Prevalence and determinants of sacroiliac joint bone marrow oedema in the general population in Germany: a population-based cross-sectional study

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Summary

Background MRI-detected bone marrow oedema in sacroiliac joints is central to diagnosing axial spondyloarthritis, influencing treatment decisions including anti-inflammatory therapy initiation. However, the prevalence of bone marrow oedema in the general population remains unknown, restricting interpretation of MRI findings and potentially leading to overdiagnosis when imaging findings are considered without clinical context. We aimed to establish the prevalence and determinants of sacroiliac bone marrow oedema in the general adult population.

Methods In this national, population-based, cross-sectional study, we analysed adults aged 20–69 years from the German National Cohort who underwent whole-body MRI between May 1, 2014, and Dec 31, 2016. Three masked experts independently assessed randomly selected participants for sacroiliac bone marrow oedema. The remaining participants were evaluated using a validated deep-learning algorithm that automatically segments and quantifies bone marrow oedema volume from fat-suppressed proton density sequences. We examined associations between the presence of bone marrow oedema (primary outcome) and demographic, lifestyle, and reproductive factors using multivariable logistic regression with sex-stratified analyses to identify differential patterns. There was no patient or public involvement in this study.

Findings Of 11 163 participants (median age 53·0 years [IQR 45·0–61·0], 5432 [48·7%] women and 5731 [51·3%] men), sacroiliac bone marrow oedema was detected in 288 (28·9% [95% CI 26·2–31·9]) of 998 participants analysed by expert readers and 3131 (30·8% [29·9–31·7]) of 10 165 participants analysed by the deep-learning algorithm, approximately 50 times higher than the 0·6% prevalence of self-reported axial spondyloarthritis diagnosis. Bone marrow oedema prevalence was higher in women (33·9% [95% CI 32·6–35·3]) than in men (27·8% [26·6–29·1]; adjusted odds ratio [OR] 1·33 [95% CI 1·23–1·45]). In women, pregnancy history was associated with bone marrow oedema compared with nulliparous women (OR 1·43 [95% CI 1·21–1·71]). In men, age (OR 1·28 per decade [95% CI 1·21–1·35]) and intensive recreational physical activity (1·24 [1·08–1·42]) showed independent associations, whereas age effects were minimal in women (1·16 per decade [1·11–1·23]). Of modifiable risk factors, BMI of 25 kg/m² and above showed the highest OR (1·62 [1·47–1·79]). Physically demanding occupational work was associated with bone marrow oedema overall (OR 1·25 [95% CI 1·14–1·36]).

Interpretation Sacroiliac bone marrow oedema affects nearly one-third of adults, showing associations with pregnancy, overweight, and occupational physical stress rather than inflammatory disease. This prevalence exceeds self-reported axial spondyloarthritis by 50 times, providing essential population reference data for contextualising MRI findings. These findings show that bone marrow oedema, the key imaging marker for sacroiliitis in Assessment of Spondyloarthritis International Society criteria, commonly occurs from non-inflammatory causes. These population-based data can inform diagnostic interpretation and support development of more specific imaging thresholds to reduce misdiagnosis and inappropriate treatments.

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Introduction

Axial spondyloarthritis is a chronic inflammatory immune-mediated disease primarily affecting the axial skeleton. Inflammation can result in irreversible structural damage to the sacroiliac joints and spine,[1] potentially leading to functional limitations and disability.[2] Treatment with advanced anti-inflammatory medication such as biological disease-modifying antirheumatic drugs can slow or halt this progression, particularly when initiated early. However, early axial spondyloarthritis presents a diagnostic challenge because conventional radiography cannot detect disease until

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Research in context

Evidence before this study

We searched MEDLINE, Embase, and Web of Science for studies published between Jan 1, 2000, and Dec 31, 2023, examining the prevalence of bone marrow oedema in sacroiliac joints in non-clinical populations. Search terms included "bone marrow edema", "sacroiliac joint", "magnetic resonance imaging", "prevalence", "healthy volunteers", "athletes", and "axial spondyloarthritis". We included studies in English and German. Previous research reported variable bone marrow oedema prevalence in 12–17% of individuals without back pain, 41% of recreational runners, and up to 57% of postpartum women. However, these studies had low sample sizes (typically <200 participants), focused on specific demographic groups, or examined selected control populations. However, no large-scale population-based study had quantified bone marrow oedema prevalence or identified its demographic determinants in an unselected general population.

Added value of this study

This study provides the first population-based assessment of bone marrow oedema in the sacroiliac joints of a general population, finding a prevalence of approximately 30%. We identified significant associations between bone marrow oedema and female sex, age, BMI, pregnancy history, and occupational physical activity, which had not previously been quantified at this scale. By developing a validated deep-learning algorithm, we enabled objective assessment of imaging findings across the entire cohort, offering unprecedented insights into demographic and lifestyle factors associated with bone marrow oedema.

Implications of all the available evidence

Sacroiliac bone marrow oedema affects 30% of the general population—50 times higher than axial spondyloarthritis prevalence—with notable associations with pregnancy, adiposity, and occupational stress rather than inflammatory disease. This high background prevalence means that isolated bone marrow oedema has low positive predictive value for axial spondyloarthritis diagnosis. The data in this study provide population-based reference values for interpreting MRI findings and support development of diagnostic algorithms incorporating patient demographics (sex, age, BMI, and pregnancy history) and bone marrow oedema burden (volume and prevalence) to improve diagnostic specificity and reduce inappropriate biological therapy initiation.

structural damage has already developed, typically after years of active inflammation.[3,4]

MRI has become an important part of early axial spondyloarthritis diagnosis because it allows early detection of active inflammation before structural damage becomes visible on radiographs.[5] The most important MRI finding for active inflammation is bone marrow oedema, which appears as hyperintense signal on fat-suppressed proton density, T2-weighted, or short tau inversion recovery sequences.[6] In the context of axial spondyloarthritis, bone marrow oedema represents active inflammatory changes in subchondral bone marrow and is one of the most important parameters in current diagnostic and classification frameworks.[7]

The Assessment of SpondyloArthritis International Society (ASAS) classification criteria formalised this concept by establishing MRI-detected bone marrow oedema as sufficient evidence of sacroiliitis, even in the absence of radiographic changes.[7] Under these criteria, individuals who have sacroiliac bone marrow oedema (that should be highly suggestive of axial spondyloarthritis in the view of the interpreter) in combination with at least one additional axial spondyloarthritis feature satisfy the imaging part of the ASAS classification criteria for axial spondyloarthritis.[8] This imaging pathway has also become an important route to early diagnosis and ultimately to early treatment. Detection of bone marrow oedema in the sacroiliac joints can therefore affect the decision of initiating advanced therapy (including biological and targeted synthetic disease-modifying antirheumatic drugs)—with implications given that these agents incur substantial treatment costs and, although safety profiles have improved substantially with accumulating evidence, carry risks that require careful patient selection.[9] The presence or absence of bone marrow oedema on MRI thus represents a decisive factor that shapes diagnostic classification, treatment access, health-care costs, and long-term patient outcomes.

However, recent studies have shown that bone marrow oedema frequently occurs without axial spondyloarthritis.[10] Studies have reported bone marrow oedema in 41% of recreational runners fulfilling ASAS MRI criteria[11] and 57% of postpartum women,[12] suggesting that mechanical stress and hormonal changes can produce bone marrow oedema indistinguishable from inflammation. These findings question the specificity of bone marrow oedema for axial spondyloarthritis; however, previous studies were hampered by small sample sizes (<200 participants), selected populations, and heterogeneous protocols. Nonetheless, comprehensive data from an unselected general adult population remain sparse.

Deep learning now enables standardised bone marrow oedema assessment at population scale, overcoming the logistical constraints of manual expert reading. Therefore, via a population-based study with participants from the German National Cohort, we aimed to establish sacroiliac bone marrow oedema prevalence in the general population using expert reading and validated artificial

intelligence-based deep-learning analysis to describe the frequency of sacroiliac oedema and to examine demographic, lifestyle, and reproductive factors associated with bone marrow oedema presence and volume.

