Self-reported Diagnosis of Rheumatoid Arthritis or Ankylosing Spondylitis Has Low Accuracy: Data from the Nord-Trøndelag Health Study

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ABSTRACT. ***Objective.*** Self-reported diagnoses of inflammatory arthritis are not accurate. The primary study aim was to ascertain self-reported diagnoses of rheumatoid arthritis (RA) and ankylosing spondylitis (AS) in the Norwegian population-based Nord-Trøndelag Health Study (HUNT) using hospital case files. The secondary aim was to provide updated estimates of the prevalence and incidence of RA and AS.

Methods. All inhabitants ≥ 20 years old from the county of Nord-Trøndelag were invited. Data from 70,805 unique participants from HUNT2 (1995–1997) and HUNT3 (2006–2008) were included. For participants who self-reported RA or AS, case files from all 3 hospitals in the catchment area were evaluated using standardized diagnostic criteria.

Results. Of 2703 self-reported cases of RA, 19.1% were verified in hospital files. Of 1064 self-reported cases of AS, 15.8% were verified. Of 259 cases self-reporting both RA and AS, 8.1% had RA and 5.4% had AS. Overall, a self-report of 1 or both diagnoses could not be verified in 82.1%, including 22.8% with insufficient information or no case file. The prevalence of RA was 768 (95% CI 705–835) per 100,000. The incidence of RA from HUNT2 to HUNT3 was 0.48 (0.41–0.56) per 1000 per year. The prevalence of AS was 264 (228–305) per 100,000. The incidence of AS from HUNT2 to HUNT3 was 0.19 (0.15–0.24) per 1000 per year.

Conclusion. Self-reported diagnoses of RA and AS are often false-positive. The prevalence and incidence of RA were comparable to reports from similar populations. The incidence of AS was higher than previously reported in a mixed population from Norway. (J Rheumatol First Release April 15 2017; doi:10.3899/jrheum.161396)

Key Indexing Terms:
RHEUMATOID ARTHRITIS ANKYLOSING SPONDYLITIS EPIDEMIOLOGY

Population-based health surveys can provide important information regarding the prevalence and incidence of inflammatory arthritis and may also include quality-of-life data and lifestyle factors. However, self-report is prone to bias. Although clinic- or hospital-based data may enable the collection of more in-depth information on disease characteristics, lower prevalence may indicate selection bias[1,2]. Comparisons with the general population are usually not possible because of the paucity of community-level data. Registry-based studies are useful if the quality of data is sufficiently high, e.g., by combining various data sources such as billing and hospitalization data, prescription registries, etc.[1,3] Registry-based data usually do not permit further analysis on disease characteristics. Thus, these different approaches each have different strengths and weaknesses.

The main aim of our present study was to investigate the quality of self-reported data on rheumatoid arthritis (RA) and ankylosing spondylitis (AS) in the population-based Nord-Trøndelag Health Study (HUNT) in Norway. All inhabitants ≥ 20 years of age in the county of Nord-Trøndelag were invited. The county is fairly representative for Norway as a whole, with a stable and ethnically homogeneous population[4]. We have previously published results showing higher incidence of RA and AS in HUNT than expected from the literature[3,5,6,7,8,9], potentially indicating a high number of false-positive self-reports. We have therefore now ascertained the diagnoses using hospital case files, also noting any alternative diagnosis explaining the patient's complaints in cases

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that were not RA or AS. The secondary aim of our study was to provide updated estimates of the prevalence and incidence of RA and AS because previous Norwegian estimates are old and scarce[7,8,10,11].

MATERIALS AND METHODS

Data were from participants in the second (1995–1997) and third (2006–2008) HUNT surveys. The study has been described previously[4]. Participants filled in questionnaires and met for a clinical examination. We used questionnaire data focusing on self-reported RA and/or AS. The file from HUNT contained 65,214 participants from HUNT2 (participation rate 69.5%) and 50,797 participants from HUNT3 (participation rate 54.1%); 33,383 participated in both these surveys. There were 70,805 unique participants included after exclusion of those with missing answers to the questions: "Has a doctor ever said that you have/have had any of these diseases: rheumatoid arthritis/ankylosing spondylitis?" (using the Norwegian denomination *Bekhterev disease*; Figure 1).

