# Intermuscular adipose tissue and lean muscle mass assessed with MRI in people with chronic back pain in Germany: a retrospective observational study

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## Summary

**Background** Chronic back pain (CBP) affects over 80 million people in Europe, contributing to substantial healthcare costs and disability. Understanding modifiable risk factors, such as muscle composition, may aid in prevention and treatment. This study investigates the association between lean muscle mass (LMM) and intermuscular adipose tissue (InterMAT) with CBP using noninvasive whole-body magnetic resonance imaging (MRI).

**Methods** This cross-sectional analysis used whole-body MRI data from 30,868 participants in the German National Cohort (NAKO), collected between 1 May 2014 and 1 September 2019. CBP was defined as back pain persisting

The Lancet Regional Health - Europe 2025;54: 101323

Published Online xxx https://doi.org/10.1016/j.lanepe.2025.101323

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>3 months. LMM and InterMAT were quantified via MRI-based muscle segmentations using a validated deep learning model. Associations were analyzed using mixed logistic regression, adjusting for age, sex, diabetes, dyslipidemia, osteoporosis, osteoarthritis, physical activity, and study site.

**Findings** Among 27,518 participants (n = 12,193/44.3% female, n = 14,605/55.7% male; median age 49 years IQR 41; 57), 21.8% (n = 6003; n = 2999/50.0% female, n = 3004/50% male; median age 53 years IQR 46; 60) reported CBP, compared to 78.2% (n = 21,515; n = 9194/42.7% female, n = 12,321/57.3% male; median age 48 years IQR 39; 56) who did not. CBP prevalence was highest in those with low (<500 MET min/week) or high (>5000 MET min/week) self-reported physical activity levels (24.6% (n = 10,892) and 22.0% (n = 3800), respectively) compared to moderate (500–5000 MET min/week) levels (19.4% (n = 12,826); $p < 0.0001$). Adjusted analyses revealed that a higher InterMAT (OR 1.22 per 2-unit Z-score; 95% CI 1.13–1.30; $p < 0.0001$) was associated with an increased likelihood of chronic back pain (CBP), whereas higher lean muscle mass (LMM) (OR 0.87 per 2-unit Z-score; 95% CI 0.79–0.95; $p = 0.003$) was associated with a reduced likelihood of CBP. Stratified analyses confirmed these associations persisted in individuals with osteoarthritis (OA-CBP LMM: 22.9 $cm^3$/kg/m; InterMAT: 7.53% vs OA-No CBP LMM: 24.3 $cm^3$/kg/m; InterMAT: 6.96% both $p < 0.0001$) and osteoporosis (OP-CBP LMM: 20.9 $cm^3$/kg/m; InterMAT: 8.43% vs OP-No CBP LMM: 21.3 $cm^3$/kg/m; InterMAT: 7.9% $p = 0.16$ and $p = 0.0019$). Higher pain intensity (Pain Intensity Numerical Rating Scale ≥4) correlated with lower LMM (2-unit Z-score deviation = OR, 0.63; 95% CI, 0.57–0.70; $p < 0.0001$) and higher InterMAT (2-unit Z-score deviation = OR, 1.22; 95% CI, 1.13–1.30; $p < 0.0001$), independent of physical activity, osteoporosis and osteoarthritis.

**Interpretation** This large, population-based study highlights the associations of InterMAT and LMM with CBP. Given the limitations of the cross-sectional design, our findings can be seen as an impetus for further causal investigations within a broader, multidisciplinary framework to guide future research toward improved prevention and treatment.

**Funding** The NAKO is funded by the Federal Ministry of Education and Research (BMBF) [project funding reference numbers: 01ER1301A/B/C, 01ER1511D, 01ER1801A/B/C/D and 01ER2301A/B/C], federal states of Germany and the Helmholtz Association, the participating universities and the institutes of the Leibniz Association.



**Keywords:** Chronic back pain; Muscle composition; Body composition; German national cohort; Physical activity

## Research in context

### Evidence before this study

We conducted a comprehensive search of PubMed, Scopus, and Google Scholar for studies investigating muscle composition in chronic back pain (CBP) using search terms such as "chronic back pain," "muscle composition," "lean muscle mass (LMM)" "intermuscular adipose tissue (InterMAT)", "physical activity," and "pain intensity" up to 31 January, 2025. Prior research showed inconsistent findings regarding the role of muscle composition in CBP, limited by small sample sizes, reliance on non-imaging or X-ray imaging techniques, and region-specific muscle assessments. This highlights the need for large-scale investigations using whole-body magnetic resonance imaging (MRI) and automated segmentation tools for precise muscle composition evaluation.

### Added value of this study

This study analyzed data from 27,518 participants in the German National Cohort (NAKO) using whole-body MRI and automated segmentation techniques. It provides strong evidence linking higher InterMAT and lower LMM to higher symptom burden and increased CBP probability, even after controlling for multiple confounders. A key advancement is the demonstration of synergistic, compensatory and suppressive interactions between LMM and InterMAT for CBP, for which clinical results of the intricate biochemical interplay are lacking. Lastly, the study established muscle composition as a potential imaging biomarker for musculoskeletal health beyond CBP, particularly in conditions such as osteoarthritis and osteoporosis.

### Implications of all the available evidence

Our findings in this large population-based cohort highlight a strong association between LMM and InterMAT with CBP, symptom burden, and musculoskeletal comorbidities. Future research should focus on longitudinal designs to explore causal pathways and underlying biological mechanisms. Assessment of muscle composition, alongside psychological, biomechanical, and lifestyle factors, represents an important component within a multifaceted framework for early risk identification and targeted interventions, potentially mitigating the socioeconomic burden of CBP.

