

Central Lancashire Online Knowledge (CLoK)

Title	Patient Characteristics Affect Hip Contact Forces during Gait
Type	Article
URL	https://clock.uclan.ac.uk/28376/
DOI	https://doi.org/10.1016/j.joca.2019.01.016
Date	2019
Citation	De Pieri, E, Lunn, DE, Chapman, Graham, Rasmussen, KP, Ferguson, SJ and Redmond, AC (2019) Patient Characteristics Affect Hip Contact Forces during Gait. <i>Osteoarthritis and Cartilage</i> , 27 (6). pp. 895-905. ISSN 1063-4584
Creators	De Pieri, E, Lunn, DE, Chapman, Graham, Rasmussen, KP, Ferguson, SJ and Redmond, AC

It is advisable to refer to the publisher's version if you intend to cite from the work.
<https://doi.org/10.1016/j.joca.2019.01.016>

For information about Research at UCLan please go to <http://www.uclan.ac.uk/research/>

All outputs in CLoK are protected by Intellectual Property Rights law, including Copyright law. Copyright, IPR and Moral Rights for the works on this site are retained by the individual authors and/or other copyright owners. Terms and conditions for use of this material are defined in the <http://clock.uclan.ac.uk/policies/>

Patient Characteristics Affect Hip Contact Forces during Gait

Enrico De Pieri ^{*1}, David E. Lunn ^{*2,3}, Graham J. Chapman ^{2,3}, Kasper P. Rasmussen ⁴, Stephen J. Ferguson ^{1 **}, Anthony C. Redmond ^{2,3}

* equally contributed to this work

¹ Institute for Biomechanics, ETH Zurich, Zurich, Switzerland

² Institute for Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK

³ NIHR Leeds Biomedical Research Centre, Leeds, UK

⁴ AnyBody Technology A/S, Aalborg, Denmark

** corresponding author

Email addresses: enrico.depieri@hest.ethz.ch; D.Lunn@leeds.ac.uk; G.J.Chapman@leeds.ac.uk; kasperpihl.r@gmail.com; sferguson@ethz.ch; A.Redmond@leeds.ac.uk

Corresponding author contact details:

Prof. Dr. Stephen J. Ferguson

Address: Höggerberggring 64, 8093 Zürich, Switzerland

Phone number: +41 44 633 93 30

Email: sferguson@ethz.ch

Running Headline: **Patient characteristics affect HCF**

24 **Abstract**

25

26 **Objective:** To examine hip contact force (HCF), calculated through multibody modelling, in a large
27 total hip replacement (THR) cohort stratified by patient characteristics such as BMI, age and
28 function.

29 **Design:** 132 THR patients undertook one motion capture session of gait analysis at a self-selected
30 walking speed. HCFs were then calculated using the AnyBody Modelling System. Patients were
31 stratified into three BMI groups, five age groups, and finally three functional groups determined by
32 their self-selected gait speed. Independent 1-dimensional linear regression **analyses** were performed
33 to separately evaluate the influence of age, BMI and functionality on HCF, by means of statistical
34 parametric mapping (SPM).

35 **Results:** The mean predicted HCF were comparable to HCFs measured with an instrumented
36 prosthesis reported in the literature. The regression analyses revealed a **statistically** significant
37 positive **relationship** between BMI and HCF, indicating that obese patients **are more likely to**
38 experience higher HCF during most of the stance phase, while a **statistically** significant **relationship**
39 with age was found only during the late swing-phase. Patients with higher functional ability
40 exhibited significantly increased peak contact forces, while patients with lower functional ability
41 displayed a pathological flattening of the typical double hump force profile.

42 **Conclusions:** HCFs experienced at the bearing surface are highly dependent on patient
43 characteristics. BMI and functional ability were determined to have the biggest influence on contact
44 force. Current preclinical testing standards do not reflect this.

45 **Keywords:** Total hip replacement, Hip contact force, Stratification, Biomechanics, Gait

46

47

48

49 **Introduction**

50

51 Total hip replacement (THR) surgery is commonly regarded as one of the most successful elective
52 orthopaedic surgeries of the 20th century ¹. It alleviates pain in patients suffering from debilitating
53 hip osteoarthritis and improves function. However there is some lifetime risk of implants requiring
54 revision, the rates of which are currently 4.4% at 10 years and 15% at 20 years². Epidemiological
55 studies have provided evidence to suggest that patient characteristics, such as age, BMI and gender
56 are important factors in the survivorship of hip implants^{2,3}. One in three patients undergoing THR at
57 < 50 years of age are expected to require revision surgery during their lifetime, with risks of one in
58 five for patients 50 to 59 years, one in ten for patients 60 to 69 years, and one in 20 for patients ≥ 70
59 years ⁴. The revision risk for younger patients is consistently higher than for older patients at all
60 time-points i.e. 5, 10, 15 and 20 years and gender also seems to affect risk ². Men aged younger than
61 70 years old have an increased revision risk compared to female patients, and at the age of 50 years
62 females have a 15% lower chance of revision compared to their male counterparts. BMI also
63 contributes to lifetime revision risk, with obese patients having twice the risk of revision at 10 years
64 compared to healthy weight and overweight patients, and it has been suggested by Culliford *et al.* ⁵
65 that for every unit increase of BMI, there is a 2% increased risk of revision of a THR.

66 The precise reason for these differences in revision rates between patient sub-groups is not clear,
67 however the variations in revision rates suggest that the demands placed on the implant likely differ
68 between patient groups. Due to the relatively small sample sizes typically employed in
69 biomechanical studies of THR cases, few studies have explored how patient characteristics can
70 differentially influence function post THR, and ultimately how those characteristics might affect
71 what demand is placed on the implant.