Methods

Study design and participants

This population-based cross-sectional study used data from the German National Cohort (NAKO Gesundheitsstudie; DRKS00037328), a prospective cohort of 205 415 individuals from the general population, established to investigate the causes and risk factors of common chronic diseases in Germany. Participants were recruited from 18 population study centres across Germany. The study is one of the largest prospective population-based cohort studies worldwide. Participants were recruited to the cohort if they were adults, aged 20–69 years. Beyond the age range, the only general exclusion criteria were insufficient German language skills and inability to provide informed consent. For the MRI substudy, standard MRI contraindications were additionally applied.[13] Participants were randomly selected from municipal registries using age-stratified and sex-stratified sampling. Baseline assessments included structured interviews, validated questionnaires, physical examinations, and imaging procedures using harmonised protocols.[13] NAKO was carried out with the approval of the relevant local ethics committees at all participating study centres and in accordance with national law and with the Declaration of Helsinki 1975 (current, revised version). There was no separate ethics approval required for this study. Written informed consent was obtained from all participants.

Between May 1, 2014, and Dec 31, 2016, a subset of the entire NAKO cohort, recruited from 11 study centres (Augsburg, Berlin Nord, Berlin-Mitte, Berlin-Süd and Brandenburg, Düsseldorf, Essen, Freiburg, Mannheim, Münster, Neubrandenburg, and Saarbrücken), underwent standardised whole-body MRI examinations at five dedicated imaging centres (Augsburg, Berlin, Essen, Mannheim, and Neubrandenburg; appendix p 18).[14] Participation in the MRI component of NAKO was voluntary and eligible participants provided separate written informed consent for imaging. Participants with contraindications for MRI (e.g., pacemakers, metallic implants, or claustrophobia) were excluded. In this study we analysed participants with complete MRI data. Individuals with incomplete pelvic coverage on MRI, or with incomplete demographic and clinical data, were excluded. Using computer-generated simple random sampling, without stratification, participants were randomly selected to be assessed by expert reading. The remaining participants underwent AI-based analysis.

There was no involvement of patients or members of the public in the design, conduct, or reporting of this research. As this study was a secondary analysis of existing cohort data with AI-based image analysis, patient involvement was not incorporated into the study design.

Procedures

We extracted demographic variables including age, sex (self-reported as male or female), smoking status, and marital status. Ethnicity data were not available and were therefore not included in the analyses. Educational attainment was dichotomised as university degree or higher versus lower, and socioeconomic status was quantified by the International Socio-economic Index of Occupational Status (ISEI-08). Clinical parameters encompassed BMI (kg/m²), high-sensitivity C-reactive protein (with concentrations >5 mg/L classified as elevated), self-reported history of psoriasis, inflammatory bowel disease, and chronic back pain. Physical activity was assessed using the Global Physical Activity Questionnaire, classifying participants as sufficiently active (≥600 metabolic equivalent min per week according to WHO criteria) or inactive (<600 metabolic equivalent min per week) and categorising occupational physical demands (physically demanding *vs* non-demanding) and intensive recreational activity engagement. For women, reproductive history included pregnancy history, number of pregnancies, livebirth history, and number of livebirths. Known axial spondyloarthritis status was self-reported based on a previous physician diagnosis during the baseline interview.

All imaging was done on identical 3-Tesla MRI systems (MAGNETOM Skyra, Siemens Healthineers, Erlangen, Germany) with identical hardware configurations. For sacroiliac bone marrow oedema assessment, we used two sequences: a three-dimensional fat-suppressed proton density sequence with 1·0 mm × 1·0 mm × 1·0 mm isotropic resolution for oedema visualisation, and a T1-weighted volumetric interpolated breath-hold examination with two-point Dixon technique (two echo times) for anatomical context. Together, these sequences provided high contrast for detecting and localising subchondral oedema in the sacroiliac joints.

Three experienced readers (DP, TD, and NK), each with more than 10 years of experience and masked to all clinical information, did independent assessments after a prereading alignment session to standardise application of the ASAS MRI definitions. Bone marrow oedema was defined as hyperintense signal on the fat-suppressed proton density sequence in the subchondral bone marrow of the sacroiliac joints, consistent with the ASAS–OMERACT definition of active inflammatory lesions.[6] Cases with at least two of three readers identifying bone marrow oedema were classified as positive. All cases with consensus-positive oedema underwent volumetric annotation with pixelwise segmentation of oedematous regions.

For the participants who underwent AI-based analysis, we developed an AI pipeline consisting of three

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See **Online** for appendix

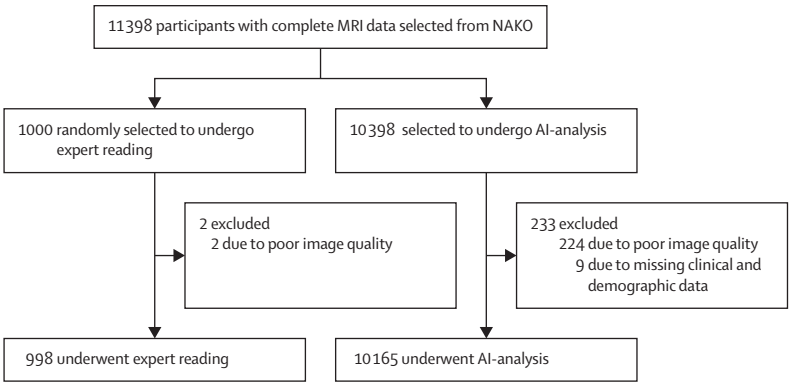


Figure 1: **Study design**
Participant selection from the NAKO MRI substudy. NAKO=German National Cohort.

	Expert-read (n=998)	AI-analysed (n=10 165)
Sex		
Female	470 (47·1%)	4962 (48·8%)
Male	528 (52·9%)	5203 (51·2%)
Age, years	53·0 (45·0–61·0)	53·0 (45·0–61·0)
BMI, kg/m²	26·9 (4·9)	26·8 (4·7)
Smoking status		
Current	198/955 (20·7%)	1916/9807 (19·5%)
Former	304/955 (31·8%)	3240/9807 (33·0%)
Never	453/955 (47·4%)	4651/9807 (47·4%)
Physical activity		
Sufficient according to GPAQ	841 (84·3%)	8703 (85·6%)
Occupational	475 (47·6%)	4618 (45·4%)
Transportation-related	678 (67·9%)	6806 (67·0%)
Recreational	741 (74·2%)	7552 (74·3%)
Intensive	613 (61·4%)	6135 (60·4%)
Family status, married	671 (67·2%)	6733 (66·2%)
Education, university degree or higher	490/910 (53·8%)	5193/9224 (56·3%)
Socioeconomic status (ISEI-08)	49·2 (15·8)	49·1 (15·3)
History of psoriasis	63/984 (6·4%)	622/10 151 (6·1%)
History of inflammatory bowel disease	12/996 (1·2%)	116/10 139 (1·1%)
Chronic back pain ever	238/996 (23·9%)	2391/10 138 (23·6%)
Chronic back pain in the last 12 months	145/993 (14·6%)	1466/10 140 (14·5%)
Known axial spondyloarthritis diagnosis	4/996 (0·4%)	63 (0·6%)
C-reactive protein concentration, mg/L	2·0 (3·5)	2·2 (3·9)
Elevated C-reactive protein (>5 mg/L)	34/432 (7·9%)	426/4636 (9·2%)
Pregnancy ever	341/444 (76·8%)	3783/4758 (79·5%)
Number of pregnancies	1·9 (1·5)	1·9 (1·5)
Livebirth ever	322/426 (75·6%)	3560/4561 (78·1%)
Number of livebirths	1·5 (1·2)	1·5 (1·1)
Bone marrow oedema volume measure, cm³	0·9 (1·6)	0·9 (1·2)
Bone marrow oedema presence (balanced cutoff)	288 (28·9%)	3131 (30·8%)

Data are n (%), median (IQR), n/N (%), or mean (SD). AI=artificial intelligence. GPAQ=Global Physical Activity Questionnaire. ISEI-08=International Socioeconomic Index of Occupational Status.