## Introduction

Back[1,2] pain is a leading cause of individuals living with disability worldwide, with approximately 90% of cases classified as the non-specific back pain, lacking an identifiable pathoanatomical cause. CBP, commonly defined as the presence of back pain for at least three months,[1,2] is a debilitating condition with detrimental effects on physical, mental, and social well-being.[3] It affects over 80 million people in Europe,[4] causing a significant burden on individuals through reduced quality of life and disability, and on society through substantial healthcare costs and lost productivity.[5,6] CBP often coexists with musculoskeletal comorbidities[7] such as osteoarthritis and osteoporosis, which complicates treatment by introducing overlapping pain mechanisms. This reinforces the need for personalized management approaches addressing both structural and functional contributors to CBP.[8]

Muscle composition, reflecting both quantity (lean muscle mass (LMM)) and quality has emerged as a key determinant of musculoskeletal health and a potential contributor to CBP.[9,10] Muscle quality can be assessed by fat accumulations, which occur both intra- and intermuscularly. While intramuscular fat[11] refers to lipid accumulation within muscle cells, intermuscular adipose tissue (InterMAT), defined as adipose tissue interspersed between and around skeletal muscle groups,[12] represents true adipose tissue and is widely studied as a parameter of muscle quality. While LMM is typically lower in patients with CBP, findings on InterMAT have been inconsistent.[13]

Previous studies investigating muscle composition in CBP have shown varying associations, yet prospective analyses of the relationship between muscle composition and clinical outcomes remain inconclusive.[14–17] This may be due to limitations such as small sample sizes,[18,19] reliance on planar imaging modalities like DXA[20] and focus on specific regions like the lumbar spine or muscle quantity alone.[21] Recent advances in whole-body magnetic resonance imaging (MRI) and automated segmentation tools now enable large-scale, precise assessments of muscle composition.[22] While whole-body MRI enables comprehensive muscle composition analysis, it is not currently recommended for routine CBP diagnosis. Our study explores whether MRI-derived biomarkers, such as InterMAT and LMM, could contribute to a broader risk assessment framework.

This study investigates the association between MRI-derived muscle composition—specifically, intermuscular adipose tissue (InterMAT) and lean muscle mass (LMM)—with CBP prevalence and symptom burden in a large, population-based cohort. We hypothesized that higher InterMAT and lower LMM would be independently associated with the presence of CBP, even after adjusting for key confounders, including osteoarthritis and osteoporosis.

## Methods

### Study design and participants

This study was conducted under the data access application NAKO-836. The NAKO is a prospective multicenter population study, with more than 205,000 participants aged between 20 and 72, enrolled at 18 centers from 1. May 2014 to 1. September 2019. The study included a subpopulation of 30,868 participants from the NAKO. For all participants whole-body MRI scans were available from five imaging centers.[23] The NAKO was approved by all local institutional review boards of the five imaging sites, and written informed consent was obtained from all participants prior to enrollment. Additionally, approval from the local Institutional Review Board of the Technical University of Munich (2024-479-S-SB; 09/2024) was received.[23]Participants were included if they had complete MRI data and self-reported pain status. Exclusion criteria were applied to remove cases with segmentation failure, missing pain assessment data, or incomplete physical activity records, ensuring data integrity and model reliability (Supplementary Figure S1). Cases with incomplete MRI segmentations or missing covariate data were excluded. Multiple imputation was not used due to the low rate of missing data (<5%)

Collected data included age, sex, race (self-identified by participants), body mass index (BMI), total physical activity (MET min/week), and the presence of diseases associated with CBP (diabetes mellitus,[24] dyslipidemia,[25] osteoporosis (OP) and osteoarthritis[26](OA). Due to data limitations, information on OA localization and severity was not available, restricting stratified analysis to a binary presence/absence classification. Physical activity levels were categorized into low (<500 MET min/week, equivalent to <8.3 MET-hours/week), moderate (500–5000 MET min/week, equivalent to 8.3–83.3 MET-hours/week), and high (>5000 MET min/week, equivalent to >83.3 MET-hours/week), following WHO and ACSM guidelines.[27,28] MRI was performed using 3 T scanners (MAGNETOM Skyra, Siemens Healthineers, Erlangen, Germany) following a standardized protocol.[29] A whole-body T2-weighted HASTE sequence (axial orientation, 5.0 mm slice thickness, voxel size 1.4 × 1.4 × 5.0 mm, echo time 81 ms) was used for segmentation. Image quality was subjectively rated as good or excellent in 97.7% of cases.[30] Participants were classified as having CBP if they reported back pain on most days for >3 months (aligned with NIH Pain Consortium and ICD-11 definitions). No clinical verification of CBP was available, which may introduce reporting bias. Symptom burden was assessed using the Pain Intensity Numerical Rating Scale (PI-NRS), classified as none (0), mild (1–3), moderate (4–6), and severe (≥7). For regression analysis, pain burden was dichotomized into low (none to mild) and high (moderate to severe).

