ORIGINAL ARTICLE

Subsequent Risk of Hospitalization for Neuropsychiatric Disorders in Patients With Rheumatic Diseases

A Nationwide Study From Sweden

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Objective: To analyze the association between rheumatoid arthritis, systemic lupus erythematosus, and ankylosing spondylitis and hospitalization for psychiatric disorders, as well as the association between hospitalization for dementia or delirium and systemic lupus erythematosus, by using a novel, large-scale approach.

Design: Cohort study with follow-up between 1973 and 2004.

Participants: The entire Swedish population.

Main Outcome Measures: Affective, psychotic, neurotic, and personality disorders as well as dementia and delirium.

Results: Individuals with rheumatic diseases had a higher risk of psychiatric disorders than the general population. Those with systemic lupus erythematosus and ankylosing spondylitis had a higher risk of subsequent psychiatric disorders than did patients with rheumatoid arthritis. The significant standardized incidence ratios for rheumatoid arthritis, systemic lupus erythematosus, and ankylosing spondylitis were 1.45, 2.38, and 1.69, respectively, for men, and 1.36, 2.16, and 1.95, respectively, for women. Differences were also found based on subtypes of the rheumatic disease and the psychiatric disorder, sex, and various follow-up intervals. Systemic lupus erythematosus carried an increased risk of dementia and delirium. Only women with rheumatoid arthritis and systemic lupus erythematosus had an increased risk of psychotic disorders and severe depression.

Conclusion: Health care providers who encounter patients with rheumatic diseases should be aware that these patients are more likely to develop neuropsychiatric disorders and that some subgroups seem to be more vulnerable than others.

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RHEUMATOID ARTHRITIS (RA), systemic lupus erythematosus (SLE), and ankylosing spondylitis (AS), also known as Bekhterev disease, are caused by misdirected autoimmune inflammation in the joints and/or spine. Concurrent inflammation in the internal organs is associated with nephritis, myocarditis, colitis, and other diseases.

These 3 rheumatic diseases are relatively common in the general population. The prevalence of RA and AS in industrialized countries is 1% to 2% and 0.5% to 4%, respectively.[1] Both RA and SLE are more common among women, whereas AS is more common among men. However, SLE exhibits the strongest sex difference; the prevalence rates are approximately 4 per 100 000 men and 45 per 100 000 women.[2,3]

In most cases, the medication for these diseases is lifelong, rigorous, and often associated with adverse effects. In addition, these chronic diseases cause long-lasting suffering for many of the affected individuals, which is characterized by chronic pain, a worsened quality of life,[4-7] and neurological and psychiatric disorders.[4,8-10] For example, SLE is associated with affective disorders[8-10] and psychosis.[8,10] There is evidence that neuropsychiatric disorders in patients with SLE are caused by immunological mechanisms[11] and a decreased regional cerebral blood flow.[12] However, psychological distress and stressful life events are also important factors in the development of maladaptive coping styles, according to a study of patients with RA and SLE from Denver, Colorado.[13] A study of patients with AS found that disease status scores correlated significantly with anxiety and depression.[14] It is, therefore, likely that these diseases have a negative effect on the mental health of affected individuals and possibly on their risk of hospitalization for psychiatric disorders.

Table 1. Diagnostic Codes

Characteristic	*International Classification of Diseases* Diagnostic Code		
	8th Edition[17]	9th Edition[18]	10th Edition[19]
Rheumatic diseases			
Ankylosing spondylitis	712.4	720.A	M45, M081
Systemic lupus erythematosus	734.1	710.A	M32
Rheumatoid arthritis	712.1, 712.3	714 (except 714.E and 714.X)	M05, M06, M080, M082
All psychiatric disorders	295, 296, 297, 298, 300, 301, 302, 306, 307, 308, 309, 311, 312	295, 296, 297, 298, 300, 301, 302, 306, 307, 308, 309, 311, 312	F20-F69
Psychotic disorders	295, 297, 298.B, 298.C, 298.E, 298.W, 298.X	295, 297, 298.B, 298.C, 298.E, 298.W, 298.X	F20-F29
Schizophrenia	295	295	F20, F21
Affective disorders	296, 298.A, 300.E, 309, 311	296, 298.A, 300.E, 309, 311	F30-F39
Severe depression with or without psychotic symptoms	296.B, 298.A	296.B, 298.A	F32.2, F32.3
Dysthymia	300.E	300.E	F34.1
Manic episode/bipolar affective disorder	296.A, 296.C, 296.D, 296.E	296.A, 296.C, 296.D, 296.E	F30, F31
Neurotic disorders	300.A, 300.B, 300.C, 300.D, 300.F, 300.G, 300.H, 300.W, 300.X	300.A, 300.B, 300.C, 300.D, 300.F, 300.G, 300.H, 300.W, 300.X	F40-F48
Personality disorders	301, 302, 312	301, 302, 312	F60-F59
Dementia	290, 294.A, 294.B	290, 294.A, 294.B	F00-F04, F067
Delirium	293	293	F05

