# Daily Energy Expenditure through the Human Life Course

2

1

- 3 Herman Pontzer<sup>1,2</sup><sup>†\*</sup>, Yosuke Yamada<sup>3,4</sup><sup>†</sup>, Hiroyuki Sagayama<sup>5</sup><sup>†</sup>, Philip N. Ainslie<sup>6</sup>, Lene F.
- 4 Andersen<sup>7</sup>, Liam J. Anderson<sup>6,8</sup>, Lenore Arab<sup>9</sup>, Issaad Baddou<sup>10</sup>, Kweku Bedu-Addo<sup>11</sup>, Ellen E.
- 5 Blaak<sup>12</sup>, Stephane Blanc<sup>13,14</sup>, Alberto G. Bonomi<sup>15</sup>, Carlijn V.C. Bouten<sup>12</sup>, Pascal Bovet<sup>16</sup>,
- 6 Maciej S. Buchowski<sup>17</sup>, Nancy F. Butte<sup>18</sup>, Stefan G. Camps<sup>12</sup>, Graeme L. Close<sup>6</sup>, Jamie A.
- 7 Cooper<sup>13</sup>, Richard Cooper<sup>19</sup>, Sai Krupa Das<sup>20</sup>, Lara R. Dugas<sup>19</sup>, Ulf Ekelund<sup>21</sup>, Sonja
- 8 Entringer<sup>22,23</sup>, Terrence Forrester<sup>24</sup>, Barry W. Fudge<sup>25</sup>, Annelies H Goris<sup>12</sup>, Michael Gurven<sup>26</sup>,
- 9 Catherine Hambly<sup>27</sup>, Asmaa El Hamdouchi<sup>10</sup>, Marjije B. Hoos<sup>12</sup>, Sumei Hu<sup>28</sup>, Noorjehan
- 10 Joonas<sup>29</sup>, Annemiek M. Joosen<sup>12</sup>, Peter Katzmarzyk<sup>30</sup>, Kitty P. Kempen<sup>12</sup>, Misaka Kimura<sup>3</sup>,
- 11 William E. Kraus<sup>31</sup>, Robert F. Kushner<sup>32</sup>, Estelle V. Lambert<sup>33</sup>, William R. Leonard<sup>34</sup>, Nader
- 12 Lessan<sup>35</sup>, Corby Martin<sup>30</sup>, Anine C. Medin<sup>7,36</sup>, Erwin P. Meijer<sup>12</sup>, James C. Morehen<sup>37,6</sup>, James P.
- 13 Morton<sup>6</sup>, Marian L. Neuhouser<sup>38</sup>, Teresa A. Nicklas<sup>18</sup>, Robert M. Ojiambo<sup>39,40</sup>, Kirsi H.
- 14 Pietiläinen<sup>41</sup>, Yannis P. Pitsiladis<sup>42</sup>, Jacob Plange-Rhule<sup>43\*\*</sup>, Guy Plasqui<sup>44</sup>, Ross L. Prentice<sup>38</sup>,
- 15 Roberto A. Rabinovich<sup>45</sup>, Susan B. Racette<sup>46</sup>, David A. Raichlen<sup>47</sup>, Eric Ravussin<sup>30</sup>, Rebecca M.
- 16 Reynolds<sup>48</sup>, Susan B. Roberts<sup>20</sup>, Albertine J. Schuit<sup>49</sup>, Anders M. Sjödin<sup>50</sup>, Eric Stice<sup>51</sup>, Samuel
- 17 S. Urlacher<sup>52</sup>, Giulio Valenti<sup>12,15</sup>, Ludo M. Van Etten<sup>12</sup>, Edgar A. Van Mil<sup>53</sup>, Jonathan C. K.
- 18 Wells<sup>54</sup>, George Wilson<sup>6</sup>, Brian M. Wood<sup>55,56</sup>, Jack Yanovski<sup>57</sup>, Tsukasa Yoshida<sup>4</sup>, Xueying
- 19 Zhang<sup>27,28</sup>, Alexia J. Murphy-Alford<sup>58</sup>, Cornelia Loechl<sup>58</sup>, Amy H Luke<sup>59</sup><sup>†</sup>, Jennifer Rood<sup>30</sup><sup>†</sup>,
- 20 Dale A. Schoeller<sup>60</sup><sup>†</sup>, Klaas R. Westerterp<sup>61</sup><sup>†</sup>, William W. Wong<sup>18</sup><sup>†</sup>, John R.
- 21 Speakman<sup>62,27,28,63</sup>\*† and the IAEA DLW database consortium#.
- 22 \*co-lead corresponding author
- 23 †co-corresponding author
- 24 \*\* deceased

- 25 # see supplementary materials
- 27 1. Evolutionary Anthropology, Duke University, Durham NC, USA
- 28 2. Duke Global Health Institute, Duke University, Durham, NC, USA
- 29 3. Institute for Active Health, Kyoto University of Advanced Science, Kyoto, Japan.
- 304National Institute of Health and Nutrition, National Institutes of Biomedical Innovation, Health<br/>and Nutrition, Tokyo, Japan.
- 32 5 Faculty of Health and Sport Sciences, University of Tsukuba, Ibaraki, Japan.
- Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool,
   UK.
- 35 7 Department of Nutrition, Institute of Basic Medical Sciences, University of Oslo, 0317 Oslo,
   36 Norway.
- 37 8 Crewe Alexandra Football Club, Crewe, UK.
- 38 9 David Geffen School of Medicine, University of California, Los Angeles.
- Unité Mixte de Recherche en Nutrition et Alimentation, CNESTEN- Université Ibn Tofail URAC39,
   Regional Designated Center of Nutrition Associated with AFRA/IAEA.
- 41 11 Department of Physiology, Kwame Nkrumah University of Science and Technology, Kumasi,
   42 Ghana.
- 43 12 Maastricht University, Maastricht, The Netherlands.

44	13	Nutritional Sciences, University of Wisconsin, Madison, WI, USA
45	14	Institut Pluridisciplinaire Hubert Curien. CNRS Université de Strasbourg, UMR7178, France.
46	15	Phillips Research, Eindoven, The Netherlands.
47	16	Institute of Social and Preventive Medicine, Lausanne University Hospital, Lausanne,
48		Switzerland.
49	17	Division of Gastroenterology, Hepatology and Nutritiion, Department of Medicine, Vanderbilt
50		University, Nashville, Tennessee, USA
51	18	Department of Pediatrics, Baylor College of Medicine, USDA/ARS Children's Nutrition Research
52		Center, Houston, Texas, USA.
53	19	Department of Public Health Sciences, Parkinson School of Health Sciences and Public Health,
54		Loyola University, Maywood, IL, USA.
55	20	Friedman School of Nutrition Science and Policy, Tufts University, 150 Harrison Ave,
56		Boston, Massachusetts, USA
57	21	Department of Sport Medicine, Norwegian School of Sport Sciences, Oslo, Norway.
58	22	Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-
59		Universität zu Berlin, and Berlin Institute of Health (BIH), Institute of Medical Psychology, Berlin,
60		Germany.
61	23	University of California Irvine, Irvine, California, USA.
62	24	Solutions for Developing Countries, University of the West Indies, Mona, Kingston, Jamaica.
63	25	University of Glasgow, Glasgow, UK.
64	26	Department of Anthropology, University of California Santa Barbara, Santa Barbara, CA, USA.
65	27	Institute of Biological and Environmental Sciences, University of Aberdeen, Aberdeen, UK
66	28	State Key Laboratory of Molecular developmental Biology, Institute of Genetics and
67		Developmental Biology, Chinese Academy of Sciences, Beijing, China
68	29	Central Health Laboratory, Ministry of Health and Wellness, Mauritius.
69	30	Pennington Biomedical Research Center, Baton Rouge, Louisiana, USA.
70	31	Department of Medicine, Duke University, Durham, North Carolina, USA.
71	32	Northwestern University, Chicago, IL, USA.
72	33	Health through Physical Activity, Lifestyle and Sport Research Centre (HPALS)
73		Division of Exercise Science and Sports Medicine (ESSM), FIMS International Collaborating
74		Centre of Sports Medicine, Department of Human Biology, Faculty of Health Sciences, University
75		of Cape Town
76	34	Department of Anthropology, Northwestern University, Evanston, IL, USA.
77	35	Imperial College London Diabetes Centre, Abu Dhabi, United Arab Emirates and Imperial College
78		London, London, United Kingdom
79	36	Department of Nutrition and Public Health, Faculty of Health and Sport Sciences, University of
80		Agder, 4630 Kristiansand, Norway.
81	37	The FA Group, Burton-Upon-Trent, Staffordshire, UK.
82	38	Division of Public Health Sciences, Fred Hutchinson Cancer Research Center and School of Public
83		Health, University of Washington, Seattle, WA, USA.
84	39	Moi University, Eldoret, Kenya.
85	40	University of Global Health Equity, Rwanda.
86	41	Helsinki University Central Hospital, Helsinki, Finland.
87	42	University of Brighton, Eastbourne, UK.
88	43	Department of Physiology, Kwame Nkrumah University of Science and Technology, Kumasi,
89		Ghana
90	44	Department of Nutrition and Movement Sciences, Maastricht University, Maastricht, The
91		Netherlands.

92	45	University of Edinburgh, Edinburgh, UK.
93	46	Program in Physical Therapy and Department of Medicine, Washington University School of
94		Medicine, St. Louis, Missouri, USA.
95	47	Biological Sciences and Anthropology, University of Southern California, California, USA.
96	48	Centre for Cardiovascular Sciences, Queen's Medical Research Institute, University of Edinburgh,
97		Edinburgh, UK.
98	49	University of Wageningen, Wageningen, The Netherlands.
99	50	Department of Nutrition, Exercise and Sports, Copenhagen University, Copenhagen, Denmark.
100	51	Stanford University, Stanford CA, USA.
101	52	Department of Anthropology, Baylor University, Waco, TX, USA.
102	53	Maastricht University, Maastricht and Lifestyle Medicine Center for Children, Jeroen Bosch
103		Hospital's-Hertogenbosch, The Netherlands.
104	54	Population, Policy and Practice Research and Teaching Department, UCL Great Ormond Street
105		Institute of Child Health, London, UK.
106	55	University of California Los Angeles, Los Angeles, USA.
107	56	Max Planck Institute for Evolutionary Anthropology, Department of Human Behavior, Ecology,
108		and Culture.
109	57	Growth and Obesity, Division of Intramural Research, NIH, Bethesda, MD, USA.
110	58	Nutritional and Health Related Environmental Studies Section, Division of Human Health,
111		International Atomic Energy Agency, Vienna, Austria.
112	59	Division of Epidemiology, Department of Public Health Sciences, Loyola University School of
113		Medicine, Maywood Illinois, USA.
114	60	Biotech Center and Nutritional Sciences University of Wisconsin, Madison, Wisconsin, USA.
115	61	Department of Human Biology, University of Maastricht, Maastricht, The Netherlands.
116	62	Center for Energy Metabolism and Reproduction, Shenzhen Institutes of Advanced Technology,
117		Chinese Academy of Sciences, Shenzhen, China
118	63	CAS Center of Excellence in Animal Evolution and Genetics, Kunming, China.

