

## Total hip arthroplasty improves pain and function but not physical activity

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**Title: Total hip arthroplasty improves pain and function but not physical activity**

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## **Abstract**

### Background:

People with hip osteoarthritis are likely to limited physical activity (PA) engagement due to pain and lack of function. Total hip arthroplasty (THA) reduces pain and improves function, potentially allowing increased PA. PA of THA patients was quantified to 12m post-operation. The hypothesis was that post-operatively levels of PA would increase.

### Methods:

PA of 30 THA patients ( $67 \pm 7$  years) was objectively measured pre-operatively and three and 12 months post-operation. Harris Hip Score (HHS), Oxford Hip Score (OHS) and six minute walk test (6MWT) were recorded. Mixed linear modelling was used to examine relationships of outcomes with time, BMI, age, gender and baseline HHS.

### Results:

Time was not a significant factor in predicting sit-to-stand transitions, upright time, steps, cadence of walking bouts  $>60$ s, or longest upright bouts. However, HHS, OHS and 6MWT all improved with time. Notably BMI was a significant predictor of upright time, steps, largest number of steps in an upright bout, HHS and 6MWT. Baseline HHS helped predict longest upright bout, cadence of walking bouts  $>60$ s and OHS. The significant effect of participant as a random intercept in the model for PA outcomes suggested habituation from pre- to post-surgery.

### Conclusions:

PA did not change from pre- to 12m post-surgery despite improvement in HHS, OHS and 6MWT. Baseline BMI was a more important predictor of upright activity and stepping than time. Pre- and post-operative PA promotion could be used to modify apparently habitual low levels of PA to enable full health benefits of THA to be gained.

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26 low levels of PA to enable full health benefits of THA to be gained.

27

## 28 **Keywords**

29 Physical activity, Total Hip Arthroplasty

30

## 31 **List of Abbreviations**

32 THA Total hip arthroplasty

33 PA Physical activity

34 HHS Harris Hip Score

35 OHS Oxford Hip Score

36 6MWT Six minute walk test

37 BMI Body mass index

38

39

40

## 41 **Introduction**

42 Total hip arthroplasty (THA) leads to reduction in pain[1–3] and improvement in functional  
43 capacity[4–6] and quality of life[7,8]. Additionally THA is associated with enhanced walking  
44 endurance (longer distances covered in the 6 minute walk test[9,10]) and improved balance  
45 (faster performance of the timed-up-and-go-test[10,11]). However, there is emerging  
46 evidence that there are only small changes in free-living physical activity (PA) following  
47 surgery[12–15]. With reduction in pain, enhancement of endurance and speed of walking  
48 following THA, it might be expected that individuals would be able to participate in health  
49 enhancing PA. However, it is possible that pre-operative habitual patterns of PA are not  
50 altered. If pre-operative patterns of PA are ingrained (at low levels), then pre-operative  
51 measurements could be extremely useful in targeting person-centred interventions to  
52 disrupt these patterns, potentially enhancing long-term health prospects. While PA may  
53 have become habituated, it is possible that changes following surgery may be dependent on  
54 a range of factors. A person's gender may have an impact on surgical outcomes, as might  
55 their weight and age at the point of surgery. Also their pre-operative clinical condition may  
56 be important in determining outcomes.

57 The aim of this study was to enhance understanding of PA following THA by using objective  
58 measurement to characterise PA from pre-operation through recovery to twelve months  
59 post-operation. The relationship between PA change with time following surgery and  
60 gender, age, BMI and baseline clinical score (Harris Hip Score) was investigated. Primary  
61 physical activity outcomes included the number of sit-to-stand transitions per day, the time  
62 upright per day and the number of steps per day. Also secondary outcomes were quantified  
63 to further characterise PA (characteristics of the longest bouts of activity), walking

64 endurance (six minute walk test) and clinical outcomes (Harris Hip Score, Oxford Hip Score).  
65 The hypothesis was that all outcomes would improve following THA.

66

## 67 **Patients and Methods**

68 This was an observational cohort study. Ethical approval was obtained from the West of  
69 Scotland Research Ethics Committee 1 (12/WS/0098). The study population was all patients  
70 being seen for a primary total hip arthroplasty operation at an NHS elective arthroplasty  
71 centre. To ensure the external validity of the study results the inclusion / exclusion criteria  
72 were kept as wide as possible. Inclusion criteria for the study were patients who were able  
73 to give informed consent, were between 50-85 years old and could return for follow-up.  
74 Patients were excluded if they were undergoing a revision hip arthroplasty, had had a total  
75 hip or knee arthroplasty in the last 12 months, had extreme locomotor limitations due to  
76 cardio-pulmonary, central or peripheral nervous system deficits or spinal conditions or were  
77 diagnosed with a terminal disease (malignancy). From July to August 2012 and January to  
78 May 2013 (break in recruitment due to illness of lead investigator) all THA patients under  
79 the care of one consultant orthopaedic surgeon (n=64) were reviewed for eligibility for the  
80 study. All eligible patients (n=57) were approached for inclusion in the study. Published  
81 data to carry out an appropriate a-priori power calculation were not available. Therefore a  
82 target sample of 30 participants was set to provide a power of 0.8 to detect a difference of  
83 1SD in outcomes with a significant level of 0.05. All the study participants gave informed  
84 consent and the complete assessment was carried out by the lead author, a registered  
85 Physiotherapist.

86 Participants were operated on by a single consultant surgeon (DA) or a trainee surgeon  
87 under his direct supervision. Using a posterior approach, all participants received either a  
88 Contemporary® cemented cup or Trident® uncemented cup with an X3 polyethylene liner  
89 and an Exeter® femoral component (Stryker Orthopaedics, Michigan, USA). The peri-  
90 operative care for all participants (from pre-assessment through to discharge) followed the  
91 institution's enhanced recovery programme[16]. The aim of this programme was to  
92 accelerate patients' rehabilitation and reduce in-hospital length of stay (to 3-4 days) by  
93 implementing a multimodal anaesthetic regime combined with pre-operative education and  
94 early mobilisation.

95 Data were collected at three time points: Pre-operatively within the two weeks before  
96 operation; three months after operation; twelve months after operation.

97 PA data were collected objectively for up to seven days using the activPAL3™ monitor  
98 (50x35x7mm, 30g) (PAL Technologies Ltd. Glasgow, UK; software version 7.1.18)[17,18].

99 Data from this instrument classified activities into sedentary (sitting/lying), standing and  
100 stride events. Thus a record of posture (upright or not) and stepping activity was generated.

101 The monitor was attached to the anterior aspect of the thigh of the non-operated leg (24  
102 hour/day wear) using a waterproof surgical dressing (Duoderm extra thin hydrocolloid  
103 dressing (Convatec) or Opsite flexifix (Smith & Nephew)). When compared to video based  
104 observation the activPAL3™ has only a 0.27% difference in upright time detection and -  
105 3.34% difference for step count in adults [19] during standardised activities. Whilst the  
106 upright time detection remains good in activities of daily living (-0.19% agreement) there is  
107 considerable undercounting of small stepping activity within these activities (-86%). This  
108 undercounting of small/slow steps associated with some ADLs is emphasised by the



109 monitor's progressively poorer performance below 0.5m/s [20]. The monitor therefore  
110 records purposeful stepping activity, but is poor at recording small/slow incidental stepping.

111 Compliance with monitor wear was assessed by self-report and post-hoc data examination  
112 by the research team. Only self-reported full 24 hours periods of wear were considered for  
113 inclusion. These records were manually inspected for apparent abnormalities. Any days with  
114 apparent abnormalities were excluded.

115

116 *Primary outcome measures:*

117 The primary outcome for the study was PA. To quantify the level of PA the following three  
118 outcome measures were averaged over all 24 hour periods recorded: Sit-to-stand  
119 transitions/day; time spent upright/day (hours/day); steps/day.

120 *Secondary outcome measures:*

121 The following characteristics of the longer bouts of activity for each recording period were  
122 calculated: Duration of longest continuous upright bout over the recording period; largest  
123 number of steps in an upright bout across the recording period (not necessarily the same  
124 bout as the longest continuous upright bout); mean cadence (steps/min) of all walking bouts  
125 of longer than 60s.

