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1	Effects of toe-in/ out toe-in gait and lateral wedge orthoses on lower extremity joint
2	kinetics; an exploration using musculoskeletal simulation and Bayesian contrasts.
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11	Keywords: biomechanics, orthoses, toe-out, toe-in, gait.
12	Abstract
13	<b>INTRODUCTION:</b> The aim of the current investigation was to examine the effects of both
14	lateral orthoses and toe-in/ toe-out foot progression angles on lower extremity joint loading
15	during walking using a musculoskeletal simulation approach.
16	METHODS: The current investigation examined 15 healthy males, walking in six different
17	conditions (neutral, lateral orthoses, toe-in, lateral toe-in, toe-out and lateral toe-out). Walking
18	kinematics were collected using an eight-camera motion capture system, and kinetics via an
19	embedded piezoelectric force plate. Lower extremity joint loading was explored using a
20	musculoskeletal simulation approach.
21	<b>RESULTS:</b> This investigation showed that peak patellofemoral joint stress was greater in the
22	neutral (3.96 KPa/BW) and lateral orthoses (4.20 KPa/BW) conditions compared to toe-in (3.33
23	KPa/BW), lateral toe-in (3.43 KPa/BW), toe-out (3.35 KPa/BW) and lateral toe-out (3.53
24	KPa/BW) and ankle joint impulse larger in the toe-in (1.65BW·s) and toe-out (1.62BW·s) foot

progression angle modalities compared to neutral (1.51BW·s) and lateral orthoses (1.53BW·s).
Furthermore, it was also shown that medial tibiofemoral impulse was statistically greater in the
toe-in (1.20BW·s) and lateral toe-in (1.15BW·s) conditions compared to neutral (1.07BW·s),
lateral orthoses (1.07BW·s), toe-out (1.09BW·s) and lateral toe-out (1.05BW·s).

29 CONCLUSIONS: Therefore, the current investigation provides evidence that altering the foot
30 progression angle may attenuate the risk from patellofemoral disorders whilst simultaneously
31 enhancing the risk from degenerative ankle pathologies. Similarly, adopting a toe-in foot
32 progression angle may also increase the risk from medial tibiofemoral degeneration.

33

## 34 Introduction

Walking is undoubtably a fundamental aspect of everyday living, and the primary locomotion modality in humans. The knee joint plays an important role in load bearing during walking and other common daily activities (1). However, excessive knee joint forces are regarded as the contributing factor to the initiation and progression of degenerative knee disorders (2-3). Therefore, due to factors such as age, excessive body mass or previous injury, the negative effects of excessive knee joint loads begin to emerge and the risk of knee disorders such as osteoarthritis (OA) increase (4).

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Knee OA represents a degenerative articular disease, caused by erosion and deterioration of the articular cartilage within the knee joint itself (5), and those with knee OA experience ongoing pain and stiffness (6). OA at the knee joint has been shown to be present in as many as 10% of individuals over the age of 55, and importantly over 90% of knee OA cases are observed in the medial tibiofemoral compartment (7-8). This is because during traditional activities of daily life over 60% of the total load borne by the tibiofemoral joint passes through the medial compartment of the knee (9).

Owing to the proposed association between excessive joint forces and the initiation/ 51 progression of joint degeneration, as well as the high incidence of medial tibiofemoral OA, 52 several strategies have emerged that aim to lower medial tibiofemoral joint loading and in turn 53 the risk from OA. Because of the challenges associated with the quantification of tibiofemoral 54 contact forces, the knee adduction moment is typically adopted as a proxy for medial 55 56 tibiofemoral loading (10-11). A commonly adopted strategy is the utilization of lateral wedge insoles/ orthoses (12), whereby the centre of pressure is forced into a more lateral position; 57 58 causing a reduction in the lever arm of the knee adduction moment (13). Importantly lateral wedge insoles have been shown to attenuate the magnitude of the knee adduction moment 59 during gait (14-15), stair ascent and descent (16). 60

61

A further conservative modality for the reduction of the knee adduction moment is alterations 62 to individuals walking gait pattern (1). Changing the foot progression angle has two variants; 63 toe-out and toe-in gait, which unlike other gait modification techniques appear to be sustainable 64 up to 10 weeks (17). Toe-in (represented by internal rotation of the foot) and toe-out 65 (characterized by external rotation of the foot) gait patterns are similarly designed to influence 66 the knee adduction moment by moving the centre of pressure mediolaterally (17). Typically 67 toe-in gait patterns have been shown to reduce the magnitude of the first peak in the knee 68 adduction moment time curve (1; 18-19), yet toe-out gait has correspondingly been found to 69 reduce the second knee adduction moment peak (1; 18-20). However, conversely Jenkyn et al., 70 (2008) showed that that toe-out walking reduced both the first and second peak of the knee 71 adduction moment curve. Similarly, both Van den Noort et al., (18) and Khan et al., (1) showed 72 that the knee adduction moment impulse was reduced with a toe-in gait pattern, yet other 73

investigations have shown that there is no effect of altering the foot progression angle on thisparameter (17).

76

As the knee adduction moment is a pseudo measurement for tibiofemoral loading, all of the 77 previous analyses concerning the effects of lateral orthoses and gait modifications have used 78 this measurement. Although the knee adduction moment and its derivatives have been linked 79 80 to medial knee joint cartilage degeneration (10), joint moments are not representative of localized joint contact loads (21). Importantly a recent investigation using instrumented knee 81 82 prostheses showed only moderate correlations between the knee adduction moment and direct medial tibiofemoral joint loading magnitudes during walking (3). Indeed Herzog et al., (21) 83 identified importantly that muscle forces are the primary contributors to joint forces and in 84 recent years advances in musculoskeletal simulation software have allowed allow muscle 85 driven calculations of lower extremity joint reaction forces (22). However, such approaches 86 have not yet been utilized to explore the effects of lateral orthoses and foot progression angle 87 gait modifications. 88

89

Similarly, whilst the effects of both lateral orthoses and modified foot progression angle gait
patterns have been examined previously, they have focussed only on indices of medial
tibiofemoral joint loading (quantified using the knee adduction moment and its derivatives).
Both wedged foot orthoses and alterations in the foot progression angles during gait are likely
to mediate alterations at more than one body segment and thus more than one joint (23).
Therefore, potential positive alterations in joint loading mediated at the medial compartment
of the tibiofemoral joint may concurrently negatively impact other lower extremity joints.