72

73 In these few studies age and BMI have been shown to influence function in THR patients. In one
74 analysis of a larger sample of patients from multiple retrospective studies, Foucher *et al.*⁶ found that
75 older patients had limited hip sagittal ROM and hip power generation compared to younger patients
76 who recovered better post-operatively. When stratifying gait function by age in a large cohort
77 (n=134) of THR patients, Bennett *et al.*^{7, 8} reported that gait kinematics and kinetics were not
78 influenced by age, except for a reduced ROM exhibited in an 80 years and over age group, a finding
79 also consistently observed in healthy control patients of a similar age range⁹. Foucher *et al.*^{6 10}
80 reported that BMI plays a role in recovery, with higher BMI patients having a reduced hip range of
81 motion (ROM) and hip abductor moment compared to healthy control participants. Furthermore,
82 lower BMI was associated with higher postoperative values of sagittal ROM, adduction moments,
83 and external rotation moments compared to THR patients with a higher BMI.

84

85 As described above, real-world patient function¹⁰ and survivorship of the hip implant² is affected by
86 the characteristics of the patient, although this is not currently reflected in preclinical wear testing
87 standards such as ISO 14242. Current preclinical testing protocols use a stylised waveform vaguely
88 representing a 'standard' THR patient's walking cycle to test the wear properties of the implant. A
89 recent study found that post-operative patient function accounts for 42% to 60% of wear, compared
90 to surgical factors which account for 10% to 33% of wear¹¹, emphasising the importance of
91 understanding how gait varies between different patient groups. No previous studies have tried to
92 understand how patient characteristics affect the absolute forces at the bearing surface, forces
93 which arguably will have the most influence on *in vivo* wear rates. Instrumented implants have been
94 used to calculate contact force at the bearing surface^{12, 13}, however the data available from these
95 implants is limited to small numbers of patients and extrapolating these data to the wider patient
96 population is not appropriate. Modern computational models of the musculoskeletal system can be
97 used to calculate joint contact forces and are becoming increasingly more clinically applicable¹⁴.
98 These models have the capability to calculate accurate joint contact forces in THR patients¹⁵, and

99 can be used to predict and compare contact forces in stratified samples derived from a large patient
100 cohort ¹⁶. The primary aim of this study therefore, was to examine hip contact force (HCF),
101 calculated through multibody modelling, in a large THR cohort when stratified by patient
102 characteristics such as BMI, age and function.

103 **Method**

104

105 ***Patients***

106

107 132 THR patients were recruited into the study through a clinical database of surgical cases.
108 Inclusion criteria for the hip replacement group were; between 1-5 years THR post-surgery, older
109 than 18 years of age, no lower limb joint replaced other than hip joint(s), fully pain free and not
110 suffering from any other orthopaedic or neurological problem which may compromise gait. Ethical
111 approval was obtained via the UK national NHS ethics (IRAS) system and all participants provided
112 informed, written consent.

113

114 ***Data Capture***

115

116 Lower limb kinematics and kinetics were collected using a ten camera Vicon system (Vicon MX,
117 Oxford Metrics, UK) sampling at 100Hz, integrated with two force plates (AMTI, Watertown, MA,
118 USA) capturing at 1000Hz in a 10m walkway. The operated limb (or most recently operated limb, in
119 bilateral cases) was used for analysis. All patients were allowed a familiarisation period prior to
120 completing 3-5 successful trials of each walking condition. A successful trial was defined as a clean
121 foot strike within the boundary of the force plate. The CAST marker set was used to track lower limb
122 segments kinematics in six degrees of freedom, with four non-orthogonal marker clusters positioned
123 over the lateral thighs, lateral shanks and sacrum as described comprehensively elsewhere ^{17, 18}. Six

124 retroreflective markers were positioned on the first, second and fifth metatarsophalangeal joints as
125 well as the malleoli and calcanei. Participants wore a pair of tight-fitting shorts and a vest onto which
126 reflective markers were affixed using double-sided tape at bony anatomical landmarks to determine
127 anatomical joint centres. Before walking trials commenced, a static trial was collected in an
128 anatomical reference position.

129

130 ***Data Processing***

131

132 All markers were labelled and gap-filled using the spline fill function in Vicon Nexus 2.5 (Vicon MX,
133 Oxford Metrics, UK), before the labelled marker coordinates and kinetic data were exported to
134 Visual 3D modelling software (C-Motion, Rockville, USA) for further analysis. Kinematic data were
135 filtered using a low-pass (6Hz) Butterworth filter. Ground reaction force (GRF) data were filtered
136 using a low-pass Butterworth filter (25Hz) and heel strike and toe-off were determined using
137 thresholds (>20N for heel strike and <20N for toe off) from the GRF.

138

139 ***Musculoskeletal modelling***

140

141 Musculoskeletal simulations were performed using commercially available software (AnyBody
142 Modeling System, Version 7.1, Aalborg, Denmark). A recently validated generic musculoskeletal
143 model ¹⁹ was scaled to match the anthropometrics of each patient. The scaling of the model
144 segments was based on the marker data collected during a static trial ²⁰. Marker trajectories and GRF
145 data from each gait trial served as input to an inverse dynamics analysis, based on a 3rd order
146 polynomial muscle recruitment criterion, to calculate muscle forces and HCFs. A total of 494 gait
147 trials were processed and analyzed through the toolkit AnyPyTools ([https://github.com/AnyBody-
148 Research-Group/AnyPyTools](https://github.com/AnyBody-Research-Group/AnyPyTools)).

149 The different components of HCFs, defined in a common femur-based reference frame ¹² were
150 computed for the operated limb over a gait cycle. The data were time-normalized from heel-strike
151 (0%), through toe-off (60%), to heel strike (100%) and interpolated to 1% steps (101 points). An
152 average per patient was then calculated based on the 3-5 trials collected.

