

ORIGINAL RESEARCH

Prevalence of anxiety and depression and the association with self-management behaviour in >12 000 patients with inflammatory rheumatic disease: a cross-sectional nationwide study

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ABSTRACT

Objective To investigate the prevalence of anxiety and depression among patients with inflammatory arthritis (IA) and evaluate the association of these mental health issues with self-management behaviour.

Methods In this nationwide cross-sectional study, we analysed data from 12 713 adult Danish patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or spondyloarthritis (SpA). Patients received an electronic questionnaire covering sociodemographics, self-management behaviour and mental health status. Questionnaire data were linked to clinical data from the Danish Rheumatology database (DANBIO) and the Danish National Patient Registry. The prevalence of anxiety and depression (by the Hospital Anxiety and Depression Scale for Anxiety (HADS-A) and Depression (HADS-D)) was estimated separately for RA/PsA/SpA. The association between mental health status and low self-management behaviour (adherence to treatment, health activation and physical activity) was estimated using multivariable logistic regression, adjusting for age, sex, educational level and comorbidity.

Results The prevalence of anxiety (HADS-A \geq 8) was highest for patients with SpA (34.5% (95% CI 32.4% to 36.6%)) and lowest for patients with RA (22.1% (95% CI 21.2% to 23.0%)), it was higher for women, younger (<55 years) and recently diagnosed (<3 years) patients and those with basic education. Similar prevalence estimates were found for depression. Across diagnoses, the clinically relevant symptoms of anxiety and depression (HADS \geq 8) were significantly associated with low self-management behaviour.

Conclusion Patients with IA showed substantial levels of anxiety and depression. A statistically significant association between anxiety and depression and low self-management behaviour was identified. These findings call for a systematic approach to identifying mental health issues in patients with IA.

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Inflammatory arthritis (IA) is frequently linked to both depression and anxiety.
- ⇒ A well-documented correlation between these mental health issues and poor health outcomes has previously been established.

WHAT THIS STUDY ADDS

- ⇒ Symptoms of anxiety and depression can be associated with self-management behaviour of individuals with IA, potentially leading to negative consequences for the progression of the disease.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ This study emphasises the importance of developing and implementing effective screening tools that are specifically designed to evaluate the mental health of individuals with IA.

INTRODUCTION

Depression and anxiety are the mental health issues most commonly associated with inflammatory arthritis (IA).^{1 2} IA is an overarching term for a group of chronic autoimmune diseases that includes rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA). Approximately 20%–40% of patients with IA have either depression, anxiety or a combination of both.^{3–6} By comparison, the prevalence of depression and anxiety in the general Danish population in 2021 was approximately 9% and 11%, respectively.⁷ Variations in prevalence rates relate to the definition of depression and anxiety and depend on the applied threshold of the measurement methods and the source

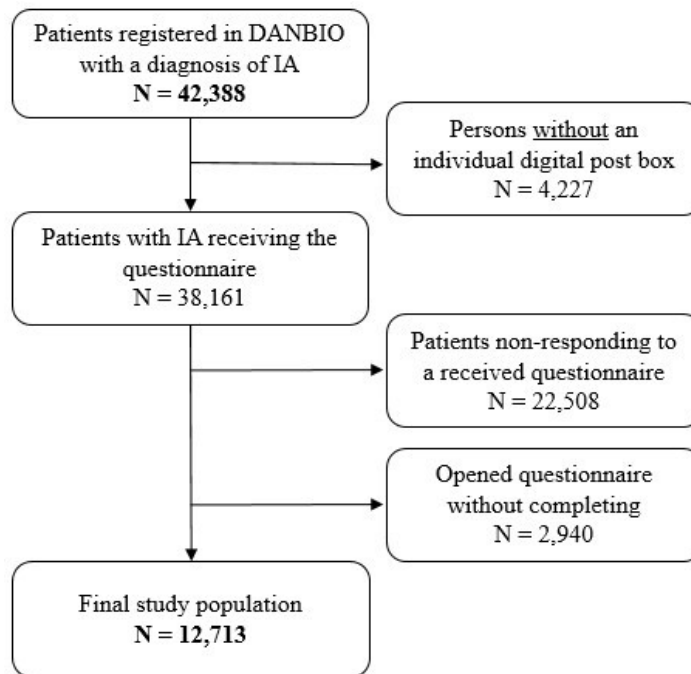


Figure 1 Flowchart of final study population for patients identified in the Danish Rheumatology database (DANBIO). IA, inflammatory arthritis.

population.³ A large prospective cohort study among more than 500 000 patients with inflammatory diseases in the UK reported a strong association between the incidence of depression and anxiety and the age at onset of the inflammatory disorder, with higher risks when the onset occurred below 40 years of age.⁸

The reasons for the increased risk of anxiety and depression in IA are multifactorial,⁹ although the exact mechanism is debated and still unexplored. Evidence points towards an association between systemic inflammation and anxiety and depression.¹⁰ It has been shown that acute phase reactants and inflammatory cytokines are increased in patients without IA who have depressive symptoms,⁹ and that patients with major depression have increased serum/and or plasma concentrations of C reactive protein.⁹ A recent prospective observational study showed baseline depression and anxiety to be inversely associated with remission in RA and partly in PsA.¹¹ The prevalence of anxiety and depression in IAs can, however, also be mediated by the socioeconomic status,⁹ and by social support and loneliness.⁸