To summarize, there is currently no scientific research that has explored the effects of lateral orthoses/ foot progression angle modifications on collective lower extremity joint loading using a musculoskeletal simulation-based approach. Therefore, the aim of the current investigation was to examine the effects both lateral orthoses and foot progression angles on lower extremity joint loading during walking using a musculoskeletal simulation approach. A study of this nature may provide further insight into the cumulative biomechanical effects of different modalities designed to reduce the risk from medial tibiofemoral OA.

105

106 The current investigation tests the hypothesis firstly that lateral orthoses and a toe-in gait

107 pattern will reduce medial tibiofemoral loading and secondly that these parameters when used

108 collectively will serve to further attenuate medial tibiofemoral forces during walking.

109

## 110 Methods

### 111 Participants

Fifteen male participants (age 31.73±4.96 years, height 1.72±0.06 m and body mass 112  $69.31\pm9.92$  kg and BMI =  $23.45\pm2.78$  kg/m<sup>2</sup>). volunteered to take part in this study. All 113 participants were free from pathology at the time of data collection and provided written 114 informed consent, in accordance with the principles outlined in the Declaration of Helsinki. 115 The inclusion criteria for the subjects included healthy adults, aged 20–45 years and having a 116 **BMI** of less than 30 kg/m<sup>2</sup> (1). The participants were excluded on the basis of any 117 musculoskeletal disorder, previous knee surgery or inability to adopt the novel gait pattern. The 118 procedure utilized for this investigation was approved; by a university ethical committee 119 (STEMH 1013). 120

## 122 *Experimental orthoses*

Commercially available full-length orthoses (Slimflex Simple, High Density, Full Length, Algeos UK) were examined in the current investigation. The orthoses were made from ethylene-vinyl acetate with a shore A rating of 65 and had a heel thickness of 11 mm including the additional wedge. The orthoses were featured a 5° lateral wedge configuration which spanned the full length of the device. To ensure consistency each participant wore the same footwear (Asics, Gel Patriot 6). The experimental footwear had a mean mass of 0.265 kg, heel thickness of 22 mm and heel drop of 10 mm.

130

## 131 Foot progression angles

As this study focused on the effects of toe-in and toe-out foot progression angles, values of 15° 132 during the stance phase were targeted (1). Therefore, the force plate was marked with a straight 133 line that ran directly through the middle of the long axis of the force plate (neutral), a 15° line 134 135 that represented the foot progression angle required for the toe-out condition for the right foot (toe-out) and a further 15° line that represented the foot progression angle required for the toe-136 in condition for the right foot (toe-in). Participants were given a 5-minute period of 137 138 familiarization for each of the three aforementioned settings in order to become accustomed to the experimental conditions (1). Following this the force plate markings were removed prior to 139 the commencement of data collection and participants were asked to replicate these foot 140 progression angles during data collection. This process was deemed to be ecologically valid as 141 individuals seeking to implement these modifications into their own gait mechanics would not 142 143 have lines drawn or feedback for each footfall during normal walking (1).

To quantify the foot progression angle during data collection, the path of the centre of pressure was determined from using the force plate. The progression angle of the foot was calculated by intersecting the position of the centre of pressure at the time of foot contact with the centre of pressure at toe-off. The toe-out (represented by a positive value) and toe-in angles (represented by a negative value) were determined as the angle formed by the intersection line relative to the directly anterior direction (24).

151

## 152 Procedures

153 Participants walked without orthoses in three conditions; straight foot (neutral), a toe-out foot progression angle (toe-out) and toe-in foot progression angle (toe-in) and also with orthoses in 154 the same conditions; lateral orthoses, lateral toe-in and lateral toe-in. Participants walked at a 155 156 velocity of 1.5 m/s (±5%), striking an embedded piezoelectric force platform (Kistler, Kistler Instruments Ltd) with their right (dominant) foot. Walking velocity was monitored using 157 infrared timing gates (Newtest, Oy Koulukatu). The stance phase was delineated as the duration 158 over which 20 N or greater of vertical force was applied to the force platform (25). Participants 159 completed five successful trials in each condition and the order that participants walked in each 160 161 footwear condition was counterbalanced. Kinematics and ground reaction forces data were synchronously collected. Kinematic data was captured at 250 Hz via an eight-camera motion 162 163 analysis system (Qualisys Medical AB) and ground reaction forces captured at 1000 Hz. 164 Dynamic calibration of the motion capture system was performed before each data collection session. 165

To define the anatomical frames of the thorax, pelvis, thighs, shanks and feet retroreflective 167 markers were placed at the C7, T12 and xiphoid process landmarks and also positioned 168 bilaterally onto the acromion process, iliac crest, anterior superior iliac spine (ASIS), posterior 169 super iliac spine (PSIS), medial and lateral malleoli, medial and lateral femoral epicondyles, 170 greater trochanter, calcaneus, first metatarsal and fifth metatarsal. Carbon-fiber tracking 171 clusters comprising of four non-linear retroreflective markers were positioned onto the thigh 172 173 and shank segments. In addition to these the foot segments were tracked via the calcaneus, first metatarsal and fifth metatarsal, the pelvic segment was tracked using the PSIS and ASIS 174 175 markers and the thorax segment was tracked using the T12, C7 and xiphoid markers.

176

177 Static calibration trials were obtained with the participant in the anatomical position in order 178 for the positions of the anatomical markers to be referenced in relation to the tracking 179 clusters/markers. A static trial was conducted with the participant in the anatomical position in 180 order for the anatomical positions to be referenced in relation to the tracking markers, following 181 which those not required for dynamic data were removed.

182

## 183 Processing

Dynamic trials were digitized using Qualisys Track Manager, in order to identify anatomical and tracking markers and then exported as C3D files to Visual 3D (C-Motion, Germantown, MD). All data were normalized to 100 % of the stance phase. Ground reaction force (GRF) and kinematic data were smoothed using cut-off frequencies of 25 and 6 Hz with a low-pass Butterworth 4th order zero lag filter (26).