153

154 ***Stratification by patient characteristics***

155

156 Patients were stratified by into three groups based on their BMI. BMI scores were calculated as
157 measured weight divided by measured height squared (kg/m^2). The three groups were; healthy
158 weight ($\text{BMI} \leq 25 \text{ kg}/\text{m}^2$); overweight ($\text{BMI} > 25 \text{ kg}/\text{m}^2$ to $\leq 30 \text{ kg}/\text{m}^2$) and obese ($\text{BMI} > 30 \text{ kg}/\text{m}^2$)²¹.
159 Patients were also stratified by age into five groups; 1) age 54 to 64 years, 2) 65 to 69 years, 3) 70 to
160 74 years, 4) 75 to 79, and 5) 80 years and over.

161

162 ***Stratification by functional ability***

163

164 A widely used alternative measure of overall functional ability is gait speed ^{22, 23}. There is some
165 negative overall correlation between chronological age and gait speed ²⁴, although age has been
166 shown to only explain 30% of the variance in gait speed ²⁵, suggesting that gait speed itself might be
167 a unique differential indicator of function compared to age. **Furthermore in a recent study ²⁶**
168 **suggested that patients walking at a higher gait speed is representative of the high functioning**
169 **patients compared to slower patients who would represent the low functioning patients. Therefore,**
170 in the main analysis, in addition to the stratification by age, patients were also stratified into three
171 functional strata determined by their self-selected gait speed. To define the functional strata, the
172 mean and standard deviations (SD) of the gait speeds for the whole cohort were determined. All
173 patients with a gait speed falling within 1SD of the mean were defined as normally functioning (NF).

174 Patients with a gait speed greater than 1SD above the mean were defined as high functioning (HF),
175 and those with a gait speed more than 1SD below the mean were defined as low functioning (LF).

176

177 ***Data Analysis***

178

179 Comparisons were made initially between the HCFs derived from the AnyBody model and the
180 measured HCFs from the Bergmann Orthoload literature¹². This was to compare absolute values and
181 ranges between the two populations and to test the validity of the computational model outputs.
182 Stratified mean peak values and 95% confidence intervals for the resultant force and the three force
183 components are also reported.

184 ***Statistical Parametric Mapping (SPM) analysis***

185

186 The computed HCFs were analysed using Statistical Parametric Mapping²⁷ (SPM, www.spm1D.org,
187 v0.4, in the Python programming language, www.python.org). Independent linear regression
188 analyses were performed to evaluate the influence of function, age, and BMI on the magnitude of
189 the HCFs, as well as on the individual force components. For each linear regression analysis, the t
190 statistic was computed at each point in the time series, thereby forming the test statistic continuum
191 $SPM\{t\}$, technical details are provided elsewhere²⁸⁻³⁰. Significance level was set at $\alpha=0.01$, and the
192 corresponding t^* critical threshold was calculated based on the temporal smoothness of the input
193 data through Random Field Theory. Finally, the probability that similar supra-threshold regions
194 would have occurred from equally smooth random waveforms was calculated. This analysis is based
195 on the assumptions of random sampling and homology of data³⁰, as well as normality in the data
196 distribution. Adherence to the latter assumption was tested by comparing the above-mentioned
197 parametric linear regression analyses with their non-parametric counterparts³⁰. The good

198 agreement between the two types of analysis, in terms of number, temporal extent, and size of the
199 supra-threshold clusters, supports the validity of the assumption of data normality.

200 The results of the three independent, 1-dimensional linear regression analyses from SPM were
201 further verified by means of 0-dimensional multiple regression analyses. The additional analyses
202 were run in SPSS (IBM SPSS Statistics for Windows, Armonk, NY, USA) at specific time points during
203 the gait cycle, corresponding with the peak loads during stance and the local minimum during mid-
204 stance (15, 32, and 48% of the gait cycle). The force values for the 132 patients at each of these time
205 points, as well as the investigated predictor variables (BMI, age, and gait speed) were normally
206 distributed. Variance inflation factor (VIF) and Tolerance statistics revealed no multi-collinearity in
207 the data, while Durbin-Watson statistics confirmed no autocorrelation between residuals. The
208 assumptions of homoscedasticity and normal distributions of the residuals were also met.

209 **Results**

210

211 *Patient Demographics*

212

213 132 patients took part in the study and the demographics can be found in Table 1.

214 - **Insert Table 1 here** -

215 *Musculoskeletal Model Simulations*

216

217 The predicted contact forces showed comparable trends and values with measured hip contact force
218 data. The mean values were comparable with those in the Orthoload published data and the ranges
219 were generally wider as might be expected from a larger dataset¹² (Figure1 and Table 2).

220

221 - Insert Table 2 and Figure 1 here -

222

223 **Peak Hip Contact Forces**

224

225 Stratified mean peak values for the resultant force and the three force components are reported in
226 full as supplementary data (Supplementary File Table 1).

227 **Statistical Parametric Mapping**

228

229 The results of the comparator multiple linear regression analyses were in agreement with the
230 outcome of the SPM analysis, confirming a statistically significant positive relationship for both BMI
231 and gait speed with HCF during both the 1st peak and 2nd peak of the stance phase, and a
232 statistically significant positive relationship for BMI and a negative one for gait speed during the mid-
233 stance valley. For the SPM analysis, only differences which were statistically significant for more than
234 2% of the gait cycle are discussed.

235

236 ***BMI***

237

238 There was a statistically significant relationship between BMI and the magnitude of the total HCF
239 (Figure 2a). Obese patients demonstrated significantly increased HCF throughout the loaded stance
240 phase (8.8 – 53.8%), mid-swing (74.6 – 79.3%), and terminal swing (88.7 – 100%). All the supra-
241 thresholds clusters exceeded the critical threshold $t^*=3.676$ with associated p-values <0.001 , 0.003 ,
242 and <0.001 respectively.

243 The same trends were observed for the proximo-distal component (Figure 2b), for which the test
244 statistics similarly exceeded the upper threshold $t^*=+3.678$ at 5.4 – 54.3% ($p<0.001$), 73.5 – 79.2%
245 ($p=0.001$), 88.4 – 100% ($p<0.001$).