The occurrence of anxiety and depression can affect a patient's self-management behaviour, which can be defined as the ability of the individual to manage symptoms, treatment and lifestyle changes, along with the psychosocial and cultural consequences of health conditions.¹² A well-established link exists between mental health issues and poor health outcomes in IAs.^{13–15}

Therefore, newly published recommendations for self-management in rheumatic and musculoskeletal diseases from the European Alliance for Associations of Rheumatology emphasise the need for periodic mental health assessments during the disease course.¹⁶ However, very few studies have investigated the association between mental health and self-management. A study from 1993 found a negative correlation between arthritis self-efficacy and physical activity, and reported depression and anxiety among patients with RA.¹⁷ However, to the best of our knowledge, similar associations have not been investigated recently or directly in patients with IA.

No consensus has yet been reached on how to measure self-management behaviour in IA (or any other chronic disease).¹⁸ However, in the late 1980s, Corbin and Strauss described how self-management covers three sets of tasks that individuals can prioritise to maintain their wellness: (1) medical management of the condition; (2) maintaining, changing and creating new behaviours and (3) dealing with the emotional aspects of living with a chronic disease that may impact problem solving.¹⁹ Therefore, self-management behaviour within IA is ideally measured by outcomes relevant to the patient. Previous measures have included adherence to treatment, patient activation in health and physical activity behaviour.²⁰

The aim of the present study was (1) to investigate the prevalence of anxiety and depression in a large cohort of patients with IA and (2) to evaluate the association between

Table 1 Baseline characteristics for 12 713 patients with IA and stratified by diagnosis

	Total N=12713	Rheumatoid arthritis N=8331	Psoriatic arthritis N=2390	Spondyloarthritis N=1992
Age in years, mean (\pm SD)	62 (13)	65 (12)	59 (12)	52 (14)
≤55, n (%)	3466 (27.3)	1539 (18.5)	816 (34.1)	1111 (55.8)
56–67, n (%)	4615 (36.3)	3022 (36.3)	962 (40.3)	631 (31.7)
>67, n (%)	4632 (36.4)	3770 (45.3)	612 (25.6)	250 (12.6)
Sex, n (%)				
Female	8060 (63.4)	5779 (69.4)	1364 (57.1)	917 (46.0)
Educational level n (%)				
Basic education	2303 (18.1)	1572 (18.9)	406 (17)	325 (16.3)
Short education	5277 (41.5)	3475 (41.7)	1038 (43.4)	764 (38.4)
Long education	5048 (39.7)	3214 (38.6)	934 (39.1)	900 (45.2)
Missing	85 (0.67)	70 (0.84)	12 (0.5)	3 (0.2)
Disease duration in years, mean (\pm SD)	12 (11)	12 (11)	11 (9)	12 (11)
0–3, n (%)	2623 (20.6)	1753 (21.0)	458 (19.2)	412 (20.7)
4–9, n (%)	3323 (26.1)	2160 (25.9)	611 (25.6)	552 (27.7)
10–20, n (%)	3230 (25.4)	2102 (25.2)	665 (27.8)	463 (23.2)
>20, n (%)	2245 (17.7)	1593 (19.1)	315 (13.2)	337 (16.9)
Missing, n (%)	1292 (10.2)	723 (8.7)	341 (14.3)	228 (11.5)
Disease activity, median (IQR)				
DAS-28-(CRP)	–	2.14 (1.39)	–	–
Missing, n (%)	–	454 (5.45)	–	–
DAPSA	–	–	9.7 (12.98)	–
Missing, n (%)	–	–	199 (8.3)	–
ASDAS	–	–	–	2.03 (1.61)
Missing, n (%)	–	–	–	206 (10.3)
MD-HAQ, median (IQR)	0.4 (0.7)	0.3 (0.7)	0.5 (0.8)	0.4 (0.7)
Missing, n (%)	543 (4.3)	326 (3.9)	137 (5.7)	80 (4.0)
Treatment, n (%)				
bDMARD	4542 (35.7)	2506 (30.1)	859 (35.9)	1177 (59.1)
csDMARD	8636 (67.9)	6710 (80.5)	1585 (66.3)	341 (17.1)
Prednisolone	673 (5.3)	595 (7.1)	56 (2.3)	22 (1.1)
Comorbidity; CCI, n (%)				
Low (score 0)	9291 (73.1)	5848 (70.2)	1821 (76.2)	1622 (81.4)
Moderate (scores 1–2)	2760 (21.7)	2002 (24.0)	457 (19.1)	301 (15.1)
Severe (scores \geq 3)	659 (5.2)	479 (5.8)	111 (4.64)	69 (3.5)
Missing, n (%)	3 (0.02)	2 (0.02)	1 (0.04)	–

ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biological disease-modifying antirheumatic drug; CCI, Charlson Comorbidity Index; csDMARD, conventional disease-modifying antirheumatic drug; DAPSA, Disease Activity in Psoriatic Arthritis; DAS28-(CPR), Disease Activity Score-28 C Reactive Protein; IA, inflammatory arthritis; MD-HAQ, Multi-Dimensional Health Assessment Questionnaire.

anxiety and depression and self-management behaviour, as indicated by the outcomes mentioned above.

