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Nathan Caron, Nicolas Peyrot, Teddy Caderby, Chantal Verkindt, Georges  
Dalleau

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**List of authors:**

Caron Nathan<sup>a</sup>, Peyrot Nicolas<sup>b</sup>, Caderby Teddy<sup>a</sup>, Verkindt Chantal<sup>a</sup>, and Dalleau Georges<sup>a</sup>.

<sup>a</sup> Laboratoire IRISSE (EA4075), UFR des Sciences Humaines et de l'Environnement, Université de la Réunion, Le Tampon, France

<sup>b</sup> Laboratoire MIP (EA4334), Faculté des Sciences et Techniques, Université du Mans, Le Mans, France.

**Corresponding author:**

Nathan CARON

Laboratoire IRISSE (EA4075), UFR des Sciences Humaines et de l'Environnement, Université de la Réunion, 117 rue du General Ailleret, F-97430 Le Tampon, La Réunion.

Mail: [nathan.caron@univ-reunion.fr](mailto:nathan.caron@univ-reunion.fr)

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1 **ABSTRACT**

2 *Objective.* The aim of this study was to develop specific prediction equations based on  
3 acceleration data measured at three body sites for estimating energy expenditure (EE) during  
4 static and active conditions **in middle-aged and older adults with and without type 2 diabetes**  
5 **(T2D)**. *Research methods.* Forty patients with T2D (age: 40-74 yr, body mass index (BMI): 21-  
6 29.4 kg.m<sup>-2</sup>) and healthy participants (age: 47-79 yr, BMI: 20.2-29.8 kg.m<sup>-2</sup>) completed trials  
7 in both static conditions and treadmill walking. For all trials, gas exchange was monitored using  
8 indirect calorimetry and vector magnitude was calculated from acceleration data measured  
9 using inertial measurement units placed to the participant's center of mass (CM), hip and ankle.  
10 Stepwise multiple regression analyses were conducted to select relevant variables to include in  
11 the three EE prediction equations, and three Monte Carlo cross-validation procedures were used  
12 to evaluate each separate equation. *Results.* Vector magnitude (p<0.0001) and personal data  
13 (gender, diabetes status and BMI; p<0.0001) were used to develop three linear prediction  
14 equations to estimate EE during static conditions and walking. Cross-validation revealed  
15 similar robust coefficients of determination (R<sup>2</sup>: 0.81 to 0.85) and small bias (mean bias: 0.008  
16 to -0.005 kcal.min<sup>-1</sup>) for all three equations. However, the equation based on CM acceleration  
17 exhibited the lowest root mean square error (0.60 kcal.min<sup>-1</sup> vs. 0.65 and 0.69 kcal.min<sup>-1</sup> for the  
18 hip and ankle equations, respectively; p<0.001). *Conclusion.* The three equations based on  
19 acceleration data and participant characteristics accurately estimated EE during sedentary  
20 conditions and walking in middle-aged **and older** adults, with or without diabetes.

21

22 Key words: Inertial measurement unit, Exercise, Energy metabolism, Public health, diabetes  
23 mellitus.

24

25 **ABBREVIATIONS**

26	BMI	Body mass index
27	CM	Center of mass
28	EE	Energy expenditure
29	EE <sub>ankle</sub>	Estimated energy expenditure from ankle acceleration
30	EE <sub>CM</sub>	Estimated energy expenditure from center of mass acceleration
31	EE <sub>hip</sub>	Estimated energy expenditure from hip acceleration
32	IMU	Inertial measurement unit
33	RMSE	Root mean square error
34	SEE	Standard error of estimate
35	T2D	Type 2 diabetes
36	VM	Vector magnitude
37	$\dot{V}O_2$	Rates of oxygen consumption
38	$\dot{V}CO_2$	Rate of carbon dioxide production
39		

## 40 1. INTRODUCTION

41 Although physical activity is an integral part of rehabilitation program, the evaluation of  
42 individual energy requirement is paramount. Aging, whether or not associated with type 2  
43 diabetes (T2D) may result in metabolic alterations. These changes may lead to a decrease in  
44 daily physical activity level (Zhao *et al.*, 2011) due to an elevated physiological relative effort.  
45 Indeed, it has been shown that, unlike young adults, older persons (Peterson & Martin, 2010)  
46 and T2D patients (Caron *et al.*, 2018b; Petrovic *et al.*, 2016) have an increased activity-related  
47 energy expenditure (EE) for a same exercise. Thus, following the exercise prescription,  
48 patients' nutrition should be adjusted to minimize the risk of dietary imbalance (i.e. malnutrition  
49 or overfeeding) or medication error (insulin therapy). In this context, the quantification of EE  
50 has gained important interest in recent years.