Data during the stance phase were exported from Visual 3D into OpenSim 3.3 software
(Simtk.org). A validated musculoskeletal model with 12 segments, 19 degrees of freedom and
92 musculotendon actuators (27) was used to estimate lower extremity joint forces. The model
featured the same segments and muscle tendon units as the standard Gait2392 Opensim model
(*https://simtk-*

195 confluence.stanford.edu:8443/display/OpenSim/Gait+2392+and+2354+Models?preview=/3 376103/3736767/Gait%202392%20vs.%20Gait%202354.pdf) but the tibiofemoral joint was 196 separated into medial and lateral compartments to allow joint reaction analyses at these areas 197 198 separately and the model also featured a patella. The model was firstly scaled for each participant to account for the anthropometrics of each individual. Then as muscle forces are 199 the main determinant of joint compressive forces (21), muscle kinetics were quantified using 200 static optimization. The static optimization simulation process calculates the muscle forces 201 required in order to recreate the experimentally measured motions. Compressive ankle, medial/ 202 lateral tibiofemoral, patellofemoral and hip joint forces were calculated via the joint reaction 203 analyses function within OpenSim using the muscle forces generated from the static 204 optimization process as inputs. The joint reaction analysis function in OpenSim calculates the 205 206 joint loads transferred between two contacting bodies, about the joint centre location identified during the static trial (28). In the current investigation, joint forces were normalized by dividing 207 by each participants body weight (BW). Compressive hip joint forces were representative of 208 the contact forces between the femur and acetabular cartilage, tibiofemoral forces between the 209 210 medial/lateral tibial and femoral cartilage, patellofemoral joint forces between the femur and 211 patella cartilage and ankle joint forces between the tibia and talar cartilage. Patellofemoral joint stress (KPa/BW) was also quantified by dividing the patellofemoral joint reaction force by the 212 patellofemoral contact area. Patellofemoral contact areas were obtained by fitting a polynomial 213 curve to the sex specific data of Besier et al., (29). From the above processing, peak normalized 214

ankle force, peak lateral tibiofemoral force, and peak patellofemoral force/ stress during the
stance phase were extracted for statistical analyses. In addition, as the hip and medial
tibiofemoral joint force curves exhibit a double peaked pattern, the normalized values at the
first and second peak for these parameters were extracted for analysis.

219

In addition, ankle, medial/ lateral tibiofemoral, patellofemoral and hip instantaneous load rates
(BW/s) were also extracted by obtaining the peak increase in force between adjacent data
points. Finally, ankle, medial/ lateral tibiofemoral, patellofemoral and hip force impulses
(BW·s) and stresses (KPa/BW·s) during the stance phase were calculated using a trapezoidal
function.

225

Finally, in order to determine the mechanisms responsible for any alterations in joint loading, the forces (BW) for the major muscles crossing the hip, knee and ankle joints were quantified at the instances of the aforementioned peak joint forces/ stresses. Similarly, for any joint whereby only statistical alterations in the joint impulse were observed between conditions, the muscle force impulses for the major muscles crossing the associated joint were also extracted.

231

## 232 Statistical analyses

Following data processing, compressive joint forces (hip, patellofemoral, ankle, medial/lateral tibiofemoral), during the stance phase were exported and temporally normalized using linear interpolation to 101 data points for statistical analysis using Statistical parametric mapping (SPM). In agreement with Pataky et al. (30), SPM was implemented in a hierarchical manner, analogous to one-way repeated measures ANOVA with post-hoc t-tests. Therefore, the entire data-set was examined first, and if a statistical main effect was reached then post-hoc tests

comparing individual conditions were conducted on each component separately. For discrete 239 parameters (peak joint forces, joint impulse, joint instantaneous load rates, muscle forces and 240 muscle force impulses), means and standard deviations were calculated for each condition. 241 Differences in discrete biomechanical parameters were examined using Bayesian one-way 242 repeated measures ANOVA with default prior scales using JASP software 0.10.2 (31). In the 243 event of a main effect, post-hoc Bayesian paired t-tests were conducted between each 244 condition. Similarly, relationships between 1. discrete joint loads and foot progression angle 245 and 2. discrete joint loads and muscle forces at the instances of peak joint loads/ muscle force 246 247 impulses across all conditions were examined using Bayesian Pearson's correlation analyses using SPSS 27.0 software (SPSS, IBM). Bayesian factors (BF) were used to explore the extent 248 to which the data supported the alternative (H<sub>1</sub>) hypothesis. Bayes factors throughout were 249 250 interpreted in accordance with the recommendations of Jeffreys, (32), with values  $\geq$ 3 indicating sufficient evidence in support of H<sub>1</sub>. In the interests of conciseness only variables that present 251 with Bayes factors  $\geq 3$  and SPM analyses showing statistical significance will be presented. 252

253

#### 254 **Results**

255 *Foot progression angles* 

256	The mean $\pm$ SD of foot progression angles were: neutral = $0.68 \pm 2.70^{\circ}$ , lateral orthoses = 1.47
257	$\pm 2.85^{\circ}$ , toe-out = $12.38 \pm 4.42^{\circ}$ , lateral toe-out = $12.44 \pm 3.58^{\circ}$ , toe-in = $-10.63 \pm 2.82^{\circ}$ and
258	lateral toe-in = $-10.54 \pm 2.37^{\circ}$ .

259

260 <u>Discrete analyses – joint loading</u>

261 <u>@@@Table 1 near here@@@</u>

For the first peak of the hip force there was decisive evidence of a main effect (BF =262 129890.84). Post-hoc analyses showed that values were larger in the lateral orthoses (BF =263 42.84), neutral (BF = 35.68), toe-out (BF = 22.47), lateral toe-out (BF = 10.91) conditions 264 compared to toe-in. Furthermore, values were also larger in the lateral orthoses (BF = 149.13), 265 neutral (BF = 7.06), toe-out (BF = 3.67), lateral toe-out (BF = 22.12) conditions compared to 266 lateral toe-in (Table 1). For the second peak of the hip force there was decisive evidence of a 267 268 main effect (BF = 24.93). Post-hoc analyses showed that values were larger in the lateral orthoses (BF = 9.28), neutral (BF = 7.37), toe-in (BF = 5.93) and lateral toe-in (BF = 3.04) 269 270 conditions compared to toe-out. Furthermore, values were also larger in the lateral orthoses (BF = 16.21), neutral (BF = 32.86) and lateral toe-out (BF = 3.16) conditions compared to 271 lateral toe-out (Table 1). 272

