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## Accepted Manuscript

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# Paraspinal muscle cross-sectional area predicts low back disability but not pain intensity

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## Abstract

**Background and context:** The lumbar paraspinal muscles, including the erector spinae and multifidus, play an important role in movement and control of the spine. However, our understanding of their contribution to low back pain and disability is unclear. Systematic reviews have reported conflicting evidence for an association between paraspinal muscle size and low back pain, and a paucity of data examining muscle cross-sectional area and low back disability.

**Purpose:** To investigate the relationship between paraspinal muscle cross-sectional area and both low back pain intensity and disability.

**Study design/ setting:** 1-year longitudinal cohort study

**Patient sample:** Participants were selected from the SpineData Registry (Denmark), which enrolls people with low back pain of 2 to 12 months duration without radiculopathy and a satisfactory response to primary intervention.

**Outcome measures:** Current, typical and worst pain in the prior 2 weeks were assessed by 11-point numeric rating scales and an average pain score was calculated, and disability was measured using the 23-item Roland-Morris Disability Questionnaire. Cross-sectional area (CSA, cm<sup>2</sup>) of the lumbar paraspinal muscles was measured at levels L3 to L5 from magnetic resonance images (MRI).

**Methods:** Participants completed the study questionnaires and underwent the lumbar spine MRI at baseline and were followed up 12 months later to repeat the questionnaires. Statistical analyses involved multivariable linear regression (cross-sectional analysis) and linear mixed-models (longitudinal analysis) with adjustment for confounders. Multiple imputation was conducted to account for missing data.

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mixture of private and public funding described in detail previously[1]. The authors have no conflicts of interest to report.

**Results:** A total of 962 participants were included and 588 (65.8%) were followed-up at 12-months. Multivariable analysis showed greater paraspinal muscle cross-sectional area was associated with lower levels of disability, after adjusting for confounders (right mean CSA: baseline beta -0.16, 95%CI -0.26 to -0.06,  $p < 0.01$ ; longitudinal beta -0.11, 95%CI -0.21 to -0.01,  $p = 0.03$ ). This was evident at all levels, except L5 which was marginal at baseline (beta -0.08, 95%CI -0.15 to -0.001,  $p = 0.045$ ) and not significant longitudinally (beta -0.05, 95%CI -0.12, 0.02,  $p = 0.18$ ). However, there were no associations between muscle cross-sectional area and pain intensity (baseline beta -0.02, 95%CI -0.06 to 0.02,  $p = 0.29$ ; longitudinal beta -0.02, 95%CI -0.06 to 0.02,  $p = 0.34$ ). Results were similar for both complete case and multiple imputation analyses.

**Conclusions:** This study found an inverse relationship between lumbar paraspinal muscle cross-sectional area and low back disability, but not pain intensity. While further investigation is needed, these findings suggest that treatment strategies directed at increasing paraspinal muscle size may be effective in reducing low back disability.

Keywords:

Low back pain; paraspinal muscles; low back disability; muscle cross-sectional area; cohort study; multiple imputation

## 1.2 Introduction

Low back pain (LBP) is the most common cause of disability globally[2] and is associated with large direct and indirect economic costs[3]. Structural changes in the lumbar spine, including those involving the inter-vertebral disc[4,5], lumbar fasciae[6–8] and paraspinal muscles[9–11], are believed to contribute to LBP. However, evidence of a direct link between structural changes and LBP is mixed and most episodes of LBP are diagnosed as “non-specific”[3,12]. Given effective treatments are limited, an understanding of specific causes of LBP and potential treatment targets is important.

The paraspinal muscles (i.e. multifidus and erector spinae) play an important role in spinal movement and control[13–15], have been investigated as potential contributors to LBP[9–11,16], and are targeted in rehabilitation for individuals with LBP[17]. Despite this, evidence from two systematic reviews of longitudinal studies indicates that the relationship between lumbar paraspinal muscle morphology and LBP is unclear[9,11]. One review found evidence for an association between reduced multifidus cross-sectional area (CSA) but not erector spinae CSA and LBP[9] and the other found neither multifidus nor erector spinae CSA on magnetic resonance imaging (MRI) to be predictive of future LBP[11]. The majority of studies included in these reviews used a pain scale as their outcome measure, such as pain intensity, frequency or duration, but did not consider disability associated with LBP.

