

Title: Estimating energy expenditure from wrist and thigh accelerometry in free-living adults:
a doubly labelled water study

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Short running head: Energy expenditure from body-worn sensors

- 1 *Abbreviations list:* Activity Energy Expenditure (AEE), Doubly-Labelled Water (DLW), Diet-
- 2 Induced Thermogenesis (DIT), Euclidean Norm Minus One (ENMO), Food Quotient (FQ),
- 3 Food Frequency Questionnaire (FFQ), High-pass Filtered Vector Magnitude (HPFVM),
- 4 Resting Energy Expenditure (REE), Total Energy Expenditure (TEE), Vector Magnitude
- 5 (VM).

6

7 **Abstract**

8 Background: Many large studies have implemented wrist or thigh accelerometry to capture
9 physical activity, but the accuracy of these measurements to infer Activity Energy
10 Expenditure (AEE) and consequently Total Energy Expenditure (TEE) has not been
11 demonstrated. The purpose of this study was to assess the validity of acceleration intensity at
12 wrist and thigh sites as estimates of AEE and TEE under free-living conditions using a gold-
13 standard criterion.

14 Methods: Measurements for 193 UK adults (105 men, 88 women, aged 40-66 years, BMI
15 $20.4\text{-}36.6\text{ kg}\cdot\text{m}^{-2}$) were collected with triaxial accelerometers worn on the dominant wrist,
16 non-dominant wrist and thigh in free-living conditions for 9-14 days. In a subsample (50 men,
17 50 women) TEE was simultaneously assessed with doubly labelled water (DLW). AEE was
18 estimated from non-dominant wrist using an established estimation model, and novel models
19 were derived for dominant wrist and thigh in the non-DLW subsample. Agreement with both
20 AEE and TEE from DLW was evaluated by mean bias, Root Mean Squared Error (RMSE)
21 and Pearson correlation.

22 Results: Mean TEE and AEE derived from DLW was $11.6\text{ (}2.3\text{) MJ}\cdot\text{day}^{-1}$ and $49.8\text{ (}16.3\text{)}$
23 $\text{kJ}\cdot\text{day}^{-1}\cdot\text{kg}^{-1}$. Dominant and non-dominant wrist acceleration were highly correlated in free-
24 living ($r=0.93$), but less so with thigh ($r=0.73$ and 0.66 , respectively). Estimates of AEE were
25 $48.6\text{ (}11.8\text{) kJ}\cdot\text{day}^{-1}\cdot\text{kg}^{-1}$ from dominant wrist, $48.6\text{ (}12.3\text{)}$ from non-dominant wrist, and 46.0
26 $\text{(}10.1\text{)}$ from thigh; these agreed strongly with AEE (RMSE $\sim 12.2\text{ kJ}\cdot\text{day}^{-1}\cdot\text{kg}^{-1}$, $r\sim 0.71$) with
27 small mean biases at the population level ($\sim 6\%$). Only the thigh estimate bias was statistically
28 significantly different from the criterion. When combining these AEE estimates with
29 estimated REE, agreement was stronger with the criterion (RMSE $\sim 1.0\text{ MJ}\cdot\text{day}^{-1}$, $r\sim 0.90$).

30 Conclusions: In UK adults, acceleration measured at either wrist or thigh can be used to
31 estimate population levels of AEE and TEE in free-living conditions with high precision.