### Procedures

The erector spinae and multifidus muscles (spanning spinal levels T1–S1) were automatically segmented using MRSegmentator, a deep learning-based tool previously validated on NAKO MRI data (DICE-score ≥0.95).[31] A three-component Gaussian-mixture model (covariance: full, initialization method: k-means, max iterations: 1000) was applied to differentiate muscle tissue from intermuscular adipose tissue (InterMAT) following the methodology of Wesselink et al.[32] Fat-water separation techniques, such as Dixon sequences, were not available in the dataset, which may limit sensitivity to intramuscular lipid infiltration. InterMAT was defined as macroscopically visible adipose tissue interspersed between and around skeletal muscle groups, as per the classification of Goodpasture[12] and Gallagher et al.[33] Segmentation masks of intermuscular fat were subtracted from total muscle segmentations to estimate fat-free muscle volume. LMM was defined as fat-free muscle volume normalized to BMI (LMM = muscle volume/BMI), following standard methodologies.[10,34] Percentile-based segmentations are shown in Fig. 1a.

### Statistical analysis

Multivariable mixed-effects logistic regression was used to analyze the association between LMM, InterMAT, and the presence of CBP, adjusting for age, sex, diabetes mellitus, dyslipidemia, OP, OA, physical activity, and study site (included as a random effect). Mixed models were chosen to account for variability across study centers and non-independent observations. Odds ratios (OR) and 95% Wald confidence intervals (CI) were calculated per 2-unit Z-score deviation of LMM and InterMAT. Variance Inflation Factors (VIF) were computed for all covariates, with a threshold of VIF >5 indicating potential collinearity. All VIF scores were below this threshold, suggesting minimal collinearity. All VIF scores are listed in Supplementary Table S2. Combined effects of InterMAT and LMM were evaluated by calculating ORs at Z-scores (–3, –1.5, 1.5, 3). Baseline log-odds were set at Z = 0. For each combination, ORs were computed with 95% CIs derived from the variance-covariance matrix. An interaction term between LMM and InterMAT was explicitly tested. To examine cumulative effects, a nomogram was constructed incorporating all variables from the multivariable model. Nomogram performance was evaluated using the concordance index (c-index), and calibration was assessed via a calibration curve derived from 1000 bootstrap resamples. Stratified comparisons were performed within OA and OP subgroups using independent t-tests to assess differences in InterMAT and LMM. No additional modeling adjustments were made within these subgroups due to sample size limitations. Symptom burden was dichotomized into low (none to mild pain) and high (moderate to severe pain, corresponding to PI-NRS ≥4). Logistic mixed-effects models were used to analyze associations, adjusting for physical activity, OA, and OP. A Bonferroni correction was applied to adjust for multiple comparisons, maintaining an alpha level of $p < 0.05$ across all tests.

### Role of the funding source

The funding sources for this study had no role in the design of the study, collection, analysis, or interpretation of data, manuscript preparation, or the decision to submit the manuscript for publication.

## Results

### Study characteristics

A total of 27,518 participants (55.7% (n = 15,325) men; median age 49 years (range: 41–57 years) were included in the analysis, of whom 21.8% (n = 6003) reported CBP. Participants with CBP were significantly older (median 53 years [IQR 46; 60 years] vs 48 years [IQR 39; 56 years]), more often female (50% vs 42.7%), had a marginally higher BMI (27.1 ± 4.9 $kg/m^2$ vs 26.3 ± 4.6 $kg/m^2$), and higher frequencies of diabetes mellitus, dyslipidemia, OP, and OA. Participants with moderate activity levels had the lowest frequency for CBP (high 24.6%/low 22.0% vs moderate 19.4%, both $p < 0.0001$). Participants with CBP had significantly higher InterMAT (7.3 ± 2.8% vs 6.44 ± 2.32%) and lower LMM values (25.32 ± 6.6 $cm^3/kg/m^2$ vs 26.98 ± 6.62 $cm^3/kg/m^2$). Descriptive characteristics of the cohort are presented in Table 1.

### Association of muscle composition with chronic back pain and symptom burden

We hypothesized that, in addition to the relationship with CBP, InterMAT and LMM correlate with symptom burden. After controlling for covariates, InterMAT (2-unit Z-score deviation = OR, 1.22; 95% CI, 1.13–1.30; $p < 0.0001$) and LMM (2-unit Z-score deviation = OR, 0.87; 95% CI, 0.79–0.95; $p = 0.003$) were independently associated with CBP. Accounting for physical activity, OA, and OP a two-unit increase in the z-score for InterMAT was significantly associated with increased odds of experiencing high symptom burden (OR = 1.17; 95% CI: 1.06–1.28; $p < 0.0001$). Conversely, a two-unit increase in the z-score for LMM was significantly associated with reduced odds of high symptom burden (OR = 0.63; 95% CI: 0.57–0.70; Bonferroni-adjusted $p < 0.0001$).

### Probability of CBP in relation to muscle composition and risk factors

The interaction between InterMAT and LMM was tested and found to be non-significant ($p = 0.552$), suggesting that the effects of InterMAT and LMM on the outcome are independent. Combinations of different age- and sex-adjusted Z-scores for LMM and InterMAT showed