Results from previous studies are relatively consistent. However, a novel approach of the present study is that we included all hospitalizations in Sweden for these rheumatic diseases between 1973 and 2004 as well as hospitalizations for subsequent affective, psychotic, neurotic, and personality disorders. The aim was to analyze the association between RA, SLE, or AS and severe psychiatric disorders leading to hospitalization. In addition, we also analyzed these associations by sex, age, and various follow-up intervals between the first hospitalization for RA, SLE, or AS and for psychiatric disorders and the association between hospitalization for SLE and dementia or delirium.

METHODS

MIGMED RESEARCH DATABASE

Patients were followed up from January 1, 1973, until hospital diagnosis, death, emigration, or the end of the study on December 31, 2004. Patients with RA, SLE, or AS were defined as those who, during the study period, were hospitalized for RA, SLE, or AS for the first time before being hospitalized for a neuropsychiatric disorder for the first time.

Data used in this study were retrieved from the MigMed database, Center for Family and Community Medicine, Karolinska Institute. MigMed is a single, comprehensive database that has been constructed using several national Swedish data registers, including, but not limited to, the Total Population Register and the Swedish Hospital Discharge Register.[15,16] Information from the various registers in the database is linked at the individual level via the 10-digit national registration number assigned to each person in Sweden for his or her lifetime. Before inclusion in the MigMed database, national registration numbers were replaced by serial numbers to ensure the anonymity of all individuals, and serial numbers were used for all data linkages. This study was approved by the Ethics Committee of the Karolinska Institute.

Diagnostic codes were retrieved from the Swedish Hospital Discharge Register according to the 8th (1973-1986), 9th (1987-1996), and 10th (1997-2004) editions of the *International Classification of Diseases* (**Table 1**).[17-19] The Swedish Hospital Discharge Register covers all hospitals in Sweden. Only first hospitalizations during the study period were included. Hospitalization for the diagnostic subcategories are referred to by the name of the disease.

INDIVIDUAL VARIABLES

Age at hospital diagnosis of neuropsychiatric disorders was categorized in 5-year groups, and the groups were merged as necessary. Geographic regions were divided into large cities (cities with a population of >200 000, ie, Stockholm, Gothenburg, and Malmö), Southern Sweden, and Northern Sweden. Geographic region was included as an individual variable to adjust for possible differences with regard to hospital admissions. In addition, time period was included to adjust for possible differences in hospitalization rates over time. The follow-up interval between first hospitalizations for RA, SLE, or AS and for any psychiatric disorder was categorized as less than 1, 1 to 4, 5 to 9, and 10 or more years.

STATISTICAL ANALYSIS

Person-years were calculated from the start of follow-up on January 1, 1973, until hospital diagnosis, death, emigration, or the end of the study on December 31, 2004. Age-standardized incidence ratios (SIRs) were calculated for the entire follow-up period, divided into 3-year periods. The SIRs were calculated as the ratio of the observed to the expected number of cases of subsequent neuropsychiatric disorders[20] in patients with rheumatic diseases. The expected number of cases was based on the expected number of cases in the general population, calculated for age (in 5-year groups), sex, time period, and geographic region. Confidence intervals (95% CIs) were calculated assuming a Poisson distribution. Interaction tests were performed to determine whether the association between the 3 rheumatic diseases and psychiatric disorders differed by age. No interaction was found.