32 Keywords: physical activity; wrist acceleration; wrist-worn sensor; thigh-worn; isotope;

33 bioenergetics; validation; energy balance

34

35

36 **Introduction**

37 Characterising the energy balance of individuals in free-living conditions requires an accurate
38 assessment of total energy expenditure. Total energy expenditure can be measured with high
39 precision using the doubly labelled water technique¹ but this is an expensive undertaking that
40 requires elaborate sample collection and analysis infrastructure, making it less feasible for
41 large-scale deployment or application in clinical settings. In most people, the largest
42 component of total energy expenditure is resting energy expenditure, which can be predicted
43 from anthropometric information with reasonable accuracy^{2,3}. Diet-induced thermogenesis is
44 less variable and ordinarily constitutes approximately 10% of total energy expenditure⁴. The
45 predominant source of uncertainty in total energy expenditure estimates is the highly-variable
46 activity energy expenditure component, which has proven difficult to capture by subjective
47 instruments such as questionnaires^{5,6}. Body-worn sensors such as accelerometers have the
48 potential to provide a relatively cheap and reliable solution to this problem⁷, if valid inference
49 models can be devised to estimate activity energy expenditure from the measurements they
50 record.

51 In recent years, wrist-worn accelerometers have become a popular measurement modality for
52 objectively capturing free-living physical activity in large-scale studies⁸⁻¹⁰. Devices worn on
53 the wrist are generally considered to be less burdensome for participants than those worn on
54 other anatomical sites¹¹. This has led to improved wear protocol adherence and thus to
55 measurements with potentially greater representation of habitual physical activity levels.
56 However, despite their recent increase in popularity, their utility in the estimation of activity
57 energy expenditure has yet to be tested against gold-standard techniques in a sufficiently
58 large sample of men and women in free-living¹². Furthermore, some large studies⁸⁻¹⁰ have
59 committed to measuring only one of either the dominant wrist or non-dominant wrist, and the
60 relationship between these two measurements also remains understudied.

61 In previous work, we derived parametric models to estimate activity energy expenditure
62 intensity from non-dominant wrist acceleration (reproduced in Table 2) using a dataset
63 (n=1050) of simultaneous non-dominant wrist and individually-calibrated combined heart
64 rate and movement sensing signals collected under free-living conditions¹³. We evaluated the
65 models in a large holdout sample (n=645) and found that they explained 44-47% of the
66 variance in activity energy expenditure with no significant mean bias at the population level.
67 However, as this comparison was against a silver-standard measurement of activity volume,
68 these estimation models could be more conclusively validated by integrating the estimated
69 activity energy expenditure signal over time, and assessing agreement of activity volume with
70 a gold-standard criterion such as doubly labelled water. This approach has been used to
71 validate combined heart rate and movement sensing¹⁴⁻¹⁶ against which the models were
72 originally derived.

73 Thigh-worn devices have typically been employed in smaller studies to measure time spent in
74 a sitting posture, in order to infer sedentary time. This is possible because the distribution of
75 gravity over the three axes can be interpreted using a simple equation to calculate thigh
76 inclination. However, thigh acceleration has received comparatively little attention as a
77 measure of physical activity intensity, though it features prominently in activity classification
78 experiments¹⁷. In epidemiological settings, thigh-worn sensors have been complemented by
79 other sensors with the intention to capture physical activity separately¹⁸.

80 The primary aim of this study was to describe the absolute validity of a previously
81 established activity energy expenditure prediction model¹³ when applied to both wrists, and
82 to evaluate the validity of this estimation in predicting total energy expenditure when
83 combined with a simple anthropometric prediction of resting energy expenditure². The
84 second aim was to use the same approach to derive and validate similar energy expenditure
85 estimation models using thigh acceleration. The third aim was to explore the relationship

86 between the dominant wrist, non-dominant wrist and thigh acceleration measures in free-
87 living, and to derive intensity models to facilitate harmonisation.

