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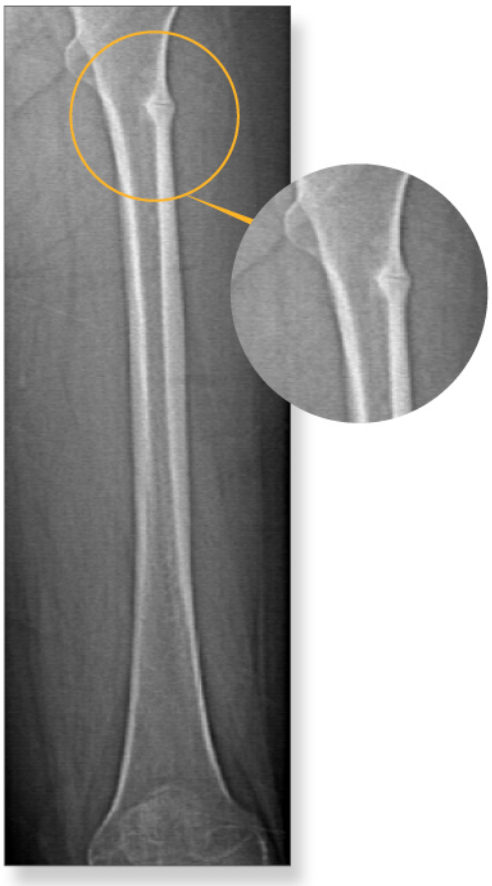

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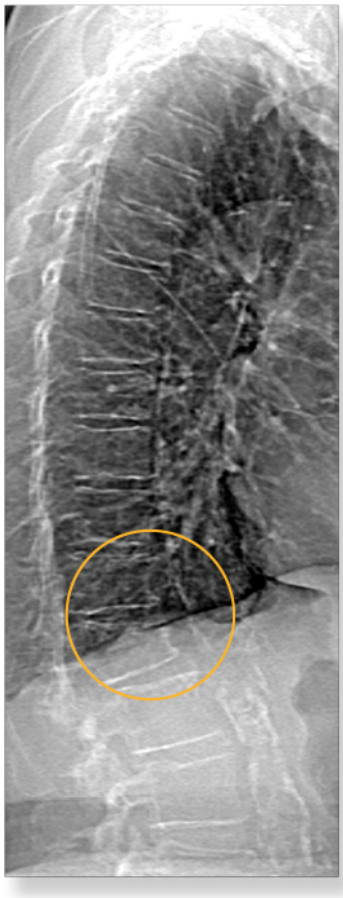

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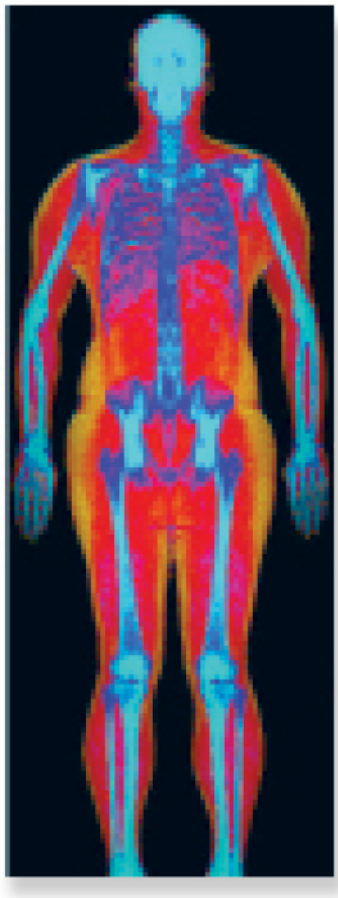

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RESEARCH ARTICLE

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Reduced Peak Bone Mass in Young Adults With Low Motor Competence

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ABSTRACT

Although suboptimal bone health has been reported in children and adolescents with low motor competence (LMC), it is not known whether such deficits are present at the time of peak bone mass. We examined the impact of LMC on bone mineral density (BMD) in 1043 participants (484 females) from the Raine Cohort Study. Participants had motor competence assessed using the McCarron Assessment of Neuromuscular Development at 10, 14, and 17 years, and a whole-body dual-energy X-ray absorptiometry (DXA) scan at 20 years. Bone loading from physical activity was estimated from the International Physical Activity Questionnaire at the age of 17 years. The association between LMC and BMD was determined using general linear models that controlled for sex, age, body mass index, vitamin D status, and prior bone loading. Results indicated LMC status (present in 29.6% males and 21.9% females) was associated with a 1.8% to 2.6% decrease in BMD at all load-bearing bone sites. Assessment by sex showed that the association was mainly in males. Osteogenic potential of physical activity was associated with increased BMD dependent on sex and LMC status, with males with LMC showing a reduced effect from increasing bone loading. As such, although engagement in osteogenic physical activity is associated with BMD, other factors involved in physical activity, eg, diversity, movement quality, may also contribute to BMD differences based upon LMC status. The finding of lower peak bone mass for individuals with LMC may reflect a higher risk of osteoporosis, especially for males; however, further research is required. © 2023 The Authors. *Journal of Bone and Mineral Research* published by Wiley Periodicals LLC on behalf of American Society for Bone and Mineral Research (ASBMR).

KEY WORDS: DXA; OTHER DISORDERS RELATED TO BONE; EXERCISE; FRACTURE PREVENTION; SCREENING

Introduction

Poor motor skills or low motor competence (LMC), which impairs the ability to participate in age appropriate activities of daily living, are a key feature of the neurodevelopmental movement disorder developmental coordination disorder (DCD).[1] LMC in the clinical form of DCD affects about 5% of the population,[1] with prevalence rates in some geographical regions being as high as 20% on standard motor assessments.[2] Typically diagnosed in developing children, this motor

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impairment often persists into adulthood,[3] with studies showing reduced overall health in adulthood for people with LMC,[4,5] including impairment in bone mineral density (BMD).[6] Suboptimal bone mass and geometry increases the risk of osteoporosis and related fragility fracture in later adulthood.[7,8] Accordingly, there is a need to identify factors that increase the risk of secondary osteoporosis, including prior diagnosis of LMC.

The status of bone health in adults with LMC has only been reported once,[6] although findings of bone health deficits in this study are supported by findings of lower bone health throughout childhood and adolescence.[9-13] However, the applicability of these studies is limited by restricted predictive power of early bone measurements.[14,15] Bone measures at the time of peak bone mass, when bone accrual and development ceases, by contrast, are strong predictors of bone health in later life and age of osteoporosis occurrence.[16] The timing of peak bone mass varies by sex and by bone region. Although there is a peak for whole-body BMD of 19.9 (95% confidence interval [CI], 17.4 to 22.4) years in females and 23.1 (95% CI, 20.8 to 25.5) years in males,[17] some sites peak as early as 16 years in females and 18 years in males.[15,18,19] For studies of the LMC community, only Ireland and colleagues'[11] finding of decreased hip BMD and bone structure changes in 17 year olds with LMC has the potential to reflect bone health at the time of peak bone mass. Further verification is thus required as to the presence of bone deficits in LMC populations at the age where peak bone mass would be expected to occur.

