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Self-reported diagnosis of rheumatoid arthritis or ankylosing spondylitis has low accuracy – data from the Nord-Trøndelag Health Study

Vibeke Videm, Ranjeny Thomas, Matthew A Brown, Mari Hoff

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 prevalences and incidences of RA and AS.

Methods

All inhabitants $\geq$ 20 years 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 self-reporting RA or AS, case files from all three hospitals in the catchment area were evaluated using standardized diagnostic criteria.

Results

Of 2,703 self-reported cases of RA, 19.1% were verified in hospital files. Of 1,065 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 one 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% confidence interval: 705-835) per 100,000. The incidence of RA from HUNT2 to HUNT3 was 0.48(0.41-0.56) per 1,000 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 1,000 per year.

Conclusion

Self-reported diagnoses of RA and AS are often false-positive. The prevalences and incidences of RA were comparable to reports from similar populations. The incidence of AS was higher than previously reported in a mixed population from Norway.

(248 words)

KEY WORDS: Rheumatoid arthritis, Ankylosing spondylitis, Epidemiology

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V Videm: MD, PhD; Professor, NTNU - Norwegian University of Science and Technology, Department of Laboratory Medicine, Children's and Women's Health; Senior Consultant, St Olavs Hospital, Department of Immunology and Transfusion Medicine, Trondheim, Norway

R Thomas: MBBS, FRACP, MD; Professor, University of Queensland, Translational Research Institute, Brisbane, Australia,

MA Brown: MBBS, MD, Director of Genomics, Queensland University of Technology, Institute of Health and Biomedical Research, Princess Alexandra Hospital, Brisbane, Australia

M Hoff: MD, PhD; Associate Professor, NTNU - Norwegian University of Science and Technology, Department of Public Health and General Practice and Department of Neuroscience; Senior Consultant, St Olavs Hospital, Department of Rheumatology, Trondheim, Norway.

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CORRESPONDING AUTHOR AND REPRINTS:

Professor Vibeke Videm

Department of Immunology and Transfusion Medicine

St. Olavs University Hospital

NO-7006 Trondheim

Norway

Tel: +47 725 73 321

Fax: +47 725 76 426

vibeke.videm@ntnu.no

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INTRODUCTION

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 life-style factors. However, self-report is prone to bias. Although clinic- or hospital-based data may enable collection of more in-depth information on disease characteristics, lower prevalences may indicate selection bias (1, 2). Comparisons with the general population are usually not possible due to 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 the 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 $\geq$ 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 homogenous population (4). We have previously published results showing higher incidences of RA and AS in HUNT than expected from the literature (3, 5-9), 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 that were not RA or AS. The secondary aim of the study was to provide updated estimates of the prevalences and incidences of RA and AS, because previous Norwegian estimates are old and scarce (7, 8, 10, 11).

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. 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's disease), 70,805 unique participants were included (Figure 1).

For participants with self-reported RA and/or AS, the diagnosis was ascertained in hospital case files from the three 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 pre-defined protocol, and the conclusions were compared to those of the treating rheumatologists (see Supplementary information). 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 two examiners, i.e. a kappa interrater agreement of 1.

In the Norwegian health care system, a diagnosis of RA and AS is given by a rheumatologist and only a rheumatologist may start disease-modifying anti-rheumatic drug (DMARD) treatment. There are no private rheumatologists in Central Norway, so all patients were followed up at the out-patient and/or in-patient clinics of the Department of Rheumatology at one of the mentioned hospitals. The case files contained notes from in-patient and out-patient visits. The role of the family physician in

the care of these patients was minor. For long-standing RA cases with incomplete information on the EULAR criteria, a rheumatologist's diagnosis according to ACR 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 IgM rheumatoid factor and anti-citrullinated protein antibodies (ACPA) in the RA cases, permitting classification as seropositive disease (one or both autoantibodies positive) or seronegative disease (no autoantibodies present). We also noted whether AS patients were *HLA-B27* positive or negative.