119 Abstract: Total daily energy expenditure ("total expenditure") reflects daily energy needs and is 120 a critical variable in human health and physiology, but its trajectory over the life course is poorly 121 studied. We analyzed a large, diverse database of total expenditure measured by the doubly 122 labeled water method for males and females aged 8 days to 95 yr. Total expenditure increased 123 with fat free mass in a power-law manner, with four distinct life stages. Fat free mass-adjusted 124 expenditure accelerates rapidly in neonates to  $\sim$ 50% above adult values at  $\sim$ 1 yr, declines slowly 125 to adult levels by  $\sim 20$  yr, remains stable in adulthood (20-60 yr) even during pregnancy, then 126 declines in older adults. These changes shed light on human development and aging and should 127 help shape nutrition and health strategies across the lifespan.

128 One Sentence Summary: Expenditure varies as we age, with four distinct metabolic life stages 129 reflecting changes in behavior, anatomy, and tissue metabolism.

130 Main Text: All of life's essential tasks, from development and reproduction to maintenance and 131 movement, require energy. Total expenditure (MJ/d) is thus central to understanding both daily 132 nutritional requirements and the body's investment among activities. Yet we know surprisingly 133 little about total expenditure in humans or how it changes over the lifespan. Most large (n>1,000) 134 analyses of human energy expenditure have been limited to basal expenditure, the metabolic rate 135 at rest (1), which accounts for only a portion (usually  $\sim$ 50-70%) of total expenditure, or have 136 estimated total expenditure from basal expenditure and daily physical activity (2-5). Doubly 137 labeled water studies provide measurements of total expenditure in free-living subjects, but have 138 been limited in sample size (n < 600), geographic and socioeconomic diversity, and/or age (6-9). 139 Body composition, size, and physical activity change over the life course, often in 140 concert, making it difficult to parse the determinants of energy expenditure. Total and basal 141 expenditures increase with age as children grow and mature (10, 11), but the relative effects of

increasing physical activity and age-related changes in tissue-specific metabolic rates are unclear
(*12-16*). Similarly, the decline in total expenditure beginning in older adults corresponds with
declines in fat free mass and physical activity but may also reflect age-related reductions in
organ metabolism (9, 17-19).

We investigated the effects of age, body composition, and sex on total expenditure using a large (n = 6,421; 64% female), diverse (n = 29 countries) database of doubly labeled water measurements for subjects aged eight days to 95 years (20), calculating total expenditure from isotopic measurements using a single, validated equation for all subjects (21). Basal expenditure, measured *via* indirect calorimetry, was available for n = 2,008 subjects, and we augmented the dataset with additional published meaures of basal expenditure in neonates and doubly labeled water-mesaured total expenditure in pregnant and post-partum women (Methods; Table S1).

153 We found that both total and basal expenditure increased with fat free mass in a power-154 law manner (Figures 1, S1, S2, Table S1), requiring us to adjust for body size to isolate potential 155 effects of age, sex, and other factors. Notably, due to the power-law relation with size, the ratio 156 of (energy expenditure/mass) does not adequately control for body size because the ratio trends 157 lower for larger individuals (Figure S1). Instead, we used regression analysis to control for body 158 size (22). A general linear model with *ln*-transformed values of energy expenditure (total or 159 basal), fat free mass, and fat mass in adults 20 - 60 y (Table S2) was used to calculate residual 160 expenditures for each subject. We converted these residuals to "adjusted" expenditures for clarity 161 in discussing age-related changes: 100% indicates an expenditure that matches the expected 162 value given the subject's fat free mass and fat mass, 120% indicates an expenditure 20% above 163 expected, etc. Using this approach, we also calculated the portion of adjusted total expenditure

164	attributed to basal expenditure (Figure 2D; Methods). Segmented regression analysis (Methods)
165	revealed four distinct phases of adjusted total and basal expenditure over the lifespan.
166	<u>Neonates (0 to 1 y)</u> : Neonates in the first month of life had size-adjusted energy expenditures
167	similar to adults, with adjusted total expenditure of $99.0 \pm 17.2\%$ (n = 35) and adjusted basal
168	expenditure of $78.1 \pm 15.0\%$ (n = 34; Figure 2). Both measures increased rapidly in the first year.
169	In segmented regression analysis, adjusted total expenditure rose $84.7 \pm 7.2\%$ per year from birth
170	to a break point at 0.7 years (95% CI: 0.6, 0.8); a similar rise and break point were evident in
171	adjusted basal expenditure (Table S4). For subjects between 9 and 15 months, adjusted total and
172	basal expenditures were nearly $\sim$ 50% elevated compared to adults (Figure 2).
173	Juveniles (1 to 20 y): Total and basal expenditure continued to increase with age throughout
174	childhood and adolescence along with fat free mass (Figure 1), but size-adjusted expenditures
175	steadily declined. Adjusted total expenditure declined at a rate of -2.8 $\pm$ 0.1% per year from
176	$147.8 \pm 22.6\%$ for subjects $1 - 2$ y to $102.7 \pm 18.1\%$ for subjects $20 - 25$ y (Tables S2, S4).
177	Segmented regression analysis identified a breakpoint in adjusted total expenditure at 20.5 y
178	(95% CI: 19.8, 21.2), after which it plateaued at adult levels (Figure 2); a similar decline and
179	break point were evident in adjusted basal expenditure (Figure 2, Table S4). No pubertal
180	increases in adjusted total or basal expenditure were evident among subjects $10 - 15$ (Figure 2,
181	Table S3). In multivariate regression for subjects 1 to 20 y, males had a higher total expenditure
182	and adjusted total expenditure (Tables S2, S3), but sex had no detectable effect on the rate of
183	decline in adjusted total expenditure with age (sex:age interaction p=0.30).
184	<u>Adults (20 to 60 y)</u> : Total and basal expenditure and fat free mass were all stable from age 20 to
185	60 (Figure 1, 2; Tables S1, S2). Sex had no effect on total expenditure in multivariate models
186	with fat free mass and fat mass, nor in analyses of adjusted total expenditure (Tables S2, S4).

187 Adjusted total and basal expenditures were stable even during pregnancy, the elevation in 188 unadjusted expenditures matching those expected from the gain in mothers' fat free mass and fat 189 mass (Figure 2C). Segmented regression analysis identified a break point at 63.0 y (95% CI: 190 60.1, 65.9), after which adjusted TEE begins to decline. This break point was somewhat earlier 191 for adjusted basal expenditure (46.5, 95% CI: 40.6, 52.4), but the relatively small number of 192 basal measures for 45 - 65 y (Figure 2D) reduces our precision in determining this break point. 193 Older adults (>60 y): At ~60 y, total and basal expenditure begin to decline, along with fat free 194 mass and fat mass (Figures 1, S3, Table S1). Declines in expenditure are not only a function of 195 reduced fat free mass and fat mass, however. Adjusted total expenditure declined by -0.7  $\pm 0.1\%$ 196 per year, and adjusted basal expendiure fell at a similar rate (Figure 2, Figure S3, Text S1, Table 197 S4). For subjects 90+ y, adjusted total expenditure was  $\sim 26\%$  below that of middle-aged adults. 198 Our analyses provide empirical measures and predictive equations for total and basal

199 expenditure from infancy to old age (Tables S1, S2), and bring to light major metabolic changes 200 across the life course. To begin, we can infer fetal metabolic rates from maternal measures 201 during pregnancy: if body size-adjusted expenditures were elevated in the fetus, then adjusted 202 expenditures for pregnant mothers, particularly late in pregnancy when the fetus accounts for a 203 substantial portion of a mother's weight, would be likewise elevated. Instead, the stability of 204 adjusted total and basal expenditures at ~100% during pregnancy (Figure 2B) indicates that the 205 growing fetus maintains a fat free mass- and fat mass-adjusted metabolic rate similar to adults, which is consistent with adjusted expenditures of neonates (both  $\sim 100\%$ ; Figure 2) in the first 206 207 weeks after birth. Total and basal expenditures, both absolute and size-adjusted values, then 208 accelerate rapidly over the first year. This early period of metabolic acceleration corresponds to a critical period in early development in which growth often falters in nutritionally-stressedpopulations (23). Increasing energy demands could be a contributing factor.

211 After rapid acceleration in total and basal expenditure during the first year, adjusted 212 expenditures progressively decline thereafter, reaching adult levels at  $\sim 20$  yr. Elevated adjusted 213 expenditures in this life stage may reflect the metabolic demands of growth and development. 214 Adult expenditures, adjusted for body size and composition, are remarkably stable, even during 215 pregnancy and post-partum. Declining metabolic rates in older adults could increase the risk of 216 weight gain. However, neither fat mass nor percentage increased in this period (Figure S3), 217 consistent with the hypothesis that energy intake is coupled to expenditure (24). 218 Following previous studies (15, 16, 19, 25, 26), we calculated the effect of organ size on 219 basal expenditure over the lifespan (Methods). Organs with a high tissue-specific metabolic rate, 220 particularly the brain and liver, account for a greater proportion of fat free mass in young 221 individuals. Thus organ-based basal expenditure, estimated from organ size and tissue-specific 222 metabolic rate, follows a power-law relationship with fat free mass, roughly consistent with 223 observed basal expenditures (Methods, Figure S6). Still, observed basal expenditure exceeded 224 organ-based estimates by ~30% in early life (1 - 20 y) and was ~20% lower than organ-based 225 estimates in subjects over 60 y (Figure S6), consistent with studies indicating that tissue-specific

226 metabolic rates are elevated in juveniles (15, 16) and reduced in older adults (19, 25, 26).