88 **Subjects and Methods**

89 Participants were recruited from the Fenland study, an ongoing cohort described in detail
90 elsewhere ¹⁹. We aimed to recruit participants who had previously indicated that they were
91 interested in participating in future studies, were aged between 40 and 70 years, with a BMI
92 between 20 and 50 kg·m⁻². Recruitment aimed to balance age, sex and BMI distributions.
93 Participants were invited to attend an assessment centre on two separate occasions, separated
94 by a free-living period of 9 to 14 days. Ethical approval for the study was obtained from
95 Cambridge University Human Biology Research Ethics Committee (Ref: HBREC/2015.16).
96 All participants provided written informed consent.
97 Weight was measured to the nearest 0.1 kg using calibrated digital scales (TANITA model
98 BC-418 MA; Tanita, Tokyo, Japan) at both visits. Height was measured to the nearest 0.1 cm
99 using a stadiometer (SECA 240; Seca, Birmingham, UK) at the first clinic visit. Body
100 composition was also measured by DXA (Lunar Prodigy Advanced, GE Healthcare, USA) as
101 part of the Fenland study.
102 Total energy expenditure was measured by doubly labelled water in 100 of the participants.
103 Prior to the first clinic visit, participants self-reported their current weight, which was used to
104 provide a body-weight specific dose of ²H₂¹⁸O (70 mg ²H₂O and 174 mg H₂¹⁸O per kg body
105 weight). Participants brought a baseline urine sample to their first clinic visit, and a second
106 baseline sample was taken at the clinic visit, prior to dosing. Participants were provided
107 labelled sampling bottles and asked to collect one urine sample per day for the next 9-10 days,
108 at a similar time each day but not the first void of the day. Participants were asked to record
109 the date and time of each measurement on the sample bottle label and separately on a
110 provided timesheet. Participants were asked to store the samples in a container in a cool, dry
111 place, such as a refrigerator, and to return those samples at their second clinic visit at the end
112 of their free-living measurement period. Isotope ratio mass spectrometry (²H, Isoprime, GV

113 Instruments, Wythenshaw, Manchester, UK and ^{18}O , AP2003, Analytical Precision Ltd,
114 Northwich, Cheshire, UK) was used to measure the isotopic enrichment of the samples. All
115 samples were measured alongside laboratory reference standards, previously calibrated
116 against the international standards Vienna-Standard Mean Ocean Water (vSMOW) and
117 Vienna-Standard Light Antarctic Precipitate (vSLAP) (International Atomic Energy Agency,
118 Vienna, Austria). Sample enrichments were corrected for interference according to Craig ²⁰
119 and expressed relative to vSMOW. Rate constants and pool sizes were calculated from the
120 slopes and intercepts of the log-transformed data, with total CO_2 production (RCO_2)
121 calculated using the multi-point method of Schoeller ²¹. RCO_2 was converted to total energy
122 expenditure ²² where the respiratory quotient was informed by the macronutrient composition
123 of the diet (see below).

124 Resting metabolic rate was measured at the start of both clinic visits during a fifteen-minute
125 rest test by respired gas analysis (OxyconPro, Jaeger, Germany). A seven-breath running
126 median was calculated and the lowest observed average rate over a five minute consecutive
127 window was found, which was scaled down by 6% to compensate for within-day elevation of
128 resting metabolic rates ²³. Basal metabolic rate was also estimated via three different
129 equations which differ in the specific body composition information utilised ^{2,24,25}. Resting
130 energy expenditure was primarily characterised as the nearest measured value to the mean
131 average estimated value, and a further sensitivity analysis was conducted using exclusively
132 measured values. The final 24-hour resting energy expenditure estimates also included an
133 adjustment for a 5% lower metabolic rate during sleep ²⁶, according to their reported mean
134 sleep duration.

135 At the second clinic visit, participants were asked to complete a Food Frequency
136 Questionnaire ²⁷, which was used to estimate dietary intake over the past year. The food
137 frequency data was processed using FETA ²⁸, and the resulting calorie-weighted

138 macronutrient profile was used to calculate the Food Quotient and diet-induced
139 thermogenesis²⁹. Diet-induced thermogenesis was normalised by the total energy expenditure
140 to total energy intake ratio, as done previously¹⁴.