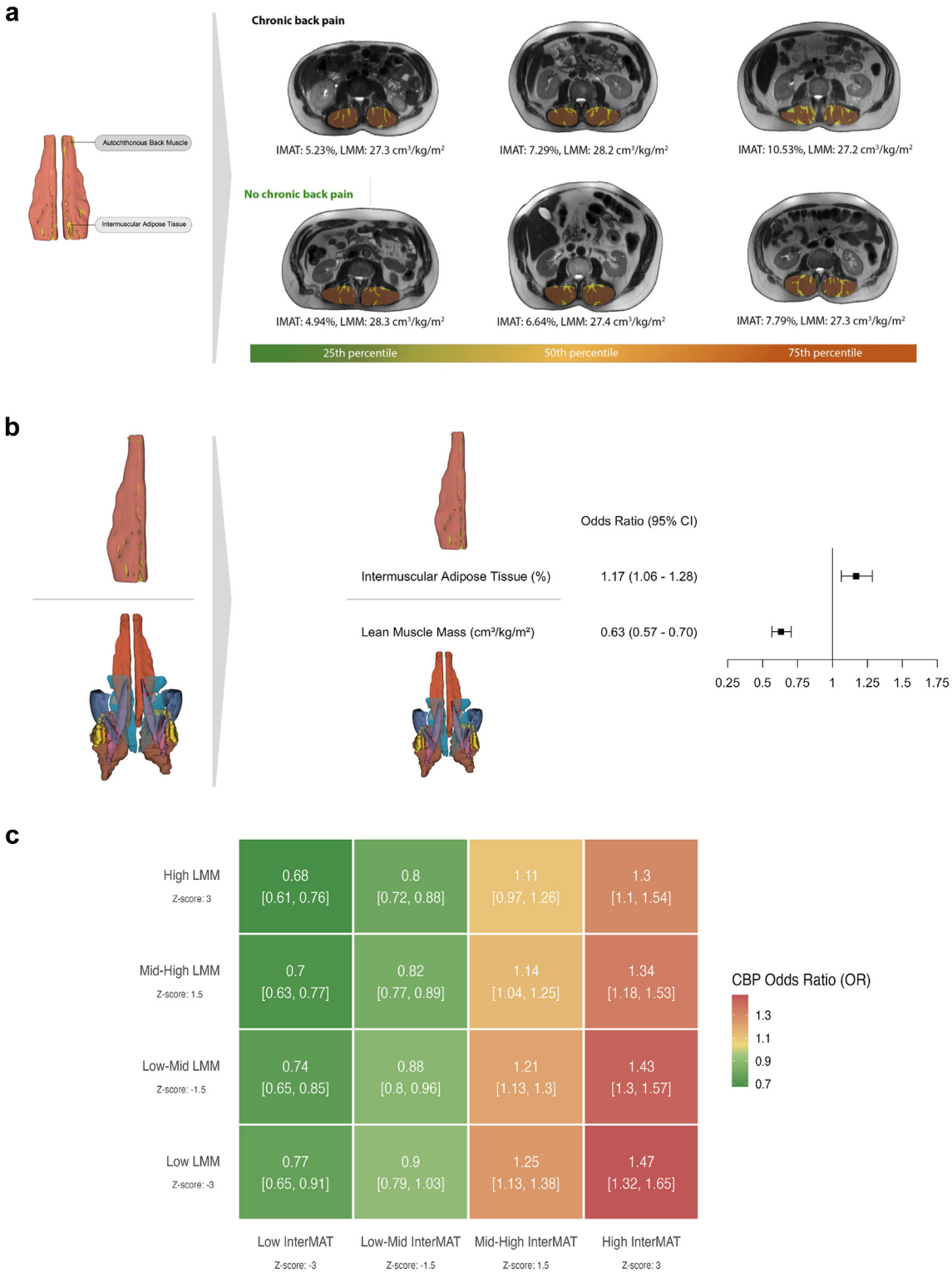


***Fig. 1:*** **MRI-Based Analysis of Intermuscular Adipose Tissue (InterMAT) and Lean Muscle Mass (LMM) in Chronic Back Pain (CBP) using data from the German National Cohort (NAKO).** (a) Representative MRI segmentations of InterMAT (yellow) and LMM (red) in participants with and without CBP, stratified by InterMAT percentiles (25th, 50th, and 75th). For comparability, MR slices corresponding to the L2-3 region were used and participants with similar LMM values were selected. (b) Association of muscle composition with CBP symptom burden.

that unfavorable deviations in both InterMAT and LMM were associated with a substantially higher OR (OR of 1.47 95% CI [1.32, 1.65] for InterMAT Z-Score: +3 and LMM Z-score −3), while favorable deviations in InterMAT and LMM were associated with a substantially lower OR (OR of 0.68 95% CI [0.61, 0.76] InterMAT Z-Score: −3 and LMM Z-score +3) for CBP. Furthermore, results suggest that higher odds of CBP due to low LMM values could be compensated by low InterMAT values (OR of 0.77 95% CI [0.65, 0.91] for InterMAT and LMM Z-score of −3), however, high InterMAT values couldn't be offset by high LMM values (OR of 1.3 95% CI [1.1, 1.54] for InterMAT and LMM Z-score of +3), indicating that synergistic associations exist between InterMAT and LMM. Moreover, the adverse association of InterMAT with CBP does not appear to be substantially mitigated by favorable LMM levels. Heatmap visualization (Fig. 1c) demonstrates that high InterMAT levels are associated with greater likelihood of CBP regardless of LMM levels, while the inverse association between of high LMM is diminished in the presence of excessive InterMAT.

The nomogram visualized in Fig. 2a integrated all variables from the multivariable logistic regression model, providing a practical tool for estimating the probability of CBP. Bootstrap validation yielded a c-index of approximately 0.67 (95% CI: [0.658, 0.675]), indicating moderate discrimination. Calibration was assessed using bootstrapping. The resulting calibration plot (Supplementary Figure S2) demonstrated good agreement between the predicted probabilities and the observed frequencies. Quantitatively, the bootstrap-calibrated secondary logistic calibration model produced an intercept of approximately $-3.33 \times 10^{-15}$ and a slope of 1.00 ($p < 2 \times 10^{-16}$), indicating excellent calibration. Moreover, based on the nomogram, OA and OP emerged as among the most influential factors for CBP.

