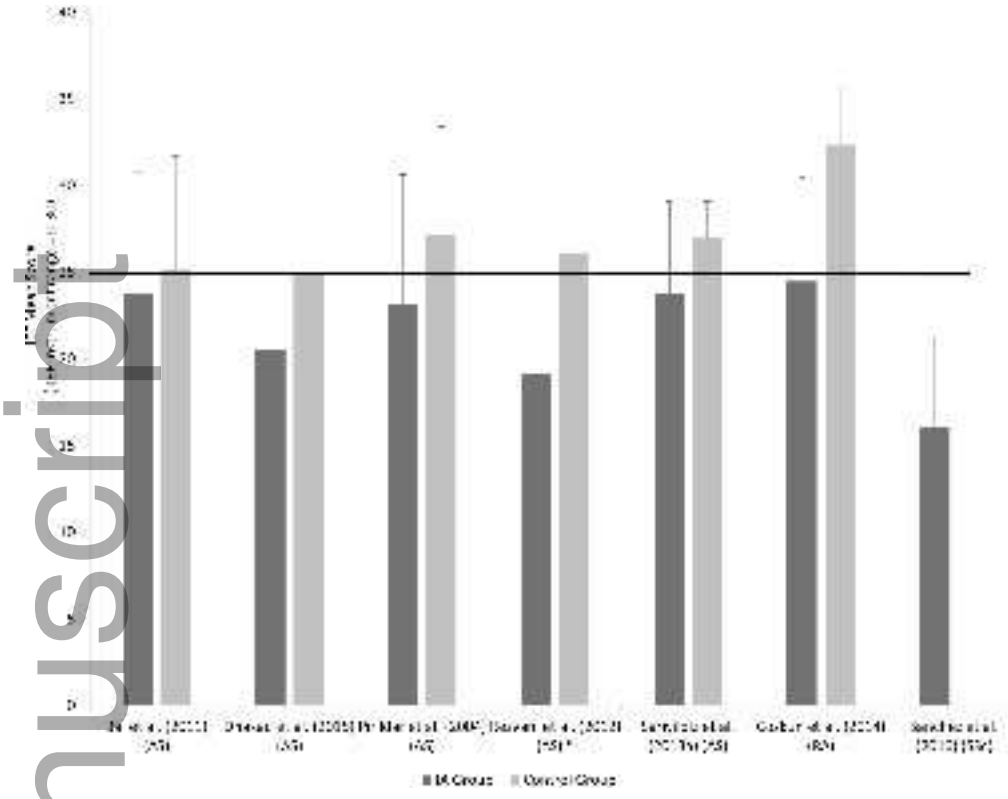

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