141 At the first clinic visit, participants were fitted with three waterproof triaxial accelerometers
142 (AX3, Axivity, Newcastle upon Tyne, UK); one device was attached to each wrist with a
143 standard wristband, and one was attached to the anterior midline of the right thigh using a
144 medical-grade adhesive dressing. The devices were setup to record raw, triaxial acceleration
145 at 100 Hz with a dynamic range of ± 8 g (where g refers to the local gravitational force,
146 roughly equal to $9.81 \text{ m}\cdot\text{s}^{-2}$). Participants were asked to wear them continuously for the
147 following 8 days and nights whilst continuing with their usual activities. They were also
148 asked to record their main sleep using a sleep diary throughout the free-living period.

149 The signals were resampled from their original irregularly timestamped intervals to a uniform
150 100 Hertz signal by linear interpolation, and then calibrated to local gravity using a well-
151 established technique^{30,31}, without adjustment for temperature changes within the record.

152 Periods of nonwear were identified as windows of an hour or more wherein the device was
153 inferred to be completely stationary¹¹, where stationary is defined as standard deviation in
154 each axis not exceeding the approximate baseline noise of the device itself (10 milli-g).

155 Vector Magnitude (VM) was then calculated from the three axes ($\text{VM}(X,Y,Z) = (X^2 + Y^2 +$
156 $Z^2)^{0.5}$), from which two acceleration intensity metrics were derived³²; Euclidean Norm Minus
157 One (ENMO) subtracts 1 g from VM and truncates any negative results to 0, and High-Pass
158 Filtered Vector Magnitude (HPFVM) applies a fourth-order high-pass filter to the signal at a
159 0.2 Hertz cut-off (3 dB). These analyses were performed using pampro v0.4.0³³.

160 In the non-doubly labelled water group (n=93), multi-level linear regression with random
161 effects at the participant level was used to characterise each of the pairwise relationships
162 between dominant wrist, non-dominant wrist and thigh acceleration intensity using

163 synchronised 5-minute level data from each source. We used these intensity relationships to
164 derive new activity energy expenditure estimation models for thigh and dominant wrist-worn
165 devices, by substituting the non-dominant wrist term in our original models with the derived
166 equation to harmonise either dominant wrist or thigh acceleration to non-dominant wrist
167 acceleration.

168 Activity energy expenditure was estimated separately from each of the acceleration signals by
169 directly applying the appropriate linear and quadratic equations given in Table 2 to 5-second
170 level data; the resulting 5-second level estimated activity energy expenditure signal was then
171 summarised to a mean-per-day average activity energy expenditure using diurnal adjustment
172 to compensate for any between-individual bias introduced by periods of nonwear³⁴. To ensure
173 a stable estimate of this circadian model, a minimum of 72 hours of valid data was required
174 per signal to be included in the analyses. Predicted total energy expenditure (in MJ-day⁻¹) was
175 calculated as the sum of predicted activity energy expenditure and predicted resting energy
176 expenditure from the simplest model (using only age, sex, height and weight)², and dividing
177 the result by 0.9 to account for diet-induced thermogenesis⁴. Agreement between these two
178 predictions against measured activity energy expenditure and total energy expenditure from
179 doubly labelled water was formally tested by calculating the pairwise mean bias and 95%
180 limits of agreement, Root Mean Squared Error (RMSE) and Pearson's correlation coefficient.
181 Linear regression was used to characterise the relationship between the acceleration
182 measurements and activity energy expenditure/total energy expenditure derived from doubly
183 labelled water. As the main focus of this paper is on absolute validity, these relative validity
184 results are supplied in the supplementary material.

185 The statistical tests were performed using Python v3.6 and Stata v14 (StataCorp, TX, USA).

186

187 **Results**

188 A descriptive summary of participant characteristics is given in Table 1. We recruited 193
189 participants, and the group measured by doubly labelled water was split equally between men
190 and women. According to the doubly labelled water measurements, mean (standard deviation)
191 total energy expenditure was 11.6 (2.3) MJ·day⁻¹, of which 6.6 (1.2) MJ·day⁻¹ was resting
192 energy expenditure. Mean (standard deviation) activity-related acceleration (ENMO) per day
193 was 32.4 (8.3) milli-g on the dominant wrist, 28.8 (7.7) milli-g on the non-dominant wrist,
194 and 27.8 (10.9) milli-g on the thigh. Mean dominant wrist acceleration was higher than non-
195 dominant wrist in 84% of participants.