RESULTS

Table 2 shows the number of cases and hospitalization rates for rheumatic diseases, hospitalization rates for psy-

Table 2. Psychiatric Disorders in the General Population and Following Rheumatic Diseases

Characteristic	Men[a]			Women[a]		
	No. of Patients	IR (per 100 000)	Mean Age, y[b]	No. of Patients	IR (per 100 000)	Mean Age, y[b]
Rheumatic diseases						
Ankylosing spondylitis	3715	3.0	43	1538	1.3	43
Systemic lupus erythematosus	1048	0.9	53	4323	3.5	46
Rheumatoid arthritis	14 849	12.2	59	34 173	26.6	58
Psychiatric disorders in the general population						
All psychiatric disorders	166 580	139.0	NA	225 935	187.9	NA
Psychotic disorders	23 874	19.6	NA	24 069	19.5	NA
Schizophrenia	10 101	8.2	NA	7998	6.7	NA
Affective disorders	50 567	42.3	NA	69 739	56.6	NA
Severe depression	6673	5.6	NA	8725	7.0	NA
Dysthymia	2142	1.8	NA	4239	3.4	NA
Manic episode/bipolar affective disorders	2633	2.2	NA	2684	2.2	NA
Neurotic disorders	17 899	14.9	NA	26 975	22.3	NA
Personality disorders	74 240	63.4	NA	105 152	89.5	NA
Psychiatric disorders following rheumatic diseases						
All psychiatric disorders	442	187.2	NA	1211	232.9	NA
Psychotic disorders	49	14.5	NA	163	27.1	NA
Schizophrenia	6	3.6	NA	20	4.3	NA
Affective disorders	197	67.5	NA	530	82.5	NA
Severe depression	27	7.2	NA	87	12.0	NA
Dysthymia	5	2.4	NA	35	6.1	NA
Manic episode/bipolar affective disorders	9	3.9	NA	16	1.7	NA
Neurotic disorders	68	32.4	NA	178	46.6	NA
Personality disorders	128	72.8	NA	340	76.7	NA

Abbreviations: IR, incidence rates; NA, not applicable.
[a]Men and women in Sweden, 1973-2004.
[b]At hospital diagnosis.

chiatric disorders in the general population, and hospitalization rates for psychiatric disorders following rheumatic diseases. Mean age at diagnosis was higher for RA than for AS and SLE. Hospitalization rates for RA, SLE, and AS varied by sex.

We compared age-specific rates of psychiatric disorders in the general population and subsequent psychiatric disorders following rheumatic diseases (**Figure**). Rates of psychiatric disorders following rheumatic diseases tended to be higher than rates of psychiatric disorders in the general population.

In most age groups, an increased risk was found among men and women with RA, SLE, and AS compared with the reference group (the general population, matched for age, sex, and other factors) (**Table 3**). Overall, the highest risks were found among men and women with SLE. Their significant SIRs were 2.38 and 2.16, respectively. For RA, the overall significant SIRs were 1.45 and 1.36 for men and women, respectively.

Men with AS had increased risks of affective, neurotic, and personality disorders (**Table 4**). Women with AS had increased risks of affective and neurotic disorders. Men with SLE had increased risks of affective and personality disorders, whereas women with SLE had an increased risk of psychotic, affective, neurotic, and personality disorders. Men and women with RA had an increased risk of affective, neurotic, and personality disorders. Women with RA also had an increased risk of psychotic disorders. The risk of severe depression was increased among women with SLE and women with RA.

Among men and women, the highest SIRs were observed when the follow-up interval between first hospitalization for RA, SLE, or AS and subsequent psychiatric disorder was less than 1 year (**Table 5**). This tendency was especially strong among patients with SLE.

For dementia, the SIR was significantly increased only among women with SLE (**Table 6**). However, the SIRs for delirium were particularly high among men and women with SLE. The significant SIRs were 3.73 and 4.99 for men and women, respectively.

In an additional analysis, we investigated whether multiple (>3) hospitalizations for RA implied an increased risk of psychiatric disorders. We found that the risk was similar compared with that of patients hospitalized only once for RA (data not shown).

COMMENT

This study shows that patients with rheumatic diseases have a higher risk of psychiatric disorders than the general population. Patients with SLE or AS tended to have a higher risk of subsequent psychiatric disorders than patients with RA, after accounting for age. In addition, differences were found in the risk of subsequent psychiatric disorders by subtype of the rheumatic disease, psychiatric disorder, sex, and various follow-up intervals. For example, only women with RA or SLE had an increased risk of psychotic disorders and severe depression. In addition, SLE carried an increased risk of dementia and delirium.