Reasons for bone health deficits in individuals with LMC are not well established. One potential cause is lower levels of physical activity in a LMC population[20-24] due to reduced habitual mechanical loading from physical activity underpinning bone formation.[25-27] Bone deficits noted in individuals with LMC are located primarily in load-bearing sites[6,11-13]. However, the relationship between physical activity and bone health changes in individuals with LMC has shown to be weak[11] or nonsignificant.[10] Given that adaptations to bone mass and strength can take up to 12 months to be detectable following exercise,[28] other studies may have provided insufficient time for adaptation and physical activity measures may provide a stronger explanation should physical activity measures be taken from an earlier time point.

The aim of this study was to determine whether there are differences in BMD in young adults with and without LMC, and whether the association between physical activity loading and BMD differs between these groups.

Subjects and Methods

Experimental design

The Raine Study is a prospective multigenerational observational study from Western Australia monitoring growth and development through the lifespan.[29] The current analysis explores the association of LMC status on measures of BMD, as well as the impact of bone loading from physical activity. Participants were grouped based on LMC status via motor competence assessments performed at follow up visits at 10, 14, and 17 years of age. BMD measures were assessed using dual-energy X-ray absorptiometry (DXA) at approximately 20 years of age. Bone loading outcomes were determined from self-reported physical activity recorded at 17 years of age.

Participants

The Raine Study recruited pregnant women (Gen1) expecting to deliver at a maternity hospital in Perth, Western Australia (King Edward Memorial Hospital) between 1989 and 1991. A total of 2900 women were recruited, with 2730 participants giving birth to 2868 children (Gen2) between 1989 and 1992. Gen2 was assessed on 11 occasions since birth at the age of 1, 2, 3, 5, 8, 10, 14, 17, 18, 20, and 22 years. Flow of participants through the study was previously reported by Straker and colleagues.[30] Comparisons of the Raine Study cohort to state government data at five time points found that the cohort was mostly representative of the Western Australian population, but were more likely to be white, first time parents, and unmarried, with births more likely to be complicated and via caesarean section.[29] Attrition analysis found infant characteristics were constant across participants and non-participants at each time point.[30] The original study and follow up studies were approved by the Human Research Ethics Committees at King Edward Memorial Hospital, Princess Margaret Hospital for Children, and the University of Western Australia. Informed consent was provided by Gen1 or another parent, until Gen2 reached 17 years of age at which point they provided consent.

Gen2 participants classified as LMC or non-LMC based upon motor competence testing at visits between 10, 14 and 17 years, and who had a whole-body DXA scan at the 20-year follow-up were included in this analysis. Participants were excluded if they had a medical condition that was likely to be bone-affecting either directly (eg, corticoadrenal insufficiency) or via malabsorption of nutrients (eg, celiac disease), or who were on medication that was bone affecting (eg, anticonvulsants, steroids). The clinical expertise of a pediatric endocrinologist was sought to guide these decisions. To assist in the classification of the LMC group, participants were excluded if they had a cognitive disability that may have affected their motor skills. Participants with a condition that was movement limiting (eg, cerebral palsy) were excluded due to the impact on both motor skills and bone. Exclusion reasons are detailed in Fig. 1.

Assessment measures and tools

Bone measurements

Participants had a single whole-body DXA scan (Norland XR-36; Norland Medical Systems, Inc., Fort Atkinson, WI, USA) at the 20-year follow-up.[31] Scan analysis was performed using built-in software (version 4.3.0) according to the manufacturer's protocol to provide estimates of total body and regional BMD (g/cm^2). The machine was calibrated prior to each scanning session and had an interscan coefficient of less than 2%. BMD measures used for analysis were whole body, head, pelvis, arms, and legs. Legs and arms were analyzed as separate limbs (preferred and non-preferred) due to the potential for loading asymmetry. The preferred limb was identified from the patient's reported preferred hand during motor testing. The head was included to provide a representation of a non-loading site. Data on total body fat mass and lean mass were also obtained from the whole-body DXA scan. Lifetime occurrence of fractures was obtained via self-report on a medical history questionnaire at 17-year and 20-year follow-up.

Motor assessment

Motor performance was assessed using the McCarron Assessment of Neuromuscular Development (MAND), a 10-item test assessing five gross and five fine motor skills.[32] Fine motor skill