126 Participants were also assessed at all time points using the Harris Hip Score[21] (completed  
127 by the lead author by measurement and interview), the Oxford Hip Score[22,23] (self-  
128 completion) and a six minute walk test [24]. The six minute walk test was conducted in a  
129 30m long corridor, which had regular rest stations at 10m intervals. The participants were

130 advised to walk up and down the corridor at a self-selected speed to achieve the maximum  
131 distance within 6 minutes. The participants were informed that they could take a break  
132 when and for how long needed at any point during the 6 minutes.

133 The age, gender, height, weight, BMI and comorbidities (from medical notes) of participants  
134 were recorded. Major complications (Death, Pulmonary Embolism/Deep vein Thrombosis,  
135 dislocation, infection, and revision) were noted.

### 136 **Data analysis and statistics**

137 Outcomes were characterised as mean (SD). To examine the change pre- to post-operation  
138 mixed linear models were used to model the relationship between each PA or clinical  
139 outcome parameter and time. As three time points were recorded time could only be  
140 modelled as quadratic. Models were adjusted for gender, baseline BMI, age and baseline  
141 Harris Hip Score (apart from Harris Hip Score). The shape of each outcome curve over time  
142 was modelled with each outcome measurement at Level 1 and each patient at Level 2. Fixed  
143 and random effects were included at the patient level (Level 2) and measurement level  
144 (Level 1). The fixed part of each model describes the average growth curve for the sample;  
145 the random part splits variation between subjects at the higher level and variation between  
146 time in the study of the same person at the lower level. The models allowed a unique  
147 growth curve to be generated for each subject based on his or her deviation from the  
148 average curve. An unstructured covariance structure was used.

149 Models were created adding covariates sequentially and comparing models using the -  
150  $2 \times \log \text{Likelihood}$  (-2LnL). Covariates were only retained if there was a significant  
151 improvement in -2LnL (reduction of 3.84). The maximum likelihood method was used to

152 estimate the coefficients so that unbiased estimates of  $-2\text{LnL}$  were calculated. Once the  
153 model had been selected the restricted maximum likelihood method was used to give  
154 unbiased estimates of the coefficients. From this model predictions were made. Residuals  
155 for both level 2 and level 1 were estimated and investigated, as was the variance of the  
156 model over time. Model parameters and 95%CI are presented along with predictions.

157 All statistical analysis was conducted in SPSS 23 (SPSS Inc, Chicago, IL) with the level of  
158 statistical significance taken to be  $p < 0.05$ .

159

## 160 Results

161 Thirty participants (21F/9M) were recruited to the study. The STROBE flow diagram giving  
162 recruitment pathway and reasons for non-participation is given in Figure 1. All surgeries  
163 were successfully carried out. For the duration of the study (one year follow-up) there were  
164 no major complications. Of the 30 participants, 3 did not have 12 month data (Figure 1). All  
165 30 participants' data were included in the mixed linear modelling. For the participants  
166 mean age was 67 years (range 50-82y), height 165cm (range 150-182cm), weight 82.9kg  
167 (range 57.8-132.6kg), BMI 31 kg/m<sup>2</sup> (range 19-43kg/m<sup>2</sup>) and pre-operative Harris Hip Score  
168 50 (range 27-66) and Oxford Hip Score 15 (range 4-30). Indication for surgery in all the  
169 participants was osteoarthritis. Along with this diagnosis 13 participants had hypertension,  
170 7 had cardiac abnormalities, 4 had Diabetes Mellitus, 7 had asthma/COPD and 2 participants  
171 had previous THA on the contralateral side. A median of six days of PA data were recorded  
172 at each time point. Mean and standard deviation of outcomes are presented (Table 1) with  
173 significant predictors within the mixed linear models (Table 2) and graphical evidence of  
174 trends with these significant predictors (Figure 2).

175 When examined using mixed linear models gender was not a significant predictor of any  
176 outcomes. Age was only a significant predictor of HHS ( $b=0.38$ ,  $p=0.047$ ) with a higher age  
177 being associated with a higher HHS (Figure 2g).

178 Time was not a significant predictor of the number of sit-to-stand transitions per day,  
179 upright time per day, steps per day, longest upright bout, the largest number of steps in an  
180 upright bout or cadence based on the outcomes of the mixed modelling (Table 1 mean data,  
181 Table 2 model outcomes). However, BMI was a significant predictor of upright time per day  
182 ( $b=-0.153$ ,  $p=-0.003$ ) (Figure 2a), steps per day ( $b=-263$ ,  $p=0.001$ ) (Figure 2b) and largest

183 number of steps in an upright bout ( $b=-144$ ,  $p=0.001$ ) (Figure 2d). In each of these cases  
184 higher BMI predicted a lower level of PA. Additionally Baseline HHS predicted variation in  
185 the longest upright bout ( $b=0.0325$ ,  $p=0.053$ ) (Figure 2c) and the cadence of walking in  
186 bouts longer than 60s ( $b=0.696$ ,  $p=0.004$ ) (Figure 2e). For all PA outcomes except the  
187 longest upright bout random intercepts explained a significant proportion of the outcome,  
188 indicating that participants tended to maintain the same level of PA in relation to the other  
189 participants across the study period.

190 Time and Time<sup>2</sup> were significant factors in the model for HHS, OHS and 6MWT outcomes (all  
191  $p<0.001$ ). Also BMI helped to predict outcomes for HHS ( $b=-0.41$ ,  $p=0.070$ ) (Figure 2f) and  
192 6MWT ( $b=-6.09$ ,  $p=0.03$ ) (Figure 2i) with higher BMI indicating lower scores. HHS baseline  
193 value helped to describe OHS ( $b=0.19$ ,  $p=0.053$ ) (Figure 2h) change over the study period.  
194 There was significant variation across the study period between participants in HHS, OHS  
195 and 6MWT as indicated by significant ( $-2\ln L$ ) contributions to the model of random  
196 intercepts.

197

## 198 **Discussion**

199 This study demonstrated that at one year post-operation primary THA patients had made  
200 little change to their free-living PA from pre-operation levels, with time not being a  
201 predictor in the mixed linear model. However, BMI was a significant predictor in the model  
202 for upright time and stepping activity. The significance of the random parameter of  
203 participant within the model coupled with the lack of a significant effect of time, suggested  
204 that participants were tending to maintain the same relative volumes of PA across the study

205 period. This appears to indicate that pre-operative PA may have become habitual (possibly  
206 related to BMI) and despite improvements in function of the joint, as seen in the  
207 improvement of clinical outcome measures, PA levels did not significantly increase post-  
208 operation.

209

210 There were a number of limitations to this study. The small size of the study and the  
211 participants being under the care of one consultant within one hospital could limit the  
212 generalisability of the results. In terms of study power, based on the standard deviation of  
213 the difference in steps per day from pre- to 12 months post-operation recorded in this study  
214 (2492), the sample used (27 full records) would have been sufficient to detect a difference  
215 of 1350 steps/day with a power of 0.8 and a confidence of 0.05. In support of the  
216 generalizability of the results, the participants' age was similar to that reported in  
217 arthroplasty registers [25,26] and similarly osteoarthritis was the main reason for operation.  
218 However, BMI (mean 31kg/m<sup>2</sup>) was higher than reported elsewhere[25,27]. It is widely  
219 accepted that by 12 months post-operatively patients have gained the maximum benefit  
220 from their THA. However, it is possible that increased function is obtained at longer follow-  
221 up or that function at one year had already begun to deteriorate due to other co-  
222 morbidities. The original activPAL™ monitor has proven validity in adults [18] and older  
223 adults[17,28]. However, the step counting facility of the activPAL3™ has limitations at slow  
224 stepping speeds as it under-counts slow, short step-length steps [20,29]. Therefore, the  
225 monitor may not have reliably detected stepping which was not 'purposeful'. A further issue  
226 is that this was an observational study of a surgical intervention. Theoretically, it would  
227 have been possible to perform an RCT with a no surgery arm to examine natural progression

228 within this population. A more subtle limitation is that this study did not measure the desire  
229 of participants to increase their level of PA post-surgery. Therefore, even with improved  
230 function participants may not have increased PA as they lacked motivation.