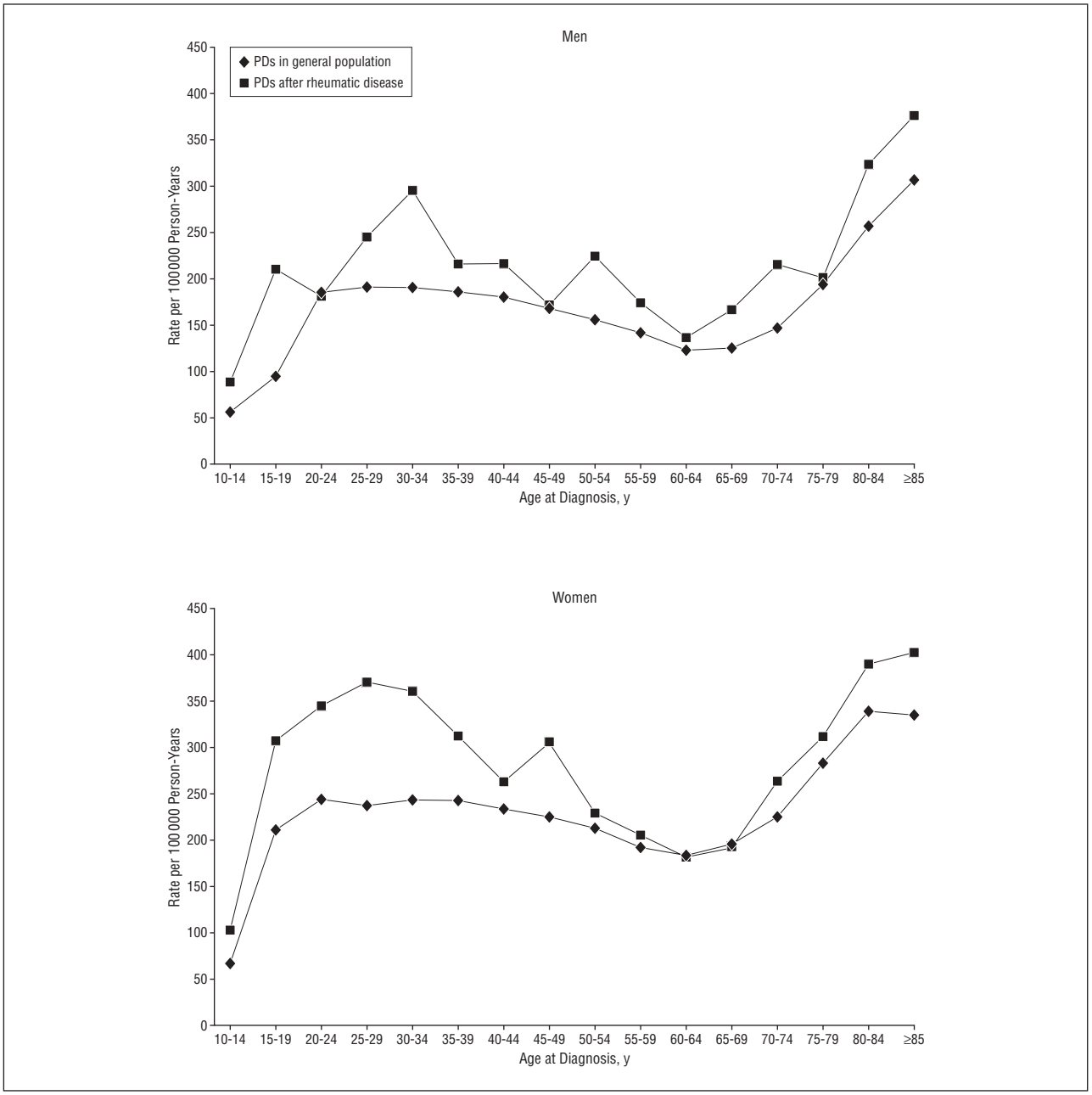

Figure. Age-specific hospitalization rates for psychiatric disorders (PDs) in the general Swedish population and subsequent PDs in patients with rheumatic diseases.

A key strength of the present study is that the study population represented the entire population of Sweden. This allowed us to present risk estimates by sex and subtypes of the 3 rheumatic diseases and the psychiatric disorders. In addition, the data in the Swedish Hospital Discharge Register are nearly 100% complete. In 2001, the main diagnosis was missing in only 0.9% of the hospitalized cases.[15] Because of the national registration number assigned to each individual in Sweden, it was possible to track the records of every person for the whole follow-up period and calculate the exact risk-time. Finally, we analyzed the associations between RA, SLE, or AS and psychiatric disorders by various follow-up intervals. We have not found similar previous studies for comparison. However, a possible explanation for the finding that the highest SIRs were observed when the follow-up interval was less than 1 year is that the individuals go through a psychological crisis when they receive their diagnosis.