Table 1: **Baseline demographic and clinical characteristics of the cohort**

deep-learning models to determine the presence of bone marrow oedema: two models for anatomical context through segmentation of pelvic structures, and one model for bone marrow oedema segmentation and quantification. The AI models were trained on the expert-read cases. AI performance was assessed using five-fold crossvalidation, wherein each expert-read case was evaluated by a model trained exclusively on the remaining cases. Details on AI development and performance metrics are provided in the appendix (pp 1–3).

Outcomes

The primary outcome was the presence of bone marrow oedema, defined as hyperintense signal on the fat-suppressed proton density sequence in the subchondral bone marrow of the sacroiliac joints.

The secondary outcome was oedema volume, a continuous measurement in cubic centimetres calculated by counting voxels classified as oedema. Additionally, in the AI-based analysis, bone marrow oedema was defined as a binary classification using a volume threshold of 0·91 cm³, calibrated to reproduce the oedema prevalence observed in the expert-annotated reference subset.

Statistical analysis

Categorical variables are presented as frequencies with percentages, and continuous variables as means with SDs. Between-group comparisons (expert-reviewed *vs* AI-analysed subsets) employed χ^2 tests for categorical variables and independent-samples *t* tests for continuous variables, with Benjamini–Hochberg adjustment for multiple comparisons. We used a predefined balanced cutoff to define AI-derived bone marrow oedema presence. A receiver operating characteristic curve in the expert-reviewed subset illustrates the performance of this cutoff relative to expert consensus (appendix p 4).

To investigate associations with bone marrow oedema, we did parallel analyses in both the expert-reviewed and AI-analysed subsets. Univariable and multivariable logistic regression models evaluated predictors of bone marrow oedema presence (binary outcome), with results reported as odds ratios (ORs) with 95% CIs. To avoid ambiguous interpretation from mutual adjustment of variables that could lie on the same causal pathway, we estimated exposure–outcome associations in separate models, using prespecified adjustment sets informed by causal assumptions to control for confounding while avoiding adjustment for potential mediators. In the overall sample, BMI models were adjusted for age, sex, and socioeconomic status; occupational physical activity models were adjusted for age, sex, BMI, and intensive physical activity; intensive physical activity models were adjusted for age, sex, BMI, and occupational physical activity; and sex and age were examined in unadjusted models. In women, BMI models were adjusted for age,

pregnancy history, and socioeconomic status; occupational physical activity models were adjusted for age, pregnancy history, BMI, and intensive physical activity; intensive physical activity models were adjusted for age, pregnancy history, BMI, and occupational physical activity; and pregnancy-related exposures were adjusted for age only. In men, BMI models were adjusted for age and socioeconomic status; occupational physical activity models were adjusted for age, BMI, and intensive physical activity; and intensive physical activity models were adjusted for age, BMI, and occupational physical activity. Estimates were not obtained where the number of events in a stratum was fewer than ten. Age was modelled as a continuous variable scaled per 10-year increase.

For the AI-analysed subset, we additionally did linear regression analyses examining associations between demographic and clinical factors and continuous bone marrow oedema volume, reporting standardised β coefficients with 95% CIs. We also did linear regression analyses for continuous bone marrow oedema volume in the expert-reviewed subset to allow comparison of volume-based associations across expert and AI-derived measurements. For linear regression models, we assessed assumptions using standard diagnostic procedures (residuals *vs* fitted, normal Q–Q, and scale–location plots) and evaluated influential observations using standardised residuals and Cook's distance. When heteroskedasticity was present, we repeated analyses using heteroskedasticity-robust SEs. Because age was modelled as a continuous variable scaled per 10-year increase, we additionally assessed functional form by refitting models with age entered as a categorical factor.

Multicollinearity was assessed using variance inflation factors; values greater than 5 prompted model refinement. We used complete-case analyses for each model (no imputation), including participants with non-missing data for the outcome, exposure, and covariates in that model.

As a sensitivity analysis, we assessed whether associations differed by sex by including interaction terms between sex and key variables in multivariable models for all participants: age, BMI, occupational physical activity, and intensive physical activity. We tested sex–predictor interactions to formally assess effect modification.

All analyses were two-sided, with $p<0·05$ considered statistically significant. All statistical analyses were done using R (version 4.2.2).

