Comparison of standing postural control and gait parameters in people with and without chronic low back pain: a cross-sectional case–control study

Catharine Siân MacRae,1,2 Duncan Critchley,3 Jeremy S Lewis,4,5 Adam Shortland1,7

ABSTRACT

Objective Differences in postural control and gait have been identified between people with and without chronic low back pain (CLBP); however, many previous studies present data from small samples, or have used methodologies with questionable reliability. This study, employing robust methodology, hypothesised that there would be a difference in postural control, and spatiotemporal parameters of gait in people with CLBP compared with asymptomatic individuals.

Methods This cross-sectional case–control study age-matched and gender-matched 16 CLBP and 16 asymptomatic participants. Participants were assessed barefoot (1) standing, over three 40 s trials, under four posture challenging conditions (2) during gait. Primary outcome was postural stability (assessed by root mean squared error of centre of pressure (CoP) displacement (CoP-RMS) and mean CoP velocity (CoP-VEL)), both in the anteroposterior direction; gait outcomes were hip range of movement and peak moments, walking speed, cadence and stride length, assessed using force plates and a motion analysis system.

Results There were no differences between groups in CoP-RMS (P=0.26), or CoP-VEL (P=0.60) for any standing condition. During gait, no differences were observed between groups for spatiotemporal parameters, maximum, minimum and total ranges of hip movement, or peak hip flexor or extensor moments in the sagittal plane.

Conclusions In contrast to previous research, this study suggests that people with mild to moderate CLBP present with similar standing postural control, and parameters of gait to asymptomatic individuals. Treatments directed at influencing postural stability (eg, standing on a wobble board) or specific parameters of gait may be an unnecessary addition to a treatment programme.

INTRODUCTION

Differences in postural control1–4 and gait5–10 have been identified between people with and without chronic low back pain (CLBP). During more challenging standing conditions people with CLBP have demonstrated increased centre of pressure (CoP) displacements and velocities,1–4 indicative of poorer postural stability.11–12 A systematic review investigating difference in standing postural sway between those with and without CLBP reports inconsistent findings.13 Although the majority of studies reported an increased postural sway in people with LBP, evidence from fewer studies, many with larger sample sizes and more robust methodologies, demonstrated no difference between groups.13 Hence, whether a true difference exists remains unclear.

During gait, people with CLBP have demonstrated reduced self-selected walking speed,5–8 stride time,9,10 stride length16 and range of hip movement5 compared with people without back pain. Due to the proposed decrease in stride length, walking speed and hip range of movement, hip joint moments are also likely to be decreased in people with CLBP compared with people without.14 Researchers have proposed that such gait changes may be an attempt by the individual to reduce pain by reducing: ground reaction forces at heel strike;15 excessive muscle activity; or joint movement.16 Alternatively, differences may be a result of altered proprioceptive feedback17 or psychological factors associated with CLBP, such as anxiety, fear avoidance and catastrophising.18 Psychological factors may lead to adaptation of normal physical activities,
such as fast walking, due to the fear of increasing pain. Although gait alterations may initially be protective, such alterations may induce mechanical problems in the long term, for example, a slower walking produces longer periods of loading on the lumbar spine during gait,\textsuperscript{19} which may be detrimental to spinal structures in the long term, whereas shorter periods of loading, thought to be less detrimental, occur during faster walking.\textsuperscript{19, 20}

These differences in postural control\textsuperscript{1–4} and gait\textsuperscript{5–10} have been proposed as contributing factors to the presence and recurrent nature of CLBP.\textsuperscript{1–4, 15} However, previous studies have used: small sample sizes\textsuperscript{2–3} (possibly introducing a type 2 error); methodological design likely to result in low reliability of data, for example, analysing data from one trial instead of multiple trials\textsuperscript{1, 5, 8–9}; outcomes that have demonstrated poor reliability; or provide results not representative of the general population (eg, all or mainly male participants\textsuperscript{8, 9}; or walking on a treadmill as opposed to on normal ground\textsuperscript{2–9, 10}).