This study also has limitations. First, we were unable to draw any conclusions about causal relationships; although an advantage of this study is that it shows that certain subgroups seem to be more vulnerable than others. Second, we lacked information on environmental risk factors for rheumatic diseases and psychiatric disorders. Third, we had no data on psychological distress and stressful life events because this study was based on the entire population. Fourth, data on outpatients are not available in nationwide registers, such as the registers used in this study. This implies that only the most

Table 3. Psychiatric Disorder Following Rheumatic Diseases by Age at Diagnosis

Age at Diagnosis of Psychiatric Disorder, y	Ankylosing Spondylitis		Systemic Lupus Erythematosus		Rheumatoid Arthritis	
	No. of Patients	SIR (95% CI)[a]	No. of Patients	SIR (95% CI)[a]	No. of Patients	SIR (95% CI)[a]
Men						
<30	4	0.79 (0.21-2.04)	6	**4.29 (1.54-9.39)**	20	**1.95 (1.19-3.02)**
30-39	28	**1.75 (1.16-2.53)**	6	**3.66 (1.32-8.02)**	14	1.32 (0.72-2.22)
40-49	31	1.39 (0.95-1.98)	3	1.59 (0.30-4.70)	27	1.37 (0.90-2.00)
50-59	34	**2.10 (1.45-2.94)**	8	**4.00 (1.71-7.92)**	47	**1.42 (1.04-1.89)**
≥60	26	**1.97 (1.29-2.89)**	7	1.24 (0.49-2.57)	181	**1.44 (1.24-1.67)**
All	**123**	**1.69 (1.41-2.02)**	**30**	**2.38 (1.61-3.41)**	**289**	**1.45 (1.29-1.63)**
Women						
<30	5	2.22 (0.70-5.23)	25	**2.46 (1.59-3.63)**	56	**1.73 (1.31-2.25)**
30-39	11	1.37 (0.68-2.45)	34	**2.33 (1.62-3.26)**	66	**1.73 (1.34-2.21)**
40-49	18	1.68 (0.99-2.66)	30	**1.87 (1.26-2.67)**	112	**1.59 (1.31-1.91)**
50-59	21	**2.70 (1.67-4.14)**	34	**2.47 (1.71-3.45)**	139	**1.24 (1.04-1.46)**
≥60	14	**2.13 (1.16-3.58)**	51	**1.96 (1.46-2.58)**	595	**1.29 (1.19-1.40)**
All	**69**	**1.95 (1.52-2.47)**	**174**	**2.16 (1.85-2.50)**	**968**	**1.36 (1.27-1.45)**

Abbreviations: CI, confidence interval; SIR, standardized incidence ratio.
[a] Boldface type indicates totals or that the 95% CI does not include 1.00.

Table 4. Subtypes of Psychiatric Disorders Following Rheumatic Diseases

Subtype	Ankylosing Spondylitis		Systemic Lupus Erythematosus		Rheumatoid Arthritis	
	No. of Patients	SIR (95% CI)[a]	No. of Patients	SIR (95% CI)[a]	No. of Patients	SIR (95% CI)[a]
Men						
All psychiatric disorders	123	**1.69 (1.41-2.02)**	30	**2.38 (1.61-3.41)**	289	**1.45 (1.29-1.63)**
Psychotic disorders	11	1.14 (0.56-2.04)	2	1.02 (0.10-3.73)	36	1.18 (0.83-1.63)
Schizophrenia	1	0.33 (0.00-1.87)	1	2.13 (0.00-12.20)	4	0.72 (0.19-1.87)
Affective disorders	49	**1.64 (1.21-2.16)**	14	**2.63 (1.43-4.43)**	134	**1.51 (1.27-1.79)**
Severe depression	6	1.27 (0.46-2.79)	1	1.20 (0.00-6.91)	20	1.42 (0.86-2.19)
Dysthymia	3	1.89 (0.36-5.59)	0	NA	2	0.41 (0.04-1.52)
Manic episode/bipolar affective disorders	3	1.79 (0.34-5.29)	2	7.41 (0.70-27.24)	4	0.98 (0.25-2.52)
Neurotic disorders	24	**2.59 (1.66-3.85)**	4	2.72 (0.71-7.04)	40	**1.96 (1.40-2.67)**
Personality disorders	39	**1.64 (1.16-2.24)**	10	**2.60 (1.24-4.81)**	79	**1.33 (1.05-1.66)**
Women						
All psychiatric disorders	69	**1.95 (1.52-2.47)**	174	**2.16 (1.85-2.50)**	968	**1.36 (1.27-1.45)**
Psychotic disorders	6	1.46 (0.53-3.21)	25	**2.44 (1.58-3.61)**	132	**1.30 (1.09-1.54)**
Schizophrenia	3	3.30 (0.62-9.76)	3	1.35 (0.25-3.98)	14	0.74 (0.40-1.24)
Affective disorders	27	**1.82 (1.20-2.65)**	76	**2.34 (1.84-2.93)**	427	**1.36 (1.24-1.50)**
Severe depression	2	0.89 (0.08-3.28)	13	**2.80 (1.48-4.79)**	72	**1.50 (1.17-1.89)**
Dysthymia	3	2.68 (0.50-7.93)	6	2.48 (0.89-5.43)	26	1.02 (0.67-1.50)
Manic episode/bipolar affective disorders	0	NA	1	0.77 (0.00-4.41)	15	1.39 (0.77-2.29)
Neurotic disorders	19	**3.47 (2.08-5.42)**	28	**2.42 (1.61-3.50)**	131	**1.52 (1.27-1.81)**
Personality disorders	17	1.56 (0.91-2.50)	45	**1.71 (1.24-2.28)**	278	**1.31 (1.16-1.47)**