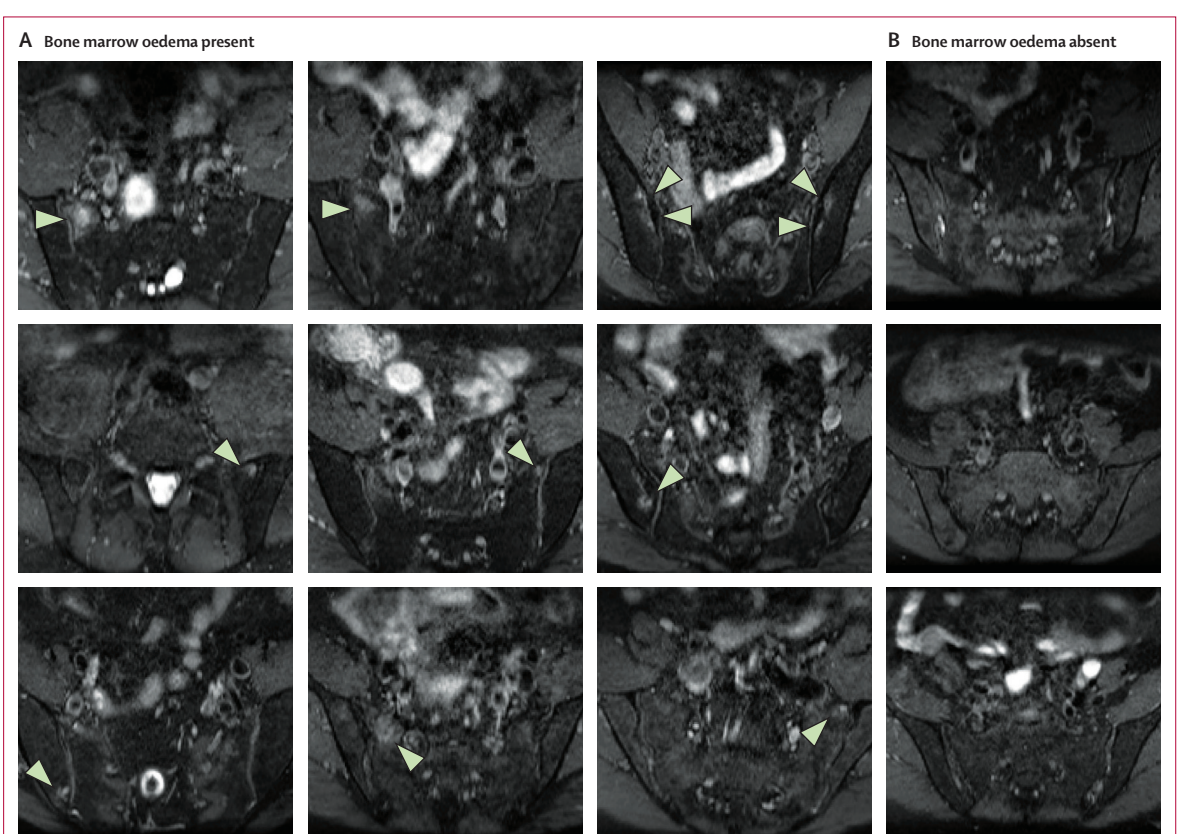


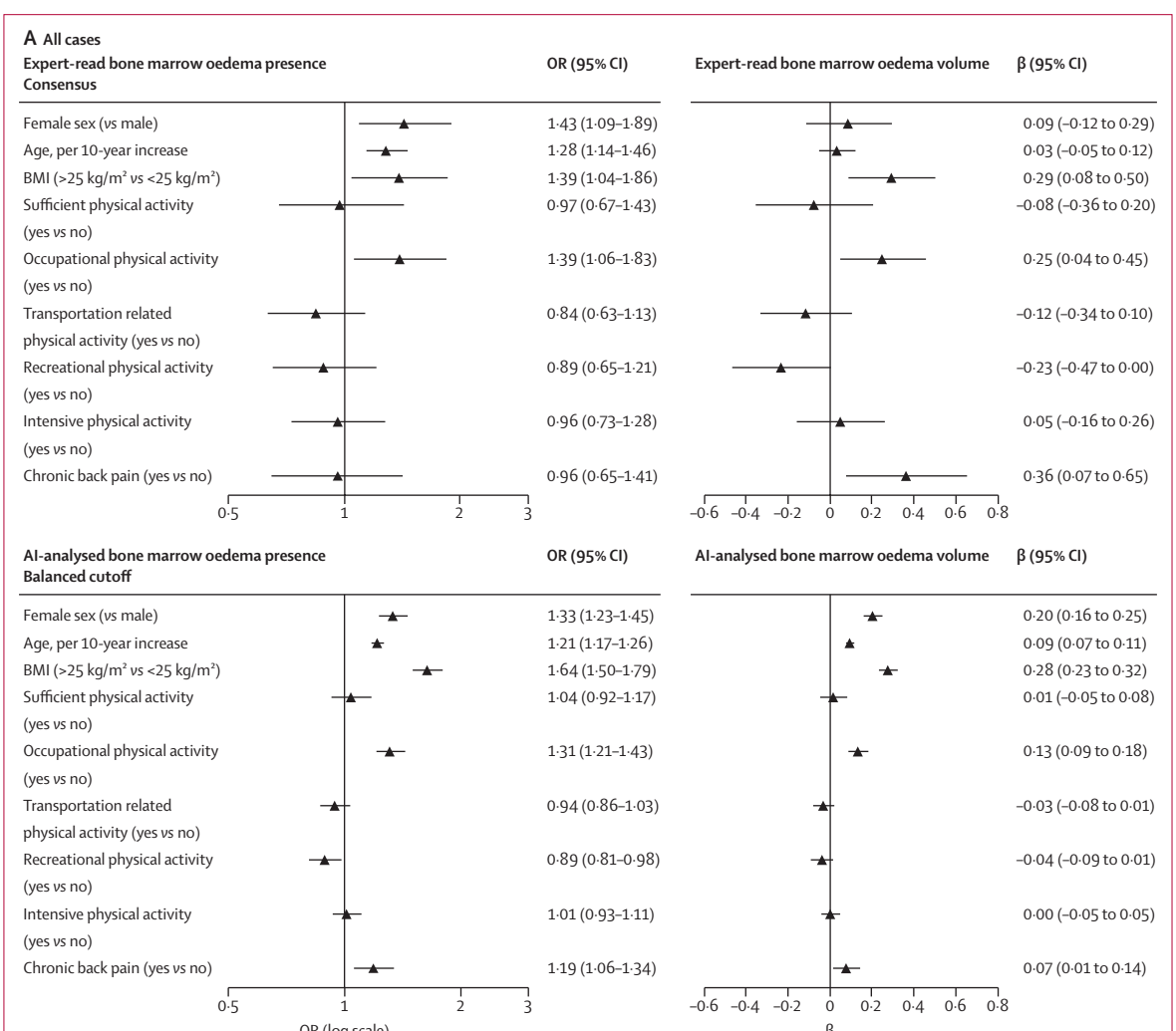
Figure 2: **Examples of bone marrow oedema on pelvic MRI**
Axial fat-suppressed proton density MRI images of the sacroiliac joints. (A) Cases with bone marrow oedema present; arrowheads indicate hyperintense subchondral signal consistent with oedema. (B) Cases without bone marrow oedema, showing normal marrow signal without focal hyperintensity.

Role of the funding source
The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results
Of the 11 398 participants with complete MRI data, 1000 (8·8%) were randomly selected to undergo expert-reading and 10 398 (91·2%) were subsequently selected for AI-analysis. After excluding two (0·2%) of 1000 participants in the expert-reading and 233 (2·2%) of 10 398 in the AI-analysed group because of poor image quality or missing clinical or demographic data, 998 participants underwent expert-reading and 10 165 underwent AI-analysis; figure 1). Participant demographics were representative of the general German population and baseline demographic and clinical characteristics were similar between groups (table 1). 5432 (48·7%) of 11 163 participants were women and 5731 (51·3%) were men. The median age was 53·0 years (IQR 45·0–61·0) and the mean BMI was 26·8 kg/m² (SD 4·7). 5093 (45·6%) participants reported physically demanding occupations. 4124 (79·3%) of 5202 women reported a history of pregnancy and 3882 (77·8%) of 4987 had given birth (table 1).

The expert-read and AI-analysed groups showed no significant differences in key baseline demographic or clinical parameters, including age, BMI, smoking status, occupational demands, reproductive history, and comorbidities. Self-reported axial spondyloarthritis prevalence was low in both groups (four [0·4%] of 996 expert-read and 63 [0·6%] of 10 165 AI-analysed participants), with 67 (0·6%) of 11 161 participants reporting a previous diagnosis.

Bone marrow oedema prevalence using the balanced classification threshold was similar between the expert-read group (288 [28·9%, 95% CI 26·2–31·9] of 998 participants) and the AI-analysed group (3131 [30·8%,



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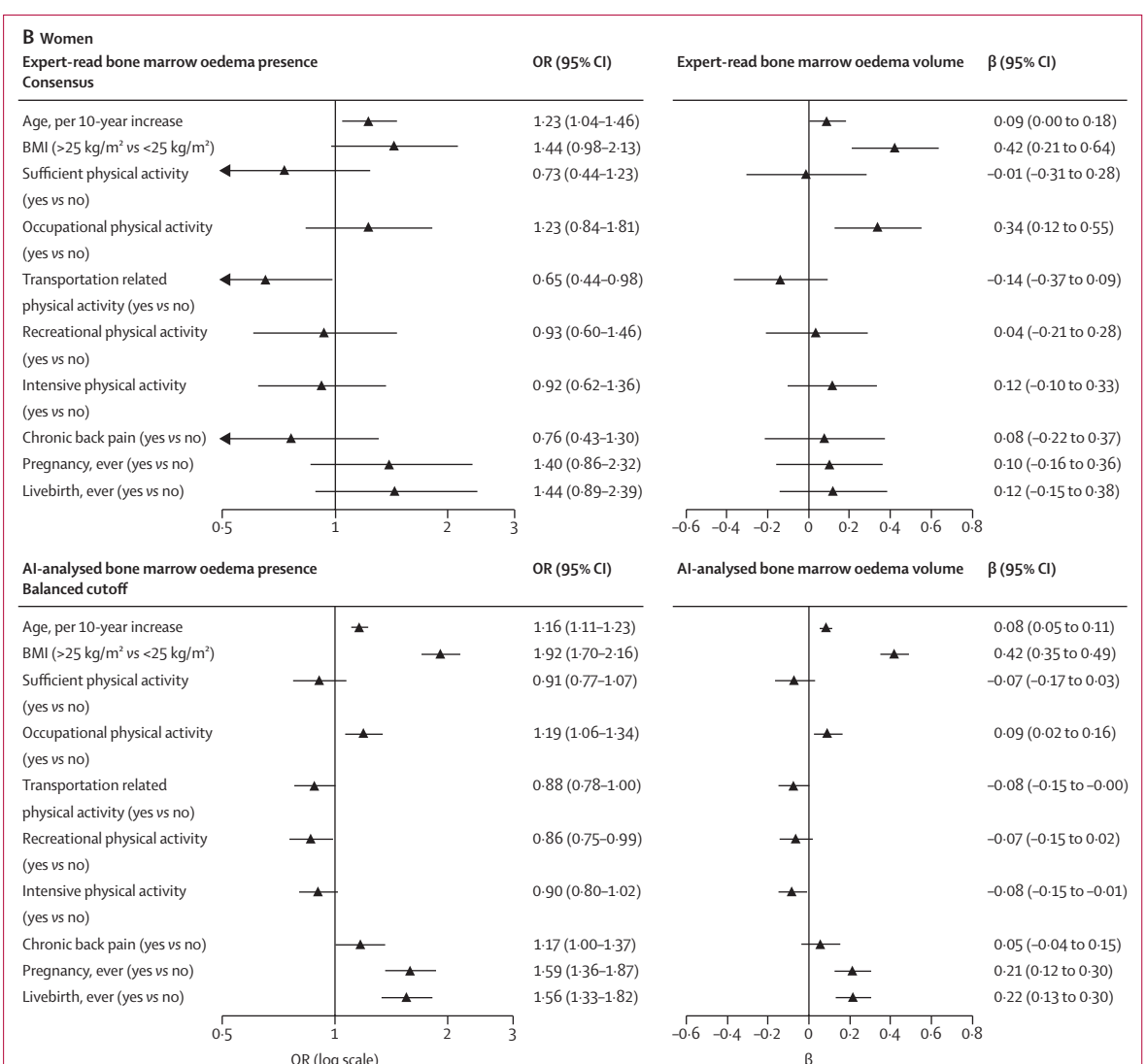
29·9–31·7] of 10 165; p=0·23). Mean oedema volume was 0·9 cm³ (SD 1·6) in the expert-read group versus 0·9 cm³ (1·2) in the AI-analysed group (p=0·26), confirming the representativeness of the expert-read subset. Bone marrow oedema occurred unilaterally in approximately half of participants, with slight disposition towards the right side (appendix pp 7, 15).