### Muscle composition as a marker of musculoskeletal health

Due to the substantially increased risk and the frequency of musculoskeletal comorbidities in CBP, a subgroup analysis was conducted for OA and OP. For both comorbidities, significant differences in InterMAT and LMM values were observed depending on the presence or absence of the risk factor (OA InterMAT = 7.15%, LMM = 23.75 $cm^3$/kg/m vs No OA InterMAT = 5.93%, LMM = 26.82 $cm^3$/kg/m; $p < 0.0001$/OP InterMAT = 8.19%, LMM = 21.13 $cm^3$/kg/m vs No OP InterMAT = 6.11%, LMM = 26.37 $cm^3$/$kg/m^2$; $p < 0.0001$). Even within the stratified groups (OA, No OA, OP, No OP), participants with CBP showed significantly higher InterMAT and lower LMM values, except for LMM within the OP group (OP-CBP LMM: 20.9 $cm^3$/kg/m vs OP-No CBP LMM: 21.3 $cm^3$/kg/m; $p = 0.16$). InterMAT and LMM values and descriptive statistics for the subgroups, are summarized in Fig. 2b and Table 2.

## Discussion

In this large, nationwide cohort study, we substantiate findings from smaller studies regarding the association between paraspinal muscle composition and CBP. Specifically, lower LMM and higher InterMAT were independently linked to the presence of CBP, even after adjusting for multiple confounders. Critically, our results support the interdependent relationship between LMM and InterMAT, and demonstrate the relevance of muscle composition within the context of musculoskeletal comorbidities, specifically OA and OP.

The role of imaging in CBP is a subject of ongoing debate, primarily due to the lack of association between degenerative changes of the spine and CBP[35] as well as pain symptomatology.[36] However, paraspinal muscle composition, often overlooked in routine diagnostics, may serve as a non-invasive biomarker for CBP. Lower LMM and higher InterMAT values were associated with the presence of CBP, even after controlling for age, sex, physical activity, BMI, diabetes mellitus, dyslipidemia, OP and OA all of which are typically associated with CBP and with drastic changes in muscle structure. These significant differences also persisted within the stratified groups of OP and OA, both common comorbidities in CBP.[7] Previous research has shown that muscle composition alterations are associated with both spinal and peripheral OA and OP, likely mediated by multifactorial mechanisms.[37–39] Notably, our findings revealed significant differences in muscle composition among participants with these comorbidities, who demonstrated significantly higher InterMAT and lower LMM values. These observations suggest that muscle composition may extend beyond being a specific parameter for CBP to serve as a holistic indicator of musculoskeletal health.

Depending on the extent of the physical activity, significantly different ratios of CBP were found, with

Multivariable logistic regression analysis demonstrated that variations in muscle composition were significantly related to CBP symptom burden, with higher InterMAT linked to increased symptom burden and higher LMM linked to reduced symptom burden, independent of physical activity and musculoskeletal comorbidities. (c) Combinatorial associations of InterMAT and LMM on CBP probability. A heatmap displaying CBP odds ratios for different combinations of InterMAT and LMM Z-scores. Higher InterMAT and lower LMM were associated with greater likelihood of CBP, with a potential synergistic association observed in individuals with both unfavorable parameters. Notably, high InterMAT values were associated with greater likelihood of CBP regardless of LMM levels, while the association between low LMM values and CBP appeared less pronounced when InterMAT values were lower.