246 In the anteroposterior direction (Figure 2c), **statistically** significant negative **relationship** was found
247 during loading response to mid-stance (10.6 – 29.9%), terminal stance (45.4 – 55.3%), and from mid-
248 swing phase (72.2 – 100%). The clusters exceeded the threshold $t^*=-3.667$ with p-values <0.001 . No
249 significant difference was observed for the medio-lateral component (Figure 2d).

250

251 ***Age***

252

253 There was a **statistically** significant negative relationship between age and the magnitude of the total
254 HCF (Figure 3a), however this was limited to the terminal swing phase (90.7 – 98.7%), with the
255 cluster exceeding the critical threshold $t^*=-3.660$ with $p<0.001$. This indicates that younger patients
256 **are more likely to** experience higher contact forces during this phase. The same trend was observed
257 for the proximo-distal component, for which the test statistics similarly exceeded the lower
258 threshold $t^*=-3.659$ at 90.7 – 98.7% of the gait cycle, with an associated p-value <0.001 (Figure 3b),
259 and for the medio-lateral component at 91.8 – 97.7% of the gait cycle ($t^*=-3.633$, $p=0.002$) (Figure
260 3d). In the anteroposterior direction, no **statistically** significant **relationship** was found (Figure 3c).

261

262 ***Function***

263

264 The mean gait speed for the functional ability stratum was $0.82 \text{ m}\cdot\text{s}^{-1}$ (SD; ± 0.08), $1.10 \text{ m}\cdot\text{s}^{-1}$ (± 0.09)
265 and $1.37 \text{ m}\cdot\text{s}^{-1}$ (± 0.09) for LF, NF and HF, respectively. There was a **statistically** significant relationship
266 between functional ability and the magnitude of the total HCF (Figure 4a). Patients with a higher
267 function demonstrated significantly increased HCF during initial contact to loading response (0 – 16%
268 gait cycle), terminal stance to initial swing (43.8 – 74.1%), and terminal swing (87.8 – 100%). A
269 **statistically significant** negative **relationship** was instead found during mid-stance (27.9-34.9%). All

270 the supra-threshold clusters exceeded the critical threshold $t^*=\pm 3.668$, with the chances of
271 observing similar clusters in repeated random samplings being $p<0.001$.
272 The same trends were observed for the proximo-distal component (the dominant component in
273 terms of magnitude), with the corresponding supra-threshold ($t>t^*=\pm 3.666$) areas spanning from 0 –
274 15.3%, 45.1 – 73%, 87.7 – 100%, and 27.4 – 35%, respectively (Figure 4b). In the anteroposterior
275 direction, statistically significant negative relationship was found during initial contact to loading
276 response (0.6 – 16.3%) and terminal swing (91.6 – 100%), indicating that higher function
277 demonstrated a significantly increased posterior force during these phases (Figure 4c), while a
278 statistically significant positive relationship was found during mid-stance (27.3 – 45.9%). All the
279 clusters exceeded the critical threshold $t^*=\pm 3.658$ with p-values <0.001 . Statistically significant
280 positive relationships were observed for the medio-lateral component during initial contact to
281 leading response (0-19.8%), terminal stance to mid-swing (43.8 – 75.4%), and late swing phase (91.6
282 – 100%) (Figure 4d).

283

284 Discussion

285

286 This is the first study to explore the effect of patient characteristics on joint loading through
287 multibody modelling in a large cohort. We found that resultant HCF varies between different patient
288 groups and identified systematic differences between strata for BMI and functional ability. The BMI
289 strata displayed statistically significant differences in the resultant force throughout most of stance
290 phase. Few differences were observed between the age strata, whereas the functional strata,
291 represented by gait speed, displayed the greatest range of statistically significant differences across
292 the time series (over approx. 60% of the whole gait cycle). Patients with a high functionality had
293 increased peak loads during the stance phase of the gait cycle, while low functioning patients
294 displayed a pathological HCF, with a flattening of the typical double hump (Figure 4a). These trends

295 were similar when observing the difference in the proximo-distal component of the HCF, albeit
296 unsurprisingly considering this is the main contributor to the resultant HCF. Our average peak HCF
297 (2449N) was of a similar magnitude to the HCFs measured with instrumented implants by Bergmann
298 *et al.*¹² (2225.7N) (Table 2). No past research has considered the effect of patient characteristics on
299 HCF and comparison to previous literature is difficult. However, previous work has found that joint
300 kinematics and forces acting around the joint are affected by different patient characteristics⁶⁻⁸ and
301 altered gait variables can affect the magnitude of joint contact forces³¹, and therefore this variability
302 in HCF would be expected.

303

304 ***BMI***

305

306 We found a systematic trend for HCFs to increase with an increasing BMI, and this was expected due
307 to the increase in body mass which has been previously reported to increase linearly with joint
308 contact force³². These systematic changes in magnitude are a consistent finding in the literature
309 comparing obese and healthy weight participants when force data are non-normalised, and the
310 differences between BMI groups tend to disappear when normalised to body mass³³, which is
311 common practice in the biomechanical literature exploring function. In our study we specifically
312 chose not to normalise HCF to body weight, as we were interested in the absolute magnitude of the
313 real world forces to which the bearing surface would be exposed. Analysing non-normalised HCFs
314 may help to explain observed BMI dependant revision rates², as increased loads in preclinical
315 hardware simulator testing has been shown to increase wear volume and wear particle size³⁴.