196 Some accelerometry measurements were not included in the analyses due to a combination of
197 devices being lost by participants (n=7), device failures (n=3), user error upon download
198 (n=3), and insufficient wear time (n=3). Of those files that overlapped with doubly labelled
199 water measurements, 3 were dominant wrist records, 3 were non-dominant wrist and 9 were
200 thigh records. There was no loss of data in the doubly labelled water, anthropometry or food
201 frequency questionnaire measurements.

202 Table 2 lists the derived equations to predict activity energy expenditure from each of the
203 sensors, as informed by the harmonisation equations which are supplied in Supplementary
204 Table 1. For brevity, Table 3 summarises the absolute validity of the quadratic HPFVM
205 models applied to measurements from both wrists and thigh with respect to activity energy
206 expenditure, and Table 3 summarises agreement with total energy expenditure derived from
207 doubly labelled water. A Bland-Altman plot illustrating the agreement of these estimates is
208 supplied in Figure 1. A table summarising the remaining models is given in Supplementary
209 Table 2.

210 The difference in performance between each estimation model was very minor; all activity
211 energy expenditure estimates had small negative mean biases (underestimates) at the

212 population level (average $-2.8 \text{ kJ}\cdot\text{day}^{-1}\cdot\text{kg}^{-1}$) but of these only the thigh model biases were
213 statistically significant. RMSEs for activity energy expenditure ranged from 11.9 to 13.5
214 $\text{kJ}\cdot\text{day}^{-1}\cdot\text{kg}^{-1}$ (24 to 27% of the mean), and 1.0 to 1.2 $\text{MJ}\cdot\text{day}^{-1}$ for total energy expenditure (8
215 to 10% of the mean). Pearson correlations ranged from 0.6 to 0.69 with activity energy
216 expenditure, and from 0.87 to 0.91 with total energy expenditure. Combined estimates using
217 two or more sensors lead to very negligible performance improvements over single-sensor
218 estimates. Signed estimation errors were nominally positively correlated with body fat
219 percentage when using our primary characterisation of resting energy expenditure ($r=0.18$ -
220 0.25), and less so with exclusively measured values ($r=0.10$ - 0.17).

221 In the non-doubly labelled water group, 88 participants had at least 3 days of valid
222 simultaneous wrist signals during free-living, and 84 had simultaneous wrist and thigh signals;
223 around 200 000 5-minute observations included in each of the regression analyses. The
224 between-individual explained variance between dominant and non-dominant wrist intensity
225 signals was approximately 86% (99% within-individual), and the average between-individual
226 explained variance between wrist and thigh intensities was approximately 49% (97% within-
227 individual). The derived linear models to harmonise the acceleration signals are listed in
228 Supplementary Table 1. The final models given to estimate activity energy expenditure from
229 dominant wrist and thigh in Table 2 were the result of substituting these harmonisation
230 equations into the original non-dominant wrist models.

231

232

233 **Discussion**

234 In this work, we have applied our previously derived activity intensity estimation models¹³ to
235 wrist acceleration signals (after harmonising the intensity of dominant wrist to non-dominant
236 wrist) and investigated their agreement with a gold-standard measure of activity energy
237 expenditure. We arrived at estimates that were highly correlated with the criterion ($r > 0.6$)
238 with small and non-significant mean biases at the population level from both wrists and low
239 RMSEs of approximately $12 \text{ kJ}\cdot\text{day}^{-1}\cdot\text{kg}^{-1}$. We have also introduced and validated new
240 intensity estimation models for thigh acceleration, demonstrating similar performance to the
241 wrist models. We observed that dominant wrist acceleration was on average 12% higher than
242 non-dominant wrist in free-living individuals, but that those measures were very highly
243 correlated ($r=0.93$), allowing us to derive conversion models which harmonise acceleration
244 intensity measured at either wrist. To our knowledge, this is the first demonstration of the
245 absolute validity of a time-integrated predictive model of activity intensity for either wrist or
246 thigh accelerometry.