The recent Global Burden of Disease Study found LBP to be responsible for more years lived with disability than any other condition and that disability adjusted life years attributed to LBP increased from 58.2 million in 1990 to 83.0 million in 2010[2]. Moreover, in an Australian study of people presenting for treatment for acute LBP, 88% of individuals reported moderate to severe pain

intensity and 76% reported moderate to extreme interference with daily function[18]. Disability is clearly an important component of LBP, but few studies have examined the relationship between paraspinal muscle size and low back disability. The aims of this study were to investigate the relationship between lumbar paraspinal muscle cross-sectional area and both LBP intensity and disability in a cohort of individuals with LBP over 1 year. We hypothesized that muscle cross-sectional area would be more closely associated with disability from LBP than pain intensity.

### 1.3 Methods

A nested cohort study was conducted within the SpineData registry (Denmark). The registry enrolls patients presenting to the Spine Centre of Southern Denmark for a new episode of care for LBP. Criteria for referral to the Spine Centre include: LBP of 2 to 12 months duration without radiculopathy and without satisfactory response to primary intervention. Typical exclusion criteria such as fracture, cancer or infection were ruled out prior to presentation at the Spine Centre. Additional detail regarding the registry has been described in detail previously [1].

Patients included in the current study were enrolled in the SpineData Registry between September 2013 and October 2014, had completed the SpineData questionnaire at baseline and one year follow up and had lumbar spine magnetic resonance imaging (MRI) available from the local radiology department within 30 days of initial presentation. According to Danish law, the study did not require ethical approval from the Region of Southern Denmark Human Research Ethics Committee (HREC). The letter of exemption is available in Danish from the authors on request. It was also exempt from ethical review by the Monash University HREC (project number: CF15/3054 -2015001289). All patients provided written informed consent for the use of their data [Danish Data Protection Agency, doc.nr. 2008-58-0035-15/22513].

Patient data relating to age, gender, height (cm) and weight (kg) were collected by electronic survey at baseline. Body mass index (BMI,  $\text{kg.m}^{-2}$ ) was calculated from height and weight. LBP intensity and disability were assessed at baseline and 12 month follow up by an electronically administered survey. Current, typical and worst pain in the prior 2 weeks were assessed by 11-point numeric rating scales (NRS: 0-10) and an average pain score was calculated [19]. Disability from LBP was assessed by the 23-item Danish language Roland-Morris Disability Questionnaire (RMDQ)[20] and pain catastrophization was assessed using two validated screening questions (“When I feel pain, it’s terrible and I feel it’s never going to get any better” and “When I feel pain, I feel I can’t stand it anymore”) scored on an 11-point NRS (0-10) [21].

Lumbar paraspinal muscle cross-sectional area (CSA,  $\text{cm}^2$ ) was measured from lumbar spine MRI’s (axial T2-weighted TSE, 1.0 Tesla, TR/TE 3000/120, matrix 224/168, FOV 327, slice width 4mm, interslice distance 1mm, Figure 1) at the inferior endplate of the L3, L4 and L5 levels on both the right and left sides by one blinded investigator (TR) in OsiriX (v5.8.2, Pixmeo SARL, Bernex, Switzerland). Measures at each spinal level were repeated on 15% of the sample and intra-class correlation coefficients (ICC) were calculated. The average CSA from L3- L5 for the left and right sides was calculated for each participant.

Descriptive statistics were calculated for demographic, outcome and clinical variables. The relationships between muscle CSA and LBP intensity, and muscle CSA and disability were analyzed using univariate and multivariable linear regression. Multivariable models were adjusted for known predictors of LBP, i.e. age, gender and BMI. Normality and model fit were assessed using QQ plots of residual and predicted values. Longitudinal analysis was carried out using univariate and

multivariable linear mixed-models with restricted maximum likelihood and a random intercept to accommodate correlation between repeated measurements on the same individual. These were also adjusted for age, gender and BMI.