To estimate the number of false-negative cases, one random age- and gender-matched participant was drawn from the same wave of HUNT for each person of a random sub-selection of participants with a self-reported diagnosis of RA or AS (n=3,434). For these controls, the diagnosis registries of the mentioned hospitals were searched for the ICD-9 codes 710, 711, 712, 713, 714, 720, 721, 725, and 274, and 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 one of 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, Armonk, NY, USA) and Stata (v.14, StataCorp LP, Lakeway Drive, USA) were used. Data are presented as frequencies (percentages) or mean (SD). The chi-square test and the t-test were used for between-group comparisons of categorical and continuous parameters, 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 incidences from HUNT2 to HUNT3, person-years of observation time were determined from the dates for each participant's inclusions for those participating in both surveys. Confidence intervals for prevalences and incidences 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 (Details in Table 1). 6 cases (1.1%) were found

via 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 2,703 participants only self-reporting RA, 516 had a correct diagnosis confirmed in the hospital records, giving a true positive rate of 19.1% (Table 2, Supplementary table 1). The diagnosis was correct in 168 of the 1,065 participants only self-reporting AS, giving a true positive rate of 15.8%. The percentages of correct diagnosis 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, psoriasis arthritis and miscellaneous other arthritis (29.1%) (Table 2, Supplementary table 1). The most common diagnoses in false-positive self-reported AS were non-rheumatologic disease (22.7%) and degenerative changes (15.3%). False-positive RA was equally frequent in both genders ($p=0.52$), whereas false-positive AS was more frequent in women (56% vs. 44% men, $p<0.0005$). False-positive cases for RA where slightly younger than the true-positives (HUNT2: 55(17) years vs. 57(13) years, $p<0.01$; HUNT3: 60(15) years vs. 65(12) years, $p<0.01$). False-positive cases for AS were slightly older than

the true-positives (HUNT2: 47(14) years vs. 43(11) years, p<0.01; HUNT3: 56(13) years vs. 52(12) years, p<0.01).

Prevalence and incidence data for RA and AS based on confirmed diagnoses are given in Table 3 and Supplementary table 2. 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). Prevalences of each condition were lower in HUNT2 than in HUNT3. The mean participant age was higher in HUNT3 (HUNT2: men 48.6(16.5) years, women 48.1(17.1) years, HUNT3: men 53.1(15.5) years, women 51.6(16.1) years). 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. Approximately 3/4 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 13.13(10.9-15.9)%.

DISCUSSION

In the present large population-based study covering approximately 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 non-rheumatologic disease and degenerative changes.

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 recent meta-study 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 as 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 of health care.

We are not aware of comparable studies regarding the validity of self-reported AS. In the National Health and Nutrition Examination Survey from the USA (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 self-reporting arthritis were unaware of which type of arthritis they had (24). This figure 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. Furthermore, 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 disagree 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 labelling of various forms of axSpA as "Bekhterev's disease" both by doctors and patients. A wide range of other diagnoses were found for the false-positive cases, including non-rheumatologic diseases. Some cases could represent undifferentiated arthritis that may later have been diagnosed as RA. Despite some significant differences, age and gender were of little help in identifying the true-positive cases due to 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 the present study had been available when these investigations were performed.

Several suggestions have been made to reduce the false-positive rates when identifying arthritis patients 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 was something else, or a non-rheumatologist 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 psoriasis arthritis as well as RA, or biologic DMARDs for colitis-associated arthritis as well as AS. Patients with mild symptoms may not be using medication or only be using non-specific drugs such as non-steroid anti-inflammatory 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 at 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) (19), but the prevalence in Oslo was lower than expected and excluded persons older than 79 years. Our data from HUNT 3 were comparable with recent Swedish data for the older women and men (27), whereas the HUNT2 prevalences were lower. The number of cases in younger participants in our study was too low for a meaningful comparison. Total prevalences from Minnesota, USA from 1995 are in agreement with HUNT2, and data from 2005 are in agreement with HUNT3 (28). Minnesota has many inhabitants of Scandinavian decent. Our data also confirm previous findings of higher prevalences of RA in Northern than Southern Europe, e.g. when comparing to recent 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 downwards. Our HUNT3 data are therefore probably more accurate. Some of the differences in prevalences from other studies may be related to participation rates among different age and gender 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). Furthermore, anonymous data from general practitioners indicated less long-lasting musculoskeletal pain in non-participants than participants in HUNT3 (36). These factors would tend to bias our prevalence estimates for RA upwards.

Our incidence data for RA are also in good agreement with data from Sweden, Norfolk/UK, 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 incidences, but that registry excluded patients older than 79 years (7).

Prevalence and incidence of AS

Prevalences of AS are known to vary greatly between populations, largely due to different carrier frequencies of *HLA-B27* (2). Previous Norwegian studies were from different parts of northern Norway, with much higher prevalences 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 prevalences were 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. Prevalences from southern Sweden were lower (32).

Even though the prevalences of AS in HUNT2 may be too low due to 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 gender 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 as 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 incidences. 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 also was similar (33). Czech and Finnish studies showed lower incidences (34, 35).