For participants with self-reported RA and/or AS, the diagnosis was ascertained in hospital case files from the 3 hospitals in Central Norway (Levanger Hospital, Namsos Hospital, and St. Olavs Hospital) using the European League Against Rheumatism (EULAR) 2010 criteria for RA and the modified New York criteria for AS[12,13]. The files were carefully evaluated by an experienced immunologist (VV) according to a predefined protocol, and the conclusions were compared with those of the treating rheumatologists (Supplementary Data available with the online version of this article). All cases with inconsistencies or unclear information were reviewed by an experienced rheumatologist (MH) for a final decision. The files from 25 randomly selected individuals previously reviewed by VV were examined by MH without knowledge of the previous conclusion. There was complete agreement between the 2 examiners, i.e., a κ interrater agreement of 1.

In the Norwegian healthcare system, a diagnosis of RA and AS is given by a rheumatologist, and only a rheumatologist may start treatment with disease-modifying antirheumatic drugs (DMARD). There are no private rheumatologists in Central Norway, so all patients were followed up at the outpatient and/or inpatient clinics of the Department of Rheumatology at one of the mentioned hospitals. The case files contained notes from inpatient and outpatient visits. The role of the family physician in the care of these patients was minor. For longstanding RA cases with incomplete information on the EULAR criteria, a rheumatologist's diagnosis according to the American College of Rheumatology criteria was accepted[14]. Self-reported cases with missing files or unclear information were excluded from the validated cases. Year of diagnosis was recorded, as well as presence of immunoglobulin M-rheumatoid factor and anticitrullinated protein antibodies (ACPA) in the RA cases, permitting classification as seropositive disease (1 or both autoantibodies positive) or seronegative disease (no autoantibodies present). We also noted whether patients with AS were *HLA-B27*–positive or –negative.

To estimate the number of false-negative cases, 1 random age- and sex-matched participant was drawn from the same wave of HUNT for each person of a random subselection of participants with a self-reported diagnosis of RA or AS (n = 3434). For these controls, the diagnosis registries of the mentioned hospitals were searched for the International Classification of Diseases, 9th ed (ICD-9) codes 710, 711, 712, 713, 714, 720, 721, 725, and 274, and the corresponding ICD-10 codes M02, M05, M06, M07, M08, M10, M11, M12, M13, M32, M35, M45, M46, M48, and L40.5. These codes were chosen because the registry also contained tentative diagnosis codes from referrals for diagnostic ascertainment from primary care physicians where the final diagnosis might be RA or AS. For all controls where one of these codes was found (n = 321), the case file was evaluated.

The frequency of *HLA-B27* carriers in the general population was estimated from the HLA-typed blood donors in the donor registry of St. Olavs Hospital, i.e., the regional blood bank in Central Norway.

Participants in HUNT gave written informed consent. Approval for the study was obtained from the Regional Committee for Medical and Health Research Ethics, Central Norway (project 4.2009.1068), the Norwegian Data Safety Authorities, and the Norwegian Department of Health. Access to case files was granted by the Nord-Trøndelag Health Trust and St. Olavs Hospital, respectively, following waiver of the need for specific individual consent from the Regional Ethics Committee because HUNT participants had already given a broad consent to case file access. The blood donors had given written informed consent that their anonymous data could be used as normal controls in studies approved by the Ethics Committee. The study was conducted in compliance with the Helsinki Agreement.

Statistics. The statistical software IBM-SPSS (v.22, IBM) and Stata (v.14, StataCorp LP) were used. Data are presented as frequencies (percentages) or mean (SD). The chi-square test and the Student t test were used for between-group comparisons of categorical and continuous variables, respectively. Based on the evaluated case files, we calculated the frequency of false-positives and false-negatives of a self-reported RA or AS diagnosis, as well as the positive and negative likelihood ratios.