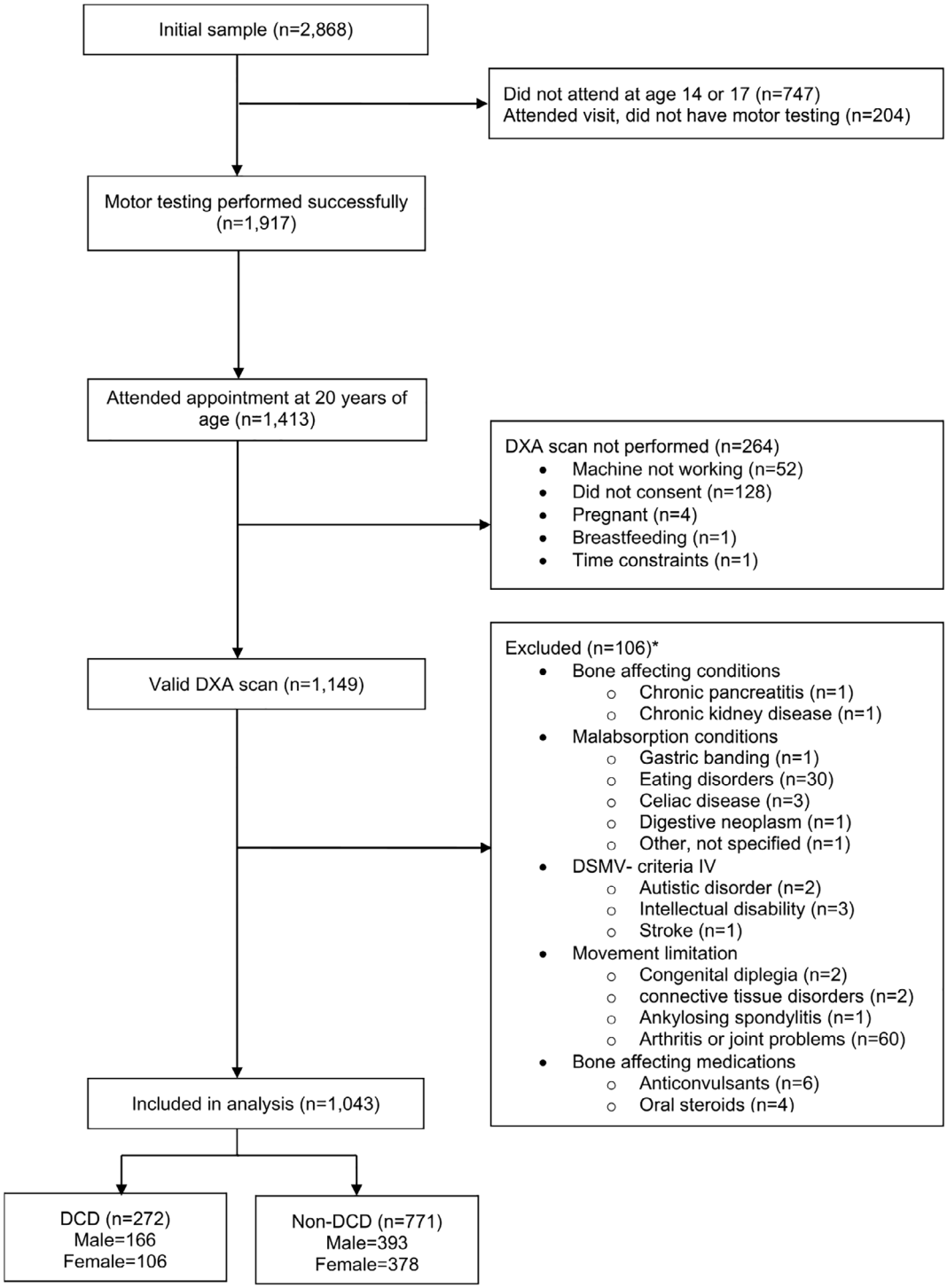

Fig. 1. Participant flow through the study. *Some participants are in multiple categories. DXA = dual-energy X-ray absorptiometry; LMC = low motor competence.

tests involved placing beads in a box within a time frame, threading beads on a row (eyes open and shut), screwing a nut onto a bolt, and sliding an object along a horizontal plane with control (rod slide). Gross motor skill tests involved assessment of hand strength using a dynamometer, the touching of finger to nose with an outstretched finger with eyes open and shut, heel to toe tandem walking, standing broad jump, and balancing on one foot with eyes open and shut.[32] Testing was performed by trained administrators using standardized demonstrations and instructions and following standardized scoring. A senior researcher trained research staff in the MAND protocol for each of the time points, oversaw the data acquisition, and conducted

the data cleaning and normative scoring. Some item scores include marks for the quality of movement as well as the quantity or speed of achievement. MAND has a very high test-retest reliability ($r = 0.99$), and concurrent validity with the Bruininks-Oseretsky Test of Motor Proficiency, a commonly used alternative motor performance test.[33] MAND is validated for individuals aged between 3 and 36 years, although the potential for validity to be impacted by ceiling effects has been identified for older adolescents and adults.[33] Items were scaled for age and summed to produce a total score, the Neuromuscular Developmental Index (NDI). The NDI is normalized with a mean score of 100, and as such individuals were classified as LMC when they had an NDI of lower than 85.[32]

Gen2 participants were tested at the 10-year, 14-year, and 17-year follow-up time points; however, only 66% of participants had complete motor testing at all time points. Twenty five percent (25%) of participants had a change in LMC status between time points, 10% changed classification from LMC to non-LMC and 15% went from non-LMC to LMC. Previous work in the Raine Study cohort found a moderate correlation between NDI scores and *Z*-scores on subsequent follow-up testing.[34] Missing value assessment showed participants who missed at least one measurement had significantly lower NDIs (eg, participants who missed their 10 year follow up had a median NDI of 93.0 at 14 years of age compared to 97.7) and were slightly younger (eg, participants who missed their 10-year follow-up had a median age of 14.1 compared to 14.2 at 14-year follow-up) than those who completed all assessments. In accordance with diagnostic criteria[1] and to avoid the potential for ceiling effects on test items,[33] participants were classified based upon their first available MAND score.

Bone loading

Physical activity levels were assessed via self-report at the Gen2 17-year and 20-year follow-ups, using the International Physical Activity Questionnaire (IPAQ), and via device-assessment using a pedometer (Yamax Digiwalker SW200; Yamax, Shropshire, UK) at the 17-year follow-up visit. IPAQ is a self-report measure that has been developed and tested for use in adults aged between 15 and 69 years.[35] It assesses the frequency, in days, and duration, in minutes, of physical activity over the past 7 days in a range of areas (leisure, occupation, domestic work, transport) and their associated intensities (walking, moderate, vigorous). The total duration spent in each activity's intensity was multiplied by the associated metabolic equivalent of tasks (METs) to obtain scores for walking, moderate and vigorous activities (MET-minute/week), which were summed to create an overall IPAQ score (MET-minute/week).[36] Short-form and long-form versions of the IPAQ were administered with the long form administered at the 17-year follow-up, and the short form administered at 20-year follow-up. IPAQ scores were converted into a loading score to assess the osteogenic potential of the physical activity. This score (effective loading rating over the week) was calculated as the frequency of the activity multiplied by the activity's effective load rating and summed across physical activity areas, using the method detailed by Ng and colleagues.[37] The predictive ability of loading scores on BMD has been assessed in this cohort with an association shown in whole-body and leg BMD.[37] An additional sedentary behavior score in minutes per week was calculated from the total number of minutes spent sitting and lying over the course of a week. Types of activities engaged in were also assessed via self-report of membership to physical activity clubs (sports, exercise, outdoor recreation) at the 17-year follow-up.

For pedometer measurements, the Yamax Digiwalker SW200 was worn on the right hip for 7 days during waking hours. A minimum of 3 valid weekdays and 1 weekend day was required for data inclusion, with a valid day having between 1000 and 40,0000 steps. The Yamax Digiwalker SW200 pedometer has established reliability in distance walked, with a 1% difference between measured distance and actual distance walked and 100% accuracy in number of steps.[38]

Vitamin D status

Participants provided a blood sample for analysis of serum 25-hydroxyvitamin D [25(OH)D] concentration following an overnight fast at the Gen2 17-year and 20-year follow-up. Samples were stored at −80°C until analyzed via liquid chromatography–tandem mass spectrometry (RDDT; vivoPharm Co., Bundoora, VIC, Australia) using an established protocol[39] with confirmed validity and reliability.[40] Because blood samples were collected year-round, results were deseasonalized using a published methodology.[41] Vitamin D was defined as deficient when results were under 50 nmol/L and insufficient at between 50 to 74.9 nmol/L.[42] Vitamin D reflected deseasonalized serum 25(OH)D3 concentration sample at the 20-year follow-up, because serum 25(OH)2 concentrations were rarely detectable in the sample.