We investigated the contributions of daily physical activity and changes in tissue-specific metabolic rate to total and basal expenditure using a simple model with two components: activity and basal expenditure (Figure 3; Meethods). Activity expenditure was modeled as a function of physical activity and body mass, assuming activity costs are proportional to weight, and could either remain constant over the lifespan or follow the trajectory of daily physical activity measured *via* accelerometry, peaking at 5 – 10 y and declining thereafter (*12, 17, 18*) (Figure 3).
Similarly, basal expenditure was modeled as a power function of fat free mass (consistent with
organ-based basal expenditure estimates; Methods) multiplied by a "tissue specific metabolism"
term, which could either remain constant at adult levels across the lifespan or follow the
trajectory observed in adjusted basal expenditure (Figure 2). For each scenario, total expenditure
was modeled as the sum of activity and basal expenditure (Methods).

238 Models that hold physical activity or tissue-specific metabolic rates constant over the 239 lifespan do not reproduce the observed patterns of age-related change in absolute or adjusted 240 measures of total or basal expenditure (Figure 3). Only when age-related changes in physical 241 activity and tissue-specific metabolism are included does model output match observed 242 expenditures, indicating that variation in both physical activity and tissue-specific metabolism 243 contribute to total expenditure and its components across the lifespan. Elevated tissue-specific 244 metabolism in early life may be related to growth or development (15, 16). Conversely, reduced 245 expenditures in later life may reflect a decline in organ level metabolism (25-27).

246 Metabolic models of life history commonly assume continuity in tissue-specific 247 metabolism over the life course, with metabolic rates increasing in a stable, power-law manner 248 (28, 29). Measures of humans here challenge this view, with deviations from the power-law 249 relationship for total and basal expenditure in childhood and old age (Fig. 1, 2). These changes 250 present a potential target for investigating the kinetics of disease, drug activity, and healing, 251 processes intimately related to metabolic rate. Further, inter-individual variation in expenditure is 252 considerable even when controlling for fat free mass, fat mass, sex, and age (Figure 1, 2, Table 253 S2). Elucidating the processes underlying metabolic changes across the life course and variation 254 among individuals may help reveal the roles of metabolic variation in health and disease.

# 255 Acknowledgements

- 256 Data in this paper are archived in the DLW database, which can be found at https://doubly-
- 257 labelled-water-database.iaea.org/home or https://www.dlwdatabase.org/. The DLW database is
- 258 generously supported by the IAEA, Taiyo Nippon Sanso and, SERCON. We are grateful to these
- 259 companies for their support and especially to Takashi Oono for his tremendous efforts at fund
- 260 raising on our behalf. The authors also gratefully acknowledge funding from the US National
- 261 Science Foundation (BCS-1824466) awarded to Herman Pontzer. The funders played no role in
- the content of this manuscript.

# 263 **Conflict of interest**

264 The authors have no conflicts of interest to declare.

# 265 Data Availability

- All data used in these analyses is freely available via the IAEA Doubly Labelled Water Database
- 267 (https://doubly-labelled-water-database.iaea.org/home or https://www.dlwdatabase.org/).

# 268 Supplementary Material

- 269 Materials and Methods
- 270 Figures S1-S10
- 271 Tables S1-S4
- 272 References (*30-54*)

# 273 References

- C. J. Henry, Basal metabolic rate studies in humans: measurement and development of new equations. *Public Health Nutr* 8, 1133-1152 (2005).
   FAO, Human energy requirements: report of a joint FAO/ WHO/UNU Expert Consultation. *Food*
- 2762.FAO, Human energy requirements: report of a joint FAO/ WHO/UNU Expert Consultation. Food277Nutr Bull 26, 166 (2005).
- 2783.K. R. Westerterp, J. O. de Boer, W. H. M. Saris, P. F. M. Schoffelen, F. ten Hoor, Measurement of279energy expenditure using doubly labelled water. Int J Sport Med 5, S74-75 (1984).
- 2804.P. D. Klein *et al.*, Calorimetric validation of the doubly-labelled water method for determination281of energy expenditure in man. *Hum Nutr Clin Nutr* **38**, 95-106 (1984).
- 282 5. J. R. Speakman, *Doubly Labelled Water: Theory and Practice*. (Chapman and Hall, London, 1997).
- A. E. Black, W. A. Coward, T. J. Cole, A. M. Prentice, Human energy expenditure in affluent
  societies: an analysis of 574 doubly-labelled water measurements. *Eur J Clin Nutr* 50, 72-92
  (1996).
- 2867.L. R. Dugas *et al.*, Energy expenditure in adults living in developing compared with industrialized287countries: a meta-analysis of doubly labeled water studies. *Am J Clin Nutr* **93**, 427-441 (2011).
- H. Pontzer *et al.*, Constrained Total Energy Expenditure and Metabolic Adaptation to Physical
   Activity in Adult Humans. *Curr Biol* 26, 410-417 (2016).
- 2909.J. R. Speakman, K. R. Westerterp, Associations between energy demands, physical activity, and291body composition in adult humans between 18 and 96 y of age. Am J Clin Nutr 92, 826-834292(2010).
- 29310.N. F. Butte, Fat intake of children in relation to energy requirements. Am J Clin Nutr 72, 1246s-2941252s (2000).
- 29511.H. L. Cheng, M. Amatoury, K. Steinbeck, Energy expenditure and intake during puberty in296healthy nonobese adolescents: a systematic review. Am J Clin Nutr **104**, 1061-1074 (2016).
- 12. D. L. Wolff-Hughes, D. R. Bassett, E. C. Fitzhugh, Population-referenced percentiles for waist worn accelerometer-derived total activity counts in U.S. youth: 2003 2006 NHANES. *PLoS One* 99. e115915 (2014).
- 30013.E. A. Schmutz *et al.*, Physical activity and sedentary behavior in preschoolers: a longitudinal301assessment of trajectories and determinants. *Int J Behav Nutr Phys Act* **15**, 35 (2018).
- 30214.J. A. Hnatiuk, K. E. Lamb, N. D. Ridgers, J. Salmon, K. D. Hesketh, Changes in volume and bouts of303physical activity and sedentary time across early childhood: a longitudinal study. Int J Behav Nutr304Phys Act 16, 42 (2019).
- 30515.A. Hsu *et al.*, Larger mass of high-metabolic-rate organs does not explain higher resting energy306expenditure in children. *Am J Clin Nutr* **77**, 1506-1511 (2003).
- 30716.Z. Wang *et al.*, A cellular level approach to predicting resting energy expenditure: Evaluation of<br/>applicability in adolescents. *Am J Hum Biol* **22**, 476-483 (2010).
- 309 17. D. L. Wolff-Hughes, E. C. Fitzhugh, D. R. Bassett, J. R. Churilla, Waist-Worn Actigraphy:
   310 Population-Referenced Percentiles for Total Activity Counts in U.S. Adults. *J Phys Act Health* 12, 447-453 (2015).
- 312 18. Y. Aoyagi, S. Park, S. Cho, R. J. Shephard, Objectively measured habitual physical activity and
   313 sleep-related phenomena in 1645 people aged 1-91 years: The Nakanojo Community Study. *Prev* 314 *Med Rep* 11, 180-186 (2018).
- 31519.D. Gallagher, A. Allen, Z. Wang, S. B. Heymsfield, N. Krasnow, Smaller organ tissue mass in the<br/>elderly fails to explain lower resting metabolic rate. *Ann N Y Acad Sci* **904**, 449-455 (2000).
- 31720.J. R. Speakman *et al.*, The International Atomic Energy Agency International Doubly Labelled318Water Database: Aims, Scope and Procedures. *Ann Nutr Metab* **75**, 114-118 (2019).
- 31921.J. R. Speakman *et al.*, A standard calculation methodology for human doubly labeled water320studies. *Cell Rep Med* 2, 100203 (2021).

221	22	D. D. Allison, C. Deultre, M. J. Coren, C. T. Dechlman, C. D. Haursefield, Statistical considerations
321 322	22.	D. B. Allison, F. Paultre, M. I. Goran, E. T. Poehlman, S. B. Heymsfield, Statistical considerations
322	23.	regarding the use of ratios to adjust data. <i>Int J Obes Relat Metab Disord</i> <b>19</b> , 644-652 (1995). H. Alderman, D. Headey, The timing of growth faltering has important implications for
323	25.	observational analyses of the underlying determinants of nutrition outcomes. <i>PLoS One</i> <b>13</b> ,
324		e0195904 (2018).
325	24	
320 327	24.	J. E. Blundell <i>et al.</i> , The drive to eat in homo sapiens: Energy expenditure drives energy intake.
327	25.	Physiol Behav <b>219</b> , 112846 (2020).
328	25.	Z. Wang <i>et al.</i> , Specific metabolic rates of major organs and tissues across adulthood: evaluation
329	26	by mechanistic model of resting energy expenditure. <i>Am J Clin Nutr</i> <b>92</b> , 1369-1377 (2010).
330	26.	Z. Wang, S. Heshka, S. B. Heymsfield, W. Shen, D. Gallagher, A cellular-level approach to
332	27.	predicting resting energy expenditure across the adult years. <i>Am J Clin Nutr</i> <b>81</b> , 799-806 (2005).
333	27.	Y. Yamada <i>et al.</i> , Extracellular water may mask actual muscle atrophy during aging. <i>J Gerontol A</i> <i>Biol Sci Med Sci</i> 65, 510-516 (2010).
333	28.	G. B. West, J. H. Brown, B. J. Enquist, A general model for ontogenetic growth. <i>Nature</i> <b>413</b> , 628-
335	20.	
336	29.	631 (2001). J. H. Brown, J. F. Gillooly, A. P. Allen, V. M. Savage, G. B. West, Toward a metabolic theory of
337	29.	ecology. Ecology 85, 1771-1789 (2004).
338	30.	R. D. Montgomery, Changes in the basal metabolic rate of the malnourished infant and their
339	50.	relation to body composition. J Clin Invest <b>41</b> , 1653-1663 (1962).
340	31.	O. G. Brooke, T. Cocks, Resting metabolic rate in malnourished babies in relation to total body
340	51.	potassium. Acta Paediatr Scand 63, 817-825 (1974).
342	32.	N. F. Butte <i>et al.</i> , Energy requirements derived from total energy expenditure and energy
343	52.	deposition during the first 2 y of life. <i>Am J Clin Nutr</i> <b>72</b> , 1558-1569 (2000).
344	33.	M. Hernández-Triana <i>et al.</i> , Total energy expenditure by the doubly-labeled water method in
345	55.	rural preschool children in Cuba. <i>Food Nutr Bull</i> <b>23</b> , 76-81 (2002).
346	34.	S. S. Summer, J. M. Pratt, E. A. Koch, J. B. Anderson, Testing a novel method for measuring
347	54.	sleeping metabolic rate in neonates. <i>Respir Care</i> <b>59</b> , 1095-1100 (2014).
348	35.	N. F. Butte <i>et al.</i> , Energy expenditure and deposition of breast-fed and formula-fed infants
349	55.	during early infancy. <i>Pediatr Res</i> <b>28</b> , 631-640 (1990).
350	36.	L. A. Gilmore <i>et al.</i> , Energy Intake and Energy Expenditure for Determining Excess Weight Gain in
351	00.	Pregnant Women. <i>Obstet Gynecol</i> <b>127</b> , 884-892 (2016).
352	37.	G. R. Goldberg <i>et al.</i> , Longitudinal assessment of energy expenditure in pregnancy by the doubly
353		labeled water method. <i>Am J Clin Nutr</i> <b>57</b> , 494-505 (1993).
354	38.	N. F. Butte, W. W. Wong, M. S. Treuth, K. J. Ellis, E. O'Brian Smith, Energy requirements during
355		pregnancy based on total energy expenditure and energy deposition. Am J Clin Nutr <b>79</b> , 1078-
356		1087 (2004).
357	39.	J. B. Weir, New methods for calculating metabolic rate with special reference to protein
358		metabolism. <i>J Physiol</i> <b>109</b> , 1-9 (1949).
359	40.	R. C. Team, R: A language and environment for statistical computing. R Foundation for Statistical
360		Computing. (Vienna, Austria, 2020).
361	41.	V. M. R. Muggeo, . Segmented: an R package to fit regression models with broken-line
362		relationships. R News 8/1, 20-25 (2008).
363	42.	M. Elia, in <i>Physiology, Stress, and Malnutrition,</i> J. M. Kinney, H. N. Tucker, Eds. (Raven Press,
364		Philadelphia, 1997), pp. 383-411.
365	43.	M. A. Holliday, D. Potter, A. Jarrah, S. Bearg, The relation of metabolic rate to body weight and
366		organ size. Pediatr Res 1, 185-195 (1967).
367	44.	M. A. Holliday, Metabolic rate and organ size during growth from infancy to maturity and during
368		late gastation and early infancy. Pediatrics 47, Suppl 2:169+ (1971).