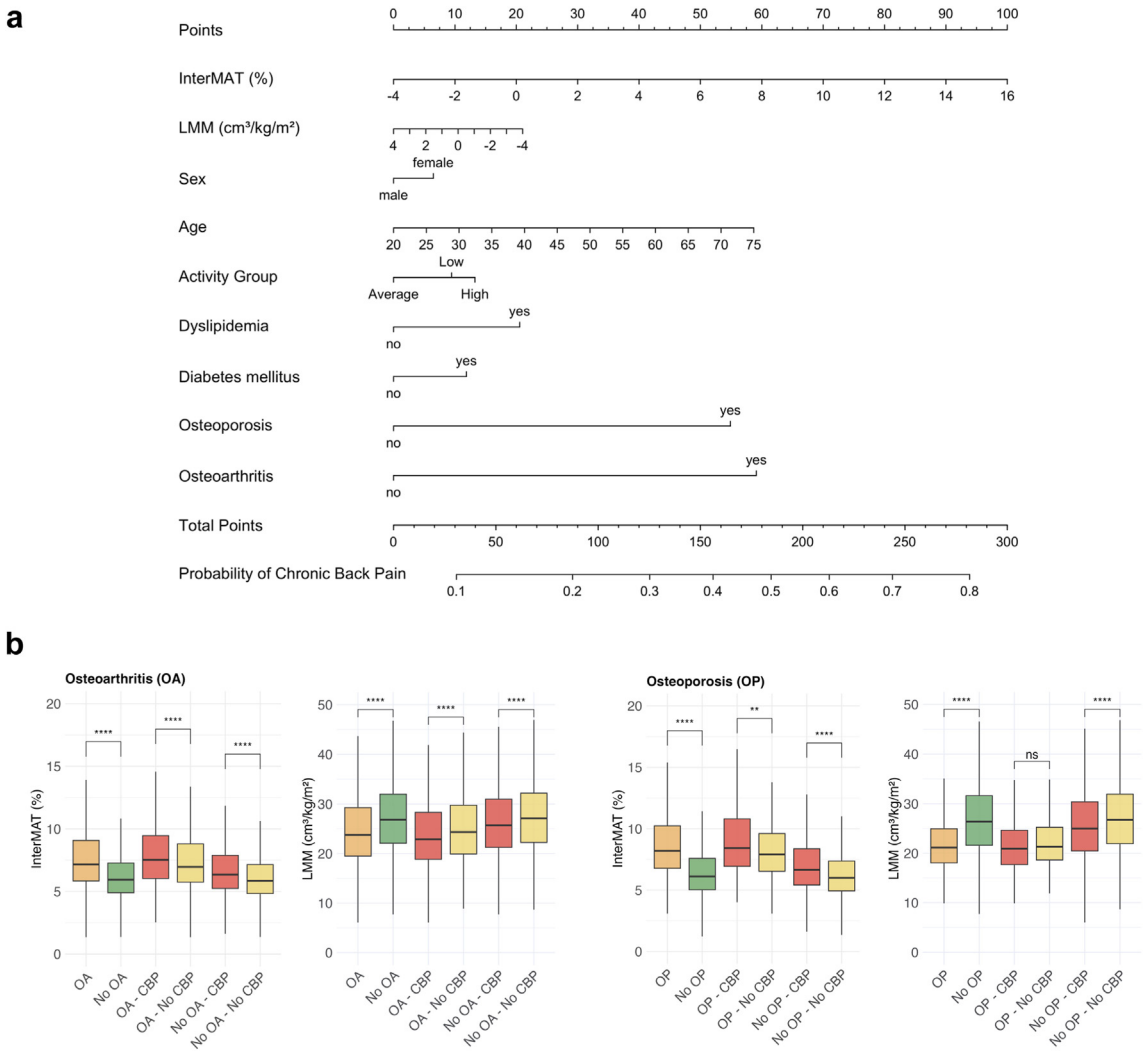


***Fig. 2:*** **Nomogram-based probability estimation and subgroup analysis of muscle Composition in Chronic Back Pain (CBP).** (a) Nomogram for Assessing CBP Probability: This nomogram integrates intermuscular adipose tissue (InterMAT), lean muscle mass (LMM), sex, age, physical activity level, and comorbidities (dyslipidemia, diabetes mellitus, osteoporosis, and osteoarthritis) to estimate an individual's probability of CBP. Each variable contributes a weighted score that is summed to yield an overall estimated probability of CBP. The nomogram is intended to illustrate the associations between these factors and CBP probability without implying direct causation or serving as a clinical decision-making aid. InterMAT and LMM are most strongly associated with CBP, with higher InterMAT and lower LMM being linked to greater probability of CBP. (b) Subgroup Analysis for Osteoarthritis (OA) and Osteoporosis (OP): Boxplots illustrate InterMAT (%) and LMM ($cm^3/kg/m^2$) across different subgroups stratified by CBP presence. Osteoarthritis (OA): Individuals with OA exhibit significantly higher InterMAT and lower LMM compared to those without OA. Among OA patients, those with CBP show further increased InterMAT and reduced LMM (****$p < 0.0001$). Osteoporosis (OP): OP is similarly associated with increased InterMAT and reduced LMM, with significant differences between CBP and non-CBP groups (**$p < 0.0019$ to ****$p < 0.0001$). However, LMM differences between OP-CBP and OP-no CBP are not significant (ns), suggesting a potentially different pathophysiological relationship.

higher percentages for low but also high physical activity, supporting a U-shaped relationship.[40] Despite prior research efforts on the effects of physical activity, the relationship is still unclear. Physically active individuals seem to have back pain less often than physically inactive individuals, but there are divergent results regarding intensity. For example, no significant differences in the frequency of back pain could be shown for low and high intensity.[41] For chronic back pain and chronic back conditions, which are more broadly defined, an inverse correlation between intensity and frequency was found. A possible explanation of our results is the different definitions of high physical activity, which was set at 5000 MET min/week or 83.3

| Characteristic | Chronic back pain (n = 6003) | No chronic back pain (n = 21,515) |
|---|---|---|
| **Age** | Median 53 (IQR 46; 60) years | Median 48 (IQR 39; 56) years |
| **Sex** | | |
| Male | 3004 (50%) | 12,321 (57.3%) |
| Female | 2999 (50%) | 9194 (42.7%) |
| **Race** | | |
| Caucasian | 5555 (92.5%) | 20,181 (93.7%) |
| African | 17 (0.3%) | 79 (0.4) |
| Asian | 19 (0.3%) | 127 (0.6%) |
| Latin American | 6 (0.1%) | 35 (0.2%) |
| Unknown/No response | 406 (6.8%) | 1093 (5.1%) |
| **BMI** | 27.1 ± 4.9 kg/m$^2$ | 26.3 ± 4.6 kg/m$^2$ |
| **Physical activity** | | |
| Average | 2492 (41.5%) | 10,334 (48.0%) |
| High | 2674 (44.5%) | 8218 (38.2%) |
| Low | 837 (13.9%) | 2963 (13.8%) |
| **Diabetes mellitus** | | |
| Missing | 13 (0.2%) | 13 (0.1%) |
| No | 5615 (93.6%) | 20,674 (96.1%) |
| Yes | 374 (6.2%) | 828 (3.8%) |
| **Hyperlipidemia** | | |
| Missing | 51 (0.8%) | 117 (0.5%) |
| No | 4113 (68.5%) | 17,129 (79.6%) |
| Yes | 1838 (30.6%) | 4269 (19.8%) |
| **Osteoporosis** | | |
| Missing | 47 (0.8%) | 33 (0.2%) |
| No | 5653 (94.2%) | 21,192 (98.5%) |
| Yes | 303 (5.0%) | 290 (1.3%) |
| **Osteoarthritis** | | |
| Missing | 50 (0.8%) | 100 (0.5%) |
| No | 3782 (63%) | 18,044 (83.9%) |
| Yes | 2171 (36.2%) | 3371 (15.7%) |
| **LMM (cm$^3$/kg/m$^2$)** | 25.32 ± 6.6 | 26.98 ± 6.62 |
| **InterMAT (%)** | 7.3 ± 2.8 | 6.44 ± 2.32 |