Anthropometric and other measures

Weight was measured to the nearest 0.1 kg using calibrated digital scales (Wedderburn Australia, Ingleburn, NSW, Australia) and height measured using a calibrated stadiometer (Holtain, Crosswell, Crymych, UK) to the nearest 0.1 cm at each follow-up visit. Body mass index (BMI) was calculated as weight(kg)/height (m^2). Weight categories were determined based upon National Institution of Health categorizations[43] with overweight being defined as a BMI of 25.0 to 29.9 and obese as being above 30.0. Information on medical history (diagnosis, medication use, accidents or injuries) were collected at the 17-year and 20-year follow-up via questionnaire. Protein (g/d), mineral (calcium, phosphorous, magnesium, potassium, zinc) in mg/d, and alcohol consumption (g/d) was determined from self-report using a semiquantitative Food Frequency Questionnaire at the 20-year follow-up. This questionnaire has been validated in Australia against weighted food records.[44] Puberty data were collected via self-report questionnaires at 14-year and 17-year follow-up appointments. Puberty was assessed via the Tanner stages of pubic hair development for males and females which is a five-stage scale.[45,46]

Statistical analysis

Statistical analyses were performed using IBM SPSS version 26 (IBM Corp., Armonk, NY, USA). Alpha was set at 0.05. Data were assessed to be missing at random. Normality was assessed using Kolmogorov-Smirnov and visual assessment. Because no variable was normally distributed, nonparametric between-group difference tests were performed using Mann-Whitney *U*, and χ^2 tests for medical condition frequency. χ^2 or the standardized test statistic is reported (U). Data are reported as mean (M), standard deviation (SD) and median (Md), interquartile range (IQR) or as proportion (%) in each category.

The relationship between LMC status and BMD (outcome) was assessed using general linear models (GLM). A preliminary model was performed controlling for current sex, age, BMI, and vitamin D status, as well as prior bone loading (fixed effects). Variables for inclusion in this model were established based on literature.[18,25,37,47] The bone loading score derived from the Gen2 17-year follow-up visit was used as the time-point of comparison to BMD at the 20-year follow-up visit due to the established effect of prior habitual physical activity on DXA-derived bone health.[48] BMD measures were log-transformed due to non-normality in residuals,[49] with resulting residuals being normal barring some minor deviation in the tails. Additional models were performed adding a LMC to sex interaction (model two), using a sedentary behavior score rather than the loading score (model three), adding a puberty variable (model four), a LMC to loading interaction variable (model five), and including a body composition variable in the form of lean mass for each body part (model six). Additionally, a simple model including only sex, age, BMI, and LMC status was examined. Estimated marginal means for sex and LMC status were derived from model two. Sex separated models were also examined. All models are described in full in the online Supporting Information (Appendix B).

From model one of the GLMs, BMD at each site were predicted based on loading score at 17-year follow-up, and BMI, age, and serum 25(OH)D levels at 20-year follow-up. These predicted values were graphed in R (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org/) to depict the relationships between bone loading and BMD by sex and LMC status. Likelihood ratio tests indicated that the models were linear and as such data was plotted as a GLM. For visual simplicity, the *x*-axis was truncated at three SD, with the shaded area representing the 95% CI.

Results

Participant characteristics

Of the 1043 participants, 272 (166 male, 106 female) were categorized as LMC. A higher proportion of males were classified as LMC compared to females. LMC participants more frequently chose the left side as their preferred limb compared to non-LMC participants (16.3% compared to 11.1%, $\chi^2 = 4.73$, $p = 0.030$). Both males and females classified as LMC had lower lean mass on DXA than their typically developing peers (Md = 54.1 kg compared to 56.7 and 34.9 compared to 36.3, U = −3.94 and − 2.21, $p < 0.001$ and 0.027, respectively) with females also having a significantly higher fat mass (25.2 kg compared to 23.4, U = 1.97, $p = 0.049$). There were no differences between groups for age or BMI; however, a significantly higher frequency of participants classified as LMC were in an overweight or obese category (24.1% compared to 20.8% and 14.3% to 8.7% respectively, $\chi^2 = 9.70$, $p = 0.021$).

Between-group differences for variables with the potential to affect bone outcomes are detailed in Table 1. Significant differences were seen in vitamin D status and physical activity. Lower levels of serum 25(OH)D were seen at 20-year follow-up (U = −2.90, $p = 0.004$), with a lower proportion of participants classified as LMC having sufficient vitamin D status (above 75 nmol/L) at both time points (17 years: 44.5% versus 47.2%, $\chi^2 = 5.49$, $p = 0.064$; 20 years: 33.8% versus 45.8%, $\chi^2 = 11.44$, $p = 0.003$ respectively). Sex-specific analysis of height differences found that LMC males were significantly shorter at 17-year follow-up compared to non-LMC (Md = 176.0 cm [IQR: 171.4 to 182.1] compared to Md = 178.4 cm [IQR = 174.1 to 183.4], U = −3.02, $p = 0.003$) with no significant difference at 20-year follow-up. Puberty analysis showed a lower frequency of puberty category five (full maturity) at the age of 17 years for the LMC group (78.6% compared to 88.4%, $\chi^2 = 6.86$, $p = 0.032$). No significant differences were observed between motor competence groups on health measures that may have impacted physical activity (depression, anxiety, joint problems, back or neck pain, respiratory problems) or usage of potentially bone affecting medication such as hormonal contraceptives. The only significant difference in dietary intake was in alcohol consumption with individuals with LMC consuming less (7.2 g/d compared to 10.8 g/d, U = −3.13, $p = 0.007$). For physical activity variables, detailed in Table 2, the only significant differences found at the 17-year follow-up were a lower level of moderate physical activity (Md = 15.0 compared to 30.0 in non-LMC, U = −2.03, $p = 0.042$) and lower frequency of moderate and vigorous physical activity engagement in the last week for the LMC group (42.4% and 33.5%, respectively, for LMC compared to 53.9% and 46.1% for non-LMC, $\chi^2 = 7.66$ and 4.48, $p = 0.006$ and 0.034). For the 20-year follow-up visit the only significant difference in physical activity was a lower level of moderate physical activity (Md = 20.00 compared to 30.00, U = −2.02, $p = 0.004$) for individuals with LMC. Membership of sports clubs was lower by 9% for the LMC than the non-LMC group ($\chi^2 = 3.90$, $p = 0.048$), but there was no significant differences in exercise club or outdoor recreation club membership. Expanded information on demographic and physical activity differences are presented in Table A1 (Appendix A) with differences by gender in Tables A2 and A3.

Differences in bone measures by motor competence status

Between-group difference tests on bone measurements showed significantly lower bone measures for males with LMC. No significant differences were seen in females, except for the preferred arm with a deficit of 0.021 g/cm^2 for LMC females compared to non-LMC (U = −2.33, $p = 0.020$) (Table 3). Between-group difference tests did not show an increased frequency of fractures for individuals with LMC ($p = 0.903$). In the whole sample, when controlling for sex, age, BMI, vitamin D status, and bone loading, LMC status showed a significant estimate of effect for all measured regions except the head (Table B1 of Appendix B). Simple models, controlling only for the effects of age, sex, and BMI showed a larger regression β coefficient than were seen when vitamin D status and bone loading were also controlled for, except in the models for the head and non-preferred leg (Table B2). The relationship was such that individuals with LMC had lower BMD at these regions compared to non-LMC individuals, that would be equivalent to a 0.024 g/cm^2 difference for a whole-body BMD between LMC and non-LMC males. Additional models controlling for the lean mass showed a significant estimate of effect only for the preferred arm and non-preferred leg (Table B3), whereas models controlling for puberty did not impact on the findings for LMC status (Table B4).