Methods

Study design and population

We conducted a cross-sectional study among patients with IA living in Denmark in January 2022. An electronic questionnaire was sent out to all eligible patients \geq 18 years of age with either RA (International Classification of Diseases,

10th revision) (ICD-10): M05.9, M06.0 M06.9), PsA (ICD-10: M073.A, M073.B) or SpA (ICD-10: M45.9, M46.1, M46.8, M46.9). Patients were identified through the DANBIO.²¹ DANBIO is a nationwide rheumatology registry for patients with inflammatory musculoskeletal diseases.²¹ Since 2006, the inclusion of all newly diagnosed patients with RA in the registry has been mandatory, and the coverage of patients with patients with RA is presently more than 90%.²²

Table 2 Prevalence of clinically relevant symptoms of anxiety among 12 713 patients with inflammatory arthritis

	Rheumatoid arthritis N=8331		Psoriatic arthritis N=2390		Spondyloarthritis N=1992	
	N	Prevalence of anxiety* % (95% CI)	N	Prevalence of anxiety* % (95% CI)	N	Prevalence of anxiety* % (95% CI)
All	8110	22.1 (21.2 to 23.0)	2337	32.1 (30.2 to 34.0)	1957	34.5 (32.4 to 36.6)
Sex						
Female	5626	23.9 (22.8 to 25.0)	1332	34.2 (31.7 to 36.8)	903	40.1 (37.0 to 43.3)
Male	2484	18.0 (16.4 to 19.5)	1005	29.4 (26.5 to 32.2)	1054	29.8 (27.0 to 32.6)
Age, years						
≤55	1527	30.6 (28.3 to 32.9)	804	40.4 (37.0 to 43.8)	1095	40.8 (37.9 to 43.7)
56–67	2957	23.6 (22.0 to 25.1)	942	32.9 (29.9 to 35.9)	618	28.2 (24.6 to 31.7)
>67	3626	17.3 (16.1 to 18.5)	591	19.6 (16.4 to 22.8)	244	22.5 (17.3 to 27.8)
Level of education						
Basic	1523	24.0 (21.9 to 26.2)	398	42.0 (37.1 to 46.8)	316	45.6 (40.1 to 51.1)
Short	3398	22.3 (20.9 to 23.7)	1021	31.4 (28.6 to 34.3)	753	35.4 (32.0 to 38.9)
Long	3136	20.6 (19.2 to 22.0)	909	28.5 (25.6 to 31.4)	886	29.9 (26.8 to 32.8)
Disease duration, years						
0–3	1717	24.7 (22.7 to 26.7)	448	35.0 (30.6 to 39.5)	405	42.2 (37.4 to 47.0)
4–9	2097	22.5 (20.7 to 24.2)	599	34.6 (30.7 to 38.4)	543	36.8 (32.8 to 40.9)
10–20	2042	19.6 (17.9 to 21.3)	649	31.1 (27.6 to 34.7)	456	31.1 (26.9 to 35.4)
>20	1543	21.6 (19.5 to 23.6)	308	24.7 (19.9 to 29.5)	329	24.9 (20.2 to 30.0)

*Prevalence of clinically relevant level of anxiety symptoms using the HADS, subscale anxiety (HADS-A≥8). HADS, Hospital Anxiety and Depression Scale.

To ensure content validity, a questionnaire was composed based on a comprehensive literature review covering the association between mental health and IA, followed by two focus group interviews concerning the same subject: one among patients with IA and one with health professionals. The questionnaire was subsequently tested for face validity among 10 patients with IA from 2 different rheumatology outpatient clinics in Denmark using cognitive semistructured interviews and the ‘think aloud technique’.²³

The questionnaire was sent via a secure Danish national digital mailbox system called ‘e-Boks’. e-Boks is an encrypted public infrastructure for electronic communication linked to the Danish civil personal registration number (CPR),²⁴ which is a unique 10-digit number given to all Danish residents at birth or on immigration. Registration on e-Boks is mandatory for all Danish citizens aged 15 and older and is currently being used by more than 5 million people.²⁵ Exemption for use can only be given to citizens with poor physical/cognitive health, poor digital skills, lack of access to digital devices or language limitations.²⁶ Non-responders received a reminder after 10 days. Patients with no access to the digital mailbox were excluded.

The index date was defined as the date of completing the questionnaire. All patients responding to and submitting the questionnaire (regardless of possible missing responses to specific items) were included in the study.