This study aimed to add to current research by using a more reliable and valid methodology to determine whether participants with CLBP have similar or different barefoot standing postural control, and gait parameters, when compared with age-matched and gender-matched asymptomatic participants. This methodology has previously been published as part of a randomised trial.\textsuperscript{20} The following hypotheses were investigated:

H₁: The CLBP group will demonstrate greater postural instability when compared with the asymptomatic group during more challenging standing conditions.

H₂: Reduced self-selected walking speed, cadence and step length will be observed in people with CLBP compared with asymptomatic individuals.

H₃: During gait, people with CLBP will present with reduced peak hip extensor moments during stance phase and reduced hip range of movement compared with asymptomatic individuals.

METHODS

This cross-sectional case–control study compared barefoot standing balance and gait data from CLBP participants with that from age-matched and gender-matched asymptomatic participants. This methodology has previously been published as part of a randomised trial.[new ref]

Participant recruitment

A convenience sample of asymptomatic adults was recruited from acquaintances and colleagues of the investigators. Participants with CLBP were recruited from four Physiotherapy Departments in London (UK) (three National Health Service hospitals, one private physiotherapy practice) following clinical referral from general practitioners and consultants as part of a previously reported randomised controlled trial (RCT).\textsuperscript{21} During the second half of the recruitment period of the RCT, 55 participants were asked to participate in the current study, 38 of which showed interest. Eighteen participants could not attend the session in the main due to work commitments. Of the remaining 20 participants, only 16 could be matched by age and gender to our asymptomatic group. Inclusion criteria for symptomatic individuals were: aged 18–65 years, with a 3-month or greater history of LBP. Exclusion criteria were constant non-mechanical LBP, lumbar radiculopathy, known spondylolisthesis, spinal stenosis or inflammatory back pain, specific spinal diagnosis inappropriate for physiotherapy interventions (eg, spinal fracture or infection); any condition inappropriate for exercise physiotherapy (eg, severe cardiovascular or metabolic disease) or for wearing rocker sole footwear (eg, Morton’s neuroma, peripheral neuropathy). Potential asymptomatic participants were contacted via email including the Participant Information Sheet, and were asked to contact CSM if they wished to partake in the study. Asymptomatic participants reported no history of LBP in the last year, were required to meet all other inclusion and exclusion criteria presented above. As increasing age is a contributing factor to poorer postural stability\textsuperscript{22} and gender may influence postural control,\textsuperscript{23} hence potential confounding factors, asymptomatic participants were matched by age and gender to symptomatic participants. An age range of 2 years above or below the age of the ‘matched’ CLBP participant was classed as acceptable. Sixteen asymptomatic participants were consented into the study.

Data collection

Data collection occurred at the ‘One Small Step Gait Laboratory’, Guys’ Hospital, London. Demographic and pain scores (numerical rating scale) representing their level of back pain on the day of assessment were recorded from all participants.

Biomechanical assessment

Participants were assessed wearing short trousers and vest or no top. Participants’ anthropometric measurements (pelvic width; leg length; knee width; ankle width; height; and weight) were recorded to inform the mechanical model formulated for each participant in Vicon’s Nexus (V.1.8.1) motion capture software (Vicon Motions Systems, Oxford, UK). The motion analysis system consisted of seven cameras, capturing retroreflective markers in three-dimensional space at a rate of 120 Hz.

Seventeen infrared reflective markers (14 mm diameter) were positioned on each participant by an experienced researcher (AS).\textsuperscript{24–26} The modified Helen Hayes marker set was implemented\textsuperscript{27} with additional markers on bilateral iliac crests, and posterior calcanei (figure 1).

Postural stability in standing

Participants were assessed barefoot, feet approximately pelvis width apart and on adjacent force plates (FP5000, AMTI, Massachusetts, USA), during four posture challenging standing conditions involving manipulation.
of visual input and support surface: (1) firm surface, eyes open; (2) firm surface, eyes closed; (3) compliant surface, eyes open; (4) compliant surface, eyes closed. Compliant surface was achieved by placing an Airex™ cushion (48.5×40.0×6.4 cm, 0.7 kg, density 38.6 kg/m⁻³, closed-cell foam) (I-group, St Louis, MO) over each force plate (figure 1).