Limitations

The main limitation was the extent of non-participation which may have biased the results. Missing information for case validation, and patients with long-standing or mild disease who may only have been followed up 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 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.

Conclusions

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 prevalences and incidences 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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FIGURE LEGEND

Figure 1: Participant inclusion to the study

Table 1 – Self-reported diagnosis in patients with validated rheumatoid arthritis (RA) or ankylosing spondylitis (AS)

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]	1 (0.5 %)[2]

[1] Identified from random selection of cases without self-reported RA or AS, and with the diagnosis given after participation in HUNT. See text for further explanation

[2] Identified from random selection of cases without self-reported RA or AS, and with the diagnosis given before participation in HUNT3

Table 2 – Validated diagnosis in persons with self-reported rheumatoid arthritis (RA) or ankylosing spondylitis (AS)[1]

Self-reported diagnosis	Validated diagnosis	N (%)
	RA	516 (19.1 %)
	Other arthritis[3]	786 (29.1 %)
	Other non-rheumatologic disease	505 (18.7 %)
	Degenerative changes	318 (11.8 %)
	AS or nrAxSpA[2]	11 (0.4 %)
	Too little information or no file	449 (16.6 %)
	AS	168 (15.8 %)
	Other non-rheumatologic disease	242 (22.7 %)
	Degenerative changes	163 (15.3 %)
	Other arthritis[3]	105 (9.9 %)
	nrAxSpA	51 (4.8 %)
	Connective tissue disease	15 (1.4 %)
	RA	1 (<0.1%)
	Too little information or no file	319 (30.0 %)
	RA	21 (8.1 %)
	AS	14 (5.4 %)
	Other arthritis[3]	44 (17.0 %)
	Degenerative changes	26 (10.0 %)
	Other non-rheumatologic disease	24 (9.3 %)
	Connective tissue disease	5 (1.9 %)
	Too little information or no file	125 (48.3 %)

[1]Percentages may not sum to 100% due to rounding

[2]Nonradiographic axial spondyloarthritis

[3]Further details are given in Supplementary table 1

Table 3 - Prevalences and incidences of rheumatoid arthritis (RA) and ankylosing spondylitis (AS)

Diagnosis	n	Total prevalence[1]	n	Prevalence in HUNT2[1]	n	Prevalence in HUNT3[1]	n	Incidence from HUNT2 to HUNT3[2]
RA, overall	544	768 (705-835)	292	507 (451-569)	365	783 (705-867)	180	0.48 (0.41-0.56)
RA, women	370	1,003 (904-1,110)	207	694 (603-794)	238	948 (832-1,075)	118	0.58 (0.48-0.70)
RA, 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)
AS, women	69	187 (146-237)	18	60 (36-95)	59	235 (179-303)	28	0.14 (0.09-0.20)
AS, men	118	348 (288-416)	51	184 (137-242)	90	418 (337-514)	42	0.25 (0.18-0.33)

[1] Prevalences are given per 100,000 individuals, with 95 % confidence intervals in parenthesis

[2] Incidences are given per 1,000 individuals per year, with 95 % confidence intervals in parenthesis. Mean time between HUNT2 and HUNT3 was 11.2 years, SD 0.6 years.

Table 4 – Characteristics of validated rheumatoid arthritis and ankylosing spondylitis patients

A) Rheumatoid arthritis (n=544)

Gender	Number	Age at diagnosis (years)[1]	Seropositive/seronegative[2]
Women	370 (68.0 %)	54 (15)	273 (76.9 %)/ 82 (23.1 %)
Men	174 (32.0 %)	57 (14)	126 (72.8 %) / 47 (27.2 %)

B) Ankylosing spondylitis (n=187)

Gender	Number	Age at diagnosis (years)	*HLA-B27* positive/negative[3]
Women	69 (36.9 %)	40 (15)	53 (81.5 %) / 12 (18.5 %)
Men	118 (63.1 %)	39 (13)	99 (92.5 %) / 8 (7.5 %)

[1] Mean (SD)

[2] ACPA (anti-citrullinated protein antibodies), IgM Rheumatoid factor or both. Percentages of tested cases; data missing for 15 women and 1 man.