Abbreviations: CI, confidence interval; NA, not applicable; SIR, standardized incidence ratio.
[a] Boldface type indicates that the 95% CI does not include 1.00.

severe cases were included in the present study, ie, those requiring hospitalization. The "true" incidence rates in the population were thus underestimated. Fifth, some associations may not have been detected because of insufficient numbers of cases in certain diagnostic subgroups, especially among men with SLE. Sixth, data on medication were not available to us, which is a limitation because psychosis is sometimes induced by corticosteroids. Finally, we were not able to test for the validity of the diagnoses because our data were based on the entire population. For example, there is an interobserver variability in clinical settings. In addition, diagnostic criteria were changed several times during the follow-up. However, we only used main diagnoses recorded in the hospital registers, which partly increases the probability that the diagnoses are valid. In addition, 61% of RA patients had more than 1 hospitalization for RA.

The results of previous studies are consistent with those of the present study. For example, the purpose of

Table 5. Psychiatric Disorders Following Rheumatic Diseases by Follow-up

Follow-Up Interval, y	Ankylosing Spondylitis		Systemic Lupus Erythematosus		Rheumatoid Arthritis	
	No. of Patients	SIR (95% CI)[a]	No. of Patients	SIR (95% CI)[a]	No. of Patients	SIR (95% CI)[a]
Men						
<1	9	**2.87 (1.30-5.46)**	7	**8.75 (3.47-18.13)**	30	**2.64 (1.78-3.77)**
1-4	27	1.31 (0.86-1.90)	14	**3.23 (1.76-5.43)**	85	1.22 (0.97-1.51)
5-9	34	**1.75 (1.21-2.45)**	2	0.59 (0.06-2.18)	65	1.15 (0.89-1.47)
≥10	53	**1.79 (1.34-2.35)**	7	1.72 (0.68-3.55)	109	**1.78 (1.46-2.14)**
All	**123**	**1.69 (1.41-2.02)**	**30**	**2.38 (1.61-3.41)**	**289**	**1.45 (1.29-1.63)**
Women						
<1	7	**4.46 (1.77-9.24)**	34	**7.59 (5.25-10.62)**	106	**2.78 (2.28-3.37)**
1-4	19	**1.84 (1.11-2.89)**	52	**1.93 (1.44-2.53)**	295	**1.23 (1.09-1.38)**
5-9	17	**1.76 (1.02-2.83)**	40	**1.81 (1.29-2.46)**	248	**1.23 (1.09-1.40)**
≥10	26	**1.88 (1.23-2.76)**	48	**1.77 (1.31-2.35)**	319	**1.36 (1.22-1.52)**
All	**69**	**1.95 (1.52-2.47)**	**174**	**2.16 (1.85-2.50)**	**968**	**1.36 (1.27-1.45)**

Abbreviations: CI, confidence interval; SIR, standardized incidence ratio.
[a] Boldface type indicates totals or that the 95% CI does not include 1.00.