273

For the first peak of the medial tibiofemoral force there was decisive evidence of a main effect 274 (BF = 298.86). Post-hoc analyses showed that values were larger in the neutral condition 275 276 compared to toe-in (BF = 5.82), lateral toe-in (BF = 4.73), toe-out (BF = 229.47) and lateral toe-out (BF = 20.24). In addition, values for this parameter were larger in lateral orthoses 277 compared to lateral toe-in (BF = 4.08), toe-out (BF = 14.12) and lateral toe-out (BF = 3.54) 278 (Table 1). For the second peak of the medial tibiofemoral force there was also decisive evidence 279 of a main effect (BF = 8543.01). Post-hoc analyses showed that values were larger in the toe-280 in condition compared to lateral orthoses (BF = 248.62), neutral (BF = 4.30), toe-out (BF =281 5.27) and lateral toe-out (BF = 15.67). In addition, values for this parameter were larger in the 282 lateral toe-in condition compared to lateral orthoses (BF = 77.03) and lateral toe-out (BF =283 3.27) (Table 1). For the medial tibiofemoral force impulse there was decisive evidence of a 284 main effect (BF = 499513.34). Post-hoc analyses showed that values were larger in the toe-in 285 286 condition compared to lateral orthoses (BF = 14.72), neutral (BF = 13.71), toe-out (BF = 14.72)

175.33) and lateral toe-out (BF = 783.24). In addition, values for this parameter were larger in the lateral toe-in condition compared to lateral orthoses (BF = 621.47) and lateral toe-out (BF = 236.42) (Table 1).

290

291 For the lateral tibiofemoral force impulse there was decisive evidence of a main effect (BF =1442262604595.22). Post-hoc analyses showed that values were larger in the lateral orthoses 292 condition compared to toe-in (BF = 225.77) and lateral toe-in (BF = 66.20) and in the neutral 293 294 compared to toe-in (BF = 31.14) and lateral toe-in (BF = 25.76). In addition, values for this parameter were larger in the toe-out condition compared to lateral orthoses (BF = 4.63), neutral 295 (BF = 7.74), toe-in (BF = 10906.26) and lateral toe-in (133.70) and also in the lateral toe-out 296 compared to lateral orthoses (BF = 11.82), neutral (BF = 34.14), toe-in (BF = 2393.76) and 297 lateral toe-in (1151.05) (Table 1). 298

299

For the peak patellofemoral force there was decisive evidence of a main effect (BF = 132.68). Post-hoc analyses showed that values were larger in the neutral condition compared to toe-in (BF = 5.82), lateral toe-in (BF = 4.73), toe-out (BF = 229.47) and lateral toe-out (BF = 20.24). In addition, values for this parameter were larger in lateral orthoses compared to lateral toe-in (BF = 4.08), toe-out (BF = 14.12) and lateral toe-out (BF = 3.54) (Table 1).

305

For the peak patellofemoral stress there was decisive evidence of a main effect (BF = 3868.64). Post-hoc analyses showed that values were larger in the neutral condition compared to toe-in (BF = 11.90), lateral toe-in (BF = 65.92), toe-out (BF = 93.58) and lateral toe-out (BF = 83.13). In addition, values for this parameter were larger in lateral orthoses compared to toe-out (BF = 19.19) (Table 1). In addition, for the patellofemoral stress impulse there was substantial evidence of a main effect (BF = 3.87). Post-hoc analyses showed that values were larger in the neutral condition compared to toe-out (BF = 31.48) and lateral toe-out (BF = 212.27). In addition, values for this parameter were larger in lateral orthoses compared to toe-out (BF = 4.88) and lateral toe-out (BF = 29.24) (Table 1).

315

For the ankle force impulse there was decisive evidence of a main effect (BF = 12448.22). Posthoc analyses showed that values were larger in the toe-out condition compared to neutral (BF = 8.43) and lateral orthoses (BF = 152.30). In addition, values for this parameter were larger in the toe-in condition compared to neutral (BF = 52.45) and lateral orthoses (BF = 184.65) and also in the lateral toe-in condition compared to lateral orthoses (BF = 34.73) (Table 1).

321

## 322 <u>Discrete analyses – muscles forces</u>

323

## @@@Table 2 near here@@@

For the gluteus medius 2 at the instance of the first peak of the hip force there was decisive 324 evidence of a main effect (BF = 381404.40). Post-hoc analyses showed that values were larger 325 326 in the lateral orthoses (BF = 10.46), neutral (BF = 755.02), toe-out (BF = 10.78), lateral toeout (BF = 57.35) conditions compared to toe-in. Furthermore, values were also larger in the 327 lateral orthoses (BF = 87.33), neutral (BF = 19.43), toe-out (BF = 98.26), lateral toe-out (BF = 19.43), toe-out (BF = 19.43), here a statement of the statement of t 328 329 251.58) conditions compared to lateral toe-in (Table 2). Similarly, for the gluteus medius 3 at the instance of the first peak of the hip force there was decisive evidence of a main effect (BF 330 = 732.05). Post-hoc analyses showed that values were larger in the lateral orthoses (BF = 331 103.36), neutral (BF = 10.60), toe-out (BF = 28.17), lateral toe-out (BF = 124.47) conditions 332

compared to lateral toe-in (Table 2). For the gluteus minimus 3 at the instance of the first peak 333 of the hip force there was substantial evidence of a main effect (BF = 6.02). Post-hoc analyses 334 335 showed that values were larger in the lateral orthoses (BF = 46.62), neutral (BF = 10.02), toeout (BF = 4.89), lateral toe-out (BF = 6.48) conditions compared to lateral toe-in (Table 2). For 336 the tensor fasciae latae at the instance of the first peak of the hip force there was decisive 337 evidence of a main effect (BF = 14450.22). Post-hoc analyses showed that values were larger 338 339 in the lateral orthoses (BF = 30.00), neutral (BF = 22.22), toe-out (BF = 4102.04), lateral toeout (BF = 47.70) conditions compared to lateral toe-in. Furthermore, values were also larger in 340 341 the toe-out compared to lateral orthoses (BF = 14.80) and toe-in (BF = 48.83) conditions (Table 2). For the rectus femoris at the instance of the first peak of the hip force there was decisive 342 evidence of a main effect (BF = 721.75). Post-hoc analyses showed that values were larger in 343 the lateral orthoses (BF = 14.97), toe-out (BF = 777619.80) and lateral toe-out (BF = 12.80) 344 conditions compared to lateral toe-in. Furthermore, values were also larger in the toe-out 345 compared to lateral orthoses (BF = 16.12) and toe-in (BF = 518.30) conditions (Table 2). 346