Participants were instructed to keep their eyes focused on a red sticker at eye height on a tripod 3 m in front of them. Participants were assessed for three 40 s trials (shown to produce acceptable reliability) for each standing condition. The middle 30 s of each trial was analysed to avoid possible initial sway errors, effects of participant fatigue or anticipation of a trial ending. Each participant received the same instructions at the start of each trial:

When I say ‘Go’ I want you to stand and maintain your balance until you hear the instruction to rest. Each trial will last for 40 s. Focus on the red sticker on the tripod ahead of you. Keep your arms relaxed by your sides.

A rest period of 20 s occurred between each trial. Sufficient trials were performed to provide three valid sets of data. A test was invalidated if the participant moved their foot position during the test, changed their arm starting position, or opened their eyes during an eyes-closed task.

Assessment of gait
Participants were asked to walk barefoot, at a pace that felt comfortable to them, from one end of the laboratory to the other, in a line which passed over three force plates. Each participant received the same instructions:

When I say go I want you to walk in a straight line to the marker at the other end of the room. Walk at a pace that feels comfortable to you.

Participants continued walking the length of the laboratory until CSM had observed three clear force plate strikes (heel strike and toe-off occurring with the foot making contact with one plate only, without contacting the plate with the contralateral foot) for each foot. The biomechanical assessment lasted approximately 30 min.

Outcome measures
The following postural stability primary outcomes were assessed during standing: (1) root mean squared error and (2) velocity of the CoP in the anteroposterior direction (CoP_RMSAP and CoP_VELAP, respectively, online supplementary appendix 1). CoP is a term that refers to the mean position of the forces acting under the feet at any instant in time. The RMSE (or SD) of the CoP position reflects the spread of these measurements over a particular time interval (in this case 30 s). The CoP_VELAP refers to the mean displacement of the CoP in the anterior-posterior direction, divided by the sample time (1/1080 s) over the course of the 30 s trial. Reliability of CoP_VEL has been reported as excellent (intraclass correlation (ICC) 0.8–0.95) and CoP_RMS reported as fair to good (ICC 0.32–0.58) for studies employing similar number of trials and trial durations as the current study.

The following outcome measures were assessed during gait: self-selected walking speed, stride length, cadence, maximum, minimum and total hip range of movement, peak hip flexor and extensor moments.

Data extraction
Force plate data (forces and moments) captured at 1080 Hz and filtered with a low pass Woltering filter (mean SE 10 mm²) were exported into Vicon’s Nexus software (V.1.8.1) to calculate biomechanical outcome measures.

Industry-standard motion capture files (.c3d) containing force data were extracted. Force plate data were filtered with a low pass (10 Hz) Butterworth filter. CoP parameters were calculated using a proprietary programme written in Visual Basic for Applications (Microsoft Excel, Reading, UK).

Sample size
A sample size calculation was not conducted due to the lack of reported data of minimal clinically important difference (MCID) for the primary outcome measures (CoP parameters). This study aimed to recruit 20 participants.
asymptomatic participants age-matched and gender-matched to symptomatic participants recruited by the authors in a previous RCT.21

Data analysis
Independent t-tests for parametric, or Mann-Whitney U tests for non-parametric data, were applied to determine differences between groups for demographic data and gait outcomes. A mixed-repeated measures analysis of variance with two within-subject factors each with two levels—vision (eyes open and eyes closed) and support surface (firm and compliant)—determined possible significant main effects and interactions of the two groups for CoP variables. The alpha level for determining statistical significance was set at 0.05. Data were analysed using IBM SPSS V.20.0.0 (IBM). Results are presented as means (SD) unless otherwise stated.

RESULTS
Recruitment and retention
During the recruitment period (June 2010 to November 2011), 16 asymptomatic participants were age-matched and gender-matched with 16 CLBP participants. The recruitment of matched asymptomatic participants, over the age of 50 years, who had not experienced LBP over the past 12 months proved difficult. This prevented recruitment of the planned sample size of 20 participants per group. There was 100% retention with all 32 participants completing the data collection process.