- 36945.D. K. Molina *et al.*, Organ Weight Reference Ranges for Ages 0 to 12 Years. Am J Forensic Med370Pathol **40**, 318-328 (2019).
- 37146.M. Sawabe *et al.*, Standard organ weights among elderly Japanese who died in hospital,372including 50 centenarians. *Pathol Int* **56**, 315-323 (2006).
- 373 47. S. Kwon, K. Honegger, M. Mason, Daily Physical Activity Among Toddlers: Hip and Wrist
  374 Accelerometer Assessments. *Int J Environ Res Public Health* 16, (2019).
- 37548.E. R. Hager *et al.*, Toddler physical activity study: laboratory and community studies to evaluate376accelerometer validity and correlates. *BMC Public Health* **16**, 936 (2016).
- 49. P. Silva *et al.*, Lifespan snapshot of physical activity assessed by accelerometry in Porto. *J Phys* 378 *Act Health* 8, 352-360 (2011).
- 37950.A. Doherty *et al.*, Large Scale Population Assessment of Physical Activity Using Wrist Worn380Accelerometers: The UK Biobank Study. *PLoS One* **12**, e0169649 (2017).
- 38151.P. S. Blair *et al.*, Childhood sleep duration and associated demographic characteristics in an382English cohort. Sleep **35**, 353-360 (2012).
- 38352.J. Kohyama, J. A. Mindell, A. Sadeh, Sleep characteristics of young children in Japan: internet384study and comparison with other Asian countries. *Pediatr Int* **53**, 649-655 (2011).
- 385 53. I. Iglowstein, O. G. Jenni, L. Molinari, R. H. Largo, Sleep duration from infancy to adolescence:
  386 reference values and generational trends. *Pediatrics* 111, 302-307 (2003).
- 38754.P. Brambilla *et al.*, Sleep habits and pattern in 1-14 years old children and relationship with388video devices use and evening and night child activities. *Ital J Pediatr* **43**, 7 (2017).

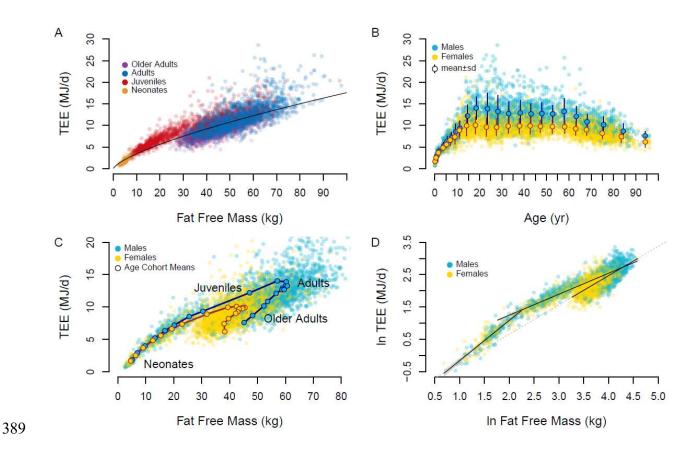
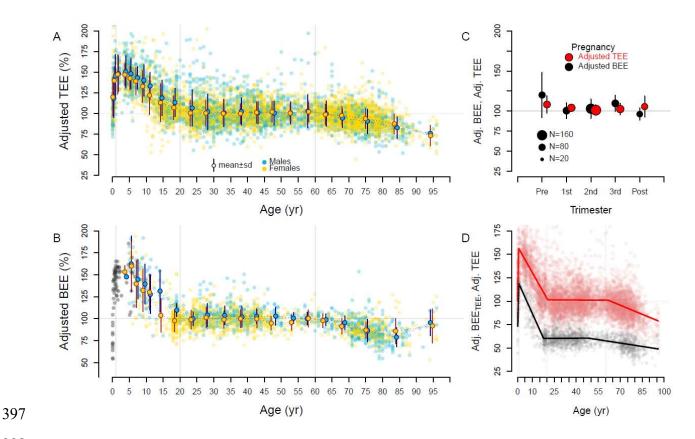
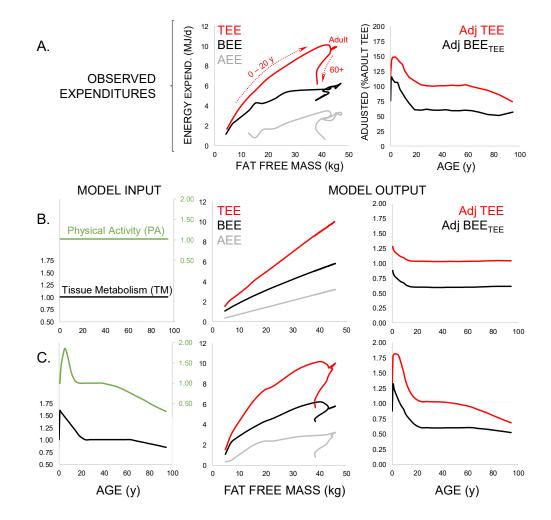


Figure 1. A. Total expenditure (TEE) increases with fat free mass in a power-law manner (black line: TEE= 0.677FFM<sup>0.708</sup>, r<sup>2</sup>=0.83, p<0.0001; Table S2) but age groups cluster about the trend line differently. **B.** Total expenditure rises in childhood, is stable through adulthood, and declines in older adults. Means±sd for agesex cohorts are shown. **C.** Age-sex cohort means show a distinct progression of total expenditure and fat free mass over the life course. **D.** Neonate, juveniles, and adults exhibit distinct relationships between fat free mass and expenditure. The dashed line, extrapolated from the regression for adults, approximates the regression used to calculate adjusted total expenditure.



398 Figure 2. Fat free mass- and fat mass-adjusted expenditures over the life course. Individual subjects and 399 age-sex cohort mean ± SD are shown. For both total (Adj. TEE) (A) and basal (Adj. BEE) expenditure (B), 400 adjusted expenditures begin near adult levels (~100%) but quickly climb to ~150% in the first year. Adjusted 401 expenditures decline to adult levels ~20y, then decline again in older adults. Basal expenditures for infants 402 and children not in the doubly labeled water database are shown in gray. C. Pregnant mothers exhibit 403 adjusted total and basal expenditures similar to non-reproducing adults (Pre: prior to pregnancy; Post: 27 404 weeks post-partum). D. Segmented regression analysis of adjusted total (red) and adjusted basal 405 expenditure (calculated as a portion of total; Adj. BEETEE; black) indicates a peak at ~1 y, adult levels at 406 ~20 y, and decline at ~60 y (see text).



407

Figure 3. Modeling the contribution of physical activity and tissue-specific metabolism to daily expenditures.
A. Observed total (TEE, red), basal (BEE, black), and activity (AEE, gray) expenditures (Table S1) show
age-related variation with respect to fat free mass (see Figure 1C) that is also evident in adjusted values
(Table S3; see Figure 2D). B. These age effects do not emerge in models assuming constant physical
activity (PA, green) and tissue-specific metabolic rate (TM, black) across the life course. C. When physical
activity and tissue-specific metabolism follow the life course trajectories evident from accelerometry and
adjusted basal expenditure, respectively, model output is similar to observed expenditures.