For calculation of RA and AS incidence from HUNT2 to HUNT3,

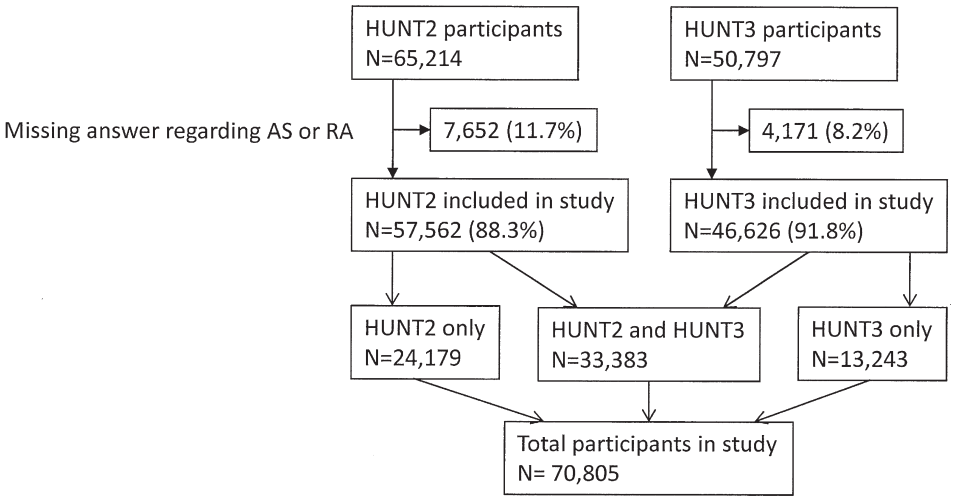

Figure 1. Participant inclusion to the study. AS: ankylosing spondylitis; RA: rheumatoid arthritis; HUNT: Nord-Trøndelag Health Study.

person-years of observation time were determined from the dates for each participant's inclusions for those participating in both surveys. CI for prevalence and incidence were calculated assuming binomial distributions.

For all calculations involving total participant numbers, the numbers from Figure 1 were used, i.e., including participants with missing or incomplete case files.

RESULTS

In total, 544 cases of RA and 187 cases of AS were identified from hospital case records. Of these, 538 RA cases (98.9%) had a self-report of RA and/or AS (Table 1). Six cases (1.1%) were found through the search in the matched controls. These persons had only participated in HUNT2 and were given their diagnosis later; thus, they were not truly false-negative cases. The false-positive rate of a self-report of RA was 82%, the false-negative rate was 0%, and the positive and negative likelihood ratios were 1.5 and 0.03, respectively. For AS, 186 cases (99.5%) had a self-report, and 1 case (0.5%) was found among the matched controls (Table 1). This single AS case was truly false-negative with the diagnosis given between participation in HUNT2 and HUNT3. The false-positive rate of a self-report of AS was 86%, the false-negative rate was < 0.1%, and the positive and negative likelihood ratios were 3.5 and 0.007, respectively.

Of the total 70,805 HUNT participants, 4.2% self-reported RA or a combination of RA and AS, and 1.9% self-reported AS or a combination of RA and AS. Of the 2703 participants who only self-reported RA, 516 had a correct diagnosis confirmed in the hospital records, giving a true positive rate of 19.1% (Table 2; Supplementary Table 1, available with the online version of this article). The diagnosis was correct in 168 of the 1064 participants only self-reporting AS, giving a true positive rate of 15.8%. The percentages of correct diagnoses were even lower for participants who self-reported both diagnoses either at the same HUNT survey or in other combinations (Table 2). Overall, for those self-reporting a diagnosis of RA, AS, or both, the diagnosis could not be verified in 82.1%, including 22.8% with too little information or no available patient file.

The most common diagnoses in false-positive self-reported RA were osteoarthritis, psoriatic arthritis (PsA), and other miscellaneous arthritis (29.1%; Table 2; Supplementary Table 1, available with the online version of this article). The most common diagnoses in false-positive self-reported AS were nonrheumatologic disease (22.7%) and degenerative changes (15.3%). False-positive RA was equally frequent in both sexes (p = 0.52), whereas false-positive AS was more frequent in women (56% vs 44% men, p < 0.0005). False-positive cases for RA were slightly younger than the true-positives [HUNT2: 55 (17) yrs vs 57 (13) yrs, p < 0.01; HUNT3: 60 (15) yrs vs 65 (12) yrs, p < 0.01]. False-positive cases for AS were slightly older than the true-positives [HUNT2: 47 (14) yrs vs 43 (11) yrs, p < 0.01; HUNT3: 56 (13) yrs vs 52 (12) yrs, p < 0.01].