Data imputation was conducted to account for loss to follow up. Missing outcome values for average pain and disability were multiply imputed by predictive mean matching. The number of replications was determined from the proportion of missing data at follow up. We used an imputation model which included: (i) covariates from the regression model and (ii) established predictors of LBP determined from previous studies[22]. Missing baseline values for covariates (muscle CSA, BMI, and pain catastrophization) were imputed with single imputation using the mean for continuous variables and median for ordinal variables [22]. The type 1 error value was set at 0.05 and all analyses were conducted in STATA (v12.0, SataCorp LP, College Station, Texas, USA).

#### 1.4 Results

Participant characteristics are shown in Table 1. Of the 962 participants recruited at baseline, 588 (65.8%) were followed up at 12 months. The mean (SD) age and BMI of the participants at baseline were 44.2 (10.0) years and 26.9 (4.9) kg.m<sup>-2</sup> respectively. The average paraspinal muscle CSA ranged from 28.5(5.4) at L5 to 29.2 (5.3) cm<sup>2</sup> at the L4 level, with an average of 28.6 cm<sup>2</sup> (4.9) for all spinal levels (i.e. L3- L5). There were differences in muscle CSA between lumbar spinal levels ( $p<0.05$ ) and between sides ( $p<0.05$ ), however, results of regression analysis were similar between the right and left sides, so only results from the right side are presented. Measurement repeatability of muscle CSA was more than 0.96 at all spinal levels (L3 0.99, L4 0.98, L5 0.96). Patient reported outcome measures improved from baseline to follow up: average pain score decreased from 5.9 (2.2) to 4.5 (2.7) ( $p<0.01$ ) and average disability score decreased from 13.2 (5.6) to 9.3 (6.7) ( $p<0.01$ ).

After multiple imputation, all 962 participants were included in the analysis at baseline and follow up. Summary statistics were similar between the complete case and imputed analyses, with regard to gender (proportion of females 54.0 vs 54.3%), age ( $44.2 \pm 10$  vs  $44.4 \pm 10$  years), BMI ( $26.9 \pm 5.0$  vs  $26.9 \pm 4.9$ ) and muscle CSA (average CSA  $28.6 \pm 4.9 \text{ cm}^2$  vs  $28.9 \pm 4.7 \text{ cm}^2$ ). In addition, patient reported outcome measures at baseline and follow up were similar between complete case and imputation analyses with respect to pain (average pain: baseline  $5.9 \pm 2.2$  vs  $5.9 \pm 2.2$ ; follow up  $4.5 \pm 2.7$  vs  $4.5 \pm 2.7$ ) and disability (baseline  $13.2 \pm 5.6$  vs  $13.0 \pm 5.9$ ; follow up  $9.3 \pm 6.7$  vs  $9.0 \pm 6.6$ ).

#### **Association between muscle CSA and low back pain intensity**

The univariate cross-sectional analysis showed no statistically significant associations between mean muscle CSA and average pain intensity at any spinal level (mean muscle CSA  $\beta$  -0.01, 95%CI -0.04 to 0.02,  $p=0.49$ ; Table 2). This was also the case for the multivariable cross-sectional analyses which involved adjustment for age, gender and BMI (mean muscle CSA  $\beta$  -0.02, 95%CI -0.06 to 0.02,  $p=0.29$ ). The direction of the results was consistently negative, the effect size was small ( $\beta$  range -0.01 to -0.03) and  $p$ -values were consistently non-significant ( $p>0.05$ ). Moreover, when multiple imputation was performed, the overall findings did not change (mean CSA  $\beta$  -0.02, 95%CI -0.06 to 0.02,  $p=0.25$ ). The longitudinal multivariable analysis produced similar results, with no association identified between mean muscle CSA and average pain in either the complete case ( $\beta$  -0.02, 95%CI -0.06 to 0.02,  $p=0.34$ ) or imputation analyses (mean CSA  $\beta$  -0.03, 95%CI -0.07, 0.01,  $p=0.13$ ).