231 The results of this study confirm the previous reports of only small changes in PA following  
232 THA [14,15,30,31]. However, there were differences in outcomes, e.g. the current study  
233 (Table 1) found lower sit-to-stand transitions per day both pre-operatively and at 3 months  
234 post-operatively and whilst the upright time/day was similar pre-operatively, there were  
235 varying levels of agreement post-operatively compared to other studies. There were  
236 differences in participant demographics, with the current study population being older and  
237 more overweight than those of previous reports, which might explain these differences.

238 The mixed model outcomes indicated that gender did not significantly predict results for any  
239 outcome parameters within this cohort and that age was only significant within the  
240 prediction model for HHS. These results are perhaps surprising in that age might have been  
241 considered important in predicting PA as the study participants covered 50-82 years of age.  
242 However, BMI or Baseline HHS appeared to be more important. BMI was a predictor of  
243 both PA and clinical score outcomes, highlighting the importance of pre-operative BMI in  
244 predicting outcomes following surgery.

245 The inclusion of the Time<sup>2</sup> term within the mixed model improved predictions of several  
246 outcomes (Harris Hip Score, Oxford Hip Score and six minute walk test), suggesting that  
247 there was a non-linear relationship with time. This is highlighted in mean scores for these  
248 outcomes where large improvements occurred to the 3 month post-operative time point,  
249 but only small changes from 3 to 12 months post-operative (Figures 2f-i).

250 In the current study additional PA measures were added to those previously reported. The  
251 longest upright bout and largest number of steps in an upright bout provide quantification  
252 of the longest times participants performed 'functional' tasks requiring the upright posture.  
253 Time was not a significant factor in predicting these outcomes (Table 2), indicating that  
254 participants were not extending their loaded use of their new hip joints. Similarly cadence  
255 of stepping for bouts longer than 60s gives an insight into the intensity of stepping over  
256 extended periods. Whilst cadence increased across the study period (Table 1), this was not  
257 significantly predicted by time (Table 2) and still remained below that of age matched peers  
258 (93 ( $\pm$ 12) against 107 steps/min) [32–34]. The longest upright bout model did not have a  
259 significant random effect of participant suggesting that there was not a consistent ranking of  
260 participants with time (Table 2). It is possible that this outcome is highly influenced by  
261 particular social events or functional activities, pointing to a need to gather contextual  
262 information to gain a full understanding of the reasons for these patterns. However, the  
263 largest number of steps in an upright bout did have significant random effects of participant,  
264 suggesting similar volumes of stepping within one bout across the study period by  
265 participants.

266 The lack of time as a significant predictor within the model coupled with the significant  
267 random effect of participant suggests that pre-operative PA (except longest upright bout)  
268 may be habituated. Therefore, if pre-operative PA was measured, interventions could be  
269 used to target those likely to have low PA post-operatively to attempt to modify long-term  
270 behaviour. Enhancing PA has demonstrated secondary benefits of improving health (e.g.  
271 lower risk of cancer, ischemic events, diabetes [35] and enhanced quality of life[36,37]). A  
272 behaviour change intervention delivered through educational material, therapy sessions



273 etc., could be used to attempt to maximise the potential gains from THA in terms of overall  
274 health improvement. The significance of BMI within several PA outcome models reinforces  
275 the need to consider this as an important factor in health promotion alongside PA  
276 promotion.

277 As expected [9,30], both Harris Hip Score and Oxford Hip Score highlighted improvement  
278 from pre- to post-operation, as did 6MWT (values similar to previous studies [12,31]).  
279 However, there was not an accompanying increase in PA levels, indicating that these  
280 measures cannot be used as surrogates for PA, i.e. that it is necessary to measure free-living  
281 PA directly to gain insight into any changes following surgery.

282

## 283 **Conclusions**

284 In this study primary total hip arthroplasty patients did not make significant changes in the  
285 volume of PA performed at one year post-operation and it appeared that participants  
286 tended to maintain the same relative level of PA in relation to their peers. However,  
287 standard clinical outcome measures improved, showing an increase in function. This may  
288 indicate that habitual free-living PA patterns are established pre-operatively, perhaps  
289 related to BMI, and these are not altered by the better function and pain reduction given by  
290 a THA. These results may indicate that intervention to modify habitual low levels of PA,  
291 associated with declining long term health, could be necessary in a proportion of primary  
292 THA patients to allow them to fully exploit the additional function that their new joint gives  
293 them.

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396

#### 397 **Suppliers**

398 <sup>a</sup> **Stryker Orthopaedics**, Michigan, USA: Exeter<sup>®</sup> femoral component, Contemporary<sup>®</sup> cemented cup,  
399 Trident<sup>®</sup> uncemented cup, X3 polyethylene liner.

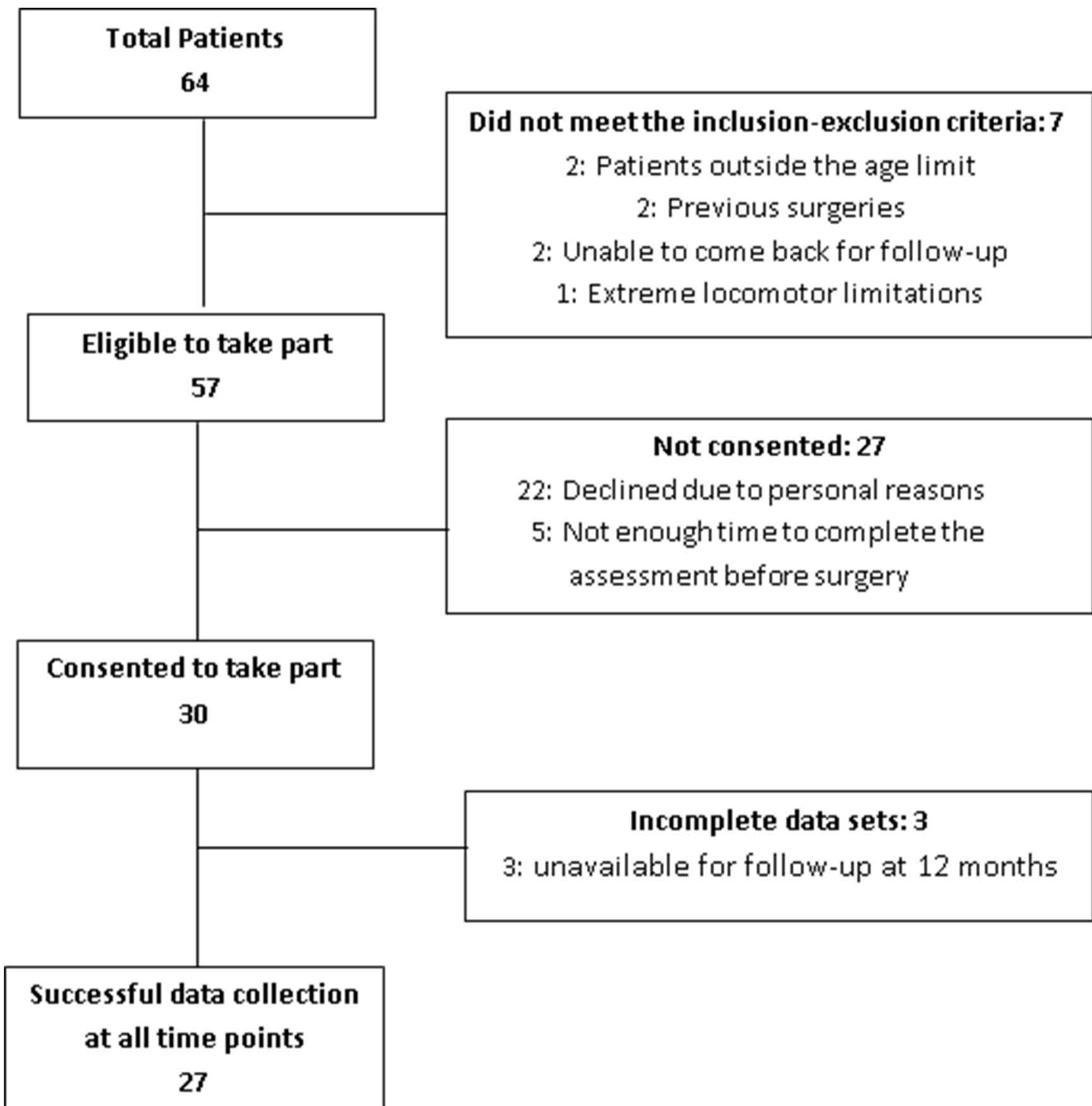
400 <sup>b</sup> **PAL Technologies Ltd.** Glasgow, UK: activPAL3<sup>™</sup>