Baseline characteristics of participants
Demographic characteristics of CLBP and asymptomatic individuals are presented in table 1. No differences were observed between groups other than self-reported pain scores. Participants with CLBP reported mild to moderate pain with a numerical rating score range of 3–8, and a mean duration of symptoms of 6.17 (SD 7.59, range 0.25–31) years.

CoP parameters during standing
Table 2 presents data for the anteroposterior CoP parameter data for CLBP and asymptomatic participants during different standing conditions. There were no differences between the groups in CoP_{RMSEAP} or CoP_{VELAP} for any of the four standing conditions (F(2.35, 70.38)=1.39, P=0.26, η²=0.04; F(1.76, 52.87)=0.47, P=0.60, η²=0.02, respectively).

Spatiotemporal parameters of gait
No differences were observed between groups for any of the spatiotemporal gait parameters assessed (table 3).

Hip moments and range of movement during gait
No differences were detected between groups for maximum, minimum and total ranges of movement at the hip in the sagittal plane during gait (table 4). No differences were observed between groups for peak hip flexor or extensor moments during gait (table 4).

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Table 2 Anteroposterior centre of pressure parameters for chronic low back pain and asymptomatic participants during different standing conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Asymptomatic (mm)</th>
<th>CoP_{RMSEAP}</th>
<th>Chronic low back pain (mm)</th>
<th>CoP_{VELAP}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes open, firm surface</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>3.76 (0.84)</td>
<td>6.57 (1.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic low back pain</td>
<td>4.21 (1.88)</td>
<td>7.14 (1.52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eyes closed, firm surface</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>3.93 (1.47)</td>
<td>7.14 (1.10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic low back pain</td>
<td>4.23 (1.38)</td>
<td>7.39 (1.24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eyes open, compliant surface</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>8.29 (1.70)</td>
<td>10.97 (1.78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic low back pain</td>
<td>9.10 (2.95)</td>
<td>12.57 (3.96)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eyes closed, compliant surface</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>8.93 (1.45)</td>
<td>17.15 (4.29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic low back pain</td>
<td>10.56 (2.85)</td>
<td>17.98 (4.38)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Summary measures represent means (SD). AP, anteroposterior; CoP, centre of pressure; RMSE, root mean squared error; VEL, velocity.

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Table 3 Spatiotemporal parameters of gait in chronic low back pain and asymptomatic individuals

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Asymptomatic group (m/s)</th>
<th>Chronic low back pain group (m/s)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking speed</td>
<td>1.32 (0.13)</td>
<td>1.25 (0.20)</td>
<td>0.26</td>
</tr>
<tr>
<td>Cadence (steps per minute)</td>
<td>115.14 (6.59)</td>
<td>112.43 (11.81)</td>
<td>0.42</td>
</tr>
<tr>
<td>Stride length</td>
<td>1.38 (0.12)</td>
<td>1.33 (0.13)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Summary measures represent means (SD). Analysis by independent t-test.
Table 4  Sagittal plane hip range of movement and peak hip joint moments during gait in people with chronic low back pain and asymptomatic individuals

<table>
<thead>
<tr>
<th></th>
<th>Asymptomatic</th>
<th>Chronic low back pain</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left maximum hip flexion (°)</td>
<td>34.35 (5.55)</td>
<td>33.70 (8.55)</td>
<td>0.78</td>
</tr>
<tr>
<td>Right maximum hip flexion (°)</td>
<td>34.46 (4.51)</td>
<td>33.82 (9.17)</td>
<td>0.79</td>
</tr>
<tr>
<td>Left maximum hip extension (°)</td>
<td>−9.71 (7.39)</td>
<td>−10.44 (9.02)</td>
<td>0.80</td>
</tr>
<tr>
<td>Right maximum hip extension (°)</td>
<td>−9.40 (6.67)</td>
<td>−9.12 (8.74)</td>
<td>0.92</td>
</tr>
<tr>
<td>Left hip range of movement (°)</td>
<td>44.07 (3.94)</td>
<td>44.14 (4.79)</td>
<td>0.97</td>
</tr>
<tr>
<td>Left hip extensor moment (Nmm/kg)</td>
<td>1029.30 (329.38)</td>
<td>955.80 (429.78)</td>
<td>0.58</td>
</tr>
<tr>
<td>Right hip extensor moment (Nmm/kg)</td>
<td>960.99 (235.24)</td>
<td>1029.57 (460.62)</td>
<td>0.94*</td>
</tr>
<tr>
<td>Left hip flexor moment (Nmm/kg)</td>
<td>−990.76 (184.25)</td>
<td>−1098.07 (231.85)</td>
<td>0.14</td>
</tr>
<tr>
<td>Right hip flexor moment (Nmm/kg)</td>
<td>−1041.87 (174.80)</td>
<td>−977.77 (194.64)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Summary measures represent means (SD).
*Represents Mann-Whitney U test for non-parametric data, otherwise independent t-test conducted.
Nmm/kg, Newton-millimetre/kilogram.