247 Our findings on the high correlation between dominant wrist and non-dominant wrist
248 acceleration in free-living individuals are consistent with a previous study in a small
249 convenience sample ($n=40$)³⁵. They also observed ~5% higher dominant wrist than non-
250 dominant wrist acceleration, but it was not a statistically significant difference, perhaps due
251 to the shorter duration of measurement and smaller sample size. In our relative validity tests,
252 we found that each wrist separately explained a similar variance in activity energy
253 expenditure, and inclusion of both wrist measurements in the linear models did not drastically
254 improve performance over either wrist measurement alone. Taken together, these results are
255 indicative of a high degree of upper-body symmetry. One implication of these findings is that
256 irrespective of hand dominance, wrist acceleration measurements are naturally conducive to
257 harmonisation across studies, making them well suited to pooled- and meta-analysis.

258 Conversely, it implies that implementing dual wrist measurements may be a largely redundant
259 exercise for studies whose primary intention is to capture activity energy expenditure.

260 However, there is a possibility that future methodological advances in the field of activity
261 recognition may be able to better utilise simultaneous wrist signals, which could yield a more
262 precise instantaneous estimation of activity energy expenditure.

263 The estimation models validated herein for the wrist were derived using a training dataset in
264 which non-dominant wrist acceleration data was collected at 60 Hz with a GeneActiv device
265 ¹³, and were successfully validated using 100 Hz data collected with an Axivity AX3. With an
266 additional harmonisation step, the model also translated to acceptably strong inferences on
267 the dominant wrist, albeit with a slightly increased error. This indicates that our models
268 capture a generalized biomechanical relationship of wrist movement, rather than being
269 superficial transformations of a specific device's output to activity energy expenditure. It
270 therefore suggests that these models are applicable to any wrist-worn device which provides
271 raw, unfiltered triaxial acceleration data expressed in SI units.

272 The associations between wrist acceleration and observations from DLW have been reported
273 before, in pregnant and non-pregnant Swedish women ¹¹. In that population it explained 27%
274 of the variance in activity energy expenditure ($\text{kJ}\cdot\text{day}^{-1}\cdot\text{kg}^{-1}$) in non-pregnant women ($n=48$),
275 but only 5% in pregnant women ($n=26$); however, those wrist measurements were evenly
276 divided between left and right wrist, which most likely lead to a mix of dominant and non-
277 dominant wrist measurements and potentially attenuated the correlations.

278 The previously established estimation models applied to the non-dominant wrist resulted in
279 robust estimates with small, non-significant mean biases, which is a strong justification for
280 using this inference scheme to infer activity energy expenditure in free-living individuals.

281 The higher average of the dominant wrist would have led to a significant overestimation had
282 we applied the original non-dominant wrist model, but our harmonisation approach

283 effectively scaled the dominant wrist measure down to the level of non-dominant wrist,
284 ultimately leading to virtually identical results. We note that physical activity was measured
285 by dominant wrist accelerometry in UK Biobank⁸. We have now demonstrated the validity of
286 this approach in a demographically comparable sample. Specifically, the absolute validity
287 result for ENMO in Supplementary Table 2 demonstrates that our linear estimation model
288 applied to ENMO at 5-second resolution yielded a valid activity energy expenditure estimate,
289 with a small mean bias and a RMSE of $13 \text{ kJ}\cdot\text{day}^{-1}\cdot\text{kg}^{-1}$ and high correlation ($r=0.61$).
290 Consequently, we can use the equations for dominant wrist in Table 2 to solve for salient
291 energy expenditure values – for example, 3 metabolic equivalents (activity energy
292 expenditure $\sim 142 \text{ J}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$) is the generally accepted threshold for “moderate” activity
293 intensity, and our ENMO equations suggest this is approximately 159 milli-g on the dominant
294 wrist.