#### **Relationship between muscle CSA and low back disability**

Multivariate cross-sectional analyses showed paraspinal muscle CSA was associated with disability from LBP, after adjustment for age, gender and BMI (mean CSA  $\beta$  -0.16, 95%CI -0.26 to -0.06,  $p < 0.01$ , Table 3). This association remained significant for all spinal levels following multiple imputation (mean CSA  $\beta$  -0.16, 95%CI -0.25 to -0.07,  $p < 0.01$ ), with the exception of L5. While the effect size was similar at L5 for the complete case and imputed data, the statistical association between muscle CSA and disability was lost when data were imputed (complete case  $\beta$  -0.08, 95%CI -0.15 to -0.001,  $p = 0.045$ ; multiple imputation  $\beta$  -0.07, 95%CI -0.14 to 0.002,  $p = 0.06$ ). Similarly, the results for the longitudinal analysis showed an association between paraspinal muscle CSA and disability (mean CSA  $\beta$  -0.11, 95%CI -0.21, -0.01,  $p = 0.03$ ) at L3 and L4, but not at L5 (complete case  $\beta$  -0.05, 95%CI -0.12, 0.02,  $p = 0.18$ ). This was also found for the imputed analysis (Table 3).

## 1.5 Discussion

This study found a consistent inverse association between lumbar paraspinal muscle CSA and low back disability, but not LBP intensity, over 1 year in a large sample of Danish adults with chronic LBP. While reduced lumbar paraspinal muscle size at the L3 and L4 spinal levels was associated with greater disability from LBP, this was not the case at the L5 level. These results indicate that smaller paraspinal muscle size is associated with higher levels of disability in people with chronic LBP, and that there is the potential for future research to examine the utility of clinical interventions aimed at addressing lumbar muscle morphology in reducing low back disability.

Our finding that a smaller lumbar paraspinal muscle CSA is associated with greater low back disability is novel. In contrast, a previous 3-year cohort study of individuals aged 70-79 years found an association between physical function and trunk muscle attenuation (i.e. increased fat area to muscle area ratio), but not muscle CSA [23]. The absence of an association between muscle CSA and

physical function may be explained by the older age of the cohort compared to that of the current study (18-60 years). Given the effects of sarcopenia on function accelerate beyond 60 years of age [24], it is possible that age related sarcopenia obviated any association with muscle size. However, consistent with our study findings, a case-control study of individuals undergoing back surgery for spondylolisthesis found decreased psoas CSA is associated with severe lumbar disability [25]. These findings suggest that lumbar trunk muscles play an important in low back disability, with changes in muscle size affecting an individual's capacity for physical movement, which in turn can lead to significant levels of disability. Further studies of muscle size and disability from LBP are needed in chronic LBP populations of a similar age to understand the mechanisms underlying this relationship.

We found no association between lumbar paraspinal muscle size and LBP intensity at any lumbar spine level [9]. Our recent systematic review found evidence for an association between multifidus muscle size and back pain, but only limited evidence for an association with other paraspinal muscles [9]. Similarly, other systematic reviews that investigated the association between muscle size and chronic, acute and recurrent LBP [10], in particular whether muscle morphology predicts LBP [11], reported mixed findings. These conflicting results may be due to studies examining not only pain intensity, but also the frequency [26] and duration [27] of pain. Moreover, it is possible that elements of the pain experience that current pain scales do not capture [28], such as fear of pain [29] and beliefs about pain [30], are associated with muscle morphology [31]. Further studies investigating other elements of the pain experience, such as psychological factors, may assist our understanding of the relationship between muscle size and low back pain.