Prevalence and incidence data for RA and AS based on confirmed diagnoses are given in Table 3 and Supplementary Table 2 (available with the online version of this article). The prevalence of RA was higher in women (2.1:1, p < 0.001) and the prevalence of AS was higher in men (1.7:1, p < 0.001). The prevalence of each condition was lower in HUNT2 than in HUNT3. The mean participant age was higher in HUNT3 [HUNT2: men 48.6 (16.5) yrs, women 48.1 (17.1) yrs; HUNT3: men 53.1 (15.5) yrs, women 51.6 (16.1) yrs]. The percentage of cases with too little information or no available patient file for diagnostic assessment was 26.9% in participants of HUNT2 only, 21.0% in participants of HUNT2 and HUNT3, and 9.7% in participants of HUNT3 only. Overall, data for diagnostic ascertainment were unavailable for 23.0% at HUNT2 and 19.1% at HUNT3. The participants without information were significantly older than those with sufficient information at HUNT2 (p < 0.0005), but not at HUNT3 (p = 0.81).

Further characteristics of the validated RA and AS cases are given in Table 4. About three-quarters of the RA cases were seropositive with no difference in frequency between men and women (p = 0.31). There were more *HLA-B27*–negative AS cases in women (18.5% vs 7.5%, p = 0.03). Age at diagnosis was not significantly different between women and men (RA: p = 0.19; AS: p = 0.53). The frequency of *HLA-B27*–positive blood donors (n = 745) was 13.1% (10.9–15.9).

Table 1. Self-reported diagnosis in patients with validated RA or AS. Values are n (%).

Self-reported Diagnosis	Validated RA, n = 544	Validated AS, n = 187
RA	516 (94.9)	4 (2.1)
AS	1 (0.2)	168 (89.8)
RA and AS	21 (3.8)	14 (7.6)
Neither RA nor AS	6 (1.1)*	1 (0.5)**

* Identified from random selection of cases without self-reported RA or AS, and with the diagnosis given after participation in HUNT. ** Identified from random selection of cases without self-reported RA or AS, and with the diagnosis given before participation in HUNT3. RA: rheumatoid arthritis; AS: ankylosing spondylitis; HUNT: Nord-Trøndelag Health Study.

DISCUSSION

In our present large population-based study covering about 11 years, self-reported RA could be verified in 19.1% and self-reported AS could be verified in 15.8%. However, the false-negative rate was very low, indicating that few cases were lost based on self-report. The overall prevalence per 100,000 was 768 (705–835) for RA and 264 (228–305) for AS. The yearly incidence per 1000 was 0.48 (0.41–0.56) for RA and 0.19 (0.15–0.24) for AS. The most common diagnoses in false-positive self-reported RA were other forms of arthritis, whereas in AS they were nonrheumatologic disease and degenerative changes.

Table 2. Validated diagnoses in persons with self-reported RA or AS. Percentages may not sum to 100% due to rounding.

Self-reported Diagnosis	Validated Diagnoses	n (%)
RA, n = 2703	RA	516 (19.1)
	Other arthritis*	786 (29.1)
	Other nonrheumatologic disease	505 (18.7)
	Degenerative changes	318 (11.8)
	AS or nr-axSpA	11 (0.4)
	Too little information or no file	449 (16.6)
AS, n = 1064	AS	168 (15.8)
	Other nonrheumatologic disease	242 (22.7)
	Degenerative changes	163 (15.3)
	Other arthritis*	105 (9.9)
	nr-axSpA	51 (4.8)
	Connective tissue disease	15 (1.4)
	RA	1 (< 0.1)
	Too little information or no file	319 (30.0)
RA and AS, n = 259	RA	21 (8.1)
	AS	14 (5.4)
	Other arthritis*	44 (17.0)
	Degenerative changes	26 (10.0)
	Other nonrheumatologic disease	24 (9.3)
	Connective tissue disease	5 (1.9)
	Too little information or no file	125 (48.3)

* Further details are given in Supplementary Table 1 (available with the online version of this article). RA: rheumatoid arthritis; AS: ankylosing spondylitis; nr-axSpA: nonradiographic axial spondyloarthritis.

Table 3. Prevalence and incidence of RA and AS. Prevalence rates are given per 100,000 individuals with 95% CI in parentheses. Incidence rates are given per 1000 individuals per year, with 95% CI in parentheses. Mean time between HUNT2 and HUNT3 was 11.2 years, SD 0.6 years.