#### 415 Supplementary Materials:

416 Pontzer et al. *Daily Energy Expenditure through the Human Life Course* 

### 417 **Contents:**

- 418 Materials and Methods
- 419 1. Doubly Labeled Water Database
- 420 2. Basal Expenditure, Activity Expenditure, and PAL
- 421 3. Predictive Models for TEE, BEE, AEE, and PAL
- 422 4. Adjusted TEE, Adjusted BEE, and Adjusted BEE<sub>TEE</sub>
- 423 5. Segmented Regression Analysis
- 424 6. Organ Size and BEE
- 425 7. Modeling the Effects of PA and Cellular Metabolism
- 426 8. Physical Activity, Activity Expenditure and PAL
- 427 9. The IAEA DLW database consortium
- 428 Figures S1-S10
- 429 Tables S1-S4

### 430 Material and Methods

431 1. <u>Doubly Labeled Water Database</u>

432 Data were taken from IAEA Doubly Labelled Water (DLW) Database, version 3.1,

433 completed April, 2020 (20). This version of the database comprises 6,743 measurements of total

- 434 expenditure using the doubly labeled water method. Of these, a total of 6,421 had valid data for
- total expenditure, fat free mass, fat mass, sex, and age. These 6,421 measurements were used in
- this analysis. This dataset was augmented with published basal expenditure measurements for
- 437 n=136 neonates and infants (30-35) that included fat free mass and fat mass. Malnourished or

438 preterm infants were excluded. For sources that provided cohort means rather than individual 439 subject measurements (32, 35) means were entered as single values into the dataset without 440 reweighting to reflect sample size. This approach resulted in 77 measures of basal expenditure, 441 fat free mass, and fat mass for n=136 subjects. We also added to the dataset published basal and 442 total expenditure measurements of n=141 women before, during, and after pregnancy (36-38) 443 that included fat free mass and fat mass. These measurements were grouped as pre-pregnancy, 1st trimester, 2<sup>nd</sup> trimester, 3<sup>rd</sup> trimester, and post-partum for analysis. 444 445 In the doubly labeled water method (5), subjects were administered a precisely measured dose of water enriched in <sup>2</sup>H<sub>2</sub>O and H<sub>2</sub><sup>18</sup>O. The subject's body water pool is thus enriched in 446 deuterium (<sup>2</sup>H) and <sup>18</sup>O. The initial increase in body water enrichment from pre-dose values is 447 448 used to calculate the size of the body water pool, measured as the dilution space for deuterium  $(N_d)$  and <sup>18</sup>O  $(N_o)$ . These isotopes are then depleted from the body water pool over time: both 449 isotopes are depleted *via* water loss, whereas <sup>18</sup>O is also lost *via* carbon dioxide production. 450 Subtracting the rate (%/d) of deuterium depletion ( $k_d$ ) from the rate of <sup>18</sup>O depletion ( $k_o$ ), and 451 452 multiplying the size of the body water pool (derived from N<sub>d</sub> and N<sub>o</sub>) provided the rate of carbon 453 doxide production, rCO<sub>2</sub>. Entries in the DLW database include the original k and N values for 454 each subject, which were then used to calculate  $CO_2$  using a common equation that has been 455 validated in subjects across the lifespan (21). The rate of CO<sub>2</sub> production, along with each 456 subject's reported food quotient, was then used to calculate energy expenditure (MJ/d) using the 457 Weir equation (39). We used the food quotients reported in the original studies to calculate total 458 energy expenditure from  $rCO_2$  for each subject.

The size of the body water pool, determined from N<sub>d</sub> and N<sub>o</sub>, was used to establish FFM,
using hydration constants for fat free mass taken from empirical studies. Other anthropometric

461 variables (age, height, body mass, sex) were measured using standard protocols. Fat mass was
462 calculated as (body mass) – (fat free mass).

#### 463 2. <u>Basal Expenditure, Activity Expenditure, and Physical Activityl Level (PAL)</u>

464 A total of 2,008 subjects in the database had associated basal expenditure, measured via 465 respirometry. For these subjects, we analyzed basal expenditure, activity expenditure, and 466 "physical activity level" (PAL). Activity expenditure was calculated as [0.9(total expenditure) – 467 (basal expenditure)] which subtracts basal expenditure and the assumed thermic effect of food 468 [estimated at 0.1(total expenditure)] from total expenditure. The PAL ratio was calculated as 469 (total expenditure)/(basal expenditure). As noted above, the basal expenditure dataset was 470 augmented with measurements from neonates and infants, but these additional measures do not 471 have associated total expenditure and could not be used to calculate activity expenditure or PAL.

#### 472 3. Predictive Models for Total, Basal, and Activity Expenditures and PAL

We used general linear models to regress measures of energy expenditure against 473 474 anthropometric variables. We used the base package in R version 4.0.3 (40) for all analyses. 475 General linear models were implemented using the lm function. These models were used to 476 develop predictive equations for total expenditure for clinical and research applications, and to 477 determine the relative contribution of different variables to total expenditure and its components. 478 Given the marked changes in metabolic rate over the lifespan (Figure 1, Figure 2) we calculated 479 these models separately for each life history stage: infants (0 - 1 y), juveniles (1 - 20 y), adults 480 (20 - 60 y), and older adults (60 + y). These age ranges were identified using segmented 481 regression analysis. Results of these models are shown in Table S2.

482

#### 4. Adjusted Expenditures

We used general linear models with fat free mass and fat mass in adults (20 - 60 y) to calculate adjusted total expenditure and adjusted basal expenditure. The 20 - 60 y age range was used as the basis for analyses because segmented regression analysis consistently identified this period as stable with respect to size-adjusted total expenditure (see below).

487 We used models 2 and 5 in Table S2, which have the form  $ln(Expenditure) \sim ln(FFM) +$ 488 ln(Fat Mass) and were implemented using the lm function in base R version 4.0.3 (40). We 489 used *ln*-transformed variables due to the inherent power-law relationship between body size and 490 both total and basal expenditure (ref. 2; see Figure 1, Figure S1). Predicted values for each 491 subject, given their fat free mass and fat mass, were calculated from the model using the 492 pred () function; these *ln*-transformed values were converted back into MJ as exp(Predicted). 493 Residuals for each subject were calculated as (Observed – Predicted) expenditure, and were then 494 used to calculate adjusted expenditures as:

[1]

# 495 Adjusted Expenditure = 1 + Residual / Predicted

496 The advantage of expressing residuals as a percentage of the predicted value is that it allows us 497 to compare residuals across the range of age and body size in the dataset. Raw residuals (MJ) do 498 not permit direct comparison because the relationship between size and expenditure is 499 heteroscedastic; the magnitude of residuals increases with size (see Figure S1). Ln-transformed 500 residuals (*ln*MJ) avoid this problem but are more difficult to interpret. Adjusted expenditures, 501 used here, provide an easily interpretable measure of deviation from expected values. An 502 adjusted expenditure value of 100% indicates that a subject's observed total or basal expenditure 503 matches the value predicted for their fat free mass and fat mass, based on the general linear 504 model derived for adults. An adjusted expenditure of 120% indicates an observed total or basal

sexpenditure value that exceeds the predicted value for their fat free mass and fat mass by 20%.
Similarly, an adjusted expenditure of 80% means the subject's measured expenditure was 20%
lower than predicted for their fat free mass and fat mass using the adult model. Adjusted total
expenditure and adjusted basal expenditure values for each age-sex cohort are given in Table S3.
Within each metabolic life history stage we used general linear models (1m function in R) to
investigate the effects of sex and age on adjusted total and basal expenditure.

511 This same approach was used to calculate adjusted basal expenditure as a proportion of 512 total expenditure (Figure 2D), hereafter termed adjusted BEE<sub>TEE</sub>. Residual<sub>BEE-TEE</sub>, the deviation 513 of observed basal expenditure from the adult total expenditure regression (eq. 2 in Table S2), 514 was calculated as (Observed Basal Expenditure – Predicted Total Expenditure) and then used to 515 calculate adjusted BEE<sub>TEE</sub> as

516 Adjusted  $BEE_{TEE} = 1 + Residual_{BEE-TEE} / Predicted Total Expenditure$ [2] 517 When adjusted  $BEE_{TEE} = 80\%$ , observed basal expenditure is equal to 80% of predicted total 518 expenditure given the subject's fat free mass and fat mass. Adjusted BEE<sub>TEE</sub> is equivalent to 519 adjusted basal expenditure (Figure S4) but provides some analytical advantages. The derivation 520 of adjusted BEE<sub>TEE</sub> approach applies identical manipulations to observed total expenditure and 521 observed basal expenditure and therefore maintains them in directly comparable units. The ratio 522 of (adjusted total expenditure)/(adjusted basal expenditure) is identical to the PAL ratio of (total 523 expenditure)/(basal expenditure), and the difference (0.9adjusted total expenditure- adjusted 524 basal expenditure) is proportional to activity expenditure (Figure S4). Plotting adjusted total 525 expenditure and adjusted BEE<sub>TEE</sub> over the lifespan (Figure 2D) therefore shows both the relative 526 magnitudes of total and basal expenditure and their relationship to one another in comparable 527 units.

528 5. <u>Segmented Regression Analysis</u>

529 We used segmented regression analysis to determine the change points in the relationship 530 between adjusted expenditure and age. We used the Segmented (version 1.1-0) package in R 531 (41). For adjusted total expenditure, we examined a range of models with 0 to 5 change points, 532 using the npsi= term in the segmented () function. This approach does not specify the 533 location or value of change points, only the number of them. Each increase in the number of change points from 0 to 3 improved the model adj.  $R^2$  and standard error considerably. 534 535 Increasing the number of change points further to 4 or 5 did not improve the model, and the 536 additional change points identifed by the segmented () function fell near the change points for 537 the 3-change point model. We therefore selected the 3-change point model as the best fit for 538 adjusted total expenditure in this dataset. Segmented regression results are shown in Table S4. A 539 similar 3-change point segmented regression approach was conducted for adjusted basal 540 expenditure (Figure S4) and adjusted BEE<sub>TEE</sub> (Figure 2D). We note that the decline in adjusted 541 basal expenditure and adjusted BEE<sub>TEE</sub> in older adults begins earlier (as identified by segmented 542 regression analysis) than does the decline in adjusted total expenditure among older adults. 543 However, this difference may reflect the relative paucity of basal expenditure measurements for 544 subjects 40 - 60 y. Additional measurements are needed to determine whether the decline in 545 basal expenditure does in fact begin earlier than the decline in total expedinture. Here, we view 546 the timing as essentially coincident and interpret the change point in adjusted total expenditure 547 (~60 y), which is determined with a greater number of measurements, as more accurate and 548 reliable.

549 Having established that 3 break points provided the best fit for this dataset, we examined 550 whether changes in the age range used to calculate adjusted total energy expenditure affected the age break-points identified by segmented regression. When the age range used to calculate

adjusted expenditure was set at 20 - 60 y, the set of break point (95% CI) was: 0.69 (0.61-0.76),

553 20.46 (19.77-21.15), 62.99 (60.14-65.85). When the age range was expanded to 15 - 70 y, break

points determined through segmented regression were effectively unchanged: 0.69 (0.62 - 0.76),

21.40 (20.60-22.19), 61.32 (58.60-64.03). Break points were also unchanged when the initial age
range for adjusted expenditure was narrowed to 30 – 50 y: 0.69 (0.62-0.77), 20.56 (19.84-21.27),

557 62.85 (59.97-65.74).