Table 6. Dementia and Delirium Following Systemic Lupus Erythematosus

	Men		Women	
	No. of Patients	SIR (95% CI)[a]	No. of Patients	SIR (95% CI)[a]
Dementia	11	1.45 (0.72-2.60)	41	**1.73 (1.24-2.35)**
Delirium	5	**3.73 (1.18-8.78)**	20	**4.99 (3.04-7.72)**

Abbreviations: CI, confidence interval; SIR, standardized incidence ratio.
[a] Boldface type indicates that the 95% CI does not include 1.00.

a recent case report was to remind health care providers of the strong association between depression and chronic medical illness, such as RA.[21] A cohort study observed 537 patients from Brazil and showed that acute psychosis is related to SLE.[22] A recent review study from Belgrade in Serbia and Montenegro found that psychiatric abnormalities are common in SLE with a prevalence of 17% to 75%.[23] Other studies have also demonstrated the association between SLE and psychiatric disorders.[4,8-10,24-27] A cross-sectional study of 82 patients with RA found a significantly increased prevalence of anxiety and depression compared with the control group.[27] Other studies of patients with RA have confirmed these findings.[28-31] Previous studies of the association between AS and psychiatric disorders are rare, although some studies based on questionnaires and depression scores have shown that the psychological status of patients with AS is affected.[14,32] The findings of an increased risk of dementia and delirium among patients with SLE suggest a primary involvement of the brain.

To sum up, this study adds further knowledge to the literature because of its novel approach; it is the first study of an entire population examining the association between 3 different rheumatic diseases and the most common neuropsychiatric disorders in men and women.

CONCLUSIONS

Patients with rheumatic diseases have a higher risk of hospitalization for psychiatric disorders than the general population, and patients with SLE have a higher risk of hospitalization for dementia and delirium. Differences in risk magnitudes were found by subtype of the rheumatic disease and psychiatric disorder, by sex, and by various follow-up intervals. These results show that health care providers who encounter patients with rheumatic diseases should be aware that these patients are more likely to develop severe neuropsychiatric disorders than the general population and that some subgroups seem to be more vulnerable than others.

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REFERENCES

1. Braun J, Sieper J. Ankylosing spondylitis. *Lancet*. 2007;369(9570):1379-1390.
2. Hopkinson ND, Doherty M, Powell RJ. The prevalence and incidence of systemic lupus erythematosus in Nottingham, UK, 1989-1990. *Br J Rheumatol*. 1993; 32(2):110-115.