51  
52 Actimetry represents a popular and objective alternative to other reference methods (i.e. doubly  
53 labelled water and indirect calorimetry) (Reilly *et al.*, 2008). **Inexpensive and unobtrusive,**  
54 **accelerometer can be integrated into different forms of wearable devises, such as a watch,**  
55 **waistband or chest belt. It is thus possible to measure accelerations at different body attachment**  
56 **sites (e.g. ankle, wrist, trunk), which offers the possibility of selecting the most appropriate**  
57 **placement of the sensor according to the physical activity practiced.** Furthermore, this  
58 technology is able to record exhaustive data for extended periods and to estimate precise  
59 minute-by-minute changes in estimated EE throughout a large number of activities. Algorithms  
60 estimating the EE typically use equations developed from multiple regression analysis between  
61 measured EE and accelerometer output (i.e. acceleration of each axis or vector magnitude  
62 (VM)) and basic participant characteristics such as age, gender, and body weight (Bouten *et al.*,  
63 1994; Chen & Sun, 1997). **As the output of the accelerometer is influenced by the anatomical**  
64 **location of the sensor, specific equations are developed depending on the body attachment site**  
65 **(Kim *et al.*, 2014).**

66  
67 The use of a motion sensor **as EE estimation tool** needs a preliminary evaluation and validation  
68 in these specific populations. To date, most published algorithms using acceleration data have  
69 been developed with small groups of healthy young adults (Bouten *et al.*, 1994; Chen & Sun,  
70 1997). Only a few have been tested in other populations such as middle-aged adults (Caron *et*  
71 *al.*, 2018a) or patients with T2D (Caron *et al.*, 2019). Although the Bouten's algorithm was  
72 reliable to estimate walking-related EE in both populations, it does not take into account the

73 age and/or physical deconditioning. This results in a tendency to underestimate EE in  
74 comparison with indirect calorimetry, which may be a source of bias in the patients' daily  
75 energy requirement.

76

77 In order to go beyond these limitations, the aim of this study was to develop specific prediction  
78 equations with user-specific algorithms based on acceleration data for estimating EE during  
79 static and active conditions in **middle-aged and older adults with and without T2D**. Three  
80 different equations have been developed according to each accelerometer attachment site (i.e.  
81 center of mass, hip and ankle).

82

## 83 **2. MATERIALS & METHODS**

### 84 **2.1 Participants**

85 Middle age to older participants, healthy or with T2D, were targeted to participate as volunteers  
86 in this study. All participants were fully informed beforehand about the test procedure, and gave  
87 their written informed consent. Exclusion criteria included peripheral neuropathy, uncontrolled  
88 fasting glycaemia ( $> 1.8 \text{ g.L}^{-1}$ ), history of orthopaedic lower limb surgery and any neurological  
89 or systemic disease. Moreover, participants were included if they were able to walk without  
90 assistive devices. This study was approved by the local ethics committee of the IRISSE unit  
91 research (EA 4075) and conducted in accordance with the Declaration of Helsinki.

92

### 93 **2.2 Measurements and design**

94 The experimental protocol was already described and previously published, for more details,  
95 see Caron et al., 2018a. Briefly, a total of forty participants volunteered in this study: **20 healthy**  
96 **(age: 47-79 yr) and 20 diabetics (age: 40-74 yr) middle-aged and older adults**. Characteristics  
97 of the participants are presented in Table 1. Participants were asked to complete two 6-min  
98 periods in seated and standing positions and to perform five 6-min level walks at different  
99 speeds ( $0.5$  to  $1.50 \text{ m.s}^{-1}$ ) in a randomised order. Each period was separated by 5 min of rest.  
100 Throughout each period, oxygen uptake ( $\dot{V}O_2$ , in  $\text{ml.min}^{-1}$ ) and carbon dioxide production  
101 ( $\dot{V}CO_2$ , in  $\text{ml.min}^{-1}$ ) were collected using a breath-by-breath gas analyser (Ergostik, Geratherm  
102 Medical AG, Geschwenda, Germany). Furthermore, three inertial measurement units (IMU)  
103 (MTw™, Xsens, Enschede, Netherlands) were used to measure the three-dimensional  
104 accelerations of the center of mass (CM), right hip and ankle, with a sampling frequency at 75  
105 Hz. Metabolic data were used to determine total energy expenditure (in  $\text{kcal.min}^{-1}$ ) for the last