295 Our findings for the thigh acceleration models demonstrate that thigh-worn accelerometers
296 capture an information-rich biomechanical signal, from which valid estimates of activity
297 energy expenditure can be made. As a consequence of the larger y-intercepts of the thigh
298 models, their minimum estimated activity energy expenditure ranges from 10 to $18 \text{ J}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$
299 ($0.15\text{-}0.25$ metabolic equivalents). To our knowledge, only one previous study has
300 described the association between thigh acceleration and activity energy expenditure from
301 doubly labelled water, in a small study of free-living cancer patients and controls³⁶; which
302 reported very low agreement between the manufacturer's proprietary activity energy
303 expenditure prediction and the criterion. While thigh-worn sensors do not yet have the same
304 popularity as wrist-worn sensors^{37,38}, large-scale data collections are planned for the future³⁹.

305 Our models enable new analyses to be conducted in those existing datasets, and may make
306 thigh-worn accelerometry a more appealing option for future studies if issues of feasibility
307 can be addressed.

308 Some have suggested that simple movement intensity approaches should be replaced by more
309 sophisticated models that utilise a broader range of signal features^{40,41}. Recent efforts to
310 estimate energy expenditure have utilised a range of machine learning approaches, such as
311 neural networks⁴²⁻⁴⁴ and random forests⁴⁰. While we are not aware of any such methodology
312 with a performance that exceeds the simpler models validated in this paper, this is an
313 interesting area of future work.

314 The results of our absolute validity tests demonstrate that deriving intensity models using a
315 "silver-standard" criterion (such as individually-calibrated heart rate and uniaxial movement
316 sensing) in a large sample of free-living adults is a sound approach. The combined sensing
317 estimate of activity energy expenditure is less precise than respiratory gas analysis which can
318 be captured in laboratory studies⁴⁵ but there are several reasons why we have been able to
319 derive superior models to previous approaches. Firstly, the dataset was collected in free-living
320 participants, and is therefore representative of the intended application, as opposed to
321 artificial scenarios and activities performed in a laboratory. Secondly, the combined sensing
322 approach embedded in a cohort study allowed the collection of a volume of data many orders
323 of magnitude greater than any laboratory study has for this purpose. Our training dataset
324 alone contained over 16.6 person-years of observation (>1.7 million data points). One
325 disadvantage of this approach is that we are unable to capture categorical labelled data, so
326 there is no opportunity to explore activity type recognition.

327 It is appropriate to compare our absolute validity results here with those of combined sensing
328 itself¹⁴. The best estimate with treadmill test calibration resulted in a RMSE of 20 kJ·day⁻¹·kg⁻¹
329 (30% of the 66 kJ·day⁻¹·kg⁻¹ criterion mean), non-significant positive mean bias of
330 approximately 4 kJ·day⁻¹·kg⁻¹ (6%) at the population level, and a correlation of 0.67 in a
331 sample of 50 UK adults. Compared to the present results, all estimations here had
332 considerably lower RMSEs of around 12 kJ·day⁻¹·kg⁻¹ (25% of the 50 kJ·day⁻¹·kg⁻¹ mean),

333 similar magnitude but negative mean biases (~6%), but generally higher correlations.
334 However, our study participants were significantly less active overall according to the
335 criterion, ultimately leading to a similar relative accuracy. Combined sensing model errors
336 were also uncorrelated to body fat percentage, whereas errors of accelerometry-only models
337 seem to display this characteristic, albeit less so in the present study ($r=0.22$ versus $r=0.63$ for
338 uniaxial trunk acceleration). Contrasting the feasibility of the methods, however, wrist
339 accelerometry has the advantages of being cheaper, less burdensome to both participants and
340 research staff, and does not require individual calibration using an exercise test. Comparing
341 performance of other devices worn on the upper limbs, validation of the now-discontinued
342 SenseWear Pro3 and Mini also achieved no significant bias with respect to total energy
343 expenditure, but with lower correlations ($r=0.84$) than any of our total energy expenditure
344 models ($r=0.9$) and wider limits of agreement⁴⁶ and with lower feasibility.
345 In summary, we have evaluated the absolute validity of intensity models of activity energy
346 expenditure from wrist and thigh accelerometry, and concluded that they provide precise and
347 accurate estimates in free-living adults. With the addition of predicted resting energy
348 expenditure to produce total energy expenditure, we found even stronger validity at the
349 population level. Considering its feasibility, wrist accelerometry emerges as a viable
350 candidate for deployment in a large scale studies, including physical activity surveillance and
351 the prediction of total energy expenditure in dietary surveys.