The study was conducted adhering to the principles outlined in the Declaration of Helsinki and registered in accordance with the Danish law on data protection and the European Union’s General Data Protection Regulation. The patients were provided with information about the study prior to answering the questionnaire, emphasising that their participation was voluntary with the right to withdraw their consent at any time. Participants gave informed consent to participate in the study before taking part. All data were stored and treated with confidentiality. Reporting of the study will follow the STROBE guidelines²⁷

Questionnaire data

The questionnaire covered a range of self-reported aspects, including sociodemographics, depression and anxiety, adherence, patient activation in health and level of physical activity. As the questionnaire was sent out at the end of a national lockdown due to the COVID-19 pandemic, it also included additional questions about COVID-19 impacts.

Outcome of interest

The outcome of interest was self-management behaviour. We operationalised self-management behaviour as adherence to treatment, patient activation in health and level of physical activity.²⁸ Adherence to treatment was measured according to the Compliance

Table 3 Prevalence of clinically relevant symptoms of depression among 12713 patients with inflammatory arthritis

	Rheumatoid arthritis N=8331		Psoriatic arthritis N=2390		Spondyloarthritis N=1,992	
	N	Prevalence of depression*% (95% CI)	N	Prevalence of depression*% (95% CI)	N	Prevalence of depression*% (95% CI)
All	8164	18.6 (17.7 to 19.4)	2340	27.2 (25.4 to 29.0)	1969	26.4 (24.5 to 28.4)
Sex						
Female	5670	19.6 (18.6 to 20.7)	1331	28.6 (26.2 to 31.1)	909	30.1 (27.2 to 33.1)
Male	2494	16.2 (14.8 to 17.7)	1009	25.4 (22.7 to 28.1)	1060	23.2 (20.7 to 25.7)
Age, years						
≤55	1529	24.7 (22.6 to 26.9)	805	33.4 (30.2 to 36.7)	1101	31.6 (28.9 to 34.4)
56–67	2989	19.8 (18.4 to 21.2)	944	28.3 (25.4 to 31.2)	622	20.7 (17.6 to 24.0)
>67	3646	15.0 (13.9 to 16.2)	592	17.1 (14.0 to 20.1)	246	17.5 (12.7 to 22.2)
Level of education						
Basic	1531	22.1 (20.0 to 24.2)	399	35.1 (30.4 to 39.8)	321	33.3 (28.2 to 38.5)
Short	3412	18.7 (17.4 to 20.0)	1015	26.3 (23.6 to 29.0)	755	26.9 (23.7 to 30.1)
Long	3163	16.6 (15.3 to 17.9)	916	24.6 (21.8 to 27.4)	891	23.5 (20.7 to 26.2)
Disease duration, years						
0–3	1722	21.3 (19.4 to 23.2)	449	29.4 (25.2 to 33.6)	406	30.3 (25.8 to 34.8)
4–9	2119	18.4 (16.8 to 20.1)	598	27.0 (23.0 to 30.5)	547	29.3 (25.4 to 33.1)
10–20	2061	16.4 (14.8 to 18.0)	649	27.7 (24.3 to 31.2)	458	25.3 (21.3 to 29.3)
>20	1561	18.3 (16.4 to 20.2)	310	21.3 (16.7 to 25.8)	333	15.9 (12.0 to 19.8)

*Prevalence of clinically relevant level of depression symptoms using the HADS, subscale depression (HADS-D≥8). HADS, Hospital Anxiety and Depression Scale.

Questionnaire Rheumatology (CQR)-5-item scale. The CQR-5 is derived from the original 19-item CQR instrument.²⁹ It consists of five statements on medication-taking behaviour, with four ordinal response options ranging from (1) ‘definitely don’t agree’ to (4) ‘definitely agree’. Lower scores indicate lower levels of adherence.²⁹ The level of adherence was classified as low or high based on an equation provided by the questionnaire developers.²⁹ In cases of missing items, the level of adherence was not calculated.

Patients’ activation in health covered two areas: The ability to tell when outpatient care is needed and the ability to handle new situations or problems with health. These areas were measured by two items from the Patient Activation Measure 13 questionnaire (PAM13),³⁰ namely item 5: ‘I am confident that I can tell whether I need to go to the doctor or whether I can handle a health problem myself’ and item 12: ‘I am confident I can figure out solutions when new situations or problems arise with my health’. The items have five ordinal response options ranging from 1 to 5: (1) ‘strongly disagree’, (2) ‘disagree’, (3) ‘agree’, (4) ‘strongly agree’ and (5) ‘not applicable’. Each item was analysed individually with dichotomised response options, where strongly disagree/disagree indicated high patient activation and disagree/strongly agree indicated low patient activation.