Sex and ethnicity data were collected through participant self-report. IQR, Interquartile Range; BMI, Body Mass Index; LMM, Lean Muscle Mass; InterMAT, Intermuscular Adipose Tissue.

***Table 1:*** **Descriptive statistics.**

| Risk factor | CBP | Count (n) | Percentage (%) | InterMAT | LMM |
|---|---|---|---|---|---|
| Osteoarthritis | | 5542 | 20.14 | 7.15 [5.84–9.08] | 23.75 [19.49–29.26] |
| | No | 3371 | 60.83 | 6.96 [5.75–8.8] | 24.32 [19.91–29.75] |
| | Yes | 2171 | 39.17 | 7.53 [6.03–9.46] | 22.86 [18.82–28.31] |
| No osteoarthritis | | 21826 | 79.32 | 5.93 [4.9–7.27] | 26.82 [22.07–31.97] |
| | No | 18044 | 82.67 | 5.86 [4.83–7.15] | 27.08 [22.24–32.18] |
| | Yes | 3782 | 17.33 | 6.35 [5.24–7.88] | 25.69 [21.24–30.98] |
| Osteoporosis | | 593 | 2.15 | 8.19 [6.78–10.23] | 21.13 [18.04–24.93] |
| | No | 290 | 48.9 | 7.9 [6.54–9.6] | 21.3 [18.63–25.22] |
| | Yes | 303 | 51.1 | 8.43 [6.94–10.8] | 20.9 [17.7–24.62] |
| No osteoporosis | | 26845 | 97.55 | 6.11 [5.02–7.58] | 26.37 [21.6–31.61] |
| | Yes | 21192 | 78.94 | 5.99 [4.94–7.37] | 26.72 [21.92–31.91] |
| | No | 5653 | 21.06 | 6.65 [5.42–8.36] | 24.98 [20.45–30.37] |

CBP, Chronic Back Pain; LMM, Lean Muscle Mass; InterMAT, Intermuscular Adipose Tissue.

***Table 2:*** **Subgroup analysis for osteoarthritis and osteoporosis.**

MET-hours/week, whereas Alzahrani et al.[41] set ≥21 MET-hours/week as the cut-off. In accordance, Fett et al.[42] showed a higher prevalence of back pain in elite athletes than in the active general population. However, it should be emphasized that our study did not differentiate between leisure time and occupational physical activity. This distinction is crucial, as occupational physical activity can often involve repetitive and strenuous movements that may contribute to musculoskeletal issues. Interestingly, individuals with higher symptom burden had lower LMM and higher InterMAT, regardless of the physical activity level. Although this finding underscores the importance of imaging techniques to identify structural changes in CBP, imaging cannot capture functional deficits. Conversely, relying solely on functional assessments like electromyography (EMG) can also be insufficient or even misleading, as EMG may show unchanged or increased muscle activation in CBP.[43] Therefore, a comprehensive evaluation of CBP must integrate both morphological and functional assessment.

Since muscle composition itself can also be modeled[44] through physical activity, our results emphasize that a general recommendation for physical activity is insufficient for CBP. Instead, targeted exercise programs are required, which, given the multidimensional nature of the condition, should ideally be tailored to the individual.[45] While our findings suggest that increasing LMM and reducing InterMAT potentially mitigates CBP symptoms, recent evidence indicates that exercises aimed to improve muscle morphometry, such as motor control exercises, show only modest effects.[14] Consequently, further research is warranted to better define the relationship between targeted exercises, muscle composition, and clinical outcomes in CBP.

The interplay between LMM and InterMAT is complex and can be modeled through various signaling pathways.[46] Our work presents initial findings on the impact of this interplay on clinical endpoints. Besides synergistic associations, which lead to substantially increased or decreased odds ratios for CBP depending on the combination of favorable or unfavorable InterMAT and LMM deviations, InterMAT appears to exert compensatory or suppressive effects on favorable or unfavorable deviations in LMM, respectively. This finding underscores the importance of considering both LMM and InterMAT in conjunction, rather than in isolation, when assessing CBP risk and developing intervention strategies.

Our work has several limitations. Foremost the cross-sectional design only shows associations for InterMAT and LMM and does not allow for causal inference or the identification of underlying mechanisms. The segmentation masks do not differentiate between the multifidus and erector spinae muscles, despite evidence suggesting distinct patterns of involvement in chronic back pain. While the literature

regarding their individual contributions remains inconclusive,[19,47,48] our methodology analyzes these muscles as a combined muscle group. Future research should focus on developing scalable segmentation models to delineate these muscle groups individually and better understand their specific roles in pain mechanisms. Physical activity was assessed via self-report, introducing potential recall bias and desirability bias.[49] For OA, information regarding localization and severity was lacking. Although both spinal and peripheral degenerative changes appear to be associated with alterations in muscle composition, the underlying mechanisms are likely not comparable, which limits the interpretability of our study. Other factors that may influence muscle composition, such as scoliosis, nutritional status, and spinal phenotypes, were not included in the analysis. Additionally, psychological factors and lifestyle factors, such as sleep deprivation, which recent studies suggest can significantly influence pain intensity,[50,51] were not evaluated. Notably, one ultrasound-based study by Pinto et al.[52] found that the association between muscle composition and both pain intensity and disability disappeared when psychological factors were accounted for. However, this study did not assess InterMAT, which may be more relevant given our results. These findings underscore that chronic back pain is a complex, multifaceted condition, and future studies should adopt comprehensive approaches that integrate both biological, psychosocial and lifestyle factors to fully explore its underlying mechanisms.