Diagnosis	n	Total Prevalence	n	Prevalence in HUNT2	n	Prevalence in HUNT3	n	Incidence from HUNT2 to HUNT3
RA								
Overall	544	768 (705–835)	292	507 (451–569)	365	783 (705–867)	180	0.48 (0.41–0.56)
Women	370	1003 (904–1110)	207	694 (603–794)	238	948 (832–1075)	118	0.58 (0.48–0.70)
Men	174	513 (440–595)	85	307 (245–379)	127	590 (492–702)	62	0.36 (0.28–0.46)
AS								
Overall	187	264 (228–305)	69	120 (93–152)	149	320 (270–375)	70	0.19 (0.15–0.24)
Women	69	187 (146–237)	18	60 (36–95)	59	235 (179–303)	28	0.14 (0.09–0.20)
Men	118	348 (288–416)	51	184 (137–242)	90	418 (337–514)	42	0.25 (0.18–0.33)

RA: rheumatoid arthritis; AS: ankylosing spondylitis; HUNT: Nord-Trøndelag Health Study.

Validity of self-reported diagnoses. Our data confirm previous results showing that the specificity of self-reported RA is high[15], but that self-report of arthritis gives many false-positives. Our data on RA are comparable with old studies from Oslo, Norway, and Baltimore, USA, indicating 21%–31% correct self-reports[16,17], and with data from the Women's Health Initiative showing 14.7% correct diagnoses[18]. Only 7% of self-reported RA cases were correct in the Nurses' Health Study and 5% in the Iowa Women's Health Study[19,20]. A Spanish study showed that self-reported health survey data indicated twice as many cases of arthritis and rheumatism than shown by electronic health records, i.e., 22.7% vs 11.3%[21].

On the other hand, a metastudy concluded that self-reported RA had acceptable accuracy with a sensitivity of 88% (59–97%) and a specificity of 93% (66–99%)[22]. Sensitivity is defined as the probability that a patient self-reports an arthritis diagnosis if he or she truly has arthritis. For population-based studies, high false-positive rates are of greater concern than sensitivity because one would include a large number of patients without disease in the arthritis group if no further diagnostic ascertainment is included, thereby "diluting" the differences between cases and controls, and overestimating the need for healthcare.

We are not aware of comparable studies regarding the

Table 4. Characteristics of validated patients with RA and AS.

Variables	n (%)	Age at Diagnosis, yrs, mean (SD)	Seropositive/seronegative*, n (%)
RA, n = 544			
Women	370 (68.0)	54 (15)	273 (76.9)/82 (23.1)
Men	174 (32.0)	57 (14)	126 (72.8)/47 (27.2)
	n (%)	Age at Diagnosis, yrs, mean (SD)	*HLA-B27*–positive/negative**, n (%)
AS, n = 187			
Women	69 (36.9)	40 (15)	53 (81.5)/12 (18.5)
Men	118 (63.1)	39 (13)	99 (92.5)/8 (7.5)

* Anticitrullinated protein antibodies, immunoglobulin M-rheumatoid factor, or both. Percentages of tested cases; data missing for 15 women and 1 man. ** Percentages of tested cases; data missing for 4 women and 11 men. RA: rheumatoid arthritis; AS: ankylosing spondylitis.

validity of self-reported AS. In the National Health and Nutrition Examination Survey from the United States (2009–2010), 0.55% self-reported AS, but there was no case validation[23].

There are several possible explanations for the high false-positive rates of self-reported arthritis. One study indicated that 30% of those who self-reported arthritis were unaware of which type of arthritis they had[24]. This number is very similar to the percentage of "other arthritis" among those self-reporting RA in our study. The number of false-positives might have been reduced if the participants had first been asked whether they had any form of physician-diagnosed arthritis before being asked questions regarding type of arthritis, allowing for not knowing the type. Further, a doctor may have indicated the possibility of a specific diagnosis before the patient has seen a rheumatologist, or a diagnosis may have been suspected, but later refuted. The patient may have misunderstood or disagreed with the doctor's conclusion, depending on their level of health literacy. Some participants may have used Internet-based information to classify their complaints without seeing a doctor. A diagnosis of RA or AS may be perceived as easier to understand, more prestigious, or more often used in the media than one of degenerative changes or a connective tissue disease. For AS, changing of diagnostic criteria may have led to the labeling of various forms of axial spondyloarthritis as "Bekhterev disease" both by doctors and patients. A wide range of other diagnoses were found for the false-positive cases, including nonrheumatologic diseases. Some cases could represent undifferentiated arthritis that may later have been diagnosed as RA. Despite some significant differences, age and sex were of little help in identifying the true-positive cases because of the large overlap with the false-positives. It cannot be excluded that the results from our previous publications on incident RA and AS[5,6] would have been altered if the validated diagnoses from our present study had been available when these investigations were performed.