352

353

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373 **Competing interests**

374 Patrick Olivier was a founding director of Axivity Ltd. (2011-2014); his spouse is currently

375 CEO and a director of Axivity (from 2014). The remaining authors declare no conflict of

376 interest.

377

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516 **Figure legends**

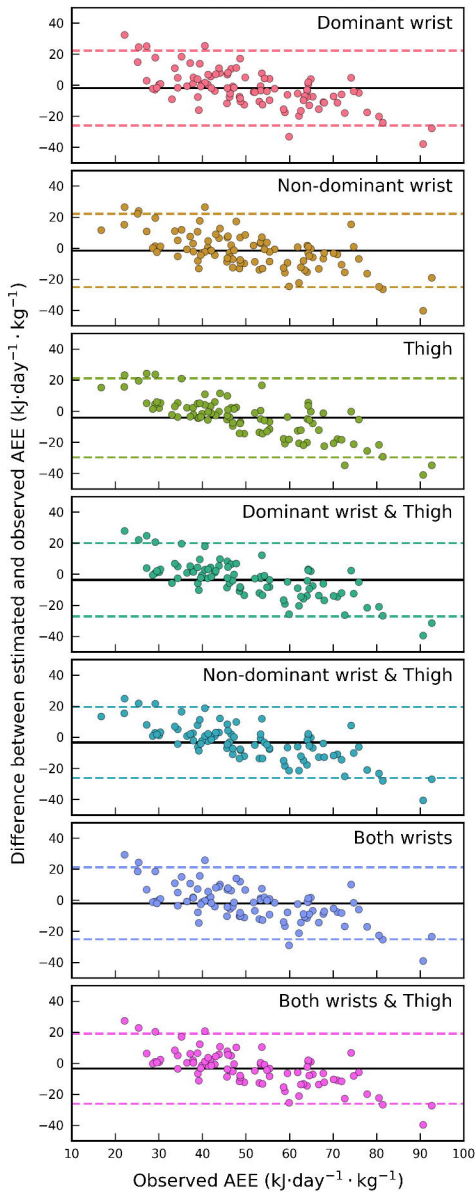
517

518 Participant characteristics, provided separately for the doubly labelled water and non-doubly
519 labelled water groups.

520 Derived linear and quadratic equations to estimate activity energy expenditure ($\text{J}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$)
521 from wrist and thigh acceleration intensity. ($4.184 \text{ J}\cdot\text{min}^{-1}\cdot\text{kg}^{-1} = 1 \text{ cal}$, and $71.225 \text{ J}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$
522 = 1 net Metabolic Equivalent Task (MET)).

523 Agreement between estimated activity energy expenditure from the HPFVM quadratic
524 models with those derived from doubly labelled water. An asterisk (*) next to a bias value
525 indicates statistical significance according to a paired t-test ($p < 0.05$).

526 Bland-Altman plots illustrating agreement between the activity energy expenditure and total
527 energy expenditure estimates from HPFVM Quadratic models with those from doubly
528 labelled water, where the X-axis indicates the observed values.

AEE ($\text{kJ}\cdot\text{day}^{-1}\cdot\text{kg}^{-1}$)TEE ($\text{MJ}\cdot\text{day}^{-1}$)