106 minute of each period using the Weir formula (Weir, 1949). Acceleration data were post-  
107 processed (low-pass and high-pass Butterworth filters with a cut-off frequency at 20 Hz and 0.2  
108 Hz, respectively) using a custom-written program in Matlab (Matlab R2015b, MathWorks,  
109 Natick, MAS, USA). Then, the mean VM integrating the three components of acceleration ( $a_x$ ,  
110  $a_y$  and  $a_z$ ) was calculated from a 30s interval for each IMU position:

$$111 \quad VM = \frac{1}{N} \sum_{i=0}^{N-1} \sqrt{a(i)_x^2 + a(i)_y^2 + a(i)_z^2} .$$

112

## 113 **2.3 Statistical analysis.**

### 114 **2.3.1 Selection of equation's variables**

115 Stepwise multiple regression analyses were conducted on the entire sample to examine the  
116 relationships of VM (for each accelerometer placement) and participant's physical  
117 characteristics to indirect calorimetry across all conditions. Personal data including age (years),  
118 gender (1=male, 0=female), diabetes status (1=adult with T2D, 0=healthy adult), BMI (in  $\text{kg}\cdot\text{m}^{-2}$ ),  
119 height (in m) and weight (in kg) were examined for inclusion in equations. Variables were  
120 examined according to their influence on EE and included in the equations if they induced a  
121 significant change in the proportion of variance explained ( $R^2$ ) based on overall  $R^2$  change from  
122 nested equations.

123

### 124 **2.3.2 Cross-validation**

125 Following these multiple regression analyses, a Monte Carlo cross-validation procedure was  
126 used to develop EE prediction equations across the three placements (Shao, 1993). This method  
127 randomly divides the participants into two subgroups (60% in a calibration group and 40% in a  
128 validation group) with equal rates of adults with and without T2D. Multiple linear regression  
129 analysis was conducted on the calibration group (n=24) to develop an equation for the  
130 prediction of EE that was then tested in the validation group (n=16). This procedure (sample  
131 division, regression analysis and validation test) was repeated 500 times for each sensor  
132 placement. The final equation represents the average across the 500 replications. At each  
133 repetition, standard error of estimate (SEE), coefficients of determination ( $R^2$ ), mean bias and  
134 mean relative bias between measured and predicted values, and root mean square error (RMSE)  
135 were calculated to evaluate the accuracy of predicted EE using the three equations (three sensor  
136 placements) in comparison with indirect calorimetry. One-way, repeated measures ANOVAs

137 on RMSE and bias were used to compare the accuracy of EE obtained between the three  
138 equations (CM, hip and ankle).

139

140 All statistical analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA).

141 Results are presented as means ( $\pm$  standard deviations) and statistical significance was set at  
142  $P < 0.05$ .

143

### 144 **3. RESULTS**

145 All healthy participants completed the entire protocol, however one participant's mechanical  
146 data set at  $1.25 \text{ m}\cdot\text{s}^{-1}$  was lost due to a technical failure. During the treadmill protocol, two  
147 participants with T2D did not complete the active trials at  $1.25$  and  $1.50 \text{ m}\cdot\text{s}^{-1}$  due to physical  
148 deconditioning. Unpaired t-tests were conducted on personal characteristics and no significant  
149 difference was found between subgroups ( $p > 0.05$ ).

150

#### 151 **3.1 Selection of equation's variables**

152 The results of multiple linear stepwise regressions to predict EE from VM and personal data  
153 (gender, age, diabetes status and BMI) for the three attachment sites are presented in Table 2.  
154 Weight and height were excluded as potential predictors because of their collinearity with BMI.  
155 Age was also removed from the three equations because it proved insignificant with regards to  
156 EE variance (0.01 to 0.1 %;  $p > 0.05$ ). Vector magnitude of acceleration accounted for 79.6, 77.8  
157 and 77.1 % of EE variation ( $p < 0.0001$ ) and BMI contributed to increasing the percentage of  
158 explained variance for the CM, hip and ankle equations by 3.8, 3.6, 3.3 % ( $p < 0.0001$ ),  
159 respectively. Moreover, even if both were significant ( $p < 0.0001$ ), gender and diabetes status  
160 explained a small additional percentage of the variance (1.6 to 2.1% for gender and 0.5 to 0.8%  
161 for diabetes status).