Models including a LMC by sex interaction showed a significant estimate of effect for the LMC by sex interaction in the models for the legs only (Table B5). Examination of estimated marginal means indicate that differences in scores by LMC status were confined to males. This effect was particularly noticeable in BMD for the whole body, pelvis, and both legs (Fig. 2). This relationship was not seen for the non-bone loading site of the head.

Table 1. Participant Characteristics at 17 and 20 Years

	17 years				20 years			
	LMC M (SD) [Md] {IQR}	Non-LMC M (SD) [Md] {IQR}	U	*p*	LMC M (SD) [Md] {IQR}	Non- LMC M (SD) [Md] {IQR}	U	*p*
Participant characteristics								
Height (cm)	172.1 (8.7) [172.0] {166.4 to 178.0}	172.7 (8.9) [172.2] {165.8 to 178.9}	−0.61	0.542	173.3 (9.0) [173.0] {167.0 to 180.0}	172.7 (9.4) [172.5] {165.4 to 179.7}	−1.00	0.315
BMI (kg/m^2)	22.8 (4.4) [22.0] {19.8 to 24.6}	22.4 (3.7) [21.8] {20.0 to 23.9}	−0.5	0.610	24.6 (5.0) [23.5] {21.2 to 26.6}	23.9 (4.3) [23.2] {21.0 to 25.7}	−1.55	0.121
Total number of injuries	0.6 (1.0) [0.0] {0.0 to 1.0}	0.7 (1.3) [0.0] {0.0 to 1.0}	−1.66	0.097	0.4 (0.8) [0.0] {0.0 to 1.0}	0.5 (0.8) [0.0] {0.0 to 1.0}	−0.85	0.394
Total fat mass (kg)					21.2 (10.5) [19.7] {12.5 to 28.0}	20.4 (9.7) [18.7] {13.3 to 25.3}	−0.73	0.467
Total lean mass (kg)					46.7 (1.2) [47.8] {37.0 to 55.4}	46.2 (11.7) [44.0] {35.8 to 56.4}	−0.47	0.639
Vitamin levels								
Deseasonalized 25(OH)D3 (nmol/L)	73.0 (26.1) [71.0] {55.4 to 86.3}	75.8 (24.8) [73.6] {58.7 to 89.3}	−1.64	0.100	70.1 (24.6) [68.3] {53.2 to 81.9}	74.6 (23.2) [72.7] {58.7 to 88.5}	−2.90	0.004
Dietary intake								
Protein (g/d)					106.0 (81.1) [88.4] {67.6 to 121.1}	103.6 (59.1) [92.2] {66.5 to 124.0}	−0.43	0.670
Calcium (mg/d)					947.2 (488.1) [842.2] {647.9 to 1147.0}	912.0 (396.0) [850.0] {638.1 to 1098.1}	−0.07	0.948
Alcohol (g/d)					15.5 (19.8) [7.2] {1.6 to 23.4}	17.7 (19.1) [10.8] {3.8 to 24.5}	−3.13	0.002
	%	%	χ^2	*p*	%	%	χ^2	*p*
Health								
Diagnosis								
Asthma	29.4	28.9	1.1	0.787	19.0	17.0	1.5	0.693
Back pain	8.5	11.0	2.9	0.412	11.7	13.1	0.8	0.859
Neck pain	4.2	5.5	1.1	0.798	4.8	6.0	3.9	0.273
Attentional problems	7.5	3.2	10.0	**0.019**	5.2	3.7	2.5	0.478
Any accidents or injury since last follow-up	38.3	44.7	2.6	0.106	29.2	32.9	1.0	0.320
Medication use								
Any prescription medication use in last 6 months	50.2	55.9	2.1	0.149	52.1	58.1	2.3	0.127
Oral contraceptives	22.7	32.5	3.9	0.146	41.7	47.8	2.5	0.282
Roaccutane	1.0	3.6	2.2	0.326	1.9	3.2	1.8	0.411
Other medication	7.3	2.5	6.8	**0.034**	4.7	5.0	0.4	0.828
Any nonprescription medication use in the last 6 months	72.5	73.2	0.0	0.847	28.3	20.8	5.1	**0.023**
Antacids	0.0	0.4	0.7	0.724	0.0	0.4	0.6	0.743
Vitamins	23.6	31.8	3.8	0.148	5.3	10.2	3.4	0.186

Abbreviations: LMC = low motor competence. M = mean, SD = standard deviation, Md = median, U = Mann Whitney U standardized score.

Analysis where models were split by sex showed that LMC had a significant estimate of effect in males for whole body BMD ($p = 0.003$), pelvis BMD ($p = 0.005$), preferred ($p < 0.001$) and non-preferred leg BMD ($p < 0.001$), and preferred ($p = 0.005$) and non-preferred arm BMD ($p = 0.015$) similar to what was demonstrated in the whole group model (Table C1 in Appendix C). However, this was not demonstrated in the models for females (Table C2). Using the male only model, the deficit in whole-body BMD in LMC males is equivalent to a 0.033 g/cm^2 deficit when compared to typically developing males. For females, the only model in which LMC showed a significant estimate of effect was for the right arm ($p = 0.003$). Puberty status did not affect these results (Tables C3 and C4), however, models that controlled for lean mass showed a significant effect for DCD status on BMD was confined to the models for BMD in the pelvis and both legs (Tables C5 and C6).

Table 2. Physical Activity Differences Based Upon LMC Status

	17 years old				20 years old			
	LMC M (SD) [Md] {IQR}	Non-LMC M (SD) [Md] {IQR}	U	*p*	LMC M (SD) [Md] {IQR}	Non-LMC M (SD) [Md] {IQR}	U	*p*
Physical activity								
Walking (minutes/d)	65.5 (69.8) [30.0] {0.0 to 120.0}	60.0 (63.1) [30.0] {10.0 to 120.0}	−0.28	0.782	83.4 (68.6) [60.0] {25.0 to 180.0}	73.8 (62.3) [60.0] {30.0 to 120.0}	−1.13	0.257
Moderate activity (minutes/d)	44.3 (60.2) [15.0] {0.0 to 60.0}	53.3 (64.3) [30.0] {0.0 to 87.5}	−2.03	0.042	50.6 (61.9) [20.0] {0.0 to 75.0}	60.2 (65.2) [30.0] {0.0 to 120.0}	−2.02	0.044
Vigorous activity (minutes/d)	53.4 (64.1) [30.0] {0.0 to 90.0}	58.6 (60.6) [45.0] {0.0 to 90.0}	−1.71	0.088	59.7 (64.9) [42.5] {0.0 to 120.0}	62.4 (60.6) [60.0] {0.0 to 90.0}	−1.02	0.306
IPAQ total score (METs/week)	4229.1 (4434.3) [2467.0] {1078.5 to 6168.0}	4302.0 (4051.6) [3099.0] {1593.0 to 5514.0}	−1.73	0.079	3536.9 (4200.4) [2125.5] {560.0 to 4320.0}	3644.6 (3623.4) [2520.0] {933.0 to 5040.0}	−1.69	0.092
Loading score (ELR/week)	148.7 (176.9) [71.4] {4.40 to 238.9}	157.4 (154.9) [113.5] {17.6 to 248.3}	−1.83	0.067	159.7 (140.7) [139.2] {15.6 to 276.5}	170.5 (133.7) [166.2] {56.2 to 275.0}	−1.33	0.185
Sedentary behavior (minutes/d)	1820.8 (385.5) [1800.0] {1530.0 to 2040.0}	1820.8 (370.1) [1800.0] {1620.0 to 2040.0}	−0.98	0.326				
Pedometer total (steps/d)	9564.3 (3192.5) [9303.0] {7002.0 to 12078.8}	9771.6 (3893.9) [9717.9) {7063.0 to 11528.3}	−0.16	0.876				