401

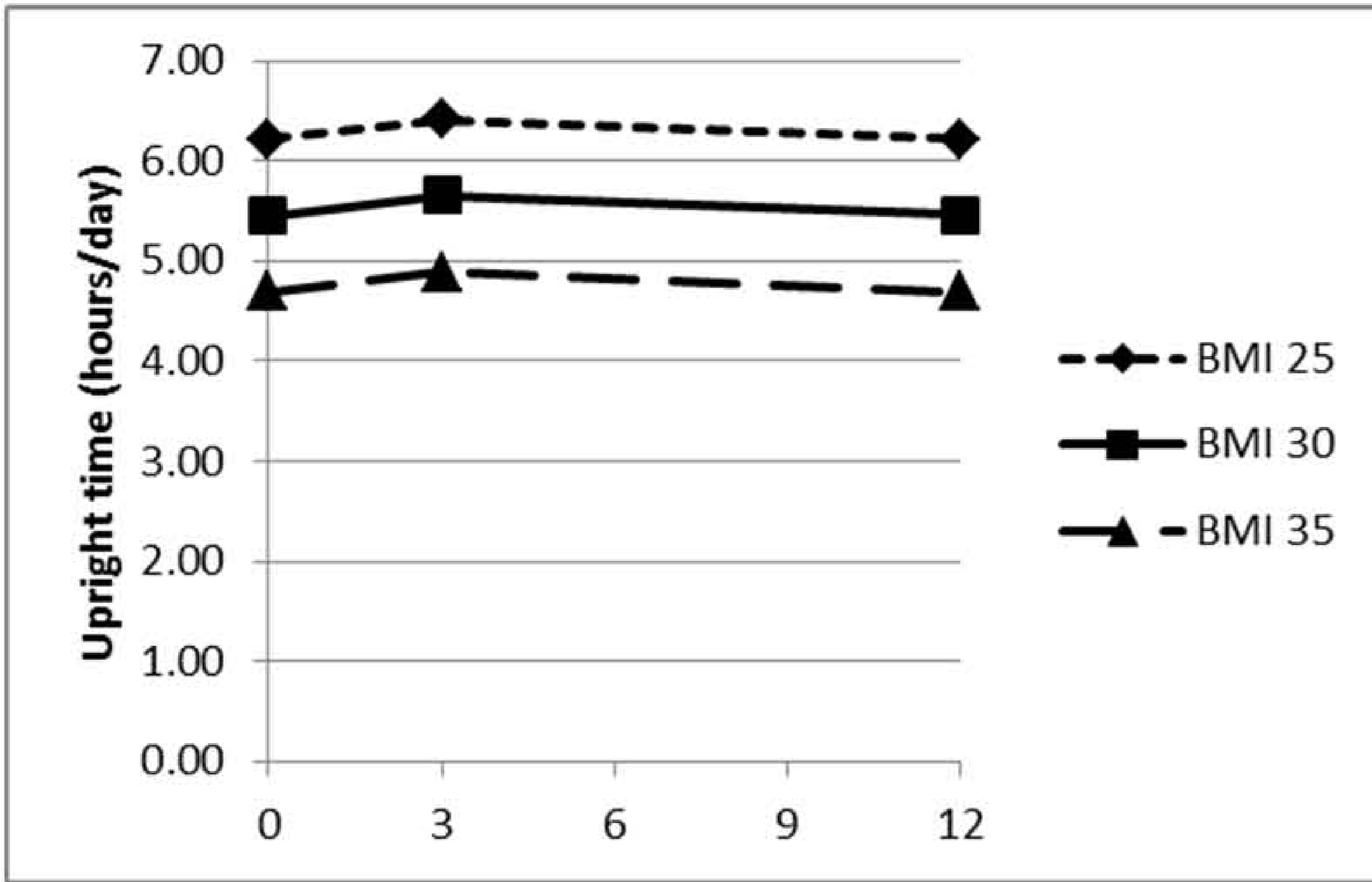
## List of Figures

**Figure 1** Strobe flow chart of participant recruitment.

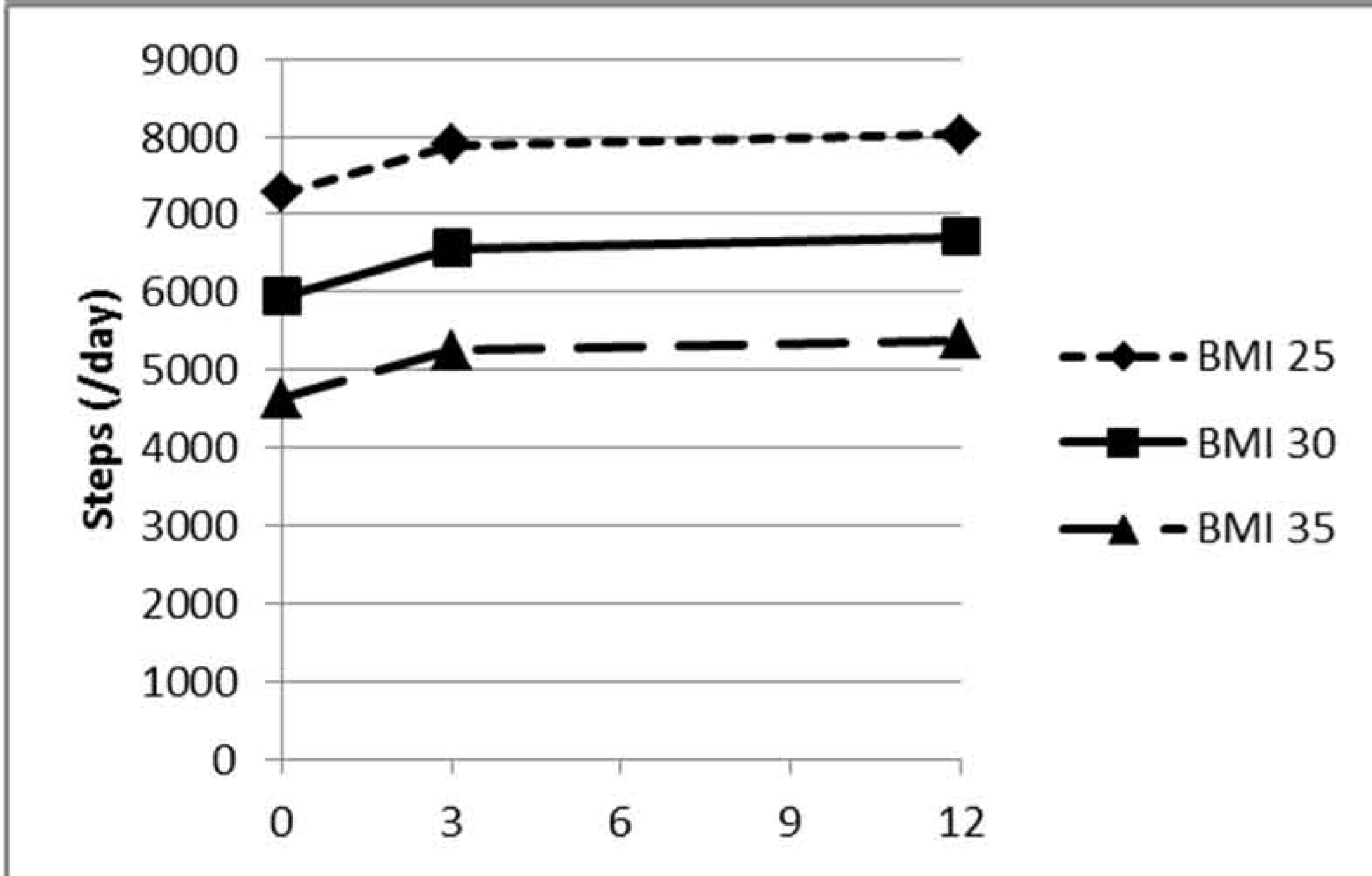
**Figure 2** Model outcomes for significant relationships by months-post operative. Note in figures a) to e) for illustrative purposes time and time<sup>2</sup> have been left in the models even though they were not significant (see Table 2 for significant model parameters). a) Upright time by BMI; b) Steps by BMI; c) Longest upright bout by Harris Hip Score baseline; d) Largest number of steps in an upright bout by BMI; e) Cadence of stepping bouts >60s by HHS baseline; f) Harris Hip Score by BMI; g) Harris Hip Score by age; h) Oxford Hip Score by Harris Hip Score baseline; i) Six minute walk test by BMI.