162

#### 163 **3.2 Cross-validation**

164 Results of the Monte Carlo cross-validation are shown in Table 3. The three predicted equations  
165 [1-3] showed comparable mean  $R^2$  and SEE ( $R^2 = 0.86, 0.85, 0.83$  and  $\text{SEE} = 0.56, 0.60$  and  
166  $0.63 \text{ kcal}\cdot\text{min}^{-1}$  for the CM, hip and ankle equations, respectively).

167

$$168 \text{EE}_{\text{CM}} = -0.818 + 0.53 \times \text{VM} + 0.066 \times \text{BMI} + 0.299 \times \text{Status} + 0.455 \times \text{Gender} \quad (\text{Eq.1})$$

$$169 \text{EE}_{\text{hip}} = -0.763 + 0.491 \times \text{VM} + 0.063 \times \text{BMI} + 0.282 \times \text{Status} + 0.47 \times \text{Gender} \quad (\text{Eq.2})$$



170  $EE_{\text{ankle}} = -0.683 + 0.216 \times VM + 0.063 \times BMI + 0.232 \times Status + 0.42 \times Gender$  (Eq.3)

171

172 where,  $VM$  ( $m.s^{-2}$ ) represents the mean vector magnitude calculated from a 30s interval,  $BMI$   
173 ( $kg.m^{-2}$ ) the body mass index,  $Status$  the diabetic condition with 1 for patients T2D and 0 for  
174 healthy person and  $Gender$  is 1 for man and 0 for woman.

175

176 During cross-validation, the three equations presented strong coefficients of determination ( $R^2$   
177 = 0.85 for CM equation, 0.83 for hip equation and 0.81 for ankle equation). Results showed  
178 that the CM equation slightly overestimated EE in comparison with indirect calorimetry (mean  
179 bias = 0.008  $kcal.min^{-1}$ ; 4.3 %), while the hip and ankle equations tended to underestimate it  
180 (mean bias = -0.005  $kcal.min^{-1}$ ; -4 % for the hip equation and -0.009  $kcal.min^{-1}$ ; - 4.1 % for the  
181 ankle equation). RMSE were 0.60, 0.65 and 0.69  $kcal.min^{-1}$  for the CM, hip and ankle equations,  
182 respectively.

183

184 When comparing all three equations, ANOVA presented no significant effect on mean  
185 difference ( $p=0.16$ ), but did show significant differences in RMSE ( $p<0.001$ ). The CM equation  
186 presented a RMSE significantly lower than hip (mean difference = -0.05  $kcal.min^{-1}$  (95%CI: -  
187 0.06 to -0.04  $kcal.min^{-1}$ ) and ankle equations (mean difference = -0.085  $kcal.min^{-1}$  (95%CI: -  
188 0.09 to -0.07  $kcal.min^{-1}$ ). RMSE obtained with hip and ankle equations were significantly  
189 different with a mean difference of -0.037  $kcal.min^{-1}$  (95%CI: -0.05 to -0.03  $kcal.min^{-1}$ ).

190

#### 191 **4. DISCUSSION**

192 Regular physical exercise is positively associated with health benefits in middle-aged adults,  
193 regardless of health status (Nordstoga *et al.*, 2019; Emerenziani *et al.*, 2015). Motion sensor  
194 (i.e. accelerometer) may be an objective tool allowing patients to accurately quantify and  
195 estimate their daily physical activity in terms of EE, and to promote a healthy lifestyle. The aim  
196 of this study was to develop equations from accelerometer data and personal characteristics to  
197 estimate EE during static conditions and walking specifically **in middle-aged and older adults**  
198 **with and without type 2 diabetes.**

199

200 Results of the regression calculation support the association between body acceleration and  
201 energy expenditure (Bouten *et al.*, 1994; Brandes *et al.*, 2012; Chen & Sun, 1997), with VM of  
202 acceleration explaining a major proportion of EE variance (77.1 to 79.6% vs.  $\approx$  3.5, 2 and 1%  
203 for BMI, gender and status, respectively). Our results are consistent with past literature