	%	%	χ^2	*p*
Performed moderate activity for leisure	33.5	42.1	4.48	**0.034**
Performed vigorous activity for leisure	42.4	53.9	7.66	**0.006**
Sports club membership	21.3	30.3	3.90	**0.048**
Exercise club membership	13.4	15.5	0.34	0.560
Outdoor recreation club membership	14.2	12.8	0.15	0.696

Abbreviations: ELR = effective loading rating; LMC = low motor competence; M = mean; Md = median; METS = metabolic equivalent of tasks; SD = standard deviation; U = Mann Whitney U standardized score.

Association between physical activity and BMD

Loading score showed a significant estimate of effect within the models for total BMD ($p = 0.001$), pelvis BMD ($p < 0.001$), and BMD at the preferred ($p = 0.002$) and non-preferred legs ($p < 0.001$), and preferred ($p < 0.001$) and non-preferred arms ($p = 0.008$). This relationship was such that a LMC female with mean characteristics but a loading score at the 25th percentile would have a whole-body BMD 0.020 g/cm^2 lower than would be seen in a female with the same characteristics but a loading score at the 75th percentile. Models for sedentary behavior (Tables B6–B8) did not show a significant estimate of effect for sedentary behavior for the whole group; however, β coefficients for LMC status were similar to that seen in the loading models.

The models for BMD in the whole body, pelvis, legs, and arms show an increase in BMD as loading levels increase for all groups, except for females with LMC, who show no increase in the pelvis and a decrease with increased loading in the arms. Graphs depicting the impact of loading on BMD outcomes, detailed in Fig. 3, showed a differing effect by LMC status and sex. More variability can be seen in females as a group compared to males. More variability is also present for males with LMC than typically developing males. In spite of differences by loading scores, males without LMC had significantly higher BMD than those with LMC, a difference that was not seen in females. Although a sharper increase in BMD with increased loading can be seen for the non-LMC group of both sexes than is seen in the LMC group, the difference based on LMC status is smaller than if observed by sex. Models designed to verify these results by including a LMC by loading interaction effect found no significant contribution from this variable (Table B9 with gender-specific models in Tables C7 and C8).

Furthermore, although the models for males showed a significant estimate of effect for loading for BMD for the whole body ($p = 0.011$), pelvis ($p = 0.005$), preferred ($p = 0.015$) and non-preferred leg ($p = 0.012$), and preferred ($p < 0.001$) and non-preferred arm ($p = 0.039$), loading did not show an estimate of effect for females. In models where lean mass was controlled for loading scores were no longer significant for the non-preferred arm. Models for sedentary behavior showed a significant estimate of effect in the preferred arm for males ($p = 0.001$) (Table C9), and pelvis for females ($p = 0.027$) (Table C10) which was unaffected by puberty (Tables C11 and C12) and lean mass (Tables C13 and C14). These effects were such that BMD decreased in males with increasing sedentary time but increased for females.

Table 3. Unadjusted between Group Differences for Dual-Energy X-ray Absorptiometry Measures

	Male				Female			
	LMC ($n = 166$) M (SD) [Md] {IQR}	Non-LMC ($n = 393$) M (SD) [Md] {IQR}	U	*p*	LMC ($n = 106$) M (SD) [Md] {IQR}	Non-LMC ($n = 378$) M (SD) [Md] {IQR}	U	*p*
BMD (g/cm^2)								
Total body	1.087 (0.112) [1.090] {1.009 to 1.159}	1.126 (0.102) [1.123] {1.056 to 1.192}	−3.285	0.001	1.008 (0.071) [1.004] {0.964 to 1.058}	1.015 (0.08) [1.013] {0.961 to 1.068}	−0.746	0.455
Head	1.756 (0.218) [1.788] {1.629 to 1.922}	1.795 (0.216) [1.768] {1.643 to 1.939}	−0.007	0.995	1.798 (0.230) [1.750] {1.626 to 1.974}	1.784 (0.205) [1.772] {1.639 to 1.909}	−0.143	0.887
Pelvis	1.191 (0.165) [1.181] {1.089 to 1.291}	1.235 (0.158) [1.226] {1.127 to 1.335}	−3.038	0.002	1.063 (0.131) [1.070] {1.000 to 1.158}	1.078 (0.119) [1.067] {1.008 to 1.156}	−0.535	0.592
Preferred leg	1.194 (0.150) [1.191] {1.096 to 1.282}	1.237 (0.131) [1.237] {1.148 to 1.331}	−3.217	0.001	1.098 (0.102) [1.090] {1.025 to 1.168}	1.102 (0.100) [1.099] {1.035 to 1.159}	−0.622	0.534
Non-preferred leg	1.200 (0.145) [1.210] {1.100 to 1.290}	1.241 (0.134) [1.240] {1.140 to 1.330}	−3.041	0.002	1.106 (0.097) [1.090] {1.028 to 1.160}	1.099 (0.099) [1.100] {1.030 to 1.160}	−0.205	0.837
Preferred arm	0.807 (0.113) [0.817] {0.728 to 0.881}	0.837 (0.095) [0.830] {0.771 to 0.899}	−2.436	0.015	0.733 (0.069) [0.734] {0.686 to 0.777}	0.754 (0.076) [0.755] {0.709 to 0.798}	−2.326	0.020
Non-preferred arm	0.791 (0.106) [0.800] {0.715 to 0.865}	0.816 (0.091) [0.820] {0.750 to 0.880}	−2.300	0.021	0.737 (0.063) [0.740] {0.690 to 0.780}	0.747 (0.075) [0.750] {0.700 to 0.790}	−1.399	0.162
Body composition measures (kg)								
Total lean mass	54.053 (7.141) [54.062] {49.630 to 57.772}	56.754 (7.107) [56.741] {52.503 to 61.238}	−3.94	<0.001	35.254 (4.970) [34.859] {32.064 to 38.819}	36.600 (4.782) [36.260] {33.494 to 40.049}	−2.21	0.027
Total fat mass	17.471 (9.639) [14.742] {10.176 to 22.637}	15.248 (7.424) [13.261] {10.038 to 18.668}	−1.62	0.106	26.905 (9.144) [25.293] {19.817 to 32.294}	25.062 (9.168) [23.389] {18.317 to 29.319}	1.97	0.049

Note: Whole group characteristics are described in Table D1 in Appendix D.
Abbreviations: LMC = low motor competence; M = mean, SD = standard deviation; Md = median; U = Mann–Whitney U standardized score.