**DISCUSSION**

In contrast to much other research, the current findings suggest that postural control during standing, and the kinetics, kinematics and spatiotemporal parameters of gait do not differ between people with CLBP of a mild to moderate intensity and asymptomatic individuals. There were no differences between people with and without CLBP in postural stability during all standing conditions assessed. During barefoot gait, both groups presented with similar peak hip moments and ranges of movement, and spatiotemporal parameters of gait. Hence, all stated hypotheses are rejected.

**CoP parameters**

There was no difference in postural stability between CLBP and asymptomatic individuals during stable and more challenging standing conditions. These findings differ from previous research1–4 possibly due to methodological variation. della Volpe et al5 assessed a smaller sample size (n=45); however, trials were only repeated once—the current study averaged three trials per condition, likely to increase reliability of data.11 Although Brumagne et al1 assessed a larger sample size (n=12 per group) and although reported significant differences between CLBP and asymptomatic groups during challenging standing conditions, these differences were small (less than 2 mm) and similar to those of both the current study and Brumagne et al’s study.1 Furthermore, Mientjes and Frank3 report a mean pain score of 0.5 in the ‘asymptomatic’ group raising concerns that the asymptomatic data may not be a true representation of a pain-free population.

The CoP parameters assessed in a research study may influence the reliability of results. CoP velocity consistently demonstrates the best overall reproducibility of all CoP parameters in the short and long terms,12 30 hence, findings from this parameter are likely to provide more reliable conclusions to those gained from CoPRMSEAP data or other CoP parameters. The current study demonstrated similar CoPVELAP in people with and without CLBP, whereas previous research has demonstrated reduced5 31 (n=24 and 22 per group, respectively) and increased2 32 33 (n=12, 12 and 10 per group, respectively) CoP velocities. These mixed results suggest it is likely that research demonstrating no difference between groups has been conducted, however, due to publication bias may not have gained acceptance for publication. Interestingly, the studies conducted with the greater sample size demonstrate poorer postural control in the asymptomatic groups, not the CLBP groups. Furthermore, findings from previous research5 31 highlight that the small differences observed between groups in this study may be due to random error associated with the reliability of the measurement technique and not clinical change.

Differences in participant demographics (eg, age, gender32 or disability3) and methodological design (eg, trial duration and repetitions3 30 32) make it difficult to...
directly compare study findings. Due to the numerous factors which may contribute to the variation in CoP outcomes reported, comparison of one study data with another is likely to reveal potential differences; however, choice of outcome measures and the number and duration of trials conducted in the current investigation improves the likelihood that data collected are reliable.

Gait
No differences were detected in spatiotemporal parameters between groups. In support of the current study findings, Al-Obaidi et al and Simmonds and Claveau demonstrated no difference in cadence and self-selected walking speed, respectively, between people with and without CLBP (with a similar age and gender to those in the current study). However, research investigating participants with similar self-reported pain (mild to moderate) to the current study demonstrated reduced walking speed, stride time and stride length in people with LBP. The current study averaged data from three trials for each participant, aiming to improve reliability, whereas other studies analysed data from only one walking trial, possibly reducing data reliability. In addition, where other studies investigated predominantly or all male participants, the current study assessed male and female participants, enabling findings to be more representative of a general population.