Physical activity behaviour was measured using an ad hoc self-report question from the Danish National Health Survey: ‘In a typical week, how much time do you spend on moderate to vigorous physical activity where you feel your heart rate and breathing increase?’ The question has five ordinal response options: ‘less than 30 min’, ‘30–89 min’, ‘90–149 min’, ‘150–299 min’ and ‘300 min or more’.⁷ Dichotomisation was done following recommendations from the WHO and the American College of Sports Medicine, who define <150 min weekly as low physical activity and ≥150 min weekly as high physical activity.^{31–33}

Exposure of interest

Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS).³⁴ HADS is a 14-item questionnaire that assesses the levels of anxiety and depression symptoms in medically ill patients using two 7-item subscales, one for anxiety (HADS-A) and one for depression (HADS-D). Each item has a four-ordinal response option from 0 to 3, giving a total score on each subscale between 0 and 21.³⁴ Scores of 8–10 suggest the presence of a mood disorder, whereas scores of 11 or higher indicate the probable presence of a mood disorder.³⁴ In this study, anxiety and depression were handled separately. Anxiety and depression symptoms were categorised into three groups: non-case (HADS-A≤7/HADS-D≤7), possible case (HADS-A 8–10/HADS-D

Table 4 Association between anxiety and depression and self-management skills

	Crude OR (95% CI)	Adjusted OR (95% CI)
Adherence to treatment		
Anxiety, HADS-A	n=11 730	n=11 668
Non-case, ≤7	ref	ref
Possible case, 8–10	1.07 (0.96 to 1.19)	1.21 (1.08 to 1.35)
Definite case, ≥11	1.07 (0.95 to 1.21)	1.40 (1.23 to 1.59)
Depression, HADS-D	n=11 784	n=11 718
Non-case, ≤7	ref	ref
Possible case, 8–10	1.20 (1.08 to 1.35)	1.34 (1.20 to 1.51)
Definite case, ≥11	1.03 (0.89 to 1.19)	1.28 (1.11 to 1.49)
Patient activation Can tell when outpatient care is needed		
Anxiety, HADS-A	n=11 880	n=11 824
Non-case, ≤7	ref	ref
Possible case, 8–10	2.44 (2.14 to 2.80)	2.32 (2.02 to 2.66)
Definite case, ≥11	4.67 (4.07 to 5.36)	4.29 (3.72 to 4.94)
Depression, HADS-D	n=11 939	n=11 879
Non-case, ≤7	ref	ref
Possible case, 8–10	3.08 (2.70 to 3.51)	2.95 (2.58 to 3.37)
Definite case, ≥11	5.41 (4.64 to 6.30)	4.90 (4.19 to 5.74)
Patient activation can handle new situations or problems with health condition		
Anxiety, HADS-A	n=11 715	n=11 658
Non-case, ≤7	ref	ref
Possible case, 8–10	2.99 (2.67 to 3.34)	2.90 (2.59 to 3.24)
Definite case, ≥11	6.02 (5.31 to 6.82)	5.66 (4.98 to 6.43)
Depression, HADS-D	n=11 776	n=11 714
Non-case, ≤7	ref	ref
Possible case, 8–10	4.02 (3.59 to 4.49)	3.88 (3.47 to 4.35)
Definite case, ≥11	7.53 (6.50 to 8.71)	7.00 (6.03 to 8.12)
Physical activity Level of physical activity weekly with increased heartrate		
Anxiety, HADS-A	n=12 341	n=12 275
Non-case, ≤7	ref	ref
Possible case, 8–10	1.35 (1.21 to 1.50)	1.31 (1.17 to 1.46)
Definite case, ≥11	1.65 (1.45 to 1.88)	1.60 (1.40 to 1.83)
Depression, HADS-D	n=12 409	n=12 340
Non-case, ≤7	ref	ref
Possible case, 8–10	1.99 (1.76 to 2.24)	1.94 (1.72 to 2.19)
Definite case, ≥11	2.46 (2.09 to 2.91)	2.39 (2.02 to 2.83)
Results of logistic regression analysis showing ORs. HADS-A, Hospital Anxiety and Depression Scale for Anxiety; HADS-D, Hospital Anxiety and Depression Scale for Depression; ref, reference group;		

8–10) and definite case (HADS-A≥11/HADS-D≥11). Clinically relevant symptoms were defined as possible and definite cases (ie, scores ≥8).

Additional questionnaire items

Level of education was categorised according to the International Standard Classification of Education³⁵ (ISCED)

into ‘basic’ (ISCED levels 1–2), ‘short’ (ISCED levels 3–4) and ‘long’ (ISCED levels 5–6).

The impact of COVID-19 was assessed with the question: ‘To what extent is your mental health influenced by the current COVID-19 situation?’ with five response options ranging from ‘not at all’ to ‘to the highest degree’. Impact was dichotomised into ‘low impact’ and ‘highly impact’.

Table 5 Baseline characteristics in 42 388 patients with IA stratified by questionnaire responders versus non-responders