Sex-stratified analyses revealed consistent patterns between the expert-read and AI-analysed groups at baseline. Compared with men, women had lower rates of intensive physical activity (278 [59·1%] of 470 *vs* 335 [63·4%] of 528 in expert-read; 2767 [55·8%] of 4962 *vs* 3368 [64·7%] of 5203 in AI-analysed) but higher prevalence of chronic back pain in the past 12 months (75 [16·0%] of 470 *vs* 70 [13·3%] of 528 in expert-read; 846 [17·0%] of 4962 *vs* 620 [11·9%] of 5203 in AI-analysed; appendix p 10). Women had higher bone marrow oedema prevalence compared with men, using the balanced threshold (152 [32·3%, 95% CI 28·1–36·8] of 470 *vs* 137 [25·9%, 22·3–29·9] of 528 in expert-read; 1684 [33·9%, 32·6–35·3] of 4962 *vs* 1447 [27·8%, 26·6–29·1] of 5203 in AI-analysed), indicating sex-specific differences (appendix p 10). Mean oedema volume was 0·79 cm³ (SD 1·19) in men and 0·98 cm³ (1·26) in women (appendix p 5). In women with a history of pregnancy, the highest mean oedema volume was observed within the first year following delivery (1·42 cm³ [SD 1·40]; appendix p 5). Mean oedema volumes in later postpartum periods were similar to each other.

In analysis stratified by age, bone marrow oedema prevalence increased with age, from 117 (20·6% [95% CI 17·4–24·2]) of 567 participants aged 20 to 30 years to 107 (38·9% [33·1–44·9]) of 275 participants aged 70 years and older (appendix p 5).



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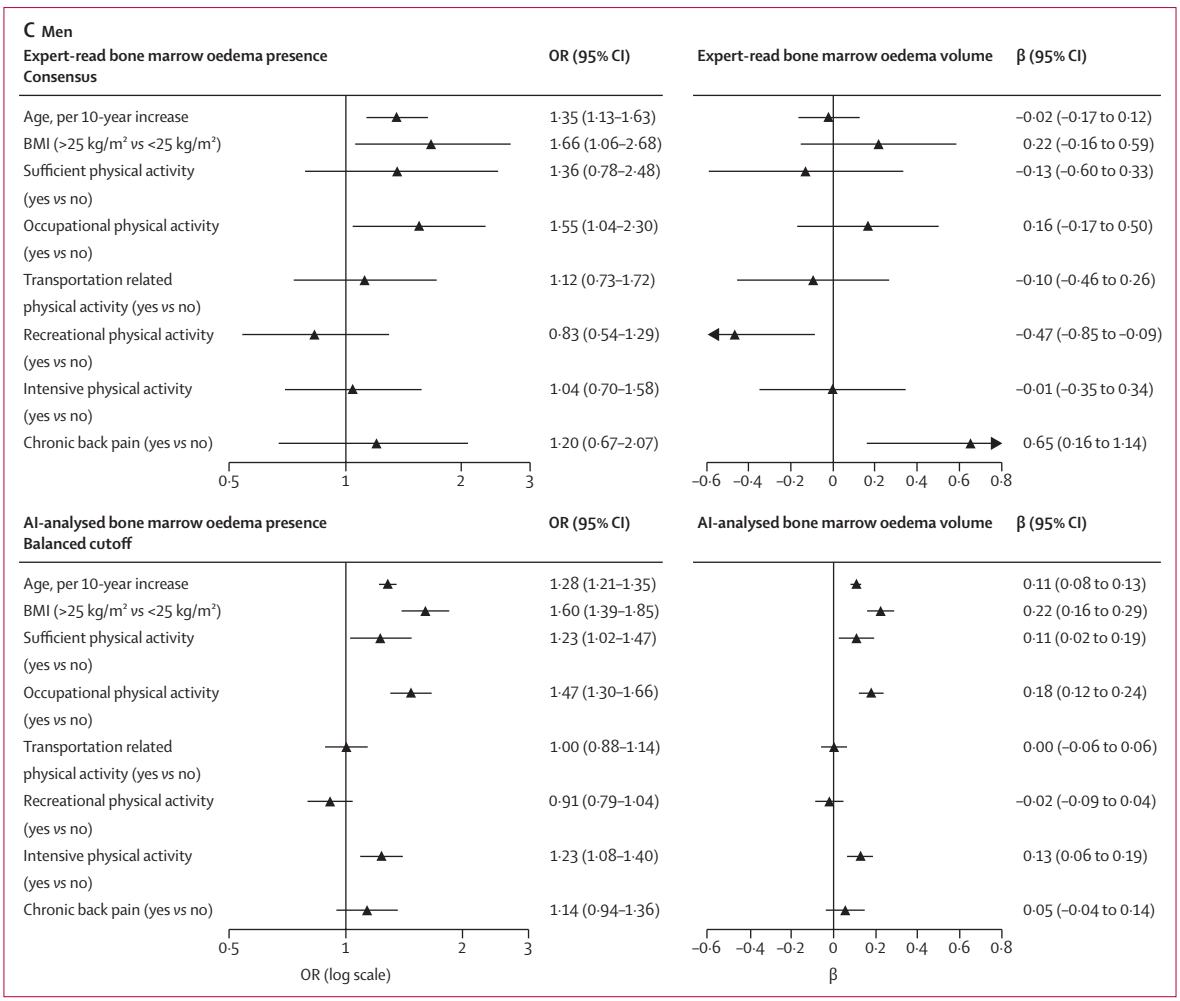

Figure 3: **Univariable associations with sacroiliac bone marrow oedema**
Forest plots showing univariable associations between demographic, lifestyle, and clinical factors and bone marrow oedema outcomes for all participants (A), women (B), and men (C). Points indicate effect estimates with 95% CIs; the vertical line indicates null effect. OR=odds ratio.