347

For the rectus femoris at the instance of the second peak of the hip force there was substantial evidence of a main effect (BF = 3.56). Post-hoc analyses showed that values were larger in the toe-in condition compared to toe-out (BF = 8.78) and in the lateral orthoses (BF = 4.03) and toe-in (BF = 6.41) conditions compared to lateral toe-out (Table 2).

352

For the vastus intermedius at the instance of the first peak of the medial tibiofemoral force, there was substantial evidence of a main effect (BF = 5.72). Post-hoc analyses showed that values were larger in the lateral orthoses (BF = 82.13) and neutral (BF = 5.76) conditions compared to toe-out (Table 2). For the vastus lateralis at the instance of the first peak of the

medial tibiofemoral force, there was substantial evidence of a main effect (BF = 8.22). Post-357 hoc analyses showed that values were greater in the lateral orthoses (BF = 25.35) and neutral 358 359 (BF = 6.58) conditions compared to toe-out and also in the neutral compared to toe-in (BF =3.16) and lateral toe-out (BF = 4.92) (Table 2). For the vastus medialis at the instance of the 360 first peak of the medial tibiofemoral force, there was substantial evidence of a main effect (BF 361 = 4.29). Post-hoc analyses showed that values were larger in the lateral orthoses (BF = 186.62) 362 363 and neutral (BF = 5.64) conditions compared to toe-out (Table 2). For the rectus femoris at the instance of the first peak of the medial tibiofemoral force, there was strong evidence of a main 364 365 effect (BF = 14.77). Post-hoc analyses showed that values were larger in the lateral orthoses (BF = 58.18), toe-in (BF = 109.18) and lateral toe-in (BF = 79.75) conditions compared to toe-366 out and also in the toe-in (BF = 7.40) compared to lateral toe-out condition (Table 2). 367

368

For the lateral gastrocnemius at the instance of the second peak of the medial tibiofemoral force, there was decisive evidence of a main effect (BF = 1023699.85). Post-hoc analyses showed that values were larger in the lateral orthoses (BF = 59.96), toe-in (BF = 30.04) and lateral toe-in (BF = 17.11) conditions compared to toe-out. Similarly, values were also larger in the lateral orthoses (BF = 1601.74), toe-in (BF = 240.40) and lateral toe-in (BF = 44.13) compared to lateral toe-out (Table 2).

375

For the vastus intermedius at the instance of peak patellofemoral stress, there was substantial evidence of a main effect (BF = 3.61). Post-hoc analyses showed that values were greater in the lateral orthoses (BF = 22.61) and neutral (BF = 6.85) conditions compared to toe-out and also in the neutral (BF = 3.90) compared to lateral toe-out (Table 2). 381 For the lateral gastrocnemius impulse there was decisive evidence of a main effect (BF =36188.95). Post-hoc analyses showed that values were greater in the toe-out compared to lateral 382 orthoses (BF = 276.36), neutral (BF = 24.91) and toe-in (BF = 38.24) also in the lateral toe-out 383 compared to lateral orthoses (BF = 80189.72), neutral (BF = 33.57) and toe-in (BF = 154.09) 384 conditions. There was also very strong evidence of a main effect for medial gastrocnemius 385 impulse (BF = 37.47). Post-hoc analyses showed that values were greater in the toe-out 386 compared to lateral orthoses (BF = 18.87) and neutral (BF 5.22) and also in the lateral toe-out 387 compared to lateral (BF = 99.06) and neutral (BF = 35.27) conditions. There was very strong 388 389 evidence of a main effect for tibialis anterior impulse (BF = 49.40). Post-hoc analyses showed 390 that values were larger in the toe-out condition compared to toe-in (BF = 17.27) and lateral toein (BF 502.53). Finally, there was also decisive evidence of a main effect for tibialis posterior 391 impulse (BF = 645123.12). Post-hoc analyses showed that values were greater in the toe-out 392 condition compared to lateral orthoses (BF = 66.82), neutral (BF = 8.69) toe-in (BF = 656.32) 393 and lateral toe-in (BF = 625.85) and also in the lateral orthoses (BF = 64.81), neutral (BF = 64.81)394 12.78) toe-in (BF = 580.43) and lateral toe-in (BF = 829.33) conditions. 395

396

## 397 <u>Statistical parametric mapping</u>

The analysis of the overall data set using SPM revealed significant main effects for hip force, medial tibiofemoral force, lateral tibiofemoral force, patellofemoral force and patellofemoral stress thus post-hoc investigation between individual conditions was required (Supplemental figure 1).

For hip force, lateral orthoses were associated with increased hip joint loading from during 403 early stance compared to both toe-in and lateral toe-in, but reduced loading in late stance in 404 relation to lateral toe-in (Figure 1). Furthermore, the neutral condition was associated with 405 increased hip loading during early stance compared to toe-in, lateral toe-in and lateral toe-out 406 and in late stance compared to toe-out and lateral toe-out (Figure 1). In addition, the toe-in 407 condition exhibited increased hip loading during late stance but reduced loading during early 408 409 stance compared to toe-out and lateral toe-out (Figure 1). In addition, the lateral toe-in condition exhibited increased hip loading during late stance but reduced loading during early-410 411 mid stance (Figure 1).

412

For patellofemoral force, lateral orthoses were associated with increased patellofemoral loading during early and late stance compared to toe-out (Figure 2). Similarly, the neutral condition exhibited increased patellofemoral loading during early stance compared to toe-out and during early and late stance compared to lateral toe-out (Figure 2). Furthermore, for patellofemoral stress lateral orthoses were associated with increased stress during early stance compared to toe-in and toe-out and during early and late stance in relation to lateral toe-out (Figure 2).