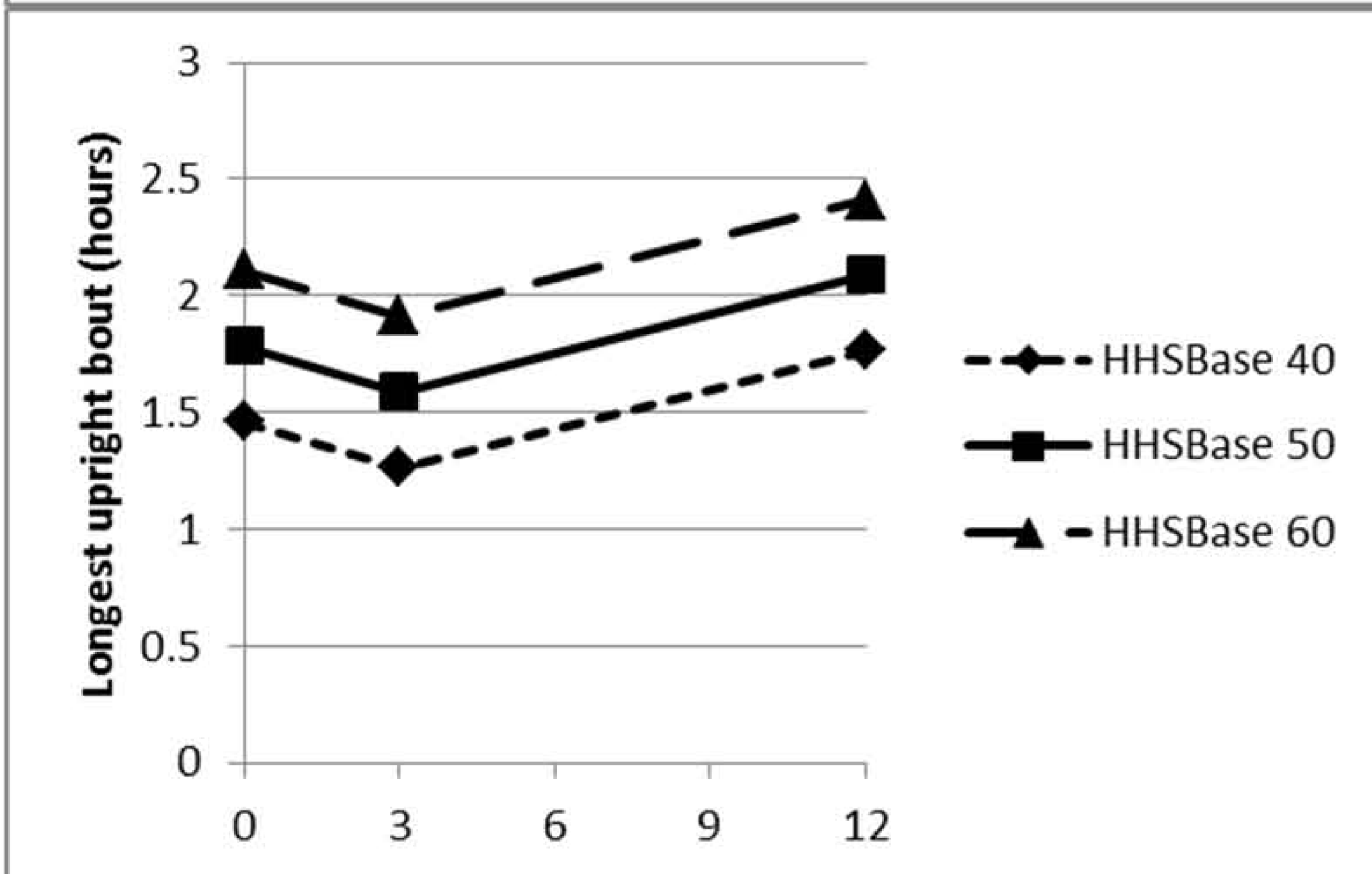
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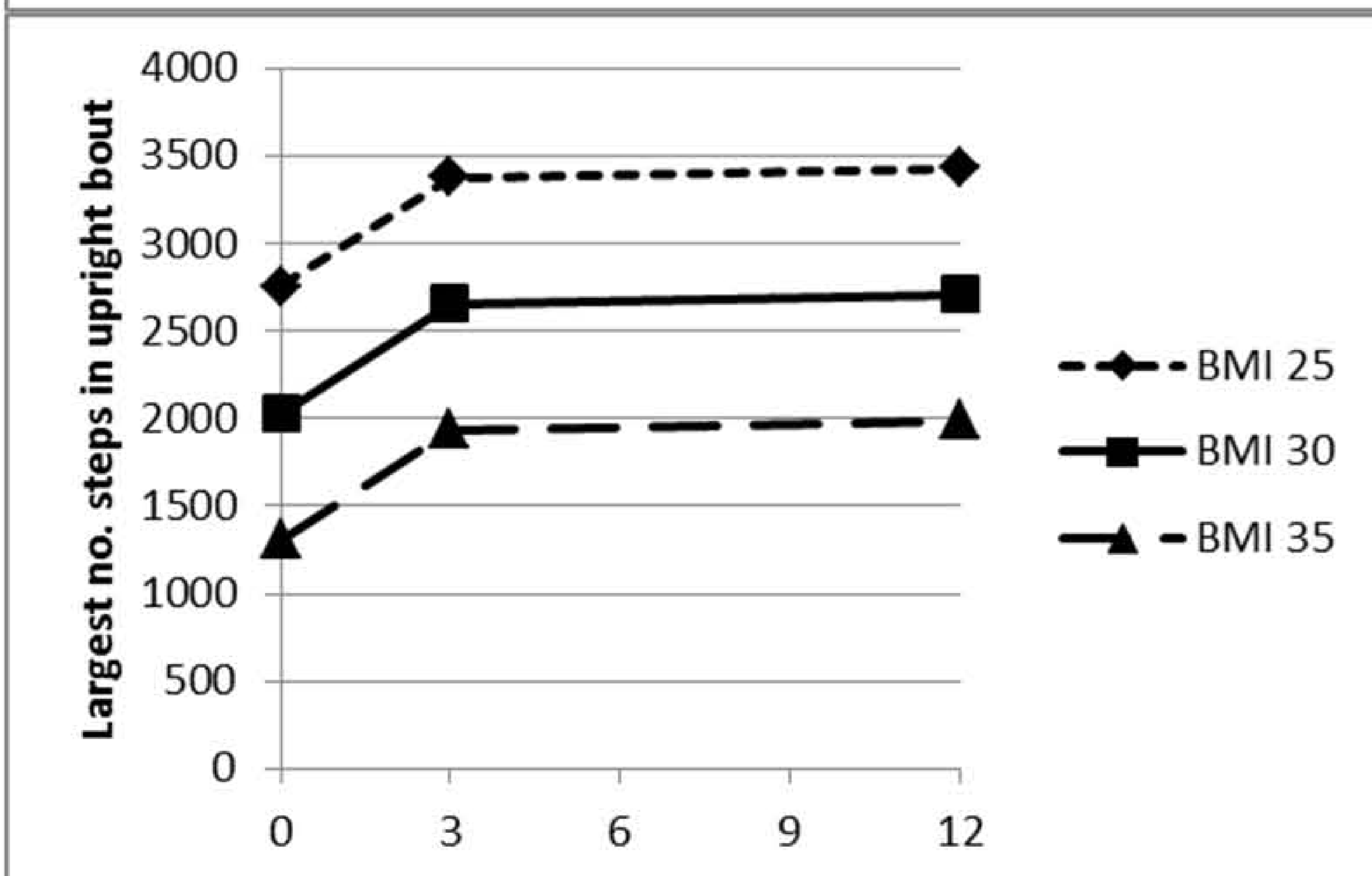
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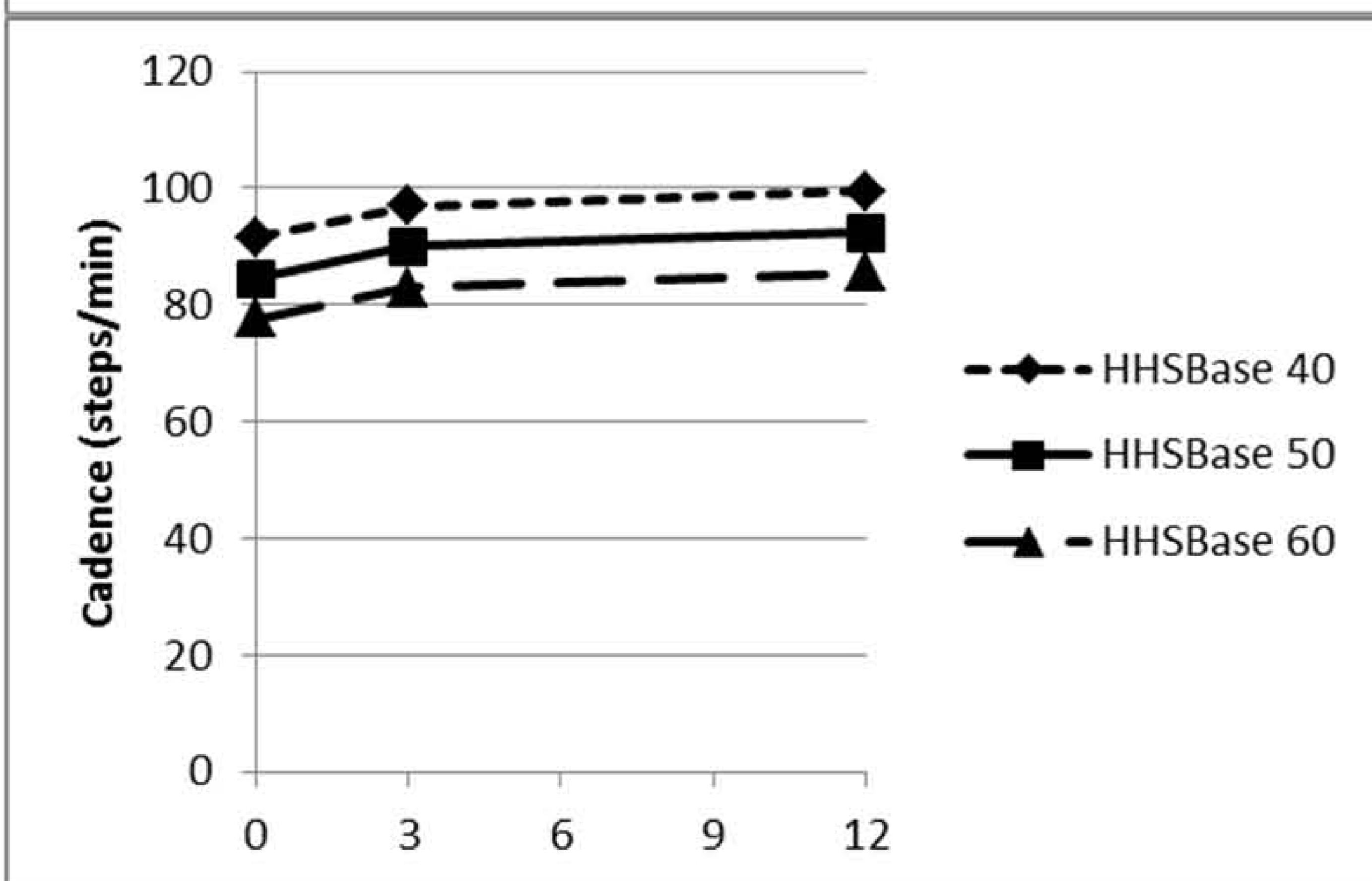