Discussion

Our results indicated LMC status was associated with decreased BMD in load-bearing bone sites for males only, possibly due to differences in physical activity engagement between the sexes through-out childhood and adolescence. This was even beyond the physical activity contribution in late adolescence that was adjusted for in analyses.[12,50] Nevertheless, these differences continued to be present after adjustment for BMI, vitamin D status, physical activity levels, and puberty status at age 17 years. For females, an association between LMC and BMD was only shown in the preferred arm. Physical activity's impact was also sex dependent, with a stronger influence from increased loading found in males than females and a larger difference present based on LMC status for males.

Bone health differences

Our findings of a gender difference in the association between bone and loading support the findings of Chivers and colleagues[12] in adolescents ($n = 39$, $M_{age} = 14.4$ years) showing bone deficits by peripheral quantitative computed tomography (pQCT) were isolated to males. As the Chivers study indicated, differences in bone quality were unable to be determined by the current study; therefore, the combined findings of these studies indicate that LMC status is not associated with bone health in females but impedes multiple areas of bone health in males. By contrast, Ireland and colleagues[11] reported a deficit in hip BMD for females with LMC compared to their non-LMC counterparts, although smaller than the deficit seen in males. Ireland also reported a decreased level of bone loading based upon LMC status, not demonstrated in the current study, which may have impacted upon bone health levels. Additionally, a potential reason for this discrepancy is environmental differences between the United Kingdom and Australia,[51] which may have affected bone health, via physical activity engagement and vitamin D levels with about 20% less participants having sufficient vitamin D in the Ireland study cohort than in the current study.[52,53] Most importantly, however, participants in the current study were approximately 2 years older than the

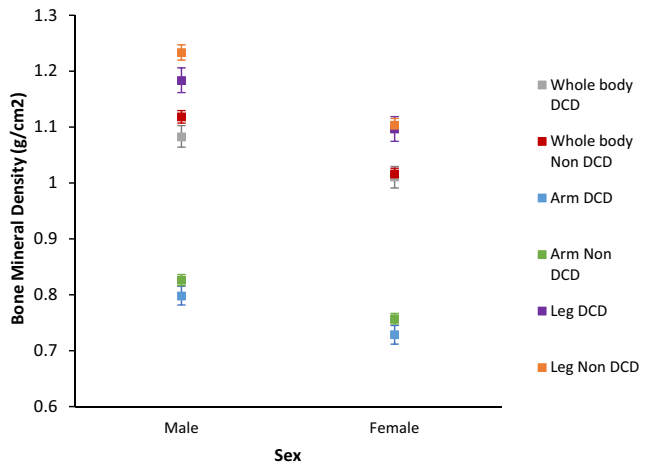

Fig. 2. Estimated marginal means for bone mineral density by sex and low motor competence status. Covariates appearing in the model are fixed at: BMI = 23.77, age = 19.95 years, loading score = 153.96 ELR/-week, serum 25-hydroxyvitamin D = 74.33 nmol/L. Leg and arm are preferred side measurements. Interaction effect is nonsignificant, except for leg ($p = 0.026$). Differences are significant for whole body for males ($p = 0.003$), leg for males ($p < 0.001$), arm for males ($p = 0.005$) and females ($p = 0.003$).

participants in Ireland's study and additional bone mass is likely to have been attained over this time.[14] Participants in the current cohort ranged in age from 19.1 to 21.8 years and were likely to be at or very close to peak bone mass with little additional bone mass accumulation expected. As such, this finding indicates that although females no longer show bone health deficits when peak bone mass is accrued, males show a continued deficit with potential for future health implications, particularly fractures.

Males with LMC may be at increased risk of fracture given their lower bone density, the higher occurrence of fractures in males,[47,50] and potentially a higher risk of injury due to their poor motor skills.[54] A systematic review has indicated the potential for an increased fracture rate (odds ratio 3.1 to 8.3 for lifetime fracture risk) in adolescents with LMC but sex-specific fracture risks are not known.[55] The current study, however, found that there was not a higher frequency of fracture or other injuries for the LMC group than non-LMC. Differences in fracture rates could be due to the form or intensity of physical activity being engaged in, as higher levels of physical activity engagement have been reported to increase fracture risk.[28,56] Although similar levels of physical activity were reported for the LMC and non-LMC group, participants with LMC were less likely to be participating in competitive sports, which may have reduced their fracture risk. An altered physical activity pattern has been reported in other studies on LMC populations with lower intensity in activity participation,[10,57] and reduced diversity.[58] Adults with LMC have also reported adjusting their behavior in order to reduce exposure to injury risks, such as avoiding slopes and stairs.[57] The presence of similar behavior in this cohort might explain vitamin D and lean mass differences between the groups, eg, less activity in outdoor spaces due to the presence of natural hazards.[59] Although differences remained for males after serum 25OHD was controlled for, vitamin D ceased to be significant in many models when lean mass was controlled for. This may indicate differences in activity are beyond the effects of vitamin D differences. Such differences in behavior, if present in this cohort, may have reduced the risk of fracture and require further examination.

Physical activity differences and relationship to bone health

The presence of differences in the relationship between loading and bone were demonstrated by sex and LMC status, with only males showing increases in BMD with loading in all regions (barring the head). This supports the findings of Chivers and colleagues[12] that showed a sex by LMC status effect for upper-body muscle density and subcutaneous fat, likely reflecting physical activity engagement. Although, a differing relationship between physical activity and bone outcomes by sex has been reported,[48] differences in the response to loading by sex and LMC status indicate that differences in the type or form of physical activity participated in may also be a factor. Bone is most responsive to dynamic loads, of at least moderate magnitude, short duration, differing load direction, and which are applied quickly.[28] Individuals with LMC have slow, inefficient movements of reduced quality[60] and as such, activities may not provide enough stimulus to trigger bone adaptation,[25-27] resulting in a reduced bone response to loading activities. The significant difference in lean mass between groups as well as the loss of significant estimate of effect for the impact of loading when lean mass was accounted for may reflect on these physical activity differences. Differences in movement quality have previously been suggested as a potential reason for reduced bone benefit from an exercise intervention as motor impairment increased.[61] Unpublished data have also shown that improvements in physical fitness measures as a result of an exercise intervention[62] were strongly influenced by motor impairment levels indicating a quality of movement effect. Further support for the role of movement quality on bone outcomes may be seen via the differing change rate in health markers to physical activity in individuals with LMC. For example, BMI in young adults with LMC changes at a much slower rate with increasing activity than is seen in young adults who do not have LMC.[24]

An examination of sedentary behavior indicated a potential explanation for some of the previously unaccounted for bone variation in females. Sedentary behavior has been previously shown to have an independent role on bone, outside of that seen from loading, thereby reinforcing the importance of other measures of physical activity than bone loading on bone health differences in a LMC population. These findings indicate that further research is needed as to the cause for bone health differences in individuals with LMC.