# 558 6. Organ Size and Basal Expenditure

559 Measuring the metabolic rate of individual organs is notoriously challenging, and the 560 available data come from only a small number of studies. The available data indicate that organs differ markedly in their mass-specific metabolic rates at rest (42). The heart (1848 kJ kg<sup>-1</sup> d<sup>-1</sup>), 561 liver (840 kJ kg<sup>-1</sup> d<sup>-1</sup>), brain (1008 kJ kg<sup>-1</sup> d<sup>-1</sup>), and kidneys (1848 kJ kg<sup>-1</sup> d<sup>-1</sup>) have much greater 562 mass-specific metabolic rates at rest than do muscle (55 kJ kg<sup>-1</sup> d<sup>-1</sup>), other lean tissue (50 kJ kg<sup>-1</sup> 563 d<sup>-1</sup>), and fat (19 kJ kg<sup>-1</sup> d<sup>-1</sup>). Consequently, the heart, liver, brain, and kidneys combined account 564 565 for  $\sim 60\%$  of basal expenditure in adults (15, 19, 43, 44). In infants and children, these 566 metabolically active organs constitute a larger proportion of body mass. The whole body mass-567 specific basal expenditure [i.e., (basal expenditure)/(body mass), or (basal expenditure)/(fat free 568 mass)] for infants and children is therefore expected to be greater than adults' due to the greater 569 proportion of metabolically active organs early in life adults (15, 19, 43, 44). Similarly, reduced 570 organ sizes in elderly subjects may result in declining basal expenditure (19). 571 To examine this effect of organ size on basal expenditure in our dataset, we used

572 published references for organ size to determine the mass of the metabolically active organs

573 (heart, liver, brain, and kidneys) as a percentage of body mass or fat free mass for subjects 0 - 12

574 y (15, 43-45), 15 to 60 y (15, 19), and 60 to 100 y (19, 46). We used these relationships to 575 estimate the combined mass of the metabolically active organs (heart, liver, brain, kidneys) for 576 each subject in our dataset. We then subtracted the mass of the metabolically active organs from 577 measured fat free mass to calculate the mass of "other fat free mass". These two measures, along 578 with measured fat mass, provided a three-compartment model for each subject: metabolically 579 active organs, other fat free mass, and fat (Figure S6A).

580 Following previous studies (15, 16, 19, 25, 26), we assigned mass-specific metabolic 581 rates to each compartment and estimated basal expenditure for each subject. We used reported 582 mass-specific metabolic rates for the heart, liver, brain, and kidneys (see above; (42)) and age-583 related changes in the proportions of these organs for subjects 0 - 12 y (15, 45), 15 to 60 y (15, 584 16, 19, 25, 26), and 60 to 100 y (19, 25, 26, 46) to calculate an age-based weighted mass-specific 585 metabolic rate for the metabolically active organ compartment. We averaged the mass-specific 586 metabolic rates of resting muscle and other lean tissue (see above; (15, 19)) and assigned a value of 52.5 kJ kg<sup>-1</sup> d<sup>-1</sup> to "other fat free mass", and we used a mass-specific metabolic rate of 19 kJ 587  $kg^{-1} d^{-1}$  for fat. 588

589 Results are shown in Figure S6. Due to the greater proportion of metabolically active 590 organs in early life, the estimated basal expenditure from the three-compartment model follows a power-law relationship with FFM (using age cohort means, BEE = 0.38 FFM<sup>0.75</sup>; Figure S6B) 591 592 that is similar to that calculated from observed basal expenditure in our dataset (see Table S2 and 593 7. Modeling the Effects of Physical Activity and Tissue Specific Metabolism, below). Estimated 594 BEE from the three-compartment model produced mass-specific metabolic rates that are 595 considerably higher for infants and children than for adults and roughly consistent with observed 596 age-related changes in (basal expenditure)/(fat free mass) (Figure S6C). Thus, changes in organ

size can account for much of the variation in basal expenditure across the lifespan observed inour dataset.

599 Nonetheless, observed basal expenditure was ~30% greater early in life, and ~20% lower 600 in older adults, than estimated basal expenditure from the three-compartment model (Figure 601 S6D). The departures from estimated basal expenditure suggest that the mass-specific metabolic 602 rates of one or more organ compartments are considerably higher early in life, and lower late in 603 life, than they are in middle-aged adults, consistent with previous assessments (15, 16, 19, 25, 604 26). It is notable, in this context, that observed basal expenditure for neonates is nearly identical 605 to basal expenditure estimated from the three-compartment model, which assumes adult-like 606 tissue metabolic rates (Figure S6B,C,D). Observed basal expenditure for neonates is thus 607 consistent with the hypothesis that the mass-specific metabolic rates of their organs are similar to 608 those of other adults, specifically the mother.

#### 609 7. Modeling the Effects of Physical Activity and Tissue Specific Metabolism

We constructed two simple models to examine the contributions of physical activity and variation in tissue metabolic rate to total and basal expenditure. In the simplest version, we used the observed relationship between basal expenditure and tat free mass for all adults 20 - 60 y determined from linear regression of *ln*(basal expenditure) and *ln*(fat free mass) (untransformed regression equation: basal expenditure = 0.32 (fat free mass)<sup>0.75</sup>, adj. r<sup>2</sup> = 0.60, df = 1684, p <

615 0.0001) to model basal expenditure as

616 Basal expenditure = 
$$0.32 \text{ TM}_{age}$$
 (fat free mass)<sup>0.75</sup> [3]

617 The TM<sub>age</sub> term is tissue metabolic rate, a multiplier between 0 and 2 reflecting a relative

618 increase ( $TM_{age} > 1.0$ ) or decrease ( $TM_{age} < 1.0$ ) in organ metabolic rate relative that expected

from the power-law regression for adults. Note that, even when  $TM_{age} = 1.0$ , smaller individuals

620	are expected to exhibit greater mass-specific basal expenditure (that is, a greater basal
621	expenditure per kg body weight) due to the power-law relationship between basal expenditure
622	and fat free mass. Further, we note that the power-law relationship between basal expenditure
623	and fat free mass for adults is similar to that produced when estimating basal expenditure from
624	organ sizes (see Organ Size and Basal Expenditure, above). Thus, variation in $TM_{age}$ reflects
625	modeled changes in tissue metabolic rate in addition to power-law scaling effects, and also, in
626	effect, in addition to changes in basal expenditure due to age-related changes in organ size and
627	proportion. To model variation in organ activity over the lifespan, we either 1) maintained $TM_{age}$
628	at adult levels ( $TM_{age} = 1.0$ ) over the entire lifespan, or 2) had $TM_{age}$ follow the trajectory of
629	adjusted basal expenditure with age (Figure S8).
630	To incorporate effects of fat mass into the model, we constructed a second version of the
631	model in which basal expenditure was modeled following the observed relationship with FFM
632	and fat mass for adults $20 - 60$ y,
633	Basal expenditure = $0.32 \text{ TM}_{age} \text{ (fat free mass)}^{0.7544} \text{ (fat mass)}^{0.0003}$ [4]
634	As with the fat free mass model (eq. 3), we either maintained $TM_{age}$ at 1.0 over the life span or
635	modeled it using the trajectory of adjusted basal expenditure.
636	Activity expenditure was modeled as a function of physical activity and body mass
637	assuming larger indivduals expend more energy during activity. We began with activity
638	expenditure, calculated as [0.9(total expenditure) – (basal expenditure)] as described above. The
639	observed ratio of (activity expenditure)/(fat free mass) for adults $20 - 60$ y was 0.07 MJ d <sup>-1</sup> kg <sup>-1</sup> .
640	We therefore modeled activity expenditure as
641	Activity expenditure = $0.07 \text{ PA}_{age}$ (fat free mass) [5]

642 To incorporate effects of fat mass, we constructed a second version using the ratio of (activity 643 expenditure)/(body weight) for adults 20 - 60y,

644	Activity expenditure = $0.04 \text{ PA}_{age}$ (body weight) [6]
645	In both equations, PA <sub>age</sub> represents the level of physical activity relative to the mean value for 20
646	-60 y adults. PA <sub>age</sub> could either remain constant at adult levels (PA <sub>age</sub> =1.0) over the lifespan or
647	follow the trajectory of physical activity measured via accelerometry, which peaks between $5 - $
648	10 y, declines rapidly through adolescence, and then declines more slowly beginning at $\sim$ 40 y
649	(12-14, 17, 18, 47-50). Different measures of physical activity (e.g., moderate and vigorous PA,
650	mean counts per min., total accelerometry counts) exhibit somewhat different trajectories over
651	the lifespan, but the patterns are strongly correlated; all measures show the greatest activity at 5-
652	10 y and declining activity in older adults (Figure S7). We chose total accelerometry counts (12,
653	17), which sum all movement per 24-hour period, to model age-related changes in $PA_{age}$ . We
654	chose total counts because activity energy expenditure should reflect the summed cost of all
655	activity, not only activity at moderate and vigorous intensities. Further, the amplitude of change
656	in moderate and vigorous activity over the lifespan is considerably larger than the observed
657	changes in adjusted total expenditure or adjusted activity expenditure (Figure S10). Determining
658	the relative contributions of different measures of physical activity to total expenditure is beyond
659	the scope of the simple modeling approach here and remains an important task for future
660	research.

# 661 <u>8. Physical Activity, Activity Expenditure and PAL</u>

To further interrogate our simple model of expenditure and the contribution of physical
activity, we examined the agreement between accelerometery-measured physical activity,
adjusted activity expenditure, and modeled PAL over the lifespan. First, as noted in our

discussion of the simple expenditure model (see above; Figures 3, S8, S9), moderate and vigorous physical activity and total accelerometry counts show a similar shape profile when plotted against age, but moderate and vigorous physical activity shows a greater amplitude of change over the lifespan (Figure S10). Moderate and vigorous physical activity reach a peak  $\sim$ 4times greater than the mean values observed for 20 – 30 y men and women, far greater than the amplitude of change in adjusted total expenditure.