316

317 ***Age***

318

319 When stratified by age there were very few differences observed in HCF in our patient cohort, with
320 **statistically** significant differences only found during the terminal swing phase in the proximo-distal

321 and resultant forces (90.7 – 98.7%) and medio-lateral component (91.8 – 97.7%), where the hip is
322 relatively unloaded. Differences in terminal swing phase may be related to the capacity for
323 individuals to energetically drive the limb forward. Compared to the functional strata, the temporal
324 range of significance was much less, indicating that grouping patients by age, as a measure of
325 function, does not differentiate well between patients. No other study has considered the effect of
326 age on HCF measures specifically, however in a gait study using conventional motion capture
327 analysis, Bennett *et al.* ^{7,8} observed little kinematic or kinetic differences between age groups in THR
328 patients. As noted previously, the absolute risk of revision in younger patients, can be up to ten
329 times higher than in older patients ² and it is likely that other factors such as overall activity level in
330 younger patients being higher or younger patients undertaking more demanding adverse loading
331 activities may contribute more than age-related variability in loads during normal walking.

332

333 ***Functional ability***

334

335 Our results suggest the functional capability of the patient, identified by biomechanical
336 characteristics, best identifies differences between patient groups. When stratifying patients by gait
337 speed, not only were peak forces increased in the HF group, but the waveform in the LF group
338 displayed pathological patterns with a flattening of the transition phase between the two peaks of
339 axial forces (Figure 4a). A trend was also observed in joint contact forces derived at different walking
340 speeds, with the slower walking speeds exhibiting a reduced force during the transition between the
341 peaks ³⁵. This GRF/HCF waveform has been associated with pathological symptoms in patients with
342 OA or other neurological pathologies ³⁶, suggesting that amongst our patient cohort, all of whom
343 during screening had self-reported as well-functioning, were patients who were indeed pathological,
344 identified by different HCF waveforms. Furthermore, those with higher walking speeds exhibit
345 increased GRFs and joint moments ³⁷, a trend also observed in our HCFs in the function strata.
346 Patient characteristics such as age and BMI are often controlled for in preclinical testing, whereas

347 the real-world functional capability of THR patient is frequently overlooked. Our results suggest that
348 the functional capability of patients could be the most influential factor in determining forces at the
349 bearing surface.

350

351 ***Limitations***

352

353 Previous work has identified that simulating different activities in preclinical testing also leads to
354 increased wear volume ³⁸. In the current study we only analysed walking and in reality patients
355 perform a number of other daily tasks which can change the overall loading conditions ³⁹. Walking is
356 the most commonly performed daily task ⁴⁰ however, and it is reasonable to suggest that walking
357 would have a **clinically relevant** impact on implant performance post-surgery. Within the multibody
358 modelling, a number of simulations were run from scaled generic models, and a certain level of error
359 associated with soft-tissue artefacts and the lack of subject-specific bone geometry and muscle
360 physiology information might persist. These models have been previously validated against in-vivo
361 data from different subjects however ^{14, 15, 19} with good agreement. The overall agreement with the
362 range of measurements from instrumented patients further supports the validity of the current
363 models' predictions.

364 **It could be expected that follow up time could have an effect on patient gait and hip contact force**
365 **and short-term follow up has shown as much ^{31, 41}. However, patients were recruited between 1-5**
366 **years post operatively in an attempt to avoid abnormalities due to post-surgery recovery and**
367 **patients mean follow-up time were similar in all groups (Table 1).**

368 **Finally, as this study was exploratory in nature we did not analyse any interactions between the**
369 **strata. It would be expected that there could be some interactions, for example, between age and**
370 **function ²³, which could potentially be more clinically relevant. However the analysis of interactions**
371 **is not possible in *spm1D* and therefore we decided to keep the focus of the paper on the temporal**

372 analysis in the individual strata, as this is relevant for other applications where full waveform data is
373 required, such as preclinical testing.

374

375

376 In conclusion, we have found that the HCF predicted at the bearing surface is highly dependent on
377 the characteristics of the patient. Conversely, current preclinical laboratory testing standards reflect
378 only one loading scenario while our study has shown systematic differences in loading patterns
379 between patient groups (Figures 2-4). To our knowledge these differences are also not considered
380 in any *in-silico* wear prediction models, although more complex waveforms, compared to ISO, have
381 resulted in greater predicted differences wear volume^{42, 43}. By extension, if future modelling included
382 patient variability, our data suggest that it is possible that differences in wear rates would also be
383 predicted. We have to accept that failure of an implant is multi factorial and patient factors and
384 surgical factors need to be taken into consideration. However if pre-clinical testing were robust
385 enough to check how implants would perform in different types of patients then patient-dependant
386 failures could potentially be better predicted. Importantly, patient variability is not considered at all
387 in current preclinical hardware simulator testing, which determines whether a device new to market
388 is fit for purpose. It was beyond the realm of this work to test this experimentally in full, but if the
389 loading profiles generated in this study were used in preclinical hardware tests, it would be expected
390 that the variability between patient groups found in this study would also be seen in experimental
391 wear testing⁴⁴. There is certainly a movement towards using different/updated testing procedures
392 with a number of authors suggesting wear testing under more adverse loads is warranted⁴⁴.
393 Improved preclinical testing, both *in silico* and *in vitro*, using more patient stratified waveforms
394 would highlight where and in whom failures are more likely to occur, allowing for better implant
395 design and more informed decision making at the time of THR planning for surgeons. Future work
396 should focus on using patient specific waveforms for *in vitro* testing to check whether the
397 differences observed in this study influence experimental wear rates.

398 **Acknowledgements**

399

400 This study was supported by the European Union's Seventh Framework Programme (FP7/2007-2013)
401 under grant agreement no. GA-310477 LifeLongJoints and by the Leeds Experimental Osteoarthritis
402 Treatment Centre which is supported by Arthritis Research UK (grant no. 20083). This research is
403 also supported by the National Institute for Health Research (NIHR) infrastructure at Leeds. The
404 views expressed in this publication are those of the author(s) and not necessarily those of the NHS,
405 the National Institute for Health Research or the Department of Health.

406 We would like to thank AnyBody Technology A/S for all the technical support, and particularly
407 Morten E. Lund, for developing the toolkit *AnyPyTools* and helping with automatizing such a large-
408 scale analysis.