In contrast to the current study, previous research has reported reduced hip range of movement in people with LBP during gait compared with asymptomatic individuals. This may be due to co-contraction of muscles crossing the hip and pelvic region limiting hip movement, or from participants reducing step length, and hence hip range, in an attempt to reduce potentially detrimental ground reaction forces at heel strike. Reduced hip range demonstrated by Vogt et al occurred during treadmill gait, hence may not be representative of natural gait. Furthermore, Vogt et al assessed hip range by attaching an electrical goniometer to the greater trochanter. This method of assessment provides less reliable data than the retroreflective marker system used in the current study; again increasing confidence that the current results are likely a more valid representation of gait in CLBP than that reported in previous research.

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Strengths and limitations
The authors did not conduct a formal sample size calculation using MCID data due to the absence of reported MCID data within the literature. However, SEs of measurements from repeatability studies for similar sample populations are reported in the literature for the more reliable postural stability outcome measure of CoP_{VELAP}. If minimal detectable change (MDC) is substituted for MCID in a sample size calculation (where alpha=0.05, beta=0.8, MDC for CoP_{VELAP}=5.4 mm, SD of groups=1.09 and 1.52 where groups contain equal number of participants) this suggests that six participants would need to be recruited.

The authors note the convenience sample recruited in this study for the asymptomatic participants may not be representative of the general population; however, potential asymptomatic participants were required to meet inclusion and exclusion criteria with a view to reducing this potential source of sampling bias. Sampling bias may have been reduced in the symptomatic sample as recruitment of participants occurred more broadly from a population with CLBP in multiple recruitment sites.

Although participants were matched for age and gender, the authors note that unaccounted confounders, such as anthropometric factors, level of physical activity, or kinesiophobia, may have influenced study results. Given the small sample size in the current study, multivariate modelling was deemed inappropriate. Research investigating the influence of anthropometric factors (including body height, limb and trunk length, and body mass) on postural balance concluded postural balance assessed with eyes open and closed is only slightly and moderately influenced by these anthropometric variables; the variables that most influenced postural balance being height and body mass index. The similarity of height and weight between groups in the current study is therefore reassuring.

The current study recruited CLBP participants from clinical populations, who had sought medical opinion regarding their symptoms, hence, represented a typical population treated within physiotherapy departments. Previous research has recruited participants from alternative sources such as university populations, which may not be representative of the subgroup of CLBP individuals who seek medical guidance; hence caution should be taken if relating findings from such studies to a person with CLBP who is attending for treatment.

Further research
The velocity of the CoP is reported as the most reliable CoP parameter; however, it is unclear if this measure is the most appropriate to detect difference in postural stability. Hence, a difference in postural control between the symptomatic and asymptomatic groups may have been present, but not detected. Alternative balance measures could be investigated, such as the forward reach test to determine whether more functional or challenging outcomes possess the necessary discriminatory value to detect differences in balance in people with and without CLBP and assist in confirming whether such differences exist.
Clinical implications

Based on the findings of this study, clinicians can be informed that standing postural stability, kinetic, kinematic and spatiotemporal parameters of gait in people with and without mild to moderate CLBP may not differ, and that treatments directed at influencing postural stability (eg, standing on a wobble board) or specific parameters of gait may be an unnecessary addition to a treatment programme.

CONCLUSIONS

In contrast to previous research, this study suggests that people with mild to moderate CLBP may present with similar standing postural control, hip moments and range of movement, and spatiotemporal parameters of gait to asymptomatic individuals.

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Contributors

CSM, the primary investigator, was involved in all aspects of the study, including methodology, data collection, analysis and interpretation of data, and was the primary author of the article. All authors contributed to methodology, data interpretation and editing of the manuscript for publication. All authors approved the final revision of the submitted manuscript. In addition, JSL received grant funding for the study, AS contributed to data collection. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

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Competing interests

None declared.

Ethics approval

Ethical approval for the recruitment of symptomatic participants (Outer North London Research Ethics Committee (REC: 10/H0724/7)) and asymptomatic participants (King’s College London Research Ethics Subcommittee (BDM/10/11–7)) was gained.

Provenance and peer review

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