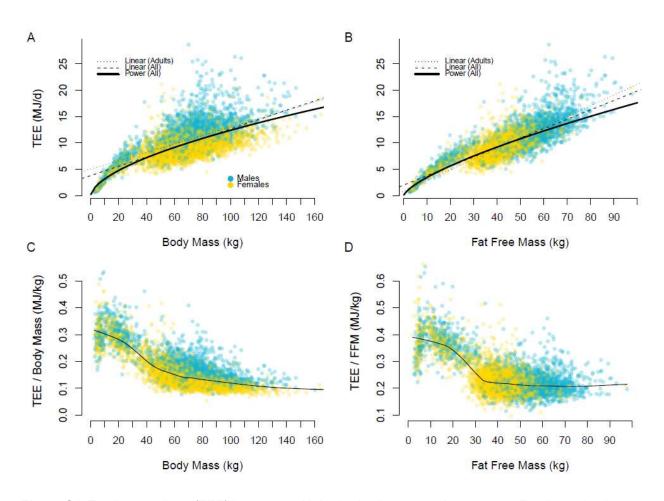
671 We used adjusted total and basal expenditures to model activity expenditure and PAL 672 over the lifespan for comparison with published accelerometry measures of physical activity. 673 Modeling activity expenditure and PAL was preferable because our dataset has no subjects less 674 than 3 y with measures of both total and basal expenditure, and only 4 subjects under the age of 6 675 y with both measures (Table S1). Using values of adjusted total expenditure and adjusted 676 BEE<sub>TEE</sub> (basal expenditure expressed as a percentage of total expenditure) for age cohorts from 677 Table S3 enabled us to model activity expenditure and PAL for this critical early period of 678 development, in which both physical activity and expenditure change substantially. We modeled 679 adjusted activity expenditure as [(adjusted total expenditure) – (adjusted  $BEE_{TEE}$ )] and PAL as 680 [(adjusted total expenditure) / (adjusted BEE<sub>TEE</sub>)], which as we show in Figure S4 corelate 681 strongly with unadjusted measures of activity expenditure and PAL, respectively.

Modeled adjusted activity expenditure and PAL showed a somewhat different pattern of change over the lifecoure than either total counts or moderate and vigorous activity measured via accelerometry (Figure S10). Modeled activity expenditure was most similar to total counts, rising through childhood, peaking between 10 and 20 y before falling to a stable adult level; the adult level was stable from  $\sim 30 - 75$  y before declining (Figure S10). Modeled PAL rose unevenly from birth through age 20, then remained largely stable thereafter.

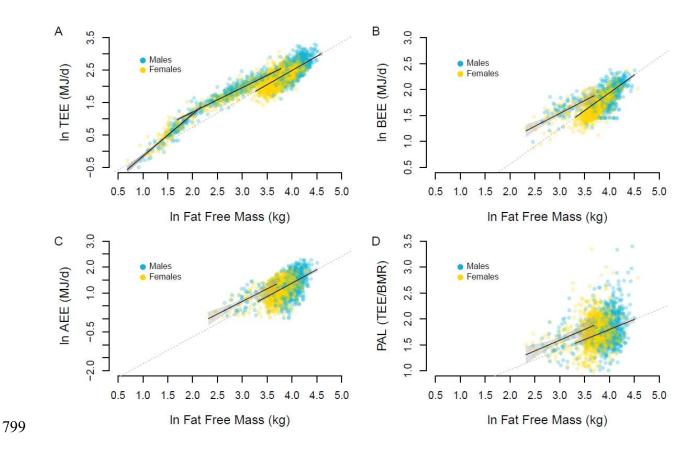
688	The agreement, and lack thereof, between the pattern of accelerometry-measured physical
689	activity and modeled activity expenditure and PAL must be assessed with caution. These
690	measures are from different samples; we do not have paired accelerometry and energy
691	expenditure measures in the present dataset. The life course pattern of accelerometry-measured
692	physical activity, particularly total counts, is broadly consistent with that of modeled activity
693	expenditure. However, more work is clearly needed to determine the effects of physical activity
694	and other factors to variation in activity expenditure and PAL over the lifecourse.
695	9.IAEA DLW database consortium
696	This group authorship contains the names of people whose data were contributed into the
697	database by the analysis laboratory but they later could not be traced, or they did not respond to
698	emails to assent inclusion among the authorship. The list also includes some researchers who did
699	not assent inclusion because they felt their contribution was not sufficient to merit authorship.
700 701 702 703 704 705 706 707 708 709	Dr Stefan Branth University of Uppsala, Uppsala, Sweden Dr Niels C. De Bruin Erasmus University, Rotterdam, The Netherlands Dr Lisa H. Colbert Kinesiology, University of Wisconsin, Madison, WI, Dr Alice E. Dutman
710 711	TNO Quality of Life, Zeist, The Netherlands
712 713 714	Dr Simon D. Eaton, University college London, London, UK
715 716 717	Dr Cara Ebbeling Boston Children's Hospital, Boston, Massachusetts, USA.
718 719 720	Dr Sölve Elmståhl Lund University, Lund, Sweden

721	Dr Mikael Fogelholm
722	Dept of Food and Nutrition, Helsinki, Finland
723	
724	Dr Tamara Harris
725	Aging, NIH, Bethesda, MD,
726	
727	Dr Rik Heijligenberg
728	Academic Medical Center of Amsterdam University, Amsterdam, The Netherlands
729	
730	Dr Hans U. Jorgensen
731	Bispebjerg Hospital, Copenhagen, Denmark
732	
733	Dr Christel L. Larsson
734	University of Gothenburg, Gothenburg, Sweden
735	
736	Dr David S. Ludwig
737	Boston Children's Hospital, Boston, Massachusetts, USA.
738	
739	Dr Margaret McCloskey
740	Royal Belfast Hospital for Sick Children, Belfast, Northern Ireland
741	
742	Dr Gerwin A. Meijer
743	Maastricht University, Maastricht, The Netherlands
744	
745	Dr Daphne L. Pannemans
746	Maastricht University, Maastricht, The Netherlands
747	
748	Dr Renaat M. Philippaerts
749	Katholic University Leuven, Leuven, Belgium
750	
751	Dr John J. Reilly
752	Universoty of Strathclyde, Glasgow, UK
753	
754	Dr Elisabet M. Rothenberg
755	Göteborg University, Göteborg, Sweden
756	
757	Dr Sabine Schulz
758	University of Maastricht, Maastricht, The Netherlands
759	
760	Dr Amy Subar
761	Epidemiology and Genomics, Division of Cancer Control, NIH, Bethesda, MD,
762	
763	Dr Minna Tanskanen
764	University of Jyväskilä, Jyväskilä, Finland
765	
766	Dr Ricardo Uauy

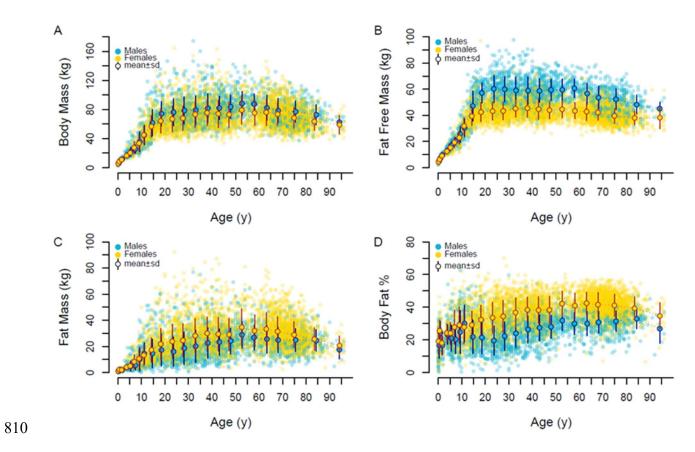
- 767 Institute of Nutrition and Food Technology (INTA), University of Chile, Santiago Chile.
- 768
- 769 Dr Rita Van den Berg-Emons
- 770 Maastricht University, Maastricht, The Netherlands
- 771
- 772 Dr Wim G. Van Gemert
- 773 Maastricht University, Maastricht, The Netherlands
- 774
- 775 Dr Erica J. Velthuis-te Wierik
- 776 TNO Nutrition and Food Research Institute, Zeist, The Netherlands
- 777
- 778 Dr Wilhelmine W. Verboeket-van de Venne
- 779 Maastricht University, Maastricht, The Netherlands
- 780
- 781 Dr Jeanine A. Verbunt
- 782 Maastricht University, Maastricht, The Netherlands



784 Figure S1. Total expenditure (TEE) increases with body size in a power-law manner. For the entire dataset 785 (n = 6,407): **A.** the power-law regression for total body mass (InTEE =  $0.593 \pm 0.004$  InMass -  $0.214 \pm$ 786 0.018, p < 0.001, adj.  $r^2 = 0.73$ , model std. err. = 0.223, df = 6419) is less predictive than the regression for 787 **B.** fat free mass (*In*TEE =  $0.708 \pm 0.004$  *In*FFM  $- 0.391 \pm 0.015$ , p < 0.001, adj. r<sup>2</sup> = 0.83, model std. err. = 788 0.176, df = 6419). For both body mass and fat free mass regressions, power-law regressions outperform 789 linear models, particularly at the smallest body sizes. For all models, for both body mass and fat free mass, 790 children have elevated total expenditure, clustering above the trend line. Children also exhibit elevated 791 basal and activity expenditures (Figure S2). Power-law regressions have an exponent < 1.0, and linear 792 regressions (dashed: linear regression through all data; dotted: linear regression through adults only) have 793 a positive intercept, indicating that simple ratios of C. (total expenditure)/(body mass) or D. (total 794 expenditure)/(fat free mass) do not adequately control for differences in body size (22) as smaller individuals 795 will tend to have higher ratios. Lines in **C** and **D** are lowess with span 1/6. In body mass regressions (panel 796 A, power and linear models) and the ratio of (total expenditure)/(body mass) (C), adult males cluster above 797 the trend line while females cluster below due to sex differences in body composition. In contrast, males 798 and females fit the fat free mass regressions (B) and ratio (D) equally well.

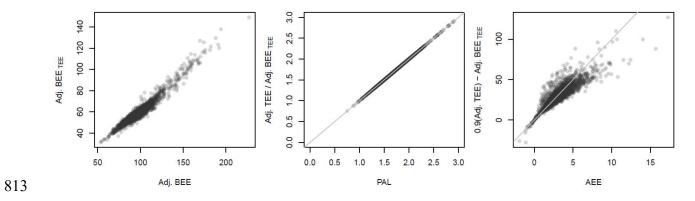


800 Figure S2. Infants and children exhibit different relationships between fat free mass and expenditure and 801 the PAL ratio. A: For total expenditure (TEE), regressions for infants (age <1 y, left regression line) and 802 adults (right regression line) intersect for neonates, at the smallest body size. However, the slopes differ, 803 with the infants' regression and 95% CI (gray region) falling outside of that for adults (age 20 - 60 y, 804 extrapolated dashed line). Juvelines (age 1 - 20 y, middle regression line) are elevated, with a regression 805 outside the 95% CI of adults. Juvenile (1 - 20 y) regressions (with 95%CI) are also elevated for basal 806 expenditure (BEE) (B), activity expenditure (AEE) (C), and PAL (D) compared to adults (20 - 60 y). Sex 807 differences in expenditure (A-D) are attributable to differences in fat free mass. Note that total and basal 808 expenditures are measured directly. Activity expenditure is calculated as (0.9TEE - BEE), and PAL is 809 calculated as (TEE/BEE); see Methods.