409

410 **Author contributions**

411

412 All authors were involved in the conception and design of the study. DEL and EDP performed data
413 acquisition, data processing and analysis. All authors were involved in interpreting the data, revising
414 the manuscript for critically important intellectual content and approved the final version to be
415 submitted.

416

417 **Role of the funding source**

418

419 The funding source had no role in the study design, collection, analysis and interpretation of the
420 data, in the writing of the manuscript, or in the decision to submit the manuscript for publication.

421

422 **Competing interest statement**

423

424 The authors have no competing interests to declare

425

426 **Supplementary data**

427

428 **Supplementary data associated with this article can be found in the online version.**

429 Data associated with this research, in C3d format, can be found at <https://doi.org/10.5518/345>. This

430 data can be subsequently used with AnyBody Modelling software to calculate joint contact forces.

431 Musculoskeletal models for all trials in the data repository have been implemented with the

432 AnyBody Modelling software and are freely available at Zenodo (DOI: 10.5281/zenodo.1254286)

433

434 **References**

435

- 436 1. Learmonth ID, Young C, Rorabeck C. The operation of the century: total hip replacement.
437 Lancet 2007; 370: 1508-1519.
- 438 2. Bayliss LE, Culliford D, Monk AP, Glyn-Jones S, Prieto-Alhambra D, Judge A, et al. The effect
439 of patient age at intervention on risk of implant revision after total replacement of the hip or
440 knee: a population-based cohort study. The Lancet; 389: 1424-1430.
- 441 3. Towle KM, Monnot AD. An Assessment of Gender-Specific Risk of Implant Revision After
442 Primary Total Hip Arthroplasty: A Systematic Review and Meta-analysis. The Journal of
443 Arthroplasty 2016; 31: 2941-2948.
- 444 4. Abdel MP, Roth Pv, Harmsen WS, Berry DJ. What is the lifetime risk of revision for patients
445 undergoing total hip arthroplasty? The Bone & Joint Journal 2016; 98-B: 1436-1440.

- 446 5. Culliford D, Maskell J, Judge A, Arden NK. A population-based survival analysis describing the
447 association of body mass index on time to revision for total hip and knee replacements:
448 results from the UK general practice research database. *BMJ Open* 2013; 3.
- 449 6. Foucher KC. Identifying clinically meaningful benchmarks for gait improvement after total
450 hip arthroplasty. *J Orthop Res* 2016; 34: 88-96.
- 451 7. Bennett D, Humphreys L, O'Brien S, Kelly C, Orr JF, Beverland DE. Gait kinematics of age-
452 stratified hip replacement patients--a large scale, long-term follow-up study. *Gait Posture*
453 2008; 28: 194-200.
- 454 8. Bennett D, Ryan P, O'Brien S, Beverland DE. Gait kinetics of total hip replacement patients-A
455 large scale, long-term follow-up study. *Gait Posture* 2017; 53: 173-178.
- 456 9. Nigg BM, Fisher V, Ronsky JL. Gait characteristics as a function of age and gender. *Gait &*
457 *Posture* 1994; 2: 213-220.
- 458 10. Foucher KC, Freels S. Preoperative factors associated with postoperative gait kinematics and
459 kinetics after total hip arthroplasty. *Osteoarthritis and Cartilage* 2015; 23: 1685-1694.
- 460 11. Ardestani MM, Amenabar Edwards PP, Wimmer MA. Prediction of Polyethylene Wear Rates
461 from Gait Biomechanics and Implant Positioning in Total Hip Replacement. *Clin Orthop Relat*
462 *Res* 2017; 475: 2027-2042.
- 463 12. Bergmann G, Bender A, Dymke J, Duda G, Damm P. Standardized Loads Acting in Hip
464 Implants. *PLOS ONE* 2016; 11: e0155612.
- 465 13. Bergmann G, Deuretzbacher G, Heller M, Graichen F, Rohlmann A, Strauss J, et al. Hip
466 contact forces and gait patterns from routine activities. *Journal of Biomechanics* 2001; 34:
467 859-871.
- 468 14. Fregly BJ, Besier TF, Lloyd DG, Delp SL, Banks SA, Pandy MG, et al. Grand challenge
469 competition to predict in vivo knee loads. *J Orthop Res* 2012; 30: 503-513.

- 470 15. Fischer MCM, Eschweiler J, Schick F, Asseln M, Damm P, Radermacher K. Patient-specific
471 musculoskeletal modeling of the hip joint for preoperative planning of total hip arthroplasty:
472 A validation study based on in vivo measurements. PLOS ONE 2018; 13: e0195376.
- 473 16. Saxby DJ, Modenese L, Bryant AL, Gerus P, Killen B, Fortin K, et al. Tibiofemoral contact
474 forces during walking, running and sidestepping. Gait & Posture 2016; 49: 78-85.
- 475 17. Benedetti MG, Catani F, Leardini A, Pignotti E, Giannini S. Data management in gait analysis
476 for clinical applications. Clinical Biomechanics 1998; 13: 204-215.
- 477 18. Cappozzo A, Catani F, Croce UD, Leardini A. Position and orientation in space of bones during
478 movement: anatomical frame definition and determination. Clin Biomech (Bristol, Avon)
479 1995; 10: 171-178.
- 480 19. De Pieri E, Lund ME, Gopalakrishnan A, Rasmussen KP, Lunn DE, Ferguson SJ. Refining muscle
481 geometry and wrapping in the TLEM 2 model for improved hip contact force prediction. PLoS
482 ONE In Press.
- 483 20. Lund ME, de Zee M, Andersen MS, Rasmussen J. On validation of multibody musculoskeletal
484 models. Proc Inst Mech Eng H 2012; 226: 82-94.
- 485 21. Organization WH. Obesity and overweight. Fact sheet no. 311. Updated January 2015. World
486 Health Organization.[Cited: 2015 November 20] Available from: [http://www.who.](http://www.who.int/mediacentre/factsheets/fs311/en)
487 [int/mediacentre/factsheets/fs311/en](http://www.who.int/mediacentre/factsheets/fs311/en) 2015.
- 488 22. Middleton A, Fritz SL, Lusardi M. Walking speed: the functional vital sign. J Aging Phys Act
489 2015; 23: 314-322.
- 490 23. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. JAMA 2011; 305:
491 50-58.
- 492 24. Bohannon RW, Williams Andrews A. Normal walking speed: a descriptive meta-analysis.
493 Physiotherapy 2011; 97: 182-189.