In analyses stratified by BMI category, bone marrow oedema was present in 2361 (34·5% [95% CI 33·4–35·7]) of 6843 participants with BMI of 25 kg/m² and higher, and 1050 (24·4% [23·1–25·7]) of 4302 participants with BMI of less than 25 kg/m² (appendix p 6). Mean oedema volume was 0·99 cm³ (SD 1·34) in participants with BMI of 25 kg/m² and higher, and 0·71 cm³ (1·00) in those with BMI of less than 25 kg/m². In analyses stratified by chronic back pain status, bone marrow oedema was present in 549 (34·1% [31·8–36·5]) of 1611 participants with chronic back pain and 2866 (30·1% [29·1–31·0]) of 9522 without chronic back pain (appendix p 6). Mean oedema volume was 0·97 cm³ (SD 1·44) in participants with and 0·87 cm³ (1·19) in those without chronic back pain.

The AI-based deep-learning model showed strong performance for bone marrow oedema segmentation and detection. For pixel-level segmentation accuracy in participants with bone marrow oedema, the model had a mean Dice similarity coefficient of 0·79 (95% CI 0·78–0·81) compared with expert annotations across five cross-validation folds, with a mean 95th-percentile Hausdorff distance of 31·7 mm (95% CI 28·3–35·3). Performance remained consistent across folds, with no significant interfold variation (p=0·34 for Dice scores; p=0·66 for Hausdorff distances).

For lesion-level detection, we evaluated the model's ability to identify individual lesions (participants could have multiple lesions). Aggregating results across all five folds, the model correctly identified 894 lesions annotated by experts (true positives) and missed 78 expert-identified lesions (false negatives). The model additionally identified 209 lesions not marked by experts (false positives). True negatives are not applicable in lesion detection because they would represent the entire background volume without lesions. This model yielded an aggregated F1 score of 0·81, improving to 0·86 with morphological opening for noise reduction. Mean per-case

	Expert-read bone marrow oedema presence, OR (95% CI)	AI-analysed bone marrow oedema presence balanced cutoff, OR (95% CI)	Expert-read bone marrow oedema volume measure, β (95% CI)	AI-analysed bone marrow oedema volume measure, β (95% CI)
All				
Female sex (*vs* male)	1·43 (1·09–1·89)	1·33 (1·23–1·45)	0·09 (–0·12 to 0·29)	0·20 (0·16 to 0·25)
Age, per 10-year increase	1·28 (1·14–1·46)	1·21 (1·17–1·26)	0·03 (–0·05 to 0·12)	0·09 (0·07 to 0·11)
BMI, ≥25 kg/m² *vs* <25 kg/m²	1·34 (0·98–1·84)	1·62 (1·47–1·79)	0·31 (0·08 to 0·54)	0·29 (0·23 to 0·34)
Occupational physical activity (yes *vs* no)	1·28 (0·96–1·72)	1·25 (1·14–1·36)	0·21 (0·00 to 0·43)	0·10 (0·06 to 0·15)
Intensive physical activity (yes *vs* no)	0·96 (0·71–1·30)	1·06 (0·97–1·16)	0·02 (–0·20 to 0·24)	0·03 (–0·01 to 0·08)
Female sex				
Age, per 10-year increase	1·23 (1·04–1·46)	1·16 (1·11–1·23)	0·09 (0·00 to 0·18)	0·08 (0·05 to 0·11)
BMI, ≥25 kg/m² *vs* <25 kg/m²	1·33 (0·87–2·04)	1·82 (1·60–2·07)	0·41 (0·19 to 0·63)	0·40 (0·33 to 0·48)
Occupational physical activity (yes *vs* no)	1·20 (0·78–1·84)	1·15 (1·02–1·31)	0·35 (0·12 to 0·57)	0·07 (0·00 to 0·15)
Intensive physical activity (yes *vs* no)	0·99 (0·64–1·52)	0·95 (0·83–1·07)	0·09 (–0·14 to 0·32)	–0·05 (–0·12 to 0·02)
Pregnancy ever (yes *vs* no)	1·18 (0·70–2·02)	1·43 (1·21–1·70)	0·03 (–0·25 to 0·31)	0·15 (0·06 to 0·25)
Pregnancy in the last 12 months (yes *vs* no)	NA*	2·90 (1·67–5·06)	NA*	0·65 (0·31 to 1·00)
Male sex				
Age, per 10-year increase	1·35 (1·13–1·63)	1·28 (1·21–1·35)	–0·02 (–0·17 to 0·12)	0·11 (0·08 to 0·13)
BMI, ≥25 kg/m² *vs* <25 kg/m²	1·44 (0·88–2·41)	1·42 (1·23–1·65)	0·19 (–0·22 to 0·59)	0·17 (0·10 to 0·23)
Occupational physical activity (yes *vs* no)	1·41 (0·93–2·14)	1·34 (1·18–1·53)	0·16 (–0·19 to 0·52)	0·13 (0·06 to 0·19)
Intensive physical activity (yes *vs* no)	1·06 (0·69–1·65)	1·24 (1·08–1·42)	–0·04 (–0·41 to 0·32)	0·13 (0·07 to 0·19)

OR=odds ratio. NA=not applicable. *NA indicates estimates that could not be reliably obtained due to very small numbers in female participants for expert-read outcomes.

Table 2: **Multivariable regression analyses of variables associated with the presence and volume of bone marrow oedema in all individuals and by sex**

F1 scores by fold ranged from 0·79 to 0·83 including noise and from 0·85 to 0·88 excluding noise, with no significant interfold variation (p=0·75). Detailed segmentation performance metrics for each validation fold are provided in the appendix (pp 3, 8–9). Figure 2 shows representative images of the range of bone marrow oedema presentations with corresponding AI segmentation overlays.

Univariable associations between demographic, lifestyle, and clinical factors and bone marrow oedema outcomes are shown in figure 3. In multivariable analyses in the overall cohort, multiple factors showed independent associations with bone marrow oedema (table 2). Age and BMI of 25 kg/m² and higher were consistently associated with bone marrow oedema across all measures. Female sex was also independently associated with bone marrow oedema (adjusted OR 1·43 [95% CI 1·09 to 1·89] for expert-read bone marrow oedema presence and 1·33 [1·23 to 1·45] for AI-analysed bone marrow oedema presence; table 2). Occupational physical activity was associated with bone marrow oedema presence (adjusted OR 1·28 [95% CI 0·96 to 1·72] for expert-read and 1·25 [1·14 to 1·36] for AI-analysed bone marrow oedema presence. In contrast, intensive physical activity showed no association in overall models (adjusted OR 0·96 [95% CI 0·71 to 1·30] for expert-read bone marrow oedema presence and 1·06 [0·97 to 1·16] for AI-analysed bone marrow oedema presence; table 2).

Sex-stratified analyses revealed distinct patterns of association between clinical factors and bone marrow oedema. In men, age showed clear associations with bone marrow oedema (adjusted OR 1·35 [95% CI 1·13 to 1·63] for expert-read and 1·28 [1·21 to 1·35] for AI-analysed bone marrow oedema presence; table 2). In women, age showed no associations across measures, however, pregnancy history was associated with bone marrow oedema in AI-analysed models (adjusted OR 1·43 [95% CI 1·21 to 1·70] and standardised β 0·15 [95% CI 0·06 to 0·25]). We additionally modelled pregnancy within the last 12 months, which showed higher effect estimates in AI-analysed models (adjusted OR 2·90 [95% CI 1·67 to 5·06]; standardised β 0·65 [95% CI 0·31 to 1·00]). BMI had positive associations with bone marrow oedema presence and volume in women, and with bone marrow oedema presence in men (table 2). Physical activity showed sex-specific effects. Occupational physical activity was associated with bone marrow oedema in both men (adjusted OR 1·34 [1·18 to 1·53]) and women (adjusted OR 1·15 [1·02 to 1·31]) in the AI-analysed model. Intensive physical activity was associated with bone marrow oedema in men (adjusted OR 1·24 [95% CI 1·08 to 1·42]) and showed no association in women (0·95 [0·83 to 1·07]) in the AI-analysed model.