420

For medial tibiofemoral force, lateral orthoses were associated with increased medial loading during early stance compared to toe-in and toe-out and reduced loading during late stance compared to toe-in and lateral toe-out (Figure 3). In addition, the neutral condition was associated with increased loading during early stance yet reduced loading in late stance compared to toe-in, lateral toe-in, toe-out and lateral toe-out conditions (Figure 3). Furthermore, the toe-in and lateral toe-in conditions were associated with increased loading during late stance but decreased loading in early stance (Figure 3). 429 For lateral tibiofemoral force, lateral orthoses were associated with increased lateral loading during early-late stance compared to toe-in and lateral toe-in (Figure 4ab). In addition, lateral 430 orthoses were associated with increased loading during early stance compared to lateral toe-431 out yet reduced loading during mid-late stance compared to toe-out and lateral toe-out (Figure 432 4cd). Similarly, the neutral condition was associated with increased lateral loading during 433 434 early-late stance compared to toe-in and lateral toe-in (Figure 4). In addition, the neutral condition was associated with increased loading during early stance compared to lateral toe-435 out yet reduced loading during late stance compared to toe-out and lateral toe-out (Figure 4). 436 437 Furthermore, the toe-in condition and lateral toe-in conditions were associated with increased 438 loading in early stance but enhanced loading during late stance compared to toe-out and lateral toe-out (Figure 4). 439

440

#### 441 *Correlation analyses*

442

#### @@@Table 3 near here@@@

443

## @@@Table 4 near here@@@

444 Correlations between the foot progression angle and joint loading indices and the associated
445 Bayes factors are presented in Table 3. Similarly, correlations between joint forces/ impulses
and muscle forces/ impulses at the instances of peak joint loads/ impulses and the associated
447 Bayes factors are presented in Table 4.

448

449 **Discussion** 

The aim of the current investigation was to examine the effects both lateral orthoses and foot progression angles on lower extremity joint loading during walking using a musculoskeletal simulation approach. As the first investigation to examine the cumulative effects of lateral orthoses/ foot progression angles on lower extremity joint loading a study of this nature may provide further insight into the biomechanical effects of different modalities designed to reduce the risk from medial tibiofemoral OA.

456

At the medial aspect of the tibiofemoral joint, the findings do not support the hypothesis and 457 similarly oppose those of Jones et al., (14) and Hinman et al., (15) in that lateral orthoses did 458 not statistically influence joint loading at the medial tibiofemoral joint in relation to no-orthoses 459 conditions. However, it is important to recognise that both Jones et al., (14) and Hinman et al., 460 (15) examined participants with existing medial tibiofemoral OA, so biomechanical responses 461 to lateral orthoses may be condition dependent. Furthermore, both the discrete and SPM based 462 analyses showed a contradictory pattern of statistical differences in relation to the influence of 463 464 the foot progression angle. Specifically, in partial agreement with previous findings, the first 465 medial tibiofemoral force peak was greater in the neutral and lateral orthoses conditions whereas the second peak was statistically larger in the toe-in conditions (1; 18-20). This 466 observation concurs with the correlation analysis between foot progression angle and the 467 second medial tibiofemoral force peak and also the correlational analyses between joint and 468 muscle kinetics (24). Therefore, as the first peak was best associated with the vasti muscle 469 kinetics, the reductions in vasti forces at the first peak in the toe-in and toe-out conditions 470 provides clear insight into the mechanisms responsible for the reductions in the first medial 471 tibiofemoral force peak in these conditions (21). However, changes in the second medial 472 tibiofemoral peak cannot be explained via the correlational analyses between joint/ muscle 473 474 kinetics.

Importantly, in addition to differences at each of the force peaks, in opposition to our 476 hypothesis, this study showed a main effect for the medial tibiofemoral impulse across the 477 stance phase, which was found to be greater in the toe-in conditions. However, both SPM and 478 discrete analyses also showed that lateral tibiofemoral loading was statistically attenuated in 479 the toe-in conditions. This observation similarly is supported by the correlation analyses 480 481 between foot progression angle and the peak lateral tibiofemoral force and also the medial tibiofemoral force impulse, and indicates that reductions in joint loading borne by the medial 482 compartment during the stance are simply shifted to the lateral aspect of the joint. However, 483 484 given the greatly enhanced incidence of medial tibiofemoral OA (7) and the association 485 between knee joint loading and initiation of cartilage degeneration (3), the current investigation indicates that toe-in gait patterns increase risk from the mechanisms linked to the aetiology of 486 487 medial knee OA.

488

Much like at the medial tibiofemoral compartment, both the discrete and SPM based analyses 489 at the hip joint showed a contradictory pattern of statistical differences. Firstly, in the neutral 490 491 and lateral orthoses conditions as well as the toe-out and lateral toe-out conditions, the smaller 492 first peak of the hip joint contact force was enhanced compared to the toe-in and lateral toe-in 493 conditions. Conversely, it was also revealed that neutral and lateral orthoses conditions as well 494 as the toe-in and lateral toe-in modalities were associated with increases in the larger second peak of the hip joint contact force in relation to the toe-out conditions. Importantly muscle 495 forces are the primary determinant of joint loading (21). Therefore the observations from the 496 497 correlational analyses showing that the first peak was best associated with adductor magnus and gluteal muscle forces and the second peak with adductor magnus, gluteal, rectus femoris 498

and tensor fasciae latae provide insight into the mechanisms responsible for the aforementioned 499 changes in hip joint loading. Specifically, therefore the reductions in gluteus medius and 500 gluteus minimus forces at the first hip joint force peak for the toe-in conditions and the 501 reductions in rectus femoris forces at the second peak indicate that the alterations in joint 502 loading were mediated via these changes in muscle kinetics. Hip joint loading is associated 503 with arthritic degeneration (33), thus, the findings from this investigation indicate firstly that 504 505 lateral orthoses do not appear to influence the risk from the parameters linked to hip joint OA and more importantly that whilst foot progression angles do influence hip joint loading at 506 507 different parts of the stance phase they appear not to be able to do so in such a way that the risk from hip OA is attenuated. Although, it should be acknowledged that it is currently unknown 508 which of the hip joint loading peaks are most strongly associated with OA initiation. 509