- 494 25. Alcock L, Vanicek N, O'Brien TD. Alterations in gait speed and age do not fully explain the
495 changes in gait mechanics associated with healthy older women. *Gait & Posture* 2013; 37:
496 586-592.
- 497 26. O'Connor JD, Rutherford M, Bennett D, Hill JC, Beverland DE, Dunne NJ, et al. Long-term hip
498 loading in unilateral total hip replacement patients is no different between limbs or
499 compared to healthy controls at similar walking speeds. *Journal of Biomechanics* 2018; 80: 8-
500 15.
- 501 27. Friston KJ, Holmes AP, Worsley KJ, Poline JP, Frith CD, Frackowiak RS. Statistical parametric
502 maps in functional imaging: a general linear approach. *Human brain mapping* 1994; 2: 189-
503 210.
- 504 28. Pataky TC. Generalized n-dimensional biomechanical field analysis using statistical
505 parametric mapping. *J Biomech* 2010; 43: 1976-1982.
- 506 29. Pataky TC. One-dimensional statistical parametric mapping in Python. *Comput Methods*
507 *Biomech Biomed Engin* 2012; 15: 295-301.
- 508 30. Pataky TC, Vanrenterghem J, Robinson MA. Zero- vs. one-dimensional, parametric vs. non-
509 parametric, and confidence interval vs. hypothesis testing procedures in one-dimensional
510 biomechanical trajectory analysis. *J Biomech* 2015; 48: 1277-1285.
- 511 31. Wesseling M, de Groot F, Meyer C, Corten K, Simon JP, Desloovere K, et al. Gait alterations
512 to effectively reduce hip contact forces. *J Orthop Res* 2015; 33: 1094-1102.
- 513 32. Sanford BA, Williams JL, Zucker-Levin AR, Mihalko WM. Hip, Knee, and Ankle Joint Forces in
514 Healthy Weight, Overweight, and Obese Individuals During Walking. In: Doyle B, Miller K,
515 Wittek A, Nielsen PMF Eds. *Computational Biomechanics for Medicine*. New York, NY:
516 Springer New York 2014:101-111.
- 517 33. Lerner ZF, Browning RC. Compressive and shear hip joint contact forces are affected by
518 pediatric obesity during walking. *Journal of Biomechanics* 2016; 49: 1547-1553.

- 519 34. Bowsher JG, Hussain A, Williams PA, Shelton JC. Metal-on-metal hip simulator study of
520 increased wear particle surface area due to 'severe' patient activity. Proceedings of the
521 Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine 2006; 220:
522 279-287.
- 523 35. Georgios G, Ilse J, Mariska W, Sam VR, Sabine V. Loading of Hip Measured by Hip Contact
524 Forces at Different Speeds of Walking and Running. Journal of Bone and Mineral Research
525 2015; 30: 1431-1440.
- 526 36. Perry J, Davids JR. Gait analysis: normal and pathological function. Journal of Pediatric
527 Orthopaedics 1992; 12: 815.
- 528 37. Ardestani MM, Ferrigno C, Moazen M, Wimmer MA. From normal to fast walking: Impact of
529 cadence and stride length on lower extremity joint moments. Gait & Posture 2016; 46: 118-
530 125.
- 531 38. Fabry C, Herrmann S, Kaehler M, Woernle C, Bader R. Generation of Physiological Movement
532 and Loading Parameter Sets for Preclinical Testing of Total Hip Replacements With Regard
533 to Frequent Daily Life Activities. Bone & Joint Journal Orthopaedic Proceedings Supplement
534 2013; 95: 194-194.
- 535 39. Varady PA, Glitsch U, Augat P. Loads in the hip joint during physically demanding
536 occupational tasks: A motion analysis study. Journal of Biomechanics 2015; 48: 3227-3233.
- 537 40. Morlock M, Schneider E, Bluhm A, Vollmer M, Bergmann G, Müller V, et al. Duration and
538 frequency of every day activities in total hip patients. Journal of Biomechanics 2001; 34: 873-
539 881.
- 540 41. Colgan G, Walsh M, Bennett D, Rice J, O'Brien T. Gait analysis and hip extensor function early
541 post total hip replacement. Journal of Orthopaedics 2016; 13: 171-176.
- 542 42. Liu F, Fisher J, Jin Z. Effect of motion inputs on the wear prediction of artificial hip joints.
543 Tribology International 2013; 63: 105-114.

544 43. Gao L, Wang F, Yang P, Jin Z. Effect of 3D physiological loading and motion on
545 elastohydrodynamic lubrication of metal-on-metal total hip replacements. Med Eng Phys
546 2009; 31: 720-729.

547 44. Zietz C, Fabry C, Reinders J, Dammer R, Kretzer JP, Bader R, et al. Wear testing of total hip
548 replacements under severe conditions. Expert Review of Medical Devices 2015; 12: 393-410.

549

550

551

552

553

554

555

556 **Figure Legends**

557

558 **Figure 1.** Predicted HCF across the patients' cohort compared to the measured HCF from the
559 Orthoload dataset (<https://orthoload.com/test-loads/standardized-loads-acting-at-hip-implants/>)¹².
560 Resultant force (blue) and single components – proximo-distal (red), antero-posterior (orange),
561 medio-lateral (green) – are reported as mean across the cohort (solid line) and overall range of
562 variation (shaded area) and compared to the corresponding mean and range of variations from the
563 Orthoload measurements (in grey). Peak values reported in Table 2 are indicated in each plot.