[3] Percentages of tested cases; data missing for 4 women and 11 men

Table 5 – Previous reports of prevalences and incidences of rheumatoid arthritis and ankylosing spondylitis

Rheumatoid arthritis	Ankylosing spondylitis
Prevalence	Prevalence
437/100,000: Oslo, Norway (19)	260/100,000: Northern Norway (8)
1115-2660/100,000: Older women, Sweden (27)	~225/100,000: Northern/Western Sweden (31)
430-1470/100,000: Older men, Sweden (27)	140/100, 000: Southern Sweden (32)
620/100,000: Minnesota, USA 1995 (28)	190/100,000: Men, Southern Sweden (32)
720/100,000: Minnesota, USA 2005 (28)	87/100,000: Women, Southern Sweden (32)
230/100,000: Men, Italy (29)	210/100,000: Ontario, Canada (33)
570/100,000: Women, Italy (29)	
Incidence	Incidence
0.41/1,000: Sweden (3)	0.07/1,000: Northern Norway (8)
0.25/1,000: Men, Sweden (3)	0.15/1,000: Ontario, Canada (33)
0.56/1,000: Women, Sweden (3)	0.06/1,000: Czech Republic (34)
0.28/1,000: Men, Norfolk, UK (30)	0.07/1,000: Finland (35)
0.59/1,000: Women, Norfolk, UK (30)	
0.41/1,000: Minnesota, USA (28)	
0.28/1,000: Men, Minnesota, USA (28)	
0.53/1,000: Women, Minnesota, USA (28)	
0.26/1,000: Oslo, Norway (7)	
0.14/1,000: Men, Oslo, Norway (7)	
0.37/1,000: Women, Oslo, Norway (7)	

Supplementary information – validation protocol

The validation protocol consisted of the following tasks:

a) Identify whether the individual has a hospital case file for one or more of the three relevant hospitals. If no: note as "missing information".
b) If yes: Identify whether the individual has ever been to the outpatient or inpatient Rheumatology clinic at one or more of the hospitals.
   If yes: read the relevant notes, go over the criteria, check lab results, X-ray/MRI/CT results, note the rheumatologist's diagnosis. Follow the notes from the first incident of a relevant diagnosis to the end of the file. Note if too little information or uncertain diagnosis.
c) If no: identify whether the individual has ever been to the outpatient or inpatient Orthopedics clinic, Multidisciplinary pain clinic, Dermatology clinic, Gastroenterology clinic, or Internal medicine clinic. Scan for relevant diagnostic codes, and inspect notes from any visits that may be relevant. Note any alternative diagnosis that could explain the individual's RA or AS answer in HUNT, check criteria, lab results, X-ray/MRI/CT results. Follow the notes from the first incident of a relevant diagnosis to the end of the file.
d) If uncertain diagnosis: add to list for colleague to check case file. Later: Agree on final conclusion.

The information was entered into a spreadsheet. The protocol had an appendix briefly stating the criteria for the relevant rheumatological diagnoses (RA, AS, nrAxSpA, PsA, IBD-associated arthritis, reactive arthritis, osteoarthritis, fibromyalgia, and gout).

Supplementary table 1 – Validated diagnoses of other arthritis in persons with self-reported rheumatoid arthritis (RA) or ankylosing spondylitis (AS)[1]

Self-reported diagnosis	Validated diagnosis	N (%)
RA (n=786)	Osteoarthritis	256 (32.6%)
	Psoriasis arthritis	233 (29.6 %)
	Miscellaneous	207 (26.3 %)
	Juvenile idiopathic arthritis	30 (3.8%)
	Gout	30 (3.8 %)
	Reactive arthritis	17 (2.2 %)
	Colitis-associated arthritis	13 (1.7 %)
AS (n=105)	Osteoarthritis	36 (34.3 %)
	Psoriasis arthritis	22 (21.0 %)
	Miscellaneous	31 (29.5 %)
	Gout	7 (6.7 %)
	Reactive arthritis	6 (5.7 %)
	Colitis-associated arthritis	3 (2.9 %)
RA and AS (n=44)	Psoriasis arthritis	16 (36.4 %)
	Osteoarthritis	10 (22.7 %)
	Miscellaneous	9 (20.5 %)
	Colitis-associated arthritis	3 (6.8 %)
	Juvenile idiopathic arthritis	2 (4.5 %)
	Gout	2 (4.5 %)
	Reactive arthritis	2 (4.5 %)

[1]Percentages may not sum to 100% due to rounding

Supplementary table 2 – Age[1]- and gender-specific prevalences of rheumatoid arthritis (RA) and ankylosing spondylitis (AS)