204 concerning a positive impact of BMI on the walking related EE (Browning *et al.*, 2006; Peyrot  
205 *et al.*, 2012), with a 3.5% of explained variance of EE. Gender was also added as an independent  
206 variable in multiple regression equations despite no consensus in past literature regarding  
207 differences in walking activity EE between gender (Abadi *et al.*, 2010). While there would not  
208 appear to be a difference in walking EE among women and men at self-selected speeds, women  
209 have a greater walking EE than men at a fixed speed, presumably because of higher step  
210 frequency (Wu, 2007). In contrast, our results demonstrated a greater EE in men than in women  
211 as observed in Waters & Mulroy (1999). However, gender slightly influenced explained  
212 variance ( $\approx 2\%$ ) and predictive precision ( $\approx -0.01 \text{ kcal}\cdot\text{min}^{-1}$  on SEE) (Table 2). Regarding the  
213 effect of age on EE, results also differ between studies (Abadi *et al.*, 2010). In the current study,  
214 age was not a significant factor in EE variance and it was therefore removed from equations.  
215 The specific age group used (middle-aged and older) in the study, which is not broad enough  
216 to induce age-related differences in EE may explain this result. Finally, our results were  
217 consistent with studies showing a higher metabolic cost for walking in patients with T2D as  
218 compared with healthy people (Caron *et al.*, 2018b; Petrovic *et al.*, 2016). Indeed, even if  
219 minimal, diabetes status was a significant factor explaining the variation in EE in all three  
220 equations (Table 2).

221  
222 Some previous studies relied on other activity monitors than those used in the current study to  
223 predict EE or activity-related EE. Previous studies conducted in our laboratory focused on the  
224 validity of Bouten's algorithm in these particular populations to estimate activity EE during  
225 walking. Despite a slight underestimation (bias ranging from  $-0.08$  to  $-0.28 \text{ kcal}\cdot\text{min}^{-1}$  in healthy  
226 middle-aged adults and patients with T2D), no significant difference was found between  
227 activity EE estimated by Bouten's algorithm and activity EE measured using indirect  
228 calorimetry during walking, (Caron *et al.*, 2018a; Caron *et al.*, 2019). In the current study, EE  
229 was underestimated only in the hip and ankle equations even though observed mean bias was  
230 negligible ( $-0.005$  and  $-0.009 \text{ kcal}\cdot\text{min}^{-1}$  for the hip and ankle equations, respectively). Finally,  
231 the study conducted by Machac *et al.*, 2013 was interested in comparing EE assessed using  
232 SenseWear™ Armband Pro3 and Omron in patients with T2D. These findings revealed that  
233 during level walking these two sensors have a tendency to overestimate EE ( $>70\%$ ).  
234 Comparatively, relative bias observed in the current study ranged from  $-4.1$  to  $4.3\%$  for level  
235 walking.

236

237 Our results present clinical relevance for exercise prescription or rehabilitation program.  
238 Currently, general guidelines recommend accumulating 30-min of physical activity at moderate  
239 intensity, five days per week (Pate, *et al.*, 1995). However, energy requirement cannot be  
240 adjusted based on these standardized exercise recommendations because the related EE may be  
241 different between two patients. However, a more widespread use of the EE as a prescription  
242 criterion for physical activity could allow practitioners to optimise beneficial effect of exercise  
243 by precisely regulating the patients' daily energy balance. In this purpose, we developed  
244 specific prediction equations for estimating EE in middle-aged healthy adults and patients with  
245 T2D. These equations can be used mainly for walking which remains one of the most  
246 recommended physical activity in both populations.

247

248 In the current study, our population was characterised by a wider, more specific age range  
249 (representative of middle-aged to older people, i.e. 40-79 yr) and included both normal-weight  
250 and overweight participants (BMI, 20.2–29.8 kg.m<sup>-2</sup>). The large diversity of personal  
251 characteristics contributed to improving the accuracy of equations in this age-BMI group but  
252 presents limitations for use with younger persons with a better physical condition. **The three**  
253 **equations being developed from data obtained during standardised activities (that may differ**  
254 **from free-living conditions), its use is limited to similar activities; e.g. to estimate the EE during**  
255 **an aerobic exercise on treadmill.** Nevertheless, because these equations can be implemented in  
256 any device measuring acceleration using the International System of Units, they offer an  
257 attractive method for EE estimation in both healthy middle-aged individuals as well as those  
258 with T2D.