564

565 **Figure 2.** Predicted hip contact forces across patients reported as a) resultant magnitude, and
566 individual components: b) proximo-distal, c) antero-posterior, and d) medio-lateral component. The
567 patients were stratified in *Healthy Weight* (blue), *Overweight* (purple) and *Obese* (red) according to

568 their BMI score. The upper panels report the averages for each patient strata (solid line) and their
569 relative 95% confidence intervals. Additionally, the loading profile from the ISO14242-1 testing
570 standard (dashed grey line) is compared to the proximo-distal forces for each group. The
571 corresponding lower panels report the results of the SPM linear regression analysis. The significance
572 α -level was set to 0.01 for each analysis and the corresponding threshold t^* are reported (horizontal
573 dashed lines). Whenever the test statistics **continuum** $SPM\{t\}$ exceeds the threshold, significance is
574 reached and the p-values associated with the supra-threshold clusters (shaded grey areas) are
575 reported.

576

577 **Figure 3.** Predicted hip contact forces across patients reported as a) resultant magnitude, and
578 individual components: b) proximo-distal, c) antero-posterior, and d) medio-lateral component. The
579 patients were stratified according to their age in five groups: 54:64 (orange), 65:69 (red), 70:74
580 (grey), 75:79 (blue) and ≥ 80 (green). The upper panels report the averages for each patient strata
581 (solid line) and their relative 95% confidence intervals. Additionally, the loading profile from the
582 ISO14242-1 testing standard (dashed grey line) is compared to the proximo-distal forces for each
583 group. The corresponding lower panels report the results of the SPM linear regression analysis. The
584 significance α -level was set to 0.01 for each analysis and the corresponding threshold t^* are
585 reported (horizontal dashed lines). Whenever the test statistics **continuum** $SPM\{t\}$ exceeds the
586 threshold, significance is reached and the p-values associated with the supra-threshold clusters
587 (shaded grey areas) are reported.

588

589 **Figure 4.** Predicted hip contact forces across patients reported as a) resultant magnitude, and
590 individual components: b) proximo-distal, c) antero-posterior, and d) medio-lateral component. The
591 patients were stratified in Low Functioning (purple), Normal Functioning (blue) and High Functioning
592 (green) according to their self-selected gait speed. The upper panels report the averages for each

593 patient strata (solid line) and their relative 95% confidence intervals. Additionally, the loading profile
594 from the ISO14242-1 testing standard (dashed grey line) is compared to the proximo-distal forces for
595 each group. The corresponding lower panels report the results of the SPM linear regression analysis.
596 The significance α -level was set to 0.01 for each analysis and the corresponding threshold t^* are
597 reported (horizontal dashed lines). Whenever the test statistics **continuum** SPM{t} exceeds the
598 threshold, significance is reached and the p-values associated with the supra-threshold clusters
599 (shaded grey areas) are reported.

600

601 **Table 1.** Patient demographics for each classification strata. Values are reported as mean (SD) unless
 602 otherwise stated.

603

		Number of patients	Female:Male	Age (Years)	BMI (kg/m ²)	Post-surgery (Years)
All		132	66:66	71.6 (7.6)	28.2(3.8)	2.8 (1.4)
BMI	Healthy Weight	29	18:11	70.1(8.2)	23.4(1.2)	2.6(1.2)
	Overweight	67	31:36	73.2(7.2)	27.6(1.3)	2.8(1.4)
	Obese	36	17:20	69.7(7.0)	33.2(2.2)	3.0(1.6)
Age	54-64	22	11:11	60.4 (2.9)	28.5(5.3)	2.9(1.5)
	65-69	37	17:20	67.0(1.4)	28.9(3.4)	2.8(1.6)
	70-74	23	14:9	72.3(1.0)	27.8(4.2)	2.1(1.1)
	75-79	28	14:14	77.4(1.2)	28.2(3.0)	2.7(1.3)
	>=80	22	10:12	82.4(3.0)	27.1(2.7)	3.0(1.5)
Function	HF	18	7:11	69.3(6.1)	27.1(2.8)	3.6(1.4)
	NF	97	48:49	71.3(7.7)	28.2(3.8)	2.7(1.4)
	LF	17	11:6	75.8(6.3)	29.3(4.4)	2.7(1.2)

604

605

606

607

608

609

610

611

Table 2. A comparison of measured peak contact forces¹² and the calculated peak contact forces from our study. Values are reported as mean and ranges (min-max). The reported values are highlighted in the corresponding graphs in Figure 1.

Dataset	Peak resultant force 1 st peak (R1) (min-max range)	Peak resultant force 2nd peak (R2) (min-max range)	Peak Proximal/Distal force 1st peak (PD1) (min-max range)	Peak Proximal/Distal force 2nd peak (PD2) (min-max range)	Peak posterior force(P1) (min-max range)	Peak Anterior forces (A1) (min-max range)	Peak Medial/Lateral force 1st peak (ML1) (min-max range)	Peak Medial/Lateral force 2nd peak (ML2) (min-max range)
LLJ dataset	2449.1 (1310.9 , 3913.5)	2279.0 (1093.8 , 3920.5)	2254.3 (1179.8 , 3694.4)	2197.3 (1030.8 , 3849.1)	-466.1 (-838.0 , -232.9)	-60.5 (-365.3 , 297.2)	826.0 (459.4 , 1353.5)	599.0 (273.2 , 1063.3)
Orthoload	2225.7 (1793.4 , 3147.0)	2149.9 (1721.2 , 2546.8)	2085.8 (1670.1 , 3006.5)	2073.6 (1643.8 , 2475.2)	-405.7 (-650.4 , -111.4)	23.5 (-193.0 , 211.7)	641.3 (366.7 , 819.5)	600.0 (341.1 , 807.2)