Diagnosis		n	Prevalence in HUNT2[2]	n	Prevalence in HUNT3[2]
RA, overall					
	< 50 years	68	210 (163-267)	32	159 (109-224)
	50-64 years	99	733 (596-892)	135	851 (714-1006)
	> 64 years	125	1065 (887-1268)	198	1862 (1614-2138)
RA, women					
	< 50 years	52	305 (228-400)	27	237 (156-344)
	50-64 years	70	1046 (817-1320)	93	1131 (914-1384)
	> 64 years	85	1394 (1115-1721)	118	2150 (1783-2569)
RA, men					
	< 50 years	16	105 (60-170)	5	57 (19-134)
	50-64 years	29	425 (285-610)	42	549 (396-741)
	> 64 years	40	710 (507-965)	80	1555 (1235-1932)
AS, overall					
	< 40 years	22	112 (70-169)	22	208 (131-315)
	>= 40 years	47	124 (91-165)	127	352 (294-419)
AS, women					
	< 40 years	7	66 (27-136)	14	227 (124-380)
	>= 40 years	11	57 (29-102)	45	238 (173-318)
AS, men					
	< 40 years	15	165 (92-272)	8	183 (79-360)
	>= 40 years	36	193 (136-268)	82	479 (381-594)

[1] Division into more age categories was not performed to avoid too small numbers and wide confidence intervals

[2] Prevalences are given per 100,000 individuals, with 95 % confidence intervals in parenthesis

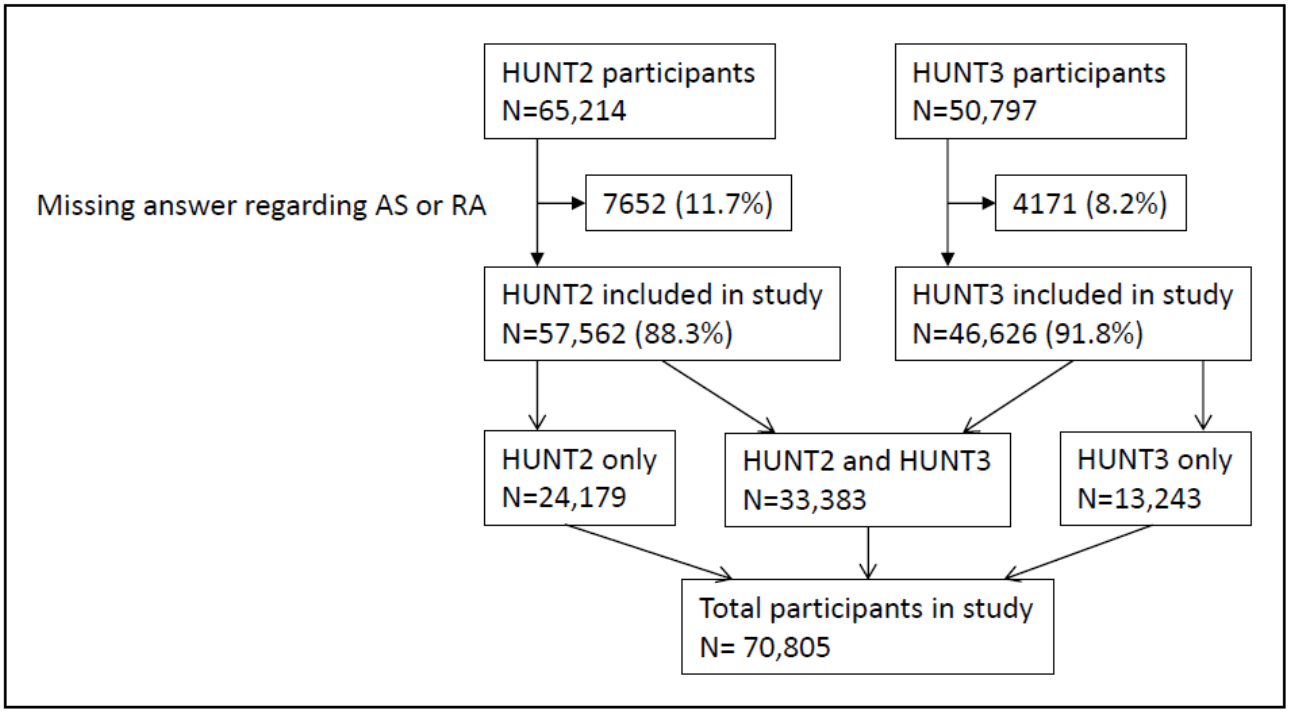
HUNT2 participants
N=65,214
HUNT3 participants
N=50,797
Missing answer regarding AS or RA
7652 (11.7%)
4171 (8.2%)
HUNT2 included in study
N=57,562 (88.3%)
HUNT3 included in study
N=46,626 (91.8%)
HUNT2 only
N=24,179
HUNT2 and HUNT3
N=33,383
HUNT3 only
N=13,243
Total participants in study
N= 70,805

Figure 1