Strengths and limitations

Strengths of this study include the use of longitudinal data from the Raine Study, a large cohort study allowing for the effects of multiple different factors upon bone to be examined. As bone reflects activity throughout life, the use of longitudinal measures strengthens the ability to determine the effects of LMC on bone because there has been sufficient time for the bone to respond to physical activity variation. The consideration of a number of established factors capable of affecting BMD further strengthens the study. The use of self-reported physical activity assessment

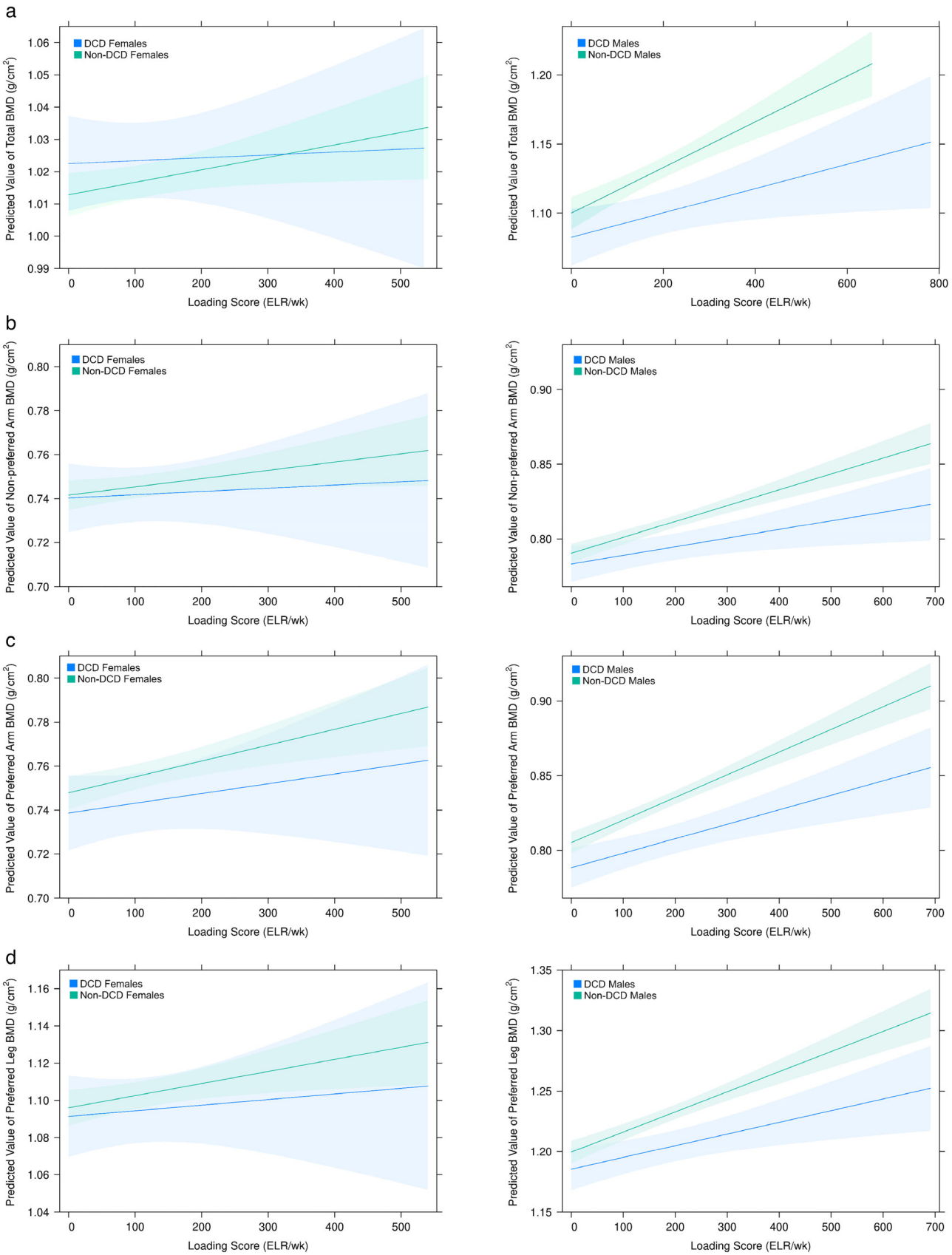

Fig. 3. Relationship between bone loading score and BMD by gender and LMC status. Models are adjusted for age, BMI, and vitamin D status. All relationships are of a linear nature (p for nonlinearity >0.050). For visual simplicity the x-axis for each group was truncated at 3 standard deviations. The shaded area represents 95% confidence intervals. BMD = bone mineral density; LMC = low motor competence.

via self-report rather than device assessment had the potential to overestimate activity levels[63]; however, device assessment on group differences in physical activity indicates this is not the case. The findings of the study are limited to the particulars of the population being measured and may not be generalizable to other populations. In particular, the rate of LMC detected in this population is much higher than general population rates. A low motor competence score and associated increased rate of LMC has been previously established in this cohort[34] and may be a reflection of population differences between a Western Australian population and that of North America where the test was devised in 1982. It is noted that this test has not been validated in an Australian population. Furthermore, differences in puberty rates may have impacted upon MAND results given that lower motor competence scores are known to be associated with a slower rate of biological maturity.[64] The use of motor competence measurements from early in the lifespan prior to when pubertal effects are present helps to counter this concern with the majority of participants having their motor competence assessed at the age of 10 years.

Conclusion

Our study demonstrates that bone health differences in children and adolescents with LMC are present in males with LMC in early adulthood. Differences in the effect of habitual bone loading upon BMD impacts upon these sex-specific associations; however, an independent role of LMC above that from loading in late adolescence can be seen to be present. This indicates other potential causations and may indicate that movement quality is a potential cause for bone health deficits in individuals with LMC. The continuance of bone health differences into young adulthood, indicates that such bone deficits are likely to be lifelong and this population may be at increased risk of osteoporosis and osteoporotic fractures. Further research is required into potential implications as well as the effects of movement quality and execution and other physical activity variables on bone health in this group.

Author Contributions

Jocelyn Tan: Conceptualization; data curation; formal analysis; methodology; visualization; writing – original draft; writing – review and editing. **Carrie-Anne Ng:** Software; visualization; writing – review and editing. **Nicolas H. Hart**: Supervision; writing-review and editing. **Timo Rantalainen:** Supervision; writing – review and editing. **Marc Sim:** Software; writing – review and editing. **David Scott:** Writing – review and editing. **Kun Zhu:** Resources; writing – review and editing. **Beth Hands:** Data curation; methodology; validation; writing – review and editing. **Paola Chivers:** Project administration; supervision; writing – review and editing.

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Peer Review

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Data Availability Statement

The data that support the findings of this study are available from The Raine Study. Restrictions apply to the availability of these data, which were used under license for this study. Data access is via https://rainestudy.org.au/information-for-researchers/available-data/.

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