	Responders N=12 713	Non-responders N=29 675	Statistical difference between groups, p value*
Age in years, mean (±SD)	62 (±13)	60 (±16)	<0.001
≤55, n (%)	3466 (27.3)	10 689 (36.0)	
56–67, n (%)	4615 (36.3)	8118 (27.3)	
>67, n(%)	4632 (36.4)	10 865 (36.6)	
Sex, n (%)			0.195
Female	8060 (63.4)	18 617 (62.7)	
Male	4653 (36.6)	11 058 (37.3)	
Diagnosis, n (%)			<0.001
Rheumatoid arthritis	8331 (65.5)	18 548 (62.5)	
Psoriatic arthritis	2390 (18.8)	5558 (18.7)	
Ankylosing spondylitis	1992 (15.7)	5569 (18.8)	
Disease duration in years, mean (±SD)	11.88 (±10.7)	12.07 (±10.3)	<0.001
0–3, n (%)	2623 (20.6)	5011 (16.9)	<0.001
4–9, n (%)	3323 (26.1)	8319 (28.0)	
10–20, n (%)	3230 (25.4)	8095 (27.2)	
>20, n (%)	2245 (17.7)	5018 (16.9)	
Missing, n (%)	1294 (10.2)	3249 (10.94)	
MD-HAQ,			<0.001
Mean (SD)	0.51 (0.51)	0.58 (0.56)	
Median (IQR)	0.4 (0.7)	0.4 (0.8)	
Missing, n (%)	543 (2.3)	2703 (9.10)	
Treatment, n (%)			
bDMARD	4542 (35.7)	9811 (33.1)	<0.001
csDMARD	8636 (67.9)	18 889 (63.6)	<0.001
Prednisolone	673 (5.3)	1729 (5.8)	0.030
Disease activity, median (IQR)			
RA patients, DAS-28	2.14 (1.39)	2.23 (1.42)	<0.001
PsA patients, DAPSA	9.7 (12.98)	9.33 (11.80)	0.0534
SpA patients, ASDAS	2.03 (1.61)	2.07 (1.68)	0.6345
Comorbidity; CCI, n (%)			
Low (score 0)	9291 (73.1)	21 341 (71.9)	<0.001
Moderate (scores 1–2)	2760 (21.7)	6375 (21.5)	
Severe (scores ≥3)	659 (5.2)	1940 (6.5)	

*Assessed using Pearson's χ^2 and Mann-Whitney tests.

ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARD, biological disease-modifying antirheumatic drug; CCI, Charlson Comorbidity Index; csDMARD, conventional disease-modifying antirheumatic drug; DAPSA, Disease Activity in Psoriatic Arthritis; DAS28-(CPR), Disease Activity Score-28 c-reactive protein; IA, inflammatory arthritis; MD-HAQ, Multi-Dimensional Health Assessment Questionnaire; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SpA, spondyloarthritis.

Register data and patient characteristics

The questionnaire data were linked to register data from the DANBIO registry²¹ and the Danish National Patient Registry (DNPR)³⁶ using CPR number, which allows the linkage of data across nationwide medical and administrative registries at the individual level.²⁴ The DNPR is an administrative registry containing information on all somatic hospital admissions and outpatient clinic visits in Denmark since 1977 and 1995, respectively.³⁷ All register

data were equally available on responders and non-responders.

Age and gender were identified according to the CPR numbers. The age of the participants was calculated at the index date, and the participants were categorised into three age groups: ≤55 years, 56–67 years and >67 years.

Disease duration was identified according to the date of the diagnoses registered in DANBIO until the index date. Information on disease activity and disease impact

was also identified from DANBIO. We used the last registration of disease activity prior to the index date. Disease activity was measured using the Disease Activity Score-28 C Reactive Protein³⁸ for RA, Disease Activity in Psoriatic Arthritis (DAPSA28)³⁹ for PsA and the Ankylosing Spondylitis Disease Activity Score⁴⁰ for SpA.

Disease impact was indicated by the functional status, as measured by the Multidimensional Health Assessment Questionnaire (MD-HAQ).⁴¹ The MD-HAQ measures self-reported functional status over the past 7 days on 10 items concerning everyday activities. Each item is scored on a 4-point Likert scale from (0) 'without any difficulty' to (3) 'unable to do'. The mean of the MD-HAQ score is calculated with a possible range of 0.0–3.0, with a higher score indicating a lower functional status.⁴¹

Data on comorbidity were obtained from the DNPR. Comorbidity burden was defined according to Charlson's Comorbidity Index and was based on diagnosis codes, excluding RA, from hospital contacts registered in the DNPR 5 years prior to the index date. Charlson Comorbidity Index scores were categorised into 'low' (score 0), 'moderate' (scores 1–2) and 'severe' (scores ≥ 3).⁴²

Statistics

All statistical analyses were performed using Stata/MP V.17.0 (StataCorp). Categorical and dichotomised data are presented as frequencies and percentage distributions. Normally distributed continuous data are presented as the mean and SD. For non-normally distributed data, the medians and IQRs were presented as well. Information on missing responses for each item was presented as frequencies and percentage distributions. For all analyses, a $p < 0.05$ was considered statistically significant.

The prevalence of clinically relevant levels of anxiety and depression symptoms (HADS-A ≥ 8 /HADS-D ≥ 8) was estimated separately for RA, PsA and SpA and presented with 95% CIs. The associations between low self-management behaviour, indicated by adherence to treatment, patient activation in health, weekly time spent on physical activity and symptoms of anxiety and depression, were estimated using multivariable logistic regression with ORs, while adjusting for age, sex, educational level and comorbidity. Crude and adjusted ORs were reported with 95% CIs. The analysis was performed collectively for IA after finding no statistically significant modification between diagnosis (RA, PsA or SpA) and HADS in relation to self-management behaviour.