Multivariable analyses stratified by chronic back pain showed similar associations in participants with and without chronic back pain across all outcomes evaluated in the main multivariable models, including expert-read bone marrow oedema presence, AI-analysed bone marrow oedema presence, expert-read volume, and AI-analysed volume (appendix p 12).

Sensitivity analyses including sex–predictor interaction terms showed significant interactions for age, BMI, and

intensive physical activity in AI-based outcomes, confirming that these associations differed by sex (appendix p 11). No significant interactions were observed for occupational physical activity or for expert-read bone marrow oedema measures.

We assessed linear regression assumptions using standard diagnostic procedures, including evaluation of residual patterns, heteroskedasticity testing, and assessment of influential observations (appendix p 13). We then did two sensitivity analyses for the linear regression models of oedema volume: we repeated models using heteroskedasticity-robust SEs to address potential non-constant variance, and we refitted models with age entered as a categorical factor to assess functional form. In both sensitivity analyses, effect estimates were similar to the primary models (appendix p 14).

Discussion

Sacroiliac bone marrow oedema is far more common than previously recognised. In this population-based study of 11 163 adults, nearly one in three participants showed MRI-detectable bone marrow oedema. This prevalence is approximately 50 times higher than the known axial spondyloarthritis prevalence in the NAKO cohort (0·6%), which aligns with German epidemiological data for ankylosing spondylitis (0·5%).[15] Although comprehensive clinical evaluation would be needed to definitively characterise axial spondyloarthritis status in all participants with bone marrow oedema, this striking disparity indicates that most sacroiliac bone marrow oedema is likely to occur in individuals without inflammatory arthritis. Conversely, given known diagnostic delays (particularly in women), some occurrences of bone marrow oedema might represent unrecognised axial spondyloarthritis.

We identified specific demographic and lifestyle factors associated with bone marrow oedema presence. Female sex was associated with presence of bone marrow oedema (OR 1·33) and elevated BMI showed the highest OR (1·62) among modifiable factors. Occupational physical activity increased odds of bone marrow oedema (OR 1·25). Notably, these associations differed markedly by sex. In women, pregnancy history had an OR of 1·43, with higher odds observed for pregnancy within the last 12 months (OR 2·90), whereas age showed minimal association. In men, both age (OR 1·28 per decade) and physical demands showed notable associations. These patterns suggest that sacroiliac bone marrow oedema frequently represents physiological or mechanical responses rather than inflammatory disease.

The AI-based analysis successfully captured the same associations identified by expert readers, including both overall patterns and sex-specific differences. This concordance validates the deep-learning framework for large-scale bone marrow oedema assessment and shows that automated analysis can reliably identify clinically relevant patterns across entire populations.

Previous studies in selected populations underestimated bone marrow oedema prevalence, probably due to small sample sizes and restricted demographics. Renson and colleagues reported prevalence of 11·6% in healthy individuals without back pain,[16] and Baraliakos and colleagues found a prevalence of 17·2% in community volunteers younger than 45 years.[10] Both studies examined specific demographic subgroups. This population-based study of 11 163 adults across the full adult age range (20–69 years) provides a large-scale estimate of sacroiliac bone marrow oedema frequency of approximately 30%, using expert-informed definitions applied consistently across the cohort.

The substantially higher prevalence we have documented has two explanations. First, we applied systematic assessment across all demographics rather than selected subgroups. Second, our detection encompassed all bone marrow oedema rather than only lesions meeting the full ASAS criteria for MRI sacroiliitis, which require bone marrow oedema to be highly suggestive of axial spondyloarthritis, based on an overall impression that takes into account lesion localisation and the presence of structural lesions. Even studies using restrictive ASAS criteria found high bone marrow oedema rates. De Winter and colleagues reported that 23·4% of healthy volunteers met full ASAS MRI criteria for sacroiliitis.[12] This finding confirms that bone marrow oedema is common regardless of detection methodology.

The original ASAS validation cohort reported only 2·6% bone marrow oedema prevalence in chronic back pain controls.[17] The substantial difference the findings in this study (30% prevalence) illustrates how control group selection influences the perceived specificity of classification criteria.[10] The unselected population in this study provides essential context for clinical MRI interpretation that was previously unavailable. This discrepancy has implications for interpreting current classification criteria. The ASAS MRI definition of a positive MRI had high specificity in the original validation cohort but might not fully account for the background bone marrow oedema prevalence we observed in the general population. Applying purely quantitative criteria without considering other parameters—including demographic context and pretest probability—risks overdiagnosis and inappropriate treatment initiation. Lesion characteristics (predominant localisation in the middle part of the joint in axial spondyloarthritis as opposed to predominant ventral localisation in mechanical conditions, and presence of axial spondyloarthritis-specific structural lesions such as erosions) could provide important discriminatory information beyond simple presence or absence.[18]

De Winter and colleagues found that only extensive, deep bone marrow oedema lesions were specific to axial spondyloarthritis, whereas smaller lesions occurred

commonly in healthy individuals.[12] Subsequent work has suggested that morphological features differentiate inflammatory from mechanical bone marrow oedema. Lesion depth exceeding 5–10 mm and extension into the posterior ligamentous portion of the sacroiliac joint could indicate inflammatory disease, whereas predominant ventral localisation suggests mechanical aetiology.[15] The volumetric data from this study support this concept. Bone marrow oedema exists on a continuum where size, number, distribution, and anatomical location distinguish pathological from physiological findings. Diagnostic approaches should integrate these morphological features with patient demographics and clinical presentation rather than relying on lesion count alone.

The demographic associations identified in this study suggest specific aetiological mechanisms. The association with pregnancy in women probably reflects biomechanical stress and hormonal influences. Elevated oestrogen and relaxin during pregnancy and postpartum periods increase ligamentous laxity and alter pelvic biomechanics, subjecting the sacroiliac joints to substantial mechanical stress.[19–21] In men, the associations with age and occupational demands align with established patterns of stress-related bone marrow oedema. Repetitive mechanical loading can exceed bone adaptive capacity, causing microdamage, increased intraosseous pressure, and fluid accumulation.[22]

These patterns parallel bone marrow oedema in other anatomical locations. Throughout the skeleton, bone marrow oedema appears as a non-specific response to mechanical stress, degenerative changes, and metabolic disturbances. Bone marrow oedema occurs in knee osteoarthritis, athletic stress reactions, and transient osteoporosis of the hip.[23,24] Clinical context determines whether bone marrow oedema represents pathological inflammation or physiological adaptation. The sacroiliac joints appear subject to similar principles.

These observations have practical implications for diagnosis. First, criteria for MRI positivity for axial spondyloarthritis might require revision to include both active inflammatory and structural lesions rather than bone marrow oedema alone, as well as anatomic localisation of the lesions within the joint.[25] Second, imaging interpretation should account for patient characteristics that modify background bone marrow oedema risk, including age, sex, BMI, pregnancy history, and occupational exposures.[26] Pastor and colleagues used this approach by developing a sex-specific algorithm for women that had 95% specificity compared with 88% for standard ASAS criteria, by requiring absence of osteophytes plus either bone marrow oedema measuring at least 8 mm in one dimension or at least one erosion.[27] Such algorithms must balance two risks: overdiagnosis of axial spondyloarthritis when bone marrow oedema reflects mechanical causes; and underdiagnosis, particularly in women, when true inflammatory disease is dismissed as pregnancy-related or degenerative change.

Osteitis condensans ilii represents another potential contributor to bone marrow oedema in this study population. Osteitis condensans ilii is a benign condition predominantly affecting multiparous women, characterised by iliac sclerosis that can be associated with bone marrow oedema on MRI in nearly half of cases.[28] Osteitis condensans ilii-related bone marrow oedema is typically localised to the anterior portion of the sacroiliac joint, whereas axial spondyloarthritis lesions predominate in the middle joint portion.[29] The absence of radiographic data in this study precludes definitive identification of osteitis condensans ilii, but the pregnancy association observed is consistent with osteitis condensans ilii epidemiology and reinforces that bone marrow oedema in women frequently reflects mechanical rather than inflammatory pathology.