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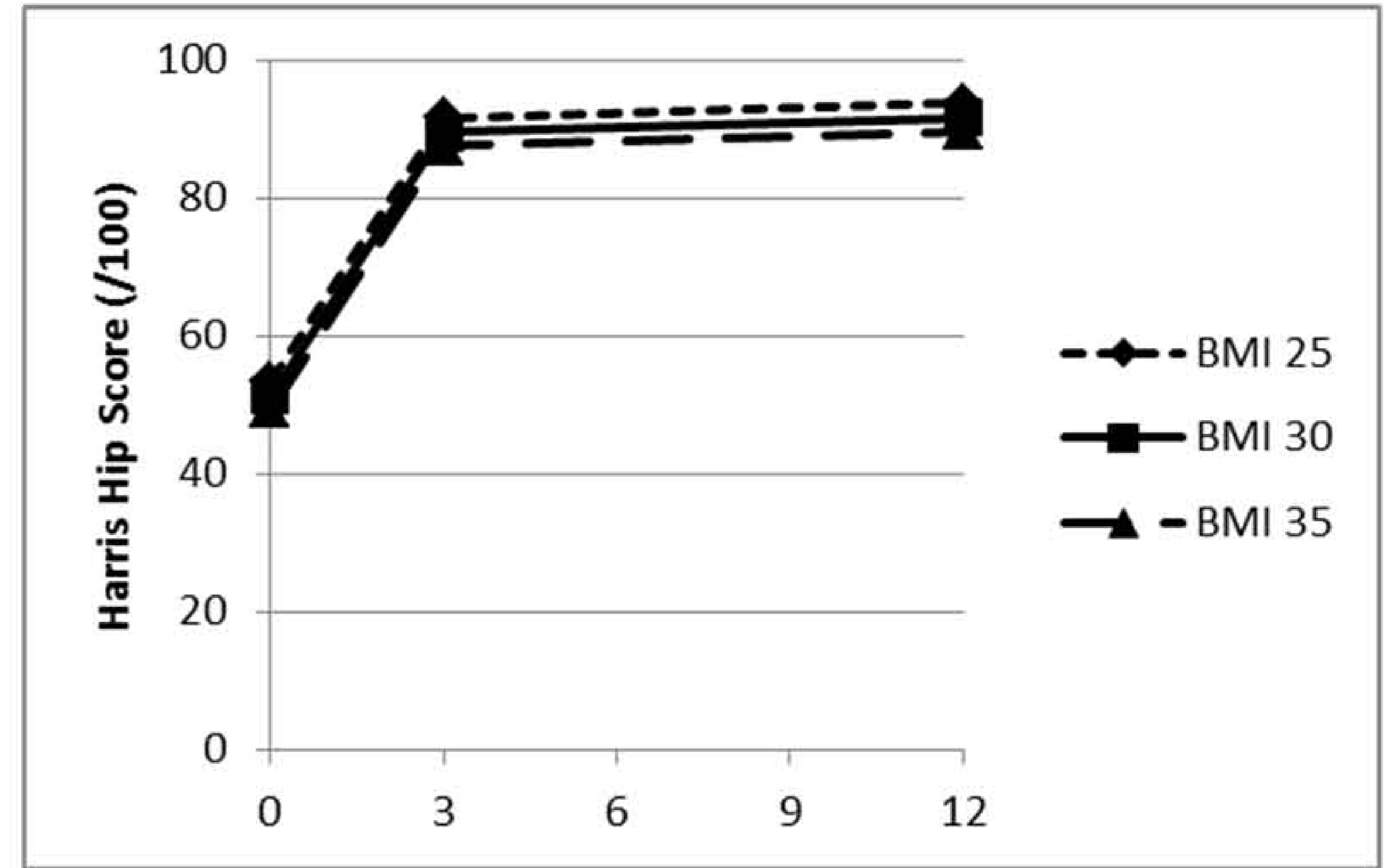
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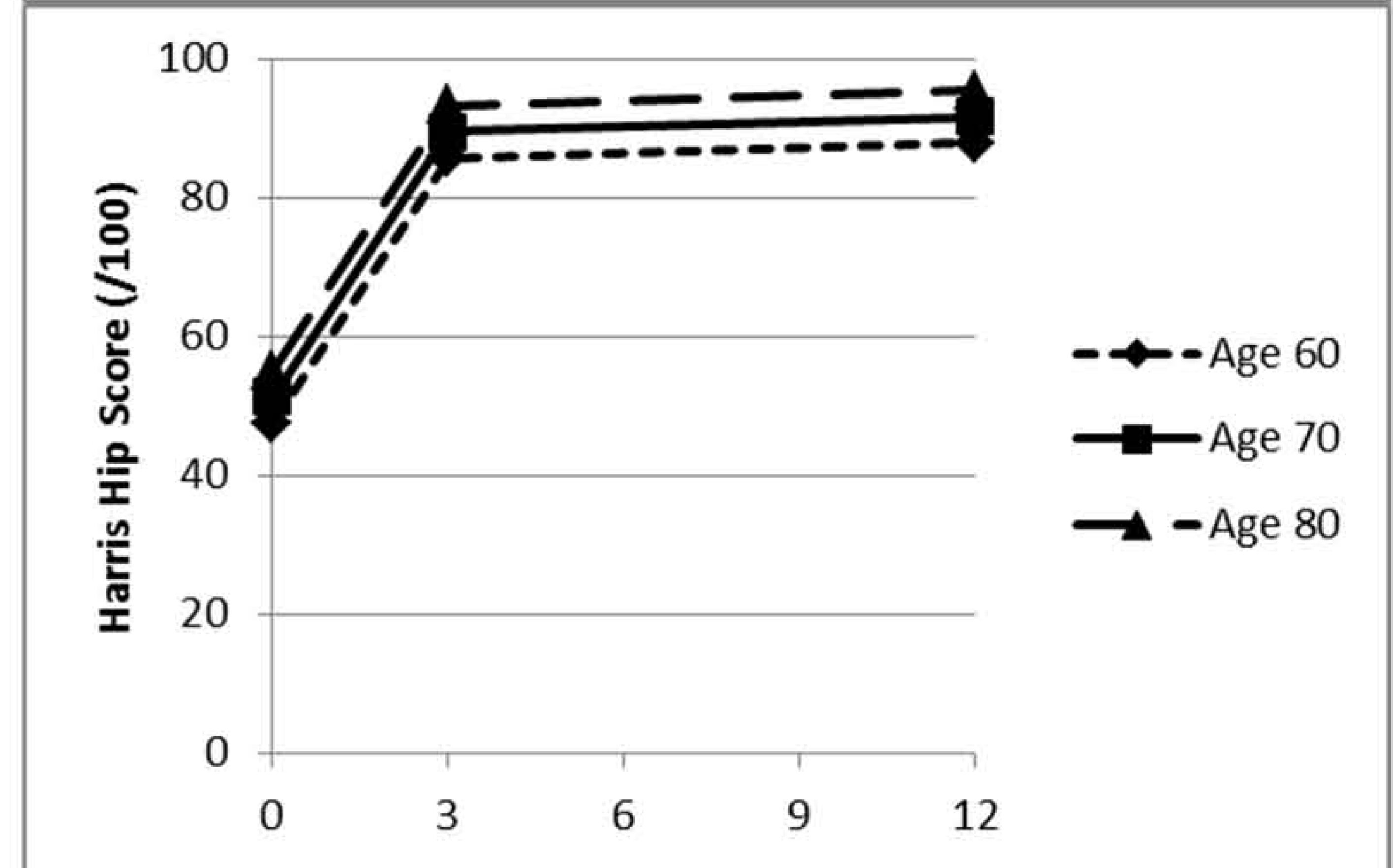
e)