3. Nightingale AL, Farmer RD, de Vries CS. Systemic lupus erythematosus prevalence in the UK: methodological issues when using the General Practice Research Database to estimate frequency of chronic relapsing-remitting disease. *Pharmacoepidemiol Drug Saf*. 2007;16(2):144-151.
4. Hanly JG, Fisk JD, McCurdy G, Fougere L, Douglas JA. Neuropsychiatric syndromes in patients with systemic lupus erythematosus and rheumatoid arthritis. *J Rheumatol*. 2005;32(8):1459-1466.
5. Ariza-Ariza R, Hernandez-Cruz B, Navarro-Sarabia F. Physical function and health-related quality of life of Spanish patients with ankylosing spondylitis. *Arthritis Rheum*. 2003;49(4):483-487.
6. Bostan EE, Borman P, Bodur H, Barca N. Functional disability and quality of life in patients with ankylosing spondylitis. *Rheumatol Int*. 2003;23(3):121-126.
7. Kobelt G, Andlin-Sobocki P, Maksymowych WP. Costs and quality of life of patients with ankylosing spondylitis in Canada. *J Rheumatol*. 2006;33(2):289-295.
8. Brey RL, Holliday SL, Saklad AR, Navarrete MG, Hermosillo-Romo D, Stallworth CL, Valdez CR, Escalante A, del Rincón I, Gronseth G, Rhine CB, Padilla P, McGlasson D. Neuropsychiatric syndromes in lupus: prevalence using standardized definitions. *Neurology*. 2002;58(8):1214-1220.
9. Ainiala H, Loukkola J, Peltola J, Korpela M, Hietaharju A. The prevalence of neuropsychiatric syndromes in systemic lupus erythematosus. *Neurology*. 2001; 57(3):496-500.
10. Sanna G, Bertolaccini ML, Cuadrado MJ, et al. Neuropsychiatric manifestations in systemic lupus erythematosus: prevalence and association with antiphospholipid antibodies. *J Rheumatol*. 2003;30(5):985-992.
11. Hanly JG. Neuropsychiatric lupus. *Rheum Dis Clin North Am*. 2005;31(2):273-298.
12. Oda K, Matsushima E, Okubo Y, Ohta K, Murata Y, Koike R, Miyasaka N, Kato M. Abnormal regional cerebral blood flow in systemic lupus erythematosus patients with psychiatric symptoms. *J Clin Psychiatry*. 2005;66(7):907-913.
13. Kozora E, Ellison MC, Waxmonsky JA, Wamboldt FS, Patterson TL. Major life stress, coping styles, and social support in relation to psychological distress in patients with systemic lupus erythematosus. *Lupus*. 2005;14(5):363-372.
14. Martindale J, Smith J, Sutton CJ, Grennan D, Goodacre L, Goodacre JA. Disease and psychological status in ankylosing spondylitis. *Rheumatology (Oxford)*. 2006; 45(10):1288-1293.
15. Rosen M, Hakulinen T. Use of disease registers. In: Ahrens W, Pigeot I, eds. *Handbook of Epidemiology*. Berlin, Germany: Springer-Verlag; 2005.
16. The National Board of Health and Welfare. *The Swedish Hospital Discharge Register and the Cause of Death Register (1961-2001)*. http://www.sos.se/epc/english/ParEng.htm. Accessed July 27, 2007.
17. World Health Organization. *International Classification of Diseases, Eighth Revision (ICD-8)*. Geneva, Switzerland: World Health Organization; 1967.
18. World Health Organization. *International Classification of Diseases, Ninth Revision (ICD-9)*. Geneva, Switzerland: World Health Organization; 1977.
19. World Health Organization. *International Classification of Diseases, 10th Revision (ICD-10)*. Geneva, Switzerland: World Health Organization; 1992.
20. Rothman KJ, Greenland S. *Modern Epidemiology*. 2nd ed. Philadelphia, PA: Lippincott-Raven Publishers; 1998.
21. Copsey Spring TR, Yanni LM, Levenson JL. A shot in the dark: failing to recognize the link between physical and mental illness. *J Gen Intern Med*. 2007;22 (5):677-680.
22. Appenzeller S, Cendes F, Costallat LT. Acute psychosis in systemic lupus erythematosus. *Rheumatol Int*. 2008;28(3):237-243.
23. Stojanovich L, Zandman-Goddard G, Pavlovich S, Sikanich N. Psychiatric manifestations in systemic lupus erythematosus. *Autoimmun Rev*. 2007;6(6):421-426.
24. Haupt M, Millen S, Janner M, Falagan D, Fischer-Betz R, Schneider M. Improvement of coping abilities in patients with systemic lupus erythematosus: a prospective study. *Ann Rheum Dis*. 2005;64(11):1618-1623.
25. Sweet JJ, Doninger NA, Zee PC, Wagner LI. Factors influencing cognitive function, sleep, and quality of life in individuals with systemic lupus erythematosus: a review of the literature. *Clin Neuropsychol*. 2004;18(1):132-147.
26. Hanly JG. ACR classification criteria for systemic lupus erythematosus: limitations and revisions to neuropsychiatric variables. *Lupus*. 2004;13(11):861-864.
27. Isik A, Koca SS, Ozturk A, Mermi O. Anxiety and depression in patients with rheumatoid arthritis. *Clin Rheumatol*. 2007;26(6):872-878.
28. VanDyke MM, Parker JC, Smarr KL, Hewett JE, Johnson GE, Slaughter JR, Walker SE. Anxiety in rheumatoid arthritis. *Arthritis Rheum*. 2004;51(3):408-412.
29. Abdel-Nasser AM, Abd El-Azim S, Taal E, El-Badawy SA, Rasker JJ, Valkenburg HA. Depression and depressive symptoms in rheumatoid arthritis patients: an analysis of their occurrence and determinants. *Br J Rheumatol*. 1998;37(4): 391-397.
30. Takeda T, Morimoto N, Kinukawa N, Nagamine R, Shutou T, Tashiro N. Factors affecting depression and anxiety in female Japanese patients with rheumatoid arthritis. *Clin Exp Rheumatol*. 2000;18(6):735-738.
31. Parker JC, Smarr KL, Slaughter JR, Johnston SK, Priesmeyer ML, Hanson KD, Johnson GE, Hewett JE, Hewett JE, Irvin WS, Komatireddy GR, Walker SE. Management of depression in rheumatoid arthritis: a combined pharmacologic and cognitive-behavioral approach. *Arthritis Rheum*. 2003;49(6):766-777.
32. Cakar E, Dincer U, Kiralp MZ, Taskaynatan MA, Yaser E, Bayman EO, Ozgul A, Dursun H. Sexual problems in male ankylosing spondylitis patients: relationship with functionality, disease activity, quality of life, and emotional status. *Clin Rheumatol*. 2007;26(10):1607-1613.