Several suggestions have been made to reduce the false-positive rates when identifying patients with arthritis in population-based studies. Linkage to central health databases is one such approach, but depends heavily on the quality of the collected data. Diagnostic codes may be missing if the main diagnosis were something else, or a nonrheumatologist may report an inaccurate diagnosis based on the patient's self-report or previous case notes.

Inclusion of self-reported medication data or data from prescription registries increases accuracy[25]. However, some drugs may be used for other conditions, e.g., DMARD for PsA as well as RA, or biologic DMARD for colitis-associated arthritis as well as AS. Patients with mild symptoms may not be using medication or may be using only nonspecific drugs such as nonsteroidal antiinflammatory drugs.

Measurement of ACPA improves diagnostic accuracy of RA, but leads to omission of seronegative cases[26]. Similarly, restricting self-reported AS only to known *HLA-B27*–positive cases will lead to case loss.

We are currently testing a questionnaire aiming to identify the most likely truly positive RA and AS cases in population-based studies. The final abbreviated and validated version of this questionnaire will be included in the forthcoming HUNT4 study to investigate whether a more specific questionnaire may help reduce the number of false-positives. However, it is unlikely that sufficiently accurate case identification is possible based on questionnaires alone, even when including questions pertaining to medication and visits to rheumatology clinics; thus, validation from a rheumatologist's case files or a highly accurate diagnostic registry is probably necessary. A good questionnaire may reduce the number of cases needing a further check. Some form of diagnostic validation should probably be included in the protocols for other population-based studies on inflammatory arthritis prior to their implementation.

Prevalence and incidence of RA. Our prevalence data for RA were higher than previous data from Oslo, Norway (Table 5)[3,7,8,19,27,28,29,30,31,32,33,34,35], but the prevalence in Oslo was

Table 5. Previous reports of prevalence and incidence of RA and AS.

Variables	RA	AS
Prevalence	437/100,000: Oslo, Norway[19] 1115–2660/100,000: Older women, Sweden[27] 430–1470/100,000: Older men, Sweden[27] 620/100,000: Minnesota, USA[28] 720/100,000: Minnesota, USA [28] 230/100,000: Men, Italy[29] 570/100,000: Women, Italy[29]	260/100,000: Northern Norway[8] ~225/100,000: Northern/Western Sweden[31] 140/100,000: Southern Sweden[32] 190/100,000: Men, Southern Sweden[32] 87/100,000: Women, Southern Sweden[32] 210/100,000: Ontario, Canada[33]
Incidence	0.41/1000: Sweden[3] 0.25/1000: Men, Sweden[3] 0.56/1000: Women, Sweden[3] 0.28/1000: Men, Norfolk, UK[30] 0.59/1000: Women, Norfolk, UK[30] 0.41/1000: Minnesota, USA[28] 0.28/1000: Men, Minnesota, USA[28] 0.53/1000: Women, Minnesota, USA[28] 0.26/1000: Oslo, Norway[7] 0.14/1000: Men, Oslo, Norway[7] 0.37/1000: Women, Oslo, Norway[7]	0.07/1000: Northern Norway[8] 0.15/1000: Ontario, Canada[33] 0.06/1000: Czech Republic[34] 0.07/1000: Finland[35]

RA: rheumatoid arthritis; AS: ankylosing spondylitis.

lower than expected and excluded persons older than 79 years. Our data from HUNT3 were comparable with Swedish data for the older women and men[27], whereas the HUNT2 prevalence was lower. The number of cases in younger participants in our study was too low for a meaningful comparison. Total prevalence from Minnesota, USA, from 1995 agrees with HUNT2, and data from 2005 agree with HUNT3[28]. Minnesota has many inhabitants of Scandinavian descent. Our data also confirm previous findings of higher prevalence of RA in Northern than Southern Europe, e.g., when comparing with Italian data[29].