We found lack of a consistent association between muscle CSA and LBP intensity and disability at L5. This is in agreement with previous studies that reported an association between obesity and lumbar

inter-vertebral disc height [32], and the length of fascia around the paraspinal compartment and high intensity LBP and disability [6] at lumbar levels 1 to 4, but not at L5. These differences may be explained by anatomical and biomechanical differences between L5 and the other lumbar levels. In the current study, muscle measures were taken at the inferior endplate of the lumbar vertebrae and therefore the L5 paraspinal muscle was measured adjacent to the lumbosacral joint (L5-S1). This joint differs anatomically from other lumbar intervertebral joints as it has an exaggerated lordotic angle which increases shear load to the pars interarticulars at this level [33]. Moreover, the relative size of the individual paraspinal muscles changes at this level, such that multifidus is larger than the erector spinae muscles, which are predominantly aponeurotic as they cross the lumbosacral junction. It is possible that anatomical and biomechanical differences at the lumbosacral junction may influence the relationship between muscle size and disability at this level.

This 1 year cohort study was strengthened by use of a prospective, longitudinal design, a large cohort of 962 people and 1 year follow up. Our measures of muscle CSA on MR imaging showed high reliability and we used validated, clinically relevant outcome measures, including the NRS for pain and the RMDQ for disability. The study was limited by a relatively low follow-up rate (65.8%), however, we performed multiple imputation, which included all 962 participants at baseline and follow-up, and found similar results in complete case and imputed analyses. Multiple imputation is an accepted technique that accounts for missing data and allows for the analysis of incomplete data sets[22]. While it is sensitive to departures from missing at random (MAR), as are similar techniques, it is valid under the MAR assumption. We believe MAR is a reasonable assumption in this cohort and thus multiple imputation is valid. In addition, allocation to MRI was not random, however, it was in line with standard practice at the Spine Centre, with some participants having an MRI before presentation (n=307), while the remaining participants were referred for MRI by their treating clinician at the Spine Centre (n= 655). Finally, while primary care practitioners may have provided

participants with various treatments before referral to the Spine Centre, we examined the relationship between muscle CSA and low back pain and disability during a 1 year time period following this referral, suggesting it is unlikely that these prior treatments would affected the results of this study.

This study found an inverse relationship between lumbar paraspinal muscle cross-sectional area and low back disability, but not pain intensity. While further investigation is needed, these findings suggest that treatment strategies directed at increasing paraspinal muscle size may be effective in reducing low back disability. This approach represents an exciting opportunity to improve treatment outcomes and assist in reducing the huge burden of LBP.

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**Table captions**

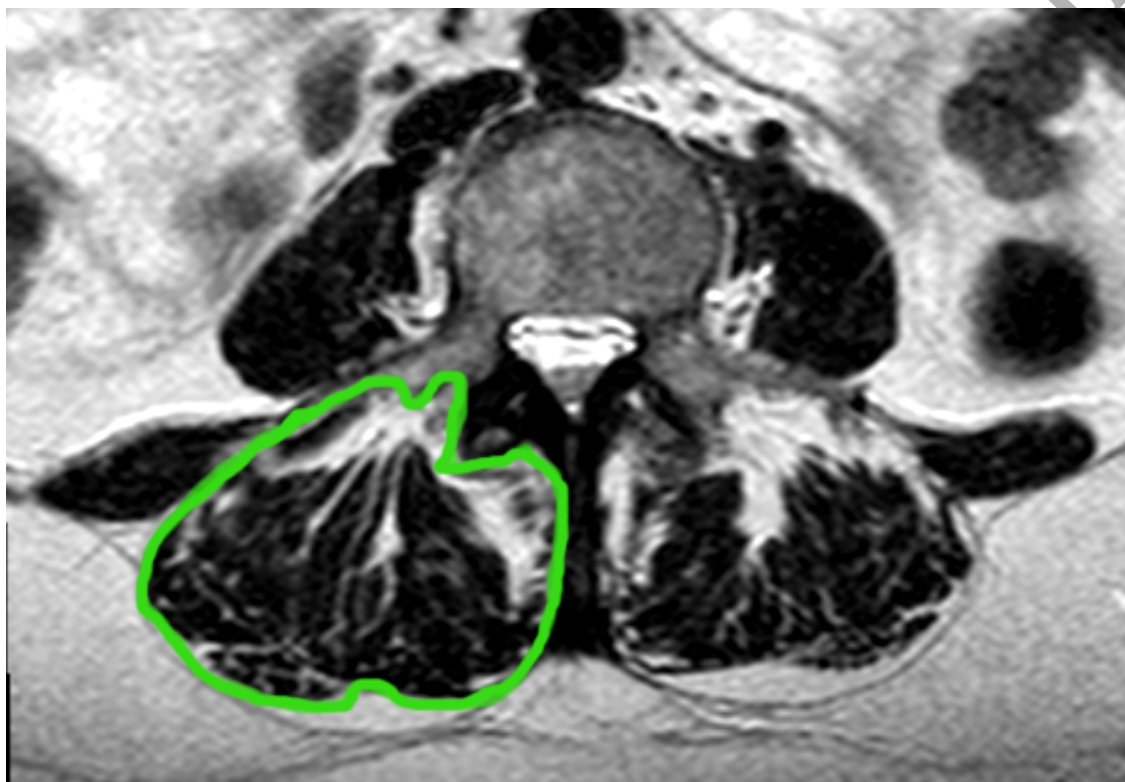
**Table 1.** Participant characteristics at baseline and 1 year follow-up.