510

At the patellofemoral joint, the current investigation showed firstly that lateral orthoses did not 511 influence patellofemoral joint loading, indicating that they may not be effective in mediating 512 513 any statistical reductions in patellofemoral joint mechanics (2). However, this study did reveal using both SPM and discrete analyses that the neutral and lateral orthoses conditions were 514 associated with statistical increases in both peak patellofemoral joint force/ stress and the 515 impulse experienced throughout the stance phase. Taking into account the correlation analyses 516 indicating that the vasti muscle group were most strongly associated with patellofemoral joint 517 stress, and the associated increases in vastus intermedius forces noted in the neutral and lateral 518 orthoses conditions, provides a mechanical explanation for the observed alterations in 519 patellofemoral loading (21). Furthermore, given the proposed association between excessive 520 joint stress and the aetiology of patellofemoral pain (2), the current investigation indicates that 521 alterations in foot progression angles irrespective of direction (i.e. toe-in or toe-out conditions) 522

are able to attenuate the magnitude of patellofemoral loading mechanisms linked to theaetiology of patellofemoral pain.

525

Examination of ankle joint kinetics showed via discrete analysis that the impulse of ankle joint 526 loading across the stance phase was statistically larger in the toe-out and toe-in conditions in 527 relation to the neutral and lateral orthoses walking modalities. The correlation analyses showed 528 that the ankle joint force impulse was associated with lateral gastrocnemius, soleus and tibialis 529 posterior muscle forces. Therefore, the associated increases in gastrocnemius and tibialis 530 impulses in the toe-out conditions, explains the observed increases in ankle joint loading in this 531 condition (21), although increases in the toe-in condition remain unresolved and may be due to 532 patterns of muscle forces not considered in this study. Nonetheless, the association between 533 ankle joint loading and the aetiology of ankle joint degeneration is well established (34), thus 534 the current investigation shows that altering the habitual foot progression angle may increase 535 536 the risk from ankle joint OA.

538	That this study utilized a musculoskeletal simulation-based procedure to quantify muscle and
539	joint forces may serve as a limitation to the current investigation. Whist musculoskeletal
540	simulation is considered an improvement over previous analyses of lateral orthoses and toe-in/
541	toe-out gait using joint moments; it does depend on the underlying mathematical model and
542	numerous mechanical assumptions are made in the construction of musculoskeletal simulation
543	models. These predominately relate to the constrained rotational degrees of freedom at the
544	lower extremity joints in addition to the lack of modelled soft tissues in particular around the
545	knee joint itself, which may lead to incorrectly predicted muscle and joint forces (35).

547 In conclusion, although the mechanics of walking in lateral orthoses and with different foot progression angles have received previous research attention; there has yet to be a cumulative 548 comparison of lower extremity joint loading, using a musculoskeletal simulation based 549 approach. The present investigation adds to the current knowledge, by examining the effects 550 of lateral orthoses as well as toe-in/ toe-out gait patterns on lower extremity joint loading. This 551 552 investigation importantly showed that patellofemoral joint stress was greater in the neutral and lateral orthosis conditions and ankle joint loading larger in the toe-in and toe-out foot 553 progression angle modalities. Furthermore, it was also shown that medial tibiofemoral impulse 554 555 was statistically greater in the toe-in conditions. Therefore, the current investigation provides 556 evidence that altering the foot progression angle to may attenuate the risk from patellofemoral disorders whilst simultaneously enhancing the risk from degenerative ankle pathologies. 557 Similarly, adopting a toe-in foot progression angle may also increase the risk from medial 558 tibiofemoral degeneration. 559

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Figure 1. Comparison of hip forces across the stance phase, in different conditions. Positive
SPM values indicate that values in the first above named condition exceed those in the other;
SPM (t) denotes the t value and critical thresholds for statistical significance are denoted via
the horizontal dotted lines.



Figure 2. Comparison of patellofemoral forces/ stress across the stance phase, in different
conditions. Positive SPM values indicate that values in the first above named condition exceed
those in the other; SPM (t) denotes the t value and critical thresholds for statistical significance
are denoted via the horizontal dotted lines.



Figure 3. Comparison of medial tibiofemoral forces across the stance phase, in different conditions. Positive SPM values indicate that values in the first above named condition exceed those in the other; SPM (t) denotes the t value and critical thresholds for statistical significance are denoted via the horizontal dotted lines.



Figure 4. Comparison of lateral tibiofemoral forces across the stance phase, in different conditions. Positive SPM values indicate that values in the first above named condition exceed those in the other; SPM (t) denotes the t value and critical thresholds for statistical significance are denoted via the horizontal dotted lines.



1. Comparison of the a. hip joint force, b. medial tibiofemoral force, c. patellofemoral force, d. lateral tibiofemoral force, e. ankle force and f. patellofemoral stress across the stance phase in all conditions. SPM (F) denotes the F value, and critical thresholds for statistical significance are denoted via the horizontal dotted line.

Table 1: Joint kinetics (Mean & standard deviations) as a function of orthoses and foot progression angle conditions.

	Lateral orthoses		Neutral		Toe-in		Lateral toe-in		Toe-out		Lateral toe-out	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Ankle force impulse (BW·s)	1.51	0.09	1.53	0.11	1.65	0.11	1.59	0.09	1.62	0.09	1.58	0.11
Lateral tibiofemoral impulse (BW·s)	0.40	0.07	0.40	0.08	0.31	0.03	0.30	0.08	0.45	0.05	0.45	0.07
First peak medial tibiofemoral force (BW)	2.50	0.26	2.55	0.19	2.38	0.26	2.35	0.32	2.28	0.30	2.35	0.28
Second peak medial tibiofemoral force (BW)	2.61	0.32	2.73	0.37	2.90	0.37	2.86	0.31	2.67	0.42	2.64	0.46
Medial tibiofemoral force impulse (BW·s)	1.07	0.10	1.07	0.09	1.20	0.17	1.15	0.09	1.09	0.16	1.05	0.11
Peak patellofemoral force (BW)	1.83	0.63	1.93	0.53	1.53	0.66	1.59	0.74	1.54	0.61	1.61	0.63
Peak patellofemoral stress (KPa/BW)	3.96	1.03	4.20	0.87	3.33	1.02	3.43	1.12	3.35	1.01	3.53	1.03
Patellofemoral stress impulse (KPa/BW·s)	0.89	0.14	0.90	0.14	0.80	0.23	0.79	0.22	0.80	0.15	0.78	0.13
First peak hip force (BW)	3.94	0.65	3.72	0.44	3.41	0.56	3.44	0.55	3.84	0.65	3.77	0.49
Second peak hip force (BW)	4.89	1.03	4.96	1.05	5.20	1.61	5.04	1.55	4.43	1.11	4.36	0.86

Table 2: Muscle forces and impulses (Mean & standard deviations) as a function of orthoses and foot progression angle conditions.