Our findings suggest an increased prevalence in RA from HUNT2 to HUNT3. This may be related to the higher number of missing data for case ascertainment for HUNT2 participants, especially in older persons who would be more likely to have RA, thereby biasing the estimates downward. Our HUNT3 data are, therefore, probably more accurate. Some of the differences in prevalence from other studies may be related to participation rates among different age and sex groups in HUNT. Both in HUNT2 and HUNT3, participation was relatively lower in the younger age groups; more so for men than for women[4]. Further, anonymous data from general practitioners indicated less long-lasting musculoskeletal pain in nonparticipants than in participants in HUNT3[36]. These factors would tend to bias our prevalence estimates for RA upward.

Our incidence data for RA are also in good agreement with data from Sweden, Norfolk/United Kingdom, and Minnesota[3,28,30], especially for women (Table 5). Some of the differences may be explained by adjustments to reference populations, as well as by the participation rates in HUNT. Previous data from Oslo showed lower incidence, but that registry excluded patients older than 79 years[7].

Prevalence and incidence of AS. Prevalence rates of AS are known to vary greatly between populations, largely because of different carrier frequencies of *HLA-B27*[2]. Previous Norwegian studies were from different parts of Northern Norway, with much higher prevalence in the city of Tromsø, which has an ethnically mixed population[8,11] (Table 5). The prevalence for the entire region was close to that in HUNT, with an increase from the 1970s to the 1990s[8]. Swedish prevalence was highest in western and northern regions, i.e., areas closer to the catchment area for HUNT[31]. Our data from HUNT3 are in good agreement with the Swedish data in men and women over 40 years, but higher in individuals below 40 years. The explanations may be similar to those for RA. Prevalence rates from Southern Sweden were lower[32].

Even though the prevalence of AS in HUNT2 may be too low because of missing data and HUNT participation frequencies, it is conceivable that there has been a true increase from HUNT2 to HUNT3 in accordance with findings from Northern Norway and Ontario, Canada[8,33]. Better imaging tools, higher diagnostic awareness, and recognition that *HLA-B27* negativity and female sex do not rule out the diagnosis are contributing factors. Our data suggest that the proportion of *HLA-B27*–negative cases may be higher in women than in men, an observation that merits further study because it may be related to misdiagnosis. It is also noteworthy that the age at diagnosis in HUNT was comparable in women and men ($p = 0.53$), in contrast to previous findings[33].

Few previous studies complicate the comparison of AS incidence. The incidence of AS in HUNT was higher than in a previous study from Northern Norway (Table 5), where the carrier frequency of *HLA-B27* reported in an old study of 176 blood donors (15.9%) was not significantly different from

our study (13.1%, p = 0.32)[8,37]. The incidence was comparable to a population-based study from Ontario where the prevalence was also similar[33]. Czech and Finnish studies showed lower incidence[34,35].

Limitations. The main limitation was the extent of nonparticipation, which may have biased the results. Missing information for case validation and patients with longstanding or mild disease who may have been followed up only in primary care could have reduced the number of identified cases. Some patients may have moved from Nord-Trøndelag, resulting in case files not being updated. However, mobility of the catchment population for HUNT has been relatively low. The EULAR 2010 and the modified New York criteria for RA and AS, respectively, were not developed for ascertainment of self-reported diagnoses. Blood donors are a selected healthy group and only those volunteering to become bone marrow donors were HLA typed, which may have biased the estimated frequency of *HLA-B27* carriers in Central Norway.

Our study confirmed that self-reported diagnoses of RA in population-based studies are not accurate, and that self-reported AS is no more accurate. Thus, validation from a rheumatologist's case files or a highly accurate diagnostic registry is necessary. The prevalence and incidence of RA in HUNT were comparable to those from similar populations. There may have been a true increase in the prevalence of AS from HUNT2 to HUNT3, especially in women. The higher frequency of *HLA-B27*–negative cases in women merits further investigation. The incidence of AS was higher than previously reported in a mixed population from Norway.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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