The level of disease activity can be considered a proxy for inflammation and in our study, it was considered to be a confounding variable for the association between inflammation, and depression and anxiety. Consequently, we performed a sensitivity analysis to adjust for this. Due to the different measures used to determine disease activity, separate analyses were performed for RA, PsA and SpA. Furthermore, as the questionnaire was distributed early in 2021 at the end of a national lockdown due to the COVID-19 pandemic, we also performed a sensitivity analysis adjusting for the potential impact of

COVID. Differences in baseline characteristics (age, sex, diagnosis, disease duration, MD-HAQ, treatment and comorbidity) between questionnaire responders and non-responders were assessed using the Pearson's χ^2 and Mann-Whitney tests.

RESULTS

Characteristics of the study population

A total of 42 388 patients with IA were identified in DANBIO. Of these, 38 161 had e-Boks and received the questionnaire. In total, 15 653 agreed to participate, but 2940 opened the questionnaire without responding. The final study population, therefore, included 12 713 patients with IA (figure 1).

The group of patients diagnosed with SpA were younger (<55 years: 55.8% vs 18.5% and 34.1% with RA and PsA, respectively), and fewer were women (46.0% vs 69.4% and 57.1% in RA and PsA, respectively) (table 1). Patients with RA were more likely to receive conventional disease-modifying antirheumatic drug (csDMARD) (80.5%). Characteristics from questionnaire data are available in online supplemental table 1.

Prevalence of anxiety symptoms

The prevalence of a clinically relevant level of anxiety symptoms was highest for patients with SpA (34.5% (95% CI 32.4% to 36.6%)) followed by PsA (32.1% (95% CI 30.2% to 34.0%)) and lowest for patients with RA (22.1% (95% CI 21.2% to 23.0%)) (table 2). For all three diagnoses, women, younger (<55 vs >67 years), more recently diagnosed patients, and those with a basic educational level, reported most anxiety symptoms (table 2).

Prevalence of depression symptoms

Overall, the prevalence appeared lower for depression symptoms than for anxiety in all three diagnoses, where patients with RA reported lower scores (18.6% (95% CI 17.7% to 19.4%)) compared with PsA (27.2% (95% CI 25.4% to 29.0%)) and SpA (26.4% (95% CI 24.5% to 28.4%)). As for anxiety, symptoms of depression were higher for women, younger and newly diagnosed patients with a basic education (table 3).

Association between depression, anxiety and self-management behaviour

Despite variation in the prevalence of depression and anxiety symptoms, especially between RA and PsA/SpA, the association between depression and anxiety and self-management behaviour was found to be independent of the three diagnosis (online supplemental figure 2, table 1).

Overall, patients presenting with a definite case of anxiety (HADS-A ≥ 11) were more likely to be non-adherent compared with non-cases (HADS-A ≤ 7) (OR 1.40 (95% CI 1.23 to 1.59)). The same pattern was found for depression (table 4). The patients' activation in healthcare was also strongly associated with the presence of anxiety. Hence, patients with either possible or

definite cases of anxiety were less likely to know when they needed medical care compared with non-cases (adjusted OR 2.32, (95% CI 2.02 to 2.66) and 4.29 (95% CI 3.72 to 4.94), respectively) and less confident that they could figure out solutions when new situations arose with their health condition (adjusted OR 2.90 (95% CI 2.59 to 3.24) and 5.66 (95% CI 4.98 to 6.43), respectively). A similar pattern was found for depression (table 4). Furthermore, a higher level of anxiety was associated with lower PA (OR 1.31 (95% CI 1.17 to 1.46) for possible cases and OR 1.60 (95% CI 1.40 to 1.83 for definite cases). A similar pattern was found for depression (table 4).

On further adjustment for disease activity, the association decreased, with the least notable influence observed for patients with RA (online supplemental tables 3–5). The strongest influence of disease activity was observed in the association between definite cases of both anxiety and depression and patient activation among patients with PsA (online supplemental table 4). However, the 95% CI intervals overlapped. Nevertheless, for patients with SpA, the OR for the association between anxiety and physical activity became non-significant (OR 1.24 (95% CI 0.94 to 1.63) for HADS-A 8–10 and OR 1.01 (95% CI 0.75 to 1.35) for HADS-A \geq 11) (online supplemental table 5).

The COVID-19 pandemic did not seem to affect the associations (online supplemental table 6).

Questionnaire responders versus non-responders

Gender distribution was similar for responders and non-responders; however, non-responders were younger (mean age of 60 compared with 62) with a slightly longer disease duration and had lower functional status, as indicated by a higher MD-HAQ score. Relatively more patients with SpA were among the non-responders. Responders were more likely to receive biological DMARD and csDMARD treatment. Furthermore, non-responders had significantly more comorbidity (table 5).

DISCUSSION

This cross-sectional study found a high prevalence of anxiety and depression symptoms among patients with IA. The prevalence was significantly higher for patients with PsA and SpA than for those with RA. Furthermore, anxiety and depression were strongly associated with low self-management behaviour, as indicated by adherence to treatment, patient activation in health and physical activity. This association did not depend on the diagnosis.