**Table 2.** Associations between lumbar paraspinal muscle cross-sectional area and low back pain intensity.

**Table 3.** Associations between lumbar paraspinal muscle cross-sectional area and low back disability.

**Figure captions**

**Figure 1.** Axial lumbar spine Magnetic Resonance Imaging (MRI) showing a measurement trace around the cross-sectional area of the paraspinal muscle.



**Table 1.** Participant characteristics at baseline and 1 year follow-up.

Participant characteristics	Complete case data		Imputed data	
	Baseline (n=894)	Follow-up (n=588)	Baseline (n=962)	Follow-up (n=962)
Females, n (%)	483 (54.0)	337 (57.3)	522 (54.3)	522 (54.3)
Age (years)	44.2 (10.0)	-	44.4 (10.0)	-
BMI (kg.m <sup>-2</sup> )	26.9 (4.9)	-	26.9 (4.9)*	-
Pain catastrophisation 1, median (IQR)	4 (2- 7)	-	4 (2- 6)	-
Pain catastrophisation 2, median (IQR)	3 (1- 5)	-	3 (1- 5)	-
Paraspinal muscle CSA (right side, cm <sup>2</sup> )				
Mean muscle CSA (L3- L5)	28.6 (4.9)	-	28.9 (4.7)*	-
L3 muscle CSA	28.7 (5.6)	-	28.8 (5.3)*	-
L4 muscle CSA	29.2 (5.3)	-	29.3 (5.1)*	-
L5 muscle CSA	28.5 (5.4)	-	28.5 (5.2)*	-
Patient reported outcome measures				
Disability from LBP	13.2 (5.6)	9.3 (6.7)	13.0 (5.9)**	9.0 (6.6)**

Average LBP intensity	5.9 (2.2)	4.5 (2.7)	5.9 (2.2)**	4.5 (2.7)**
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Results presented as mean (standard deviation) except where otherwise indicated

BMI – Body mass index; Pain catastrophisation 1 – When I feel pain, it's terrible and I feel it's never going to get any better (0- 10); Pain catastrophisation2 – When I feel pain, I feel I can't stand it anymore (0- 10); CSA – cross-sectional area; LBP - Low back pain; L3, L4, L5 – lumbar spine level 3, 4, 5

\*Indicates value derived by single imputation

\*\*Indicates value derived by multiple imputation

**Table 2.** Association between lumbar paraspinal muscle cross-sectional area and low back pain intensity

	Univariate analysis (n= 894)		Multivariable analysis* (n=894)		Multivariable analysis with imputed values** (n=962)	
Cross-sectional analysis	Beta coefficient (95%CI)	p-value	Beta coefficient (95%CI)	p-value	Beta coefficient (95%CI)	p-value
Mean CSA	-0.01 (-0.04, 0.02)	0.49	-0.02 (-0.06, 0.02)	0.29	-0.02 (-0.06, 0.02)	0.25
L3	-0.01 (-0.04, 0.02)	0.46	-0.02 (-0.06, 0.02)	0.30	-0.03 (-0.06, 0.01)	0.17