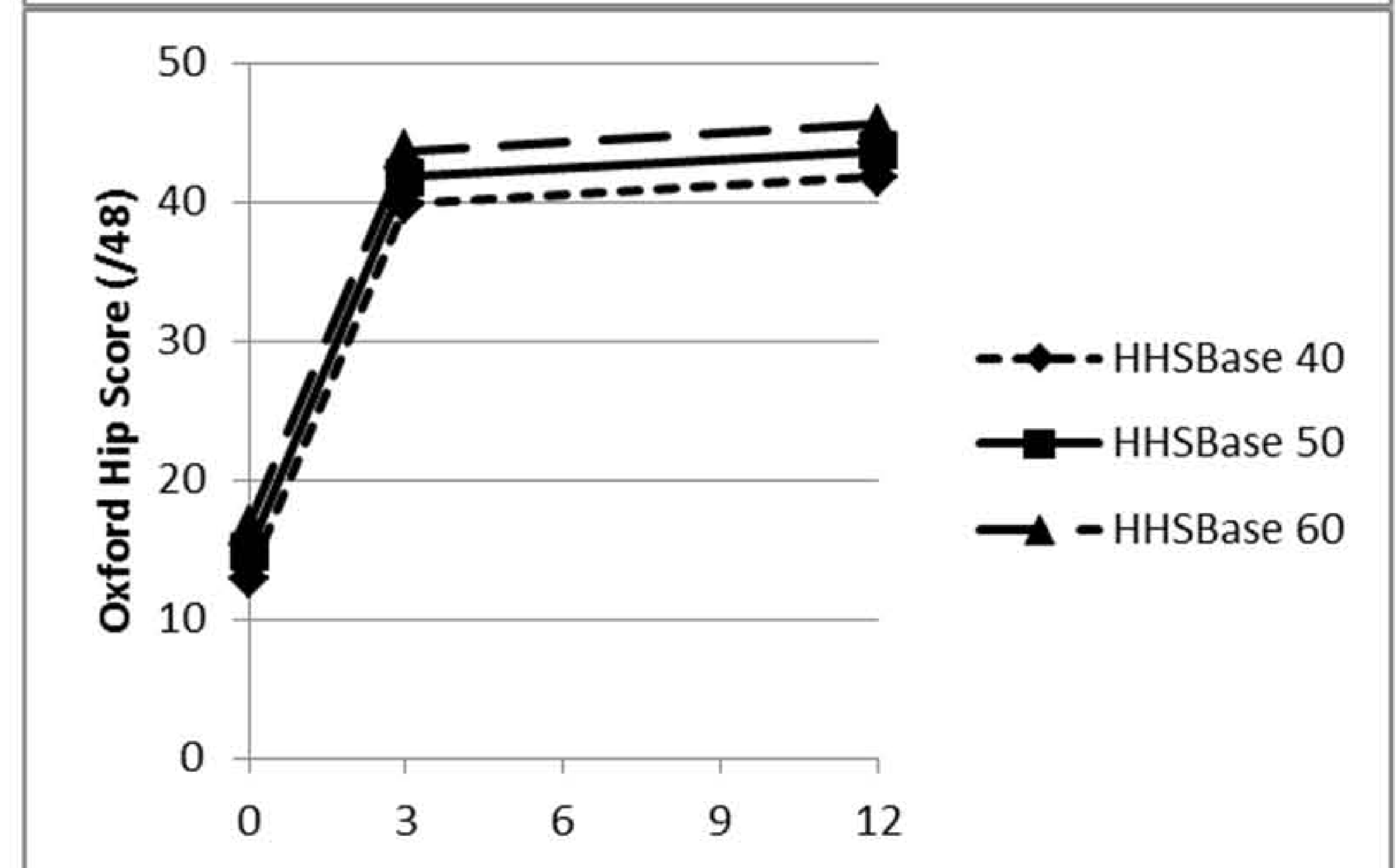
f)