A previous systematic review reported a pooled prevalence of 38% (95% CI 30% to 45%) for depression (HADS \geq 7/8) among patients with SpA,⁴ which is higher than the 26.4% identified in our study. This difference could reflect the lower mean age of the participants in the eight reviewed studies. Therefore, our use of the prevalence estimated for patients who were \leq 55 years of age in our study (31.6%) would make the findings more comparable and similar. A meta-analysis examining the

prevalence of anxiety and depression among patients with PsA reported a pooled prevalence of 19% (95% CI 11% to 29%) and 17% (95% CI 13% to 21%), respectively⁴³; however, that study only included definite cases with HADS \geq 11.

Studies addressing the association between mental health in IA and self-management are limited. For patients with RA, a negative correlation between self-efficacy, physical activity, depression and anxiety was acknowledged by Taal *et al.*¹⁷ A recent Turkish study investigating the effects of depression on medication adherence of patients with SpA found that non-adherent patients reported more depressive symptoms.⁴⁴ Our study confirms that anxiety and depression are associated with low physical activity and low adherence to medication among patients with RA, PsA and SpA. We also identified patient activation as having the strongest association; to the best of our knowledge, no other study has previously established this finding.

Disease activity appears to influence the association between mental health status and our self-management behaviour measures for all patients. The most notable finding is that the association between mental health status and physical activity lost its statistical significance for patients with SpA after adjustment for disease activity. Nevertheless, this finding is likely a result of confounding by indication, as patients with SpA are encouraged to exercise on a regular basis, and physical activity promotion and instructions constitute a cornerstone of the treatment.⁴⁵

No standard exists regarding how to measure self-management behaviour, making comparisons between studies difficult. In previous research, self-efficacy has often been used as a proxy outcome for self-management behaviour.^{18 20} However, we refrained from using self-efficacy as we consider the concept of self-efficacy to be a mechanism and a prerequisite for self-management behaviour⁴⁶ and that self-efficacy is thus more likely to be an effect modifier for the association rather than an outcome. A recent Danish systematic review on self-management measurements in rheumatology revealed that PAM-13 has often been utilised as a direct measure of self-management.²⁰ In addition, we chose to investigate adherence to treatment and physical activity because these aspects are highly relevant for the treatment of IA. This choice of method is in line with the guidelines from a group of international self-management experts who recommend that self-management intervention should include a combination of at least two of the following: stimulation of independent sign/symptom monitoring, medication management, enhancing problem-solving and decision-making skills for medical treatment management, and changing their physical activity, dietary and/or smoking behaviour.²⁸ It can be argued that a lower level of physical activity is expected among patients suffering from depression. Maybe because depression and anxiety affect functional decline indirectly through other processes such as cardiovascular diseases or

inflammation, or because depression leads to decreased levels of executive control and thereby decreased exercise or changes in eating habits.⁹ In our study, however, we found that the severity of anxiety and depression did not substantially change the association to physical activity. This suggests that this issue affects a considerable number of patients with IA, and as such, should be considered in routine clinical practice.

The strength of our study is its very large sample size, which enabled us to identify the association between mental health and self-management among IA patients with a high degree of precision. Another strength is the linked dataset, which combined self-reported data with clinical-based and register-based data from DANBIO and DNPR. We consider this to be unique and helpful in obtaining a deeper understanding of how different determinants may impact self-management behaviour in patients with IA. Nevertheless, our study has some limitations that merit further discussion. First, our use of a cross-sectional questionnaire study design did not allow an identification of the causal path between levels of self-management behaviour and symptoms of anxiety and depression. Another limitation was that the questionnaire was distributed electronically through the electronic 'e-Boks' mailboxes; therefore, patients without 'e-Boks' were not included in the study. One cause of exemption from using the electronic mailbox is poor physical health, and this could potentially have made us underestimate the prevalence of anxiety and depression symptoms among patients with IA.

In addition, our questionnaire was distributed at the end of the third lockdown due to the COVID-19 pandemic in Denmark, which might have affected the mental health of this patient group and could have led to higher estimates. This possibility is supported by findings by a Japanese research group, which identified an increased prevalence of anxiety and depression in patients with RA during the pandemic than before it.⁴⁷ However, Koppert *et al* investigated the psychological impact of the peak of the COVID-19 pandemic on patients with chronic inflammatory rheumatic disease and found only a modest psychological impact of the COVID-19 pandemic in patients with inflammatory rheumatic disease.⁴⁸ Additionally, our non-response analysis revealed that non-responders were younger and more likely to have had a SpA diagnosis. Since the prevalence estimates were higher for these groups, this selection bias may have resulted in an underestimation of the prevalence. However, as we consider the bias to be non-differential, this selection bias would not change the association.

In summary, the symptoms of anxiety and depression seem to have an impact on self-management behaviour in IA, with potentially negative impacts on the disease. Studies in other areas have suggested that systematic screening may be effective in addressing mental health problems in clinical practice.⁴⁹ Hence, future studies should focus on tools for screening the mental health of patients with IA. This may enable feedback to individuals

about symptom severity and the provision of contacts for social support interventions or other relevant healthcare services.

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