

## Article

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# Patient Characteristics Affect Hip Contact Forces during Gait

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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 20<sup>th</sup> century <sup>1</sup>. 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 years<sup>2</sup>. 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<sup>2,3</sup>. 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 <sup>4</sup>. 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 <sup>2</sup>. 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.* <sup>5</sup>  
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.*<sup>6</sup> 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.*<sup>7, 8</sup> 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 range<sup>9</sup>. Foucher *et al.*<sup>6 10</sup>  
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 function<sup>10</sup> and survivorship of the hip implant<sup>2</sup> 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 wear<sup>11</sup>, 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<sup>12, 13</sup>, 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 applicable<sup>14</sup>.  
98 These models have the capability to calculate accurate joint contact forces in THR patients<sup>15</sup>, and

99 can be used to predict and compare contact forces in stratified samples derived from a large patient  
100 cohort <sup>16</sup>. 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 <sup>17, 18</sup>. 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 <sup>19</sup> 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 <sup>20</sup>. Marker trajectories and GRF  
145 data from each gait trial served as input to an inverse dynamics analysis, based on a 3<sup>rd</sup> 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 <sup>12</sup> 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 ( $\text{kg}/\text{m}^2$ ). 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 ( $\text{BMI} > 30 \text{ kg}/\text{m}^2$ )<sup>21</sup>.  
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 <sup>22, 23</sup>. There is some  
165 negative overall correlation between chronological age and gait speed <sup>24</sup>, although age has been  
166 shown to only explain 30% of the variance in gait speed <sup>25</sup>, suggesting that gait speed itself might be  
167 a unique differential indicator of function compared to age. **Furthermore in a recent study <sup>26</sup>**  
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 literature<sup>12</sup>. 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 Mapping<sup>27</sup> (SPM, [www.spm1D.org](http://www.spm1D.org),  
187 v0.4, in the Python programming language, [www.python.org](http://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 elsewhere<sup>28-30</sup>. 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 data<sup>30</sup>, 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 counterparts<sup>30</sup>. 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 dataset<sup>12</sup> (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;  $\pm 0.08$ ),  $1.10 \text{ m}\cdot\text{s}^{-1}$  ( $\pm 0.09$ )  
265 and  $1.37 \text{ m}\cdot\text{s}^{-1}$  ( $\pm 0.09$ ) 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.*<sup>12</sup> (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 characteristics<sup>6-8</sup> and  
301 altered gait variables can affect the magnitude of joint contact forces<sup>31</sup>, 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 force<sup>32</sup>. 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 mass<sup>33</sup>, 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 rates<sup>2</sup>, as increased loads in preclinical  
315 hardware simulator testing has been shown to increase wear volume and wear particle size<sup>34</sup>.

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.*<sup>7,8</sup> 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<sup>2</sup> 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<sup>35</sup>. This GRF/HCF waveform has been associated with pathological symptoms in patients with  
342 OA or other neurological pathologies<sup>36</sup>, 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<sup>37</sup>, 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 <sup>38</sup>. 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 <sup>39</sup>. Walking is  
356 the most commonly performed daily task <sup>40</sup> 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 <sup>14, 15, 19</sup> 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 <sup>31, 41</sup>. 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 <sup>23</sup>, 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<sup>42, 43</sup>. 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 testing<sup>44</sup>. 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 warranted<sup>44</sup>.  
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.

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399

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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.

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## 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/>)<sup>12</sup>.  
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  $\alpha$ -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  $\geq 80$  (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  $\alpha$ -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  $\alpha$ -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 <sup>2</sup> )	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)

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**Table 2.** A comparison of measured peak contact forces<sup>12</sup> 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 <sup>st</sup> 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)