	Lateral	orthoses	Neut	ral	Тое	e-in	Lateral	toe-in	Toe-	out	Lateral	toe-out
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Gluteus medius 2 first hip force peak (BW)	0.29	0.08	0.29	0.08	0.24	0.06	0.21	0.04	0.32	0.08	0.31	0.07
Gluteus medius 3 first hip force peak (BW)	0.30	0.14	0.30	0.08	0.27	0.13	0.21	0.10	0.33	0.16	0.33	0.13
Gluteus minimus 3 first hip force peak (BW)	0.10	0.03	0.10	0.02	0.09	0.02	0.08	0.02	0.11	0.03	0.09	0.02
Tensor fasciae latae first hip force peak (BW)	0.09	0.04	0.10	0.04	0.08	0.04	0.05	0.03	0.13	0.03	0.11	0.04
Rectus femoris first hip force peak (BW)	0.45	0.34	0.51	0.26	0.37	0.36	0.29	0.34	0.60	0.38	0.50	0.33
Gluteus medius 1 second hip force peak (BW)	0.47	0.17	0.46	0.11	0.35	0.14	0.38	0.15	0.41	0.11	0.42	0.13
Rectus femoris second hip force peak (BW)	1.03	0.63	1.05	0.46	1.24	0.85	1.10	0.79	0.81	0.73	0.78	0.67
Vastus intermedius first medial tibiofemoral force peak (BW)	0.48	0.20	0.50	0.10	0.42	0.16	0.44	0.18	0.38	0.18	0.42	0.14
Vastus lateralis first medial tibiofemoral force peak (BW)	0.86	0.36	0.92	0.19	0.74	0.31	0.78	0.32	0.68	0.33	0.75	0.26
Vastus medialis first medial tibiofemoral force peak (BW)	0.41	0.16	0.42	0.09	0.37	0.14	0.37	0.15	0.31	0.15	0.35	0.12
Rectus femoris first medial tibiofemoral force peak (BW)	0.33	0.35	0.33	0.21	0.24	0.24	0.22	0.23	0.43	0.34	0.33	0.24
Lateral gastrocnemius second medial tibiofemoral force peak (BW)	0.28	0.06	0.29	0.04	0.26	0.08	0.26	0.07	0.33	0.07	0.32	0.06
Vastus intermedius patellofemoral force peak (BW)	0.49	0.17	0.51	0.09	0.43	0.16	0.46	0.17	0.40	0.15	0.43	0.14
Lateral gastrocnemius impulse (BW·s)	0.06	0.01	0.07	0.01	0.07	0.02	0.06	0.01	0.08	0.02	0.07	0.01
Medial gastrocnemius impulse (BW·s)	0.28	0.04	0.28	0.04	0.32	0.09	0.30	0.04	0.33	0.06	0.31	0.05
Tibialis anterior impulse (BW·s)	0.04	0.02	0.04	0.01	0.04	0.02	0.04	0.01	0.04	0.01	0.05	0.02
Tibialis posterior impulse (BW·s)	0.04	0.02	0.07	0.05	0.03	0.03	0.03	0.03	0.15	0.08	0.15	0.08

Table 3: Correlations between joint kinetic parameters and foot progression angles with associated Bayes factors.

	r	BF
Lateral tibiofemoral impulse	0.73	1.78E+11
Second peak medial tibiofemoral force	-0.37	8.21
Medial tibiofemoral force impulse	-0.34	10.12

Table 4: Correlations between joint kinetic parameters and muscles forces/impulses with associated Bayes factors.

First hip force	e peak		Second hip force peak					
	r	BF		r	BF			
Adductor magnus 1	0.56	156069.21	Adductor magnus 1	0.61	4451247.16			
Adductor magnus 2	0.56	112579.04	Adductor magnus 2	0.55	50498.31			
Adductor magnus 3	0.50	4737.95	Adductor magnus 3	0.40	72.08			
Gluteus maximus 1	0.59	863819.92	Rectus femoris	0.96	2.75E+40			
Gluteus maximus 2	0.58	471381.57	Gluteus medius 2	-0.53	16994.49			
Gluteus maximus 3	0.52	14173.44	Gluteus medius 3	-0.49	2226.24			
Gluteus medius 2	0.33	7.32	Gluteus minimus 1	0.82	3.29E+17			
Gluteus medius 3	0.49	2590.80	Gluteus minimus 2	0.82	1.54E+17			
Gluteus medius 2	0.38	32.49	Gluteus minimus 3	0.59	799133.16			
Gluteus medius 3	0.56	144058.66	Tensor fasciae latae	0.76	1.08E+13			
First medial tibiofe	moral pe	ak	Second medial tibiofemoral peak					
	r	BF		r	BF			
Vastus intermedius	0.70	5.85E+09	Lateral gastrocnemius	0.30	3.23			
Vastus lateralis	0.70	5.55E+09	Medial gastrocnemius	0.72	8.45E+10			
Vastus medialis	0.68	1.09E+09						
Peak patellofeme	oral stres	<u>s</u>	Peak lateral tibiofemoral force					
	r	BF		r	BF			
Vastus intermedius	0.71	1.64E+10	Vastus lateralis	0.31	4.30			
Vastus lateralis	0.71	2.29E+10	Biceps femoris long head	0.30	3.29			
Vastus medialis	0.70	9.66E+09						
Ankle imp	ulse							
	r	BF						
Lateral gastrocnemius	0.54	37890.15						
Medial gastrocnemius	0.49	2787.68						
Soleus	0.45	486.95						
Tibialis posterior	0.31	3.59						