This study demonstrates the value of incorporating muscle composition assessment into a comprehensive risk evaluation framework for CBP management across Europe. Advanced imaging techniques enable objective quantification of muscle composition. When integrated with psychological, biomechanical, and lifestyle factors, this multifactorial approach can support healthcare systems in developing targeted interventions, such as personalized exercise programs and tailored lifestyle modifications, potentially mitigating the significant economic and societal burden of CBP.

#### Contributors

Conceptualization: SZ, KB, LA; Data curation: FBa, CS, JW, SR, EC, AP, MS, MG, JL,TN,CM; Formal analysis: SZ, HH, CS, FBu, TL; Investigation: HH, FBu, MG, AK; Methodology: SZ, MG, TL, BW; Project administration: KB, LA, MS, DT, TK, AP, MM, MH; Software: HH, KB; Resources: JNK, DT, MM, MH, CS, FBa, JNK, DT, JSM, AP, TP JW, SR, TN; Supervision: KB, LA, MM, MH, BW, MM, MH; Validation: JL, SHK, MG, EC; Visualization: SZ, FBu; Writing—original draft: SZ, HH, KB, LA Writing—review & editing: KB, LA, EC, CM, AK JL, MG, CS, FBa, TL, SHK, TP JNK, DT, AP, SR, MS, TK, TN, BW, JW, JSM, MM, MH. SZ and KB have accessed and verified the underlying data. All authors had full access to all the data in the study, reviewed the final version of the manuscript and had the responsibility for the decision to submit the paper for publication.

#### Data sharing statement

The data underlying this article were accessed from the German National Cohort (NAKO Gesundheitsstudie). Data can be provided by the NAKO data transfer site (https://transfer.nako.de) based on a written request. Requests should be submitted to the GNC data transfer site.

#### Declaration of interests

SZ is a fellow in the TUM School of Medicine and Health Clinician Scientist. DT has received honoraria from Bayer, Germany, Philips, Germany, GE Healthcare. Furthermore, he holds shares in StratifAI GmbH, Germany, Synagen GmbH, Germany. JNK declares consulting services for Bioptimus, France; Owkin, France; DoMore Diagnostics, Norway; Panakeia, UK; AstraZeneca, UK; Mindpeak, Germany; and MultiplexDx, Slovakia. Furthermore, he holds shares in StratifAI GmbH, Germany, Synagen GmbH, Germany, and has received a research grant by GSK, and has received honoraria by AstraZeneca, Bayer, Daiichi Sankyo, Eisai, Janssen, Merck, MSD, BMS, Roche, Pfizer and Fresenius. JL received compensation for delivering an educational lecture at the Forum for Continuing Medical Education (FomF) and received honoraria from AstraZeneca and Novartis. She is a fellow in the TUM School of Medicine and Health Clinician Scientist and the DKTK School of Oncology and received travel grants by the DKTK, the Association for Molecular Pathology Europe Congress and was awarded Google's Gemma Academic Program. BW has received honoraria from Novartis and Philips and has received honoraria by the DFG, Dt. Krebshilfe, NIH, BMBF, BMWi. He holds shares in Need Inc. CLS has received honoraria from Siemens Healthineers and Bayer Healthcare and received research grants from BMBF/DLR and Siemens. TK has received a research grant from the German Federal Ministry for Education and Research (BMBF). LCA is a is an Albrecht-Struppler-Clinician Scientist Fellow, funded by the Federal Ministry of Education and Research (BMBF) and the Free State of Bavaria under the Excellence Strategy of the Federal Government and the Länder, as well as by the Technical University of Munich–Institute for Advanced Study. She is a deputy editor for Radiology Advances. KB has received research grants from the European Union (101079894), Bayern Inovativ, German Federal Ministry of Education and Research, Else Kröner Foundation, Max Kade Foundation and Wilhelm-Sander Foundation and speaker fees from Canon Medical Systems Corporation and GE HealthCare. He is Advisor for the EU Horizon 2020 LifeChamps project (875329) and the EU IHI Project IMAGIO (101112053). TN, CM, AP, FBu, EC, FBa, MG, JSM, JW, TL, MH, MM, SHK, TP, AK, HH, MS and SR have no conflicts to declare.

#### Acknowledgements

This project was conducted with data (Application No. NAKO-836) from the German National Cohort (NAKO) (www.nako.de). The NAKO is funded by the Federal Ministry of Education and Research (BMBF) [project funding reference numbers: 01ER1301A/B/C, 01ER1511D, 01ER1801A/B/C/D and 01ER2301A/B/C], federal states of Germany and the Helmholtz Association, the participating universities and the institutes of the Leibniz Association. We thank all participants who took part in the NAKO study and the staff of this research initiative. Open Access funding enabled and organized by Projekt DEAL.

#### Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2025.101323.

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