This study has limitations. The cross-sectional design prevents identifying whether bone marrow oedema persists, resolves, or predicts future axial spondyloarthritis development. Longitudinal follow-up would address these important questions. HLA-B27 status and detailed symptom data were not available, precluding definitive classification of axial spondyloarthritis status in participants with bone marrow oedema. This limitation has bidirectional implications. We cannot exclude subclinical axial spondyloarthritis in some participants, but equally, some individuals—particularly women who experience longer diagnostic delays—might have undiagnosed non-radiographic axial spondyloarthritis. This uncertainty highlights the potential for both overdiagnosis and underdiagnosis when imaging is interpreted without clinical context. Furthermore, this analysis characterised bone marrow oedema presence and volume but did not systematically assess lesion location within the sacroiliac joint as well as structural lesions, largely related to the technical limitations of the obtained imaging in this study. Given that lesion location affects diagnostic specificity, future studies incorporating detailed lesion mapping and simultaneous evaluation of structural lesions could enhance clinical applicability. Regarding methodology, the AI algorithm had good but imperfect concordance with expert readers (mean Dice coefficient 0·79), potentially introducing some misclassification, although the consistency between the expert-read and AI-analysed groups suggests minimal impact on the conclusions. Although recent work has similarly applied deep learning to bone marrow oedema detection in axial spondyloarthritis,[30] supporting the feasibility of automated MRI assessment, external validation in independent populations remains an important future direction. Lastly, we did not have data on the timing of pregnancies relative to MRI acquisition and thus cannot exclude that some women were imaged during the postpartum period, showing higher frequency of bone marrow oedema. However, given the mean age

of the cohort (51·9 years), the majority of parous women would have been many years post-delivery, suggesting that the observed association reflects long-term biomechanical changes rather than transient postpartum oedema.

Sacroiliac bone marrow oedema affects 30% of the general population, approximately 50 times higher than expected axial spondyloarthritis prevalence, with associations with female sex, pregnancy, elevated BMI, and occupational physical demands. These demographic and lifestyle associations indicate that most bone marrow oedema reflects mechanical stress and physiological adaptation rather than inflammatory disease. Recent updates of the MRI definitions in the context of axial spondyloarthritis emphasise the importance of considering lesion morphology, location, and clinical context. These population-based data provide essential reference values for accurate MRI interpretation and support the development of refined diagnostic and classification approaches that integrate patient demographics, bone marrow oedema characteristics, and the presence or absence of structural lesions rather than relying on bone marrow oedema presence alone. These findings could inform future consensus discussions on imaging criteria for axial spondyloarthritis.

Contributors

KB and DP conceptualised the study and supervised the image analysis. CLS, SR, and TK were responsible for data curation, funding acquisition, investigation, methodology, project administration, resources, software, and supervision. AZ, JLV, and KB developed and validated the deep learning models. NK, DP, and TD interpreted imaging data. DP, KB, JLV, and LX did image segmentation. HJWLA, KB, DP, MT, XB, NK, and LCA provided methodological expertise. MT did the statistical analysis. KB, DP, and MT wrote the first draft of the manuscript. KB, MT, AZ, and DP directly accessed and verified the underlying data reported in this manuscript. All authors had full access to all of the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

XB reports grants from Novartis, AbbVie, Celltrion, Janssen, and Moonlake; consulting fees from, support for travelling to meetings from, payments or honoraria from, and participation on advisory boards for AbbVie, Advanz, Alexion, Alphasigma, Amgen, Bristol Myers Squibb (BMS), Cesas, Celltrion, Clarivate, Galapagos, Greywolfe, Johnson and Johnson, Lilly, Moonlake, Novartis, Peervoice, Pfizer, Roche, Sandoz, Springer, Stada, Takeda, UCB, and Zuellig; editorial board membership of *Annals of Rheumatic Diseases*; past presidency of ASAS; and being EULAR President Elect. DP reports research grants from AbbVie, BMS, Lilly, Johnson and Johnson, Novartis, Pfizer, and UCB; consulting fees from AbbVie, Lilly, GSK, Greywolf, Johnson and Johnson, Merck, Moonlake, Novartis, Pfizer, and UCB; speaker honoraria from AbbVie, Canon, Celltrion, Lilly, Globemed, Johnson and Johnson, Novartis, Pfizer, Medscape, Peervoice, and UCB; and serving on the ASAS executive committee and GRAPPA steering committee. FP reports grants from Novartis, Lilly, and UCB; consulting fees from AbbVie, Celgene, Janssen, UCB, and Novartis; speaker honoraria from Amgen, AbbVie, BMS, Celgene, Janssen, Merck Sharp & Dohme (MSD), Novartis, Pfizer, Roche, UCB, Galapagos, Medscape, and Hexal; support for attending meetings from Celgene, Janssen, Pfizer, Novartis, and UCB; participation on data safety monitoring boards or advisory boards from AbbVie, Celgene, Janssen, Novartis, UCB, and Pfizer; leadership or fiduciary roles for ASAS, Y-ASAS, GRAPPA, Y-GRAPPA, EMEUNET, EULAR, DGRh, DEGUM and Rheumazentrum Berlin; and receipt of study materials from Aidian Oy. TD reports grants from Canon MS; speaker honoraria from Canon MS, Lilly, MSD, Novartis, Pfizer, and UCB; and participation on advisory boards for AbbVie, Lilly, and UCB. NK reports speaker honoraria from AbbVie, Pfizer, UCB, Novartis, and PharmaServe–Lilly. HH reports grants from UCB, Novartis, and Sobi; speaker fees from Boehringer Ingelheim, Janssen, MSD, Novartis, Sobi, Roche, Pfizer, and AbbVie; meeting or travel support from AbbVie, UCB, and Novartis; and participation on advisory boards for UCB and Janssen. MP reports meeting or travel support from AbbVie, UCB, Pfizer, and Novartis; and receipt of equipment, materials, or other services from Novartis and AbbVie. VRR reports grants from Pfizer, Lilly, AbbVie, and UCB; and meeting or travel support from Novartis and UCB. JR reports speaker honoraria from Janssen and UCB; and meeting or travel support from AbbVie, Novartis, Janssen, and UCB. K-GH reports consulting fees from AbbVie; speaker honoraria from Novartis, Pfizer, and AbbVie; and stock in BerlinFlame (co-founder). CLS reports grants from Siemens Healthineers; and speaker honoraria from Siemens Healthineers and Bayer Healthcare. JBW reports grants from the German Research Foundation, NAM, and Siemens Healthineers; and consulting fees from Onc.AI. FB reports grants from Bayer Healthcare and Siemens Healthineers; speaker honoraria from Bayer Healthcare; and serving as board member of the German Radiological Society. H-UK reports grants and speaker honoraria from Siemens Healthineers, Philips, and Boehringer Ingelheim; and advisory board participation for Median and Contextflow. KB reports grants from the German Federal Ministry of Research, Technology and Space, Free State of Bavaria (Bayern Innovativ), the Wilhelm Sander Foundation, the Max Kade Foundation, and the EU; speaker fees from Canon Medical Systems and GE Healthcare; and data safety monitoring board participation for Philips (IHI Project IMAGIO). LCA reports grants from the German Federal Ministry of Research, Technology and Space, Free State of Bavaria (Bayern Innovativ), the Wilhelm Sander Foundation, the EU, the TUM Institute of Advanced Studies, and the German Research Foundation. TP reports leadership or fiduciary roles as a member of the NAKO board of directors (unpaid position), who are leading the NAKO study. All other authors declare no competing interests.

Data sharing

This study uses data from NAKO. Data access requests should be submitted to NAKO through their formal application process at https://nako.de/. Proposals will be reviewed by the NAKO data access committee. Upon approval and completion of a data access agreement, data will be shared for the purpose specified in the approved proposal. All code and models created for this project are publicly available at https://github.com/andreasZhukov/DeepSpA-BME-Detection.

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