259

260 Three regression equations based on accelerometer data (according to three sensor body-  
261 placements) and personal data were derived to predict EE during static conditions and walking  
262 in a heterogeneous sample of healthy and diabetic middle-aged and older adults. All three  
263 equations showed comparable strong correlation and great agreement between estimated and  
264 measured EE. Nonetheless, for free-living activities, further studies are needed to validate these  
265 equations using a reference method as doubly labelled water to measure related EE.

266

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271

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328

Table 1: Characteristics of the participants.

Parameters	T2D (n = 20)	Healthy (n = 20)	All participants (n = 40)
Female/Male	12/8	12/8	24/16
Age, years	57.5 ± 8.0	57.3 ± 6.7	57.4 ± 7.4
Weight, kg	70.9 ± 12.3	68.1 ± 13.4	69.5 ± 12.8
Height, m	1.63 ± 0.1	1.65 ± 0.1	1.64 ± 0.1
BMI, kg.m <sup>-2</sup>	25.8 ± 2.7	25.1 ± 2.9	25.4 ± 2.8
FBG, g.L <sup>-1</sup>	1.47 ± 0.16*	0.89 ± 0.12	1.20 ± 0.30
Diabetes duration, yr	10.6 (6.1)	/	/

Values are means ± standard deviation. T2D, type 2 diabetes; BMI, body mass index; FBG, fasting blood glucose. \*: Significant group difference with P < 0.05.

Table 2 - Results of stepwise multiple regression analyses to predict EE from VM, BMI, diabetes status, gender and age for each sensor placement.

Equation	Parameter	R <sup>2</sup> adjusted	R <sup>2</sup> adjusted % of variation	SEE (kcal.min <sup>-1</sup> )	p-value
CM	VM	.796	79.6	0.692	p<0.0001
	BMI	.834	3.8	0.624	p<0.0001
	Gender	.854	2.0	0.568	p<0.0001
	Status	.862	0.8	0.609	p<0.0005
	Age	.863	0.01	0.568	0.22
Hip	VM	.778	77.8	0.722	p<0.0001
	BMI	.814	3.6	0.608	p<0.0001
	Gender	.835	2.1	0.662	p<0.0001
	Status	.842	0.7	0.649	p<0.001
	Age	.845	0.1	0.603	0.20
Ankle	VM	.771	77.1	0.733	p<0.0001
	BMI	.804	3.3	0.679	p<0.0001
	Gender	.820	1.6	0.642	p<0.0001
	Status	.825	0.5	0.671	p<0.008
	Age	.826	0.1	0.638	0.061

VM, Vector magnitude (m.s<sup>-2</sup>); BMI, Body mass index (kg.m<sup>-2</sup>).

Status, T2D = 1 and healthy = 0; Gender, M = 1 and F = 0.

Table 3 -Regression coefficients for estimating EE with each sensor placement.

Parameter	CM Equation		Hip Equation		Ankle Equation	
	Coefficients (95% CI)	SEE	Coefficients (95% CI)	SEE	Coefficients (95% CI)	SEE
Intercept	-0.818 (-1.61 to -0.02)	0.437	-0.763 (-1.61 to 0.08)	0.337	-0.683 (-1.58 to 0.22)	0.126
VM	0.530 (0.50 to 0.56)	0.014	0.491 (0.46 to 0.53)	0.014	0.216 (0.20 to 0.23)	0.005
BMI	0.066 (0.03 to 0.10)	0.013	0.063 (0.03 to 0.10)	0.014	0.063 (0.03 to 0.10)	0.005
Status	0.299 (0.11 to 0.49)	0.075	0.282 (0.08 to 0.48)	0.080	0.232 (0.02 to 0.44)	0.030
Gender	0.455 (0.26 to 0.65)	0.076	0.470 (0.26 to 0.68)	0.082	0.420 (0.20 to 0.64)	0.030

VM, Vector magnitude ( $\text{m}\cdot\text{s}^{-2}$ ); BMI, Body mass index ( $\text{kg}\cdot\text{m}^{-2}$ ); Status, T2D = 1 and Healthy = 0; Gender, M = 1 and F = 0.