L4	-0.01 (-0.04, 0.02)	0.45	-0.03 (-0.06, 0.01)	0.17	-0.02 (-0.06, 0.01)	0.21
L5	-0.002 (-0.03, 0.02)	0.87	-0.01 (-0.04, 0.02)	0.57	-0.01 (-0.04, 0.02)	0.62
Longitudinal analysis	(n= 588)		(n= 588)		(n= 962)	
Mean CSA	-0.002 (-0.03, 0.03)	0.91	-0.02 (-0.06, 0.02)	0.34	-0.03 (-0.07, 0.01)	0.13
L3	-0.002 (-0.03, 0.02)	0.83	-0.02 (-0.06, 0.02)	0.36	-0.03 (-0.06, 0.01)	0.11
L4	-0.004 (-0.03, 0.02)	0.74	-0.02 (-0.06, 0.01)	0.19	-0.02 (-0.06, 0.01)	0.16
L5	<-0.001 (-0.03, 0.03)	0.99	-0.01 (-0.04, 0.02)	0.42	-0.01 (-0.04, 0.01)	0.32

CSA – cross-sectional area; 95%CI – 95% Confidence Interval; L3, 4, 5 – Lumbar spine level 3, 4, 5; Mean CSA – mean cross-sectional area of L3- 5

\*Adjusted for age, gender and body mass index

\*\* Multivariable model adjusted for age, gender and body mass index. Missing values of outcome variables derived by multiple imputation and missing values of predictor variables derived by single imputation

**Table 3.** Association between lumbar paraspinal muscle cross-sectional area and low back disability

	Univariate analysis (n= 894)		Multivariable analysis* (n= 894)		Multivariable analysis with imputed values** (n= 962)	
Cross-sectional analysis	Beta coefficient (95%CI)	p-value	Beta coefficient (95%CI)	p-value	Beta coefficient (95%CI)	p-value
Mean CSA	-0.07 (-0.15, 0.01)	0.08	-0.16 (-0.26, -0.06)	<0.01	-0.16 (-0.25, -0.07)	<0.01
L3	-0.07 (-0.14, 0.002)	0.06	-0.20 (-0.30, -0.10)	<0.01	-0.17 (-0.26, -0.08)	<0.01
L4	-0.07 (-0.14, 0.003)	0.06	-0.15 (-0.25, -0.06)	<0.01	-0.14 (-0.23, -0.06)	<0.01
L5	-0.05 (-0.12, 0.02)	0.13	-0.08 (-0.15, -0.001)	0.045	-0.07 (-0.14, 0.002)	0.06
Longitudinal analysis	(n= 588)		(n= 588)		(n= 962)	
Mean CSA	-0.002 (-0.08, 0.08)	0.99	-0.11 (-0.21, -0.01)	0.03	-0.12 (-0.21, -0.02)	0.02
L3	-0.003 (-0.07, 0.07)	0.96	-0.14 (-0.23, -0.04)	<0.01	-0.12 (-0.21, -0.03)	0.01
L4	-0.03 (-0.10, 0.04)	0.44	-0.13 (-0.22, -0.04)	<0.01	-0.12 (-0.20, -0.03)	0.01
L5	-0.02 (-0.08, 0.05)	0.66	-0.05 (-0.12, 0.02)	0.18	-0.05 (-0.12, 0.03)	0.22

CSA – cross-sectional area; 95%CI – 95% Confidence Interval; L3, 4, 5 – Lumbar spine level 3, 4, 5; Mean CSA – average cross-sectional area of L3- 5

\*Adjusted for age, gender and body mass index

\*\* Multivariable model adjusted for age, gender and body mass index. Missing values of outcome variables derived by multiple imputation and missing values of predictor variables derived by single imputation