g)



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i)

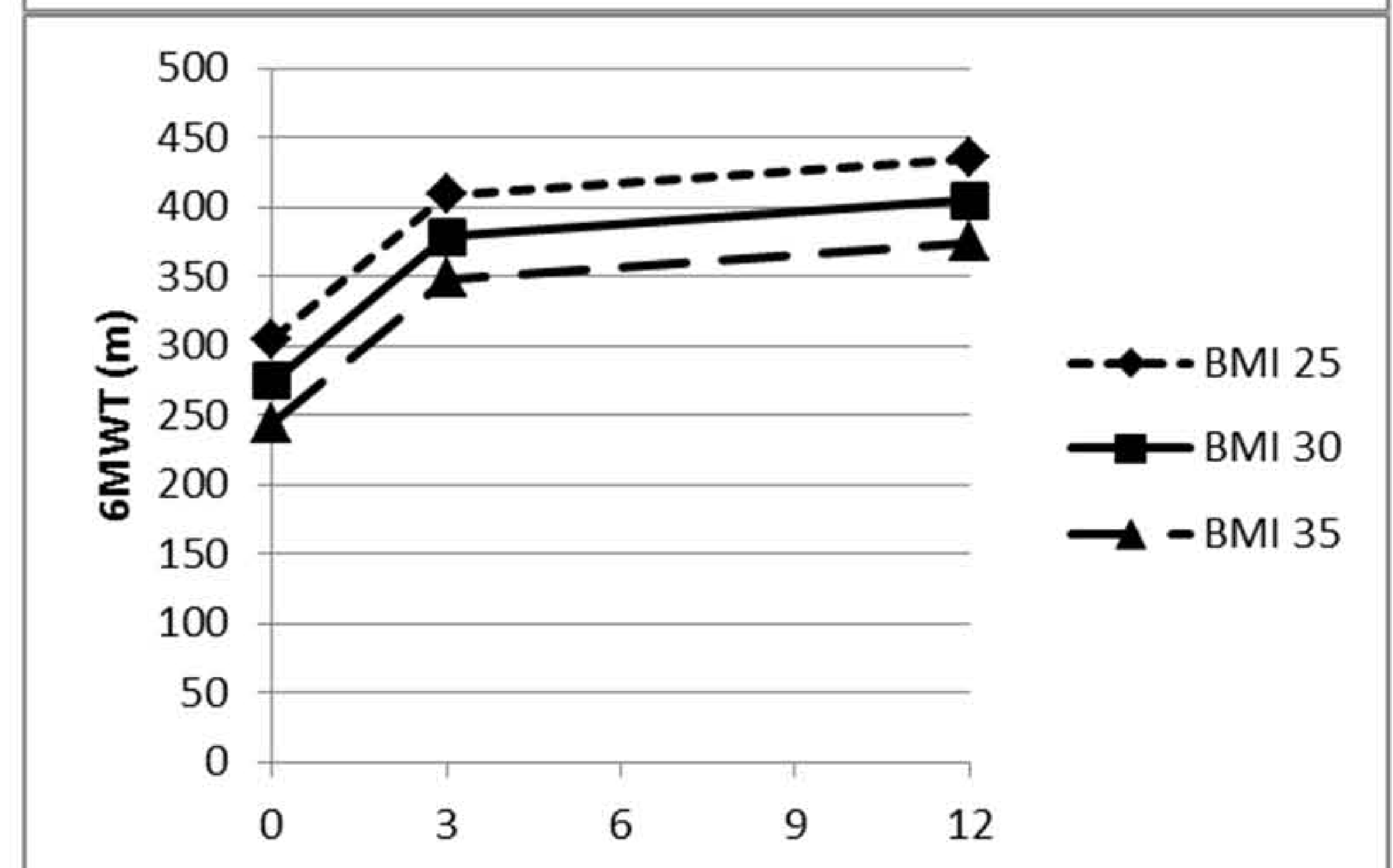




Table 1 Outcomes at each time point.

Outcome	Pre-operative (Mean SD)	3m Post-operative (Mean SD)	12m Post-operative (Mean SD)
Primary outcomes			
Sit-to-stand transitions (/day)	46 (11)	44 (11)	44 (11)
Upright time (hours/day)	5.35 (2.07)	5.55 (1.74)	5.42 (1.61)
Steps (/day)	5320 (3015)	5943 (2675)	6155 (2631)
Secondary outcomes			
Longest upright bout (hours)	1.78 (1.48)	1.58 (0.82)	2.09 (1.96)
Largest number of steps in an upright bout	1934 (1480)	2559 (1841)	2671 (1705)
Cadence of bouts >60s (steps/min)	85 (16)	91 (13)	93 (12)
Harris Hip Score (/100)	50 (10)	88 (10)	91 (11)
Oxford Hip Score (/48)	15 (6)	42 (7)	44 (6)
Six minute walk test (m)	270 (93)	374 (87)	399 (104)

Table 2 Mixed linear model results, both fixed and random parameters for all outcomes. Those elements of the model that are included produced an improvement in 2LnL of a minimum of 3.84. Variables were centred as: BMI 30 kg/m<sup>2</sup>, Age 70 years, HHS Baseline 50. Beta = change in outcome per unit of model element: Time (months), BMI (kg/m<sup>2</sup>), Age (years), HHS (Harris Hip Score) Baseline (score/100). 95% confidence intervals are given.

Outcome	Fixed parameters											Random parameter		
	Intercept		Time		Time <sup>2</sup>		BMI		Age		HHS Baseline		Intercept	
	Beta	P value	Beta	P value	Beta	P value	Beta	P value	Beta	P value	Beta	P value	Covariance	P value
Primary outcomes														
Sit-to-stand transitions (/day)	44.4	<0.001											75.7	0.002
	(40.8,47.9)												(40.2,142.5)	
Upright time (hours/day)	5.52	<0.001					-0.153	0.003					1.630	0.002
	(4.99,6.05)						(-0.248,-0.057)						(0.862,3.087)	
Steps (/day)	5950	<0.001					-263	0.001					3270000	0.003
	(5184,6715)						(-401,-126)						(1680000,6365000)	
Secondary outcomes														
Longest upright bout (hours)	1.81	<0.001									0.0325	0.053		
	(1.50,2.12)										(-0.0004,0.0655)			
Largest number of steps in an upright bout	2453	<0.001					-144	0.001					783500	0.031
	(2023,2883)						(-221,-67)						(315500,1945300)	
Cadence of bouts >60s (steps/min)	89.1	<0.001									0.696	0.004	75.3	0.018
	(84.9,93.2)										(0.240,1.151)		(32.8,172.4)	
Harris Hip Score (/100)	51.3	<0.001	15.84	<0.001	-1.04	<0.001	-0.41	0.070	0.38	0.047			15.47	0.184
	(47.7,54.9)		(13.96,17.72)		(-1.18,-0.89)		(-0.85,0.04)		(0.01,0.76)				(3.53,67.70)	
Oxford Hip Score (/48)	14.9	<0.001	11.16	<0.001	-0.73	<0.001					0.19	0.053	14.33	0.029
	(12.5,17.2)		(9.99,12.33)		(-0.82,-0.64)						(-0.003,0.383)		(5.85,35.11)	
Six minute walk test (m)	274	<0.001	42.62	<0.001	-2.646	<0.001	-6.09	0.03					5016	0.002
	(241,307)		(30.54,54.69)		(-3.582,-1.709)		(-11.36,-0.83)						(2671,9419)	

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