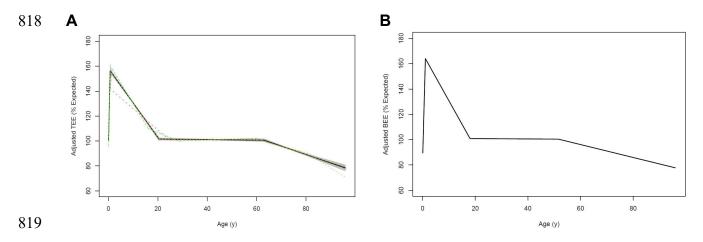


811 **Figure S3.** Changes in body composition over the lifespan: **A.** Body mass; **B.** Fat free mass; **C.** Fat Mass;

<sup>812</sup> and **D.** Body fat percentage.



**Figure S4.** Left: Adjusted  $BEE_{TEE}$  corresponds strongly to adjusted basal expenditure (Adj. BEE). <u>Center:</u> The ratio of adjusted total expenditure (adj. TEE) to adjusted  $BEE_{TEE}$  is identical to the PAL ratio. <u>Right:</u> The difference (0.9adjusted total expenditure – adjusted  $BEE_{TEE}$ ) is proportional to activity energy expenditure (AEE). Gray lines: center panel: y = x, right panel: y = 10x.

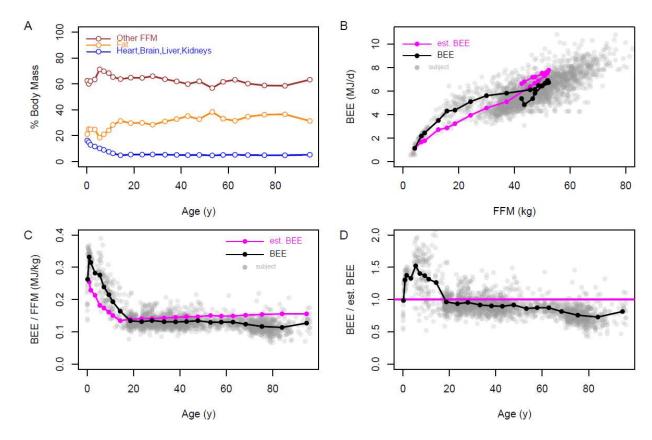


820 **Figure S5.** Segmented regression analysis of adjusted TEE (**A**) and adjusted BEE (**B**). In both panels,

821 the black line and gray shaded confidence region depicts the 3 change-point regression. For adjusted

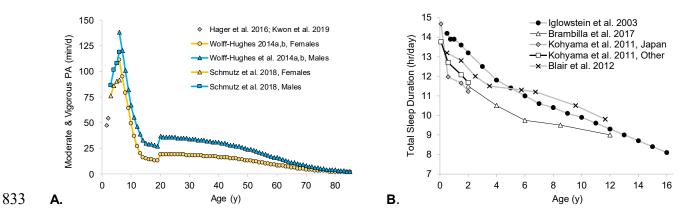
822 TEE, segmented regressions are also shown for 2 change points (red), 4 change points (yellow), and 5

823 change points (green). Segmented regression statistics are given in Table S4.



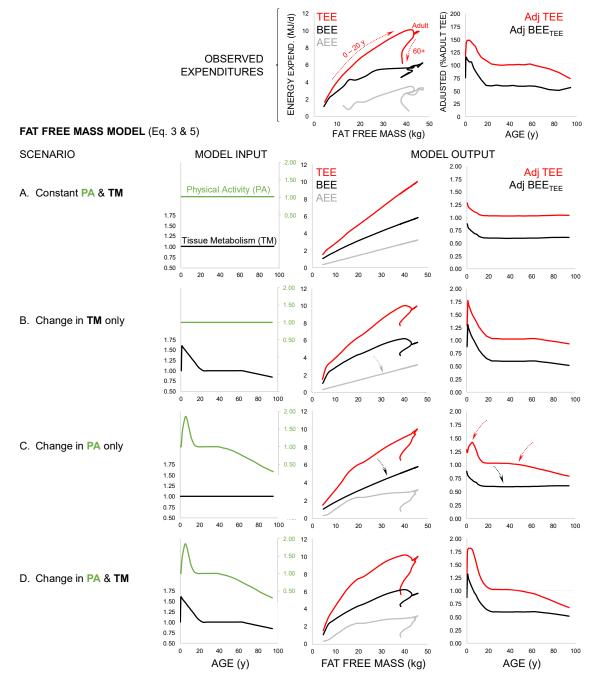
824

825 Figure S6. Organ sizes and BEE. A. The relative proportions of metabolically active organs (heart, 826 brain, liver, kidneys), other fat free mass (FFM), and fat changes over the life course. Age cohort means 827 are shown. B. Consequently, estimated basal expenditure (BEE) from the three-compartment model 828 increases with fat free mass (FFM) in a manner similar to observed basal expenditure, with C. greater 829 whole body mass-specific basal expenditure (BEE/FFM) early in life. D. Observed basal expenditure is 830 ~30% greater early in life, and ~20% lower after age 60 y, than estimated basal expenditure from the 831 three-compartment model (shown as the ratio of BEE/est.BEE). In panels B, C, and D, age-cohort means 832 for observed (black) and estimated (magenta) basal expenditure are shown.

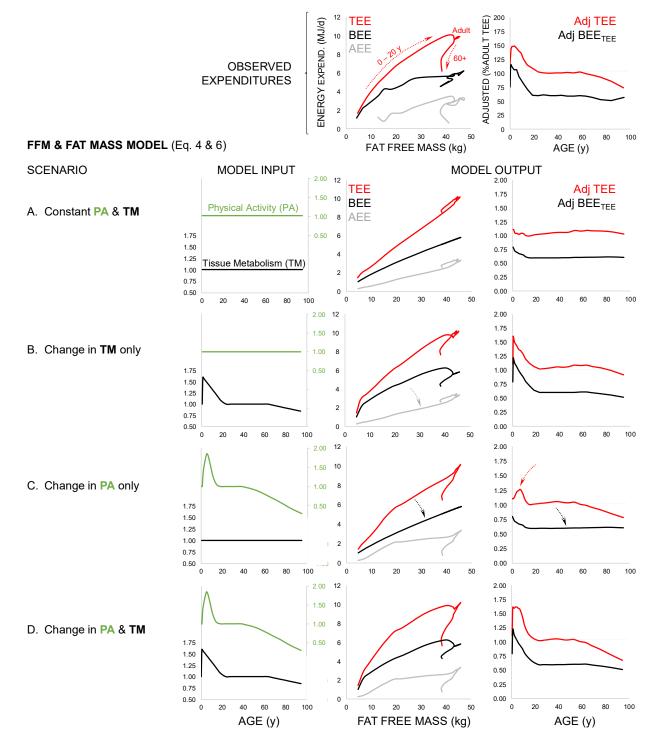


834 **Figure S7.** Modeling physical activity across the lifespan. **A.** Across studies and countries,

835 accelerometer-measured physical activity rises through infancy and early childhood, peaking between 5 836 and 10y before declining to adult levels in the teenage years (12-14, 17, 18, 47-50). Physical activity 837 declines again, more slowly, in older adults. The onset of decline in older adults varies somewhat across 838 studies, beginning between ~40 y and ~60 y. Here, physical activity is shown as minutes/day of moderate 839 and vigorous physical activity. Other measures (e.g., total accelerometer counts; mean counts/min, vector 840 magnitude) follow a similar pattern of physical activity over the life span (12, 17). B. The increase in 841 physical activity from 0 to ~10 y is mirrored by the steady decline in total daily sleep duration during this 842 period (51-54).

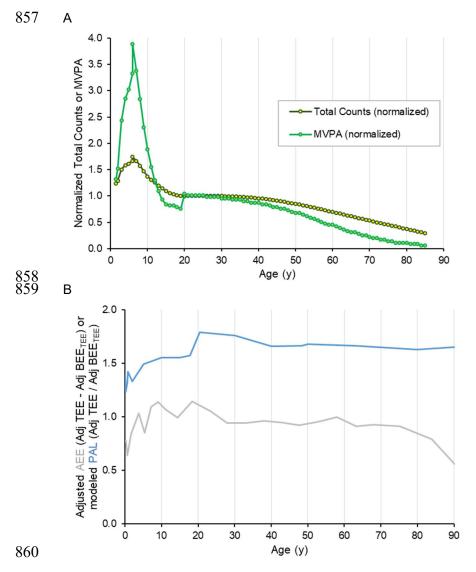


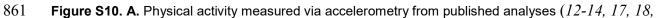
844 Figure S8. Results of the fat free mass model. Observed expenditures exhibit a marked age effect on the 845 relationship between expenditure and fat free mass that is evident in both absolute (Figure 1C) and adjusted 846 (Figure 2D) measures. A. If physical activity (PA) and cellular metabolism (TM) remain constant at adult 847 levels, age effects do not emerge from the model. B. When only TM varies, age effects emerge for total 848 expenditure (TEE) and basal expenditure (BEE), but not activity expenditure (AEE; gray arrow). C. 849 Conversely, if only physical activity varies age effects emerge for AEE and TEE but not BEE (black arrows). 850 Adjusted TEE also peaks later in childhood and declines earlier in adulthood (red arrows) than observed. 851 **D.** Varying both PA and TM gives model outputs similar to observed expenditures.

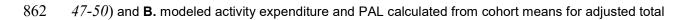


852

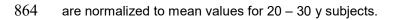
**Figure S9.** Results of the fat free mass and fat mass model. Model outputs are similar to those of the fat free mass model (Figure S8). The scenario that best matches the observed relationships between fat free mass, age, and expenditure is D, in which AEE is influenced by age-related variation in both physical activity and cellular metabolism. Abbreviations as in Fig S8.







863 expenditure and adjusted BEE<sub>TEE</sub> in Table S3. Accelerometry measures and modeled activity expenditure



1	(70,8	(65,70]	(60.6	(55 6	(50.5	(45.5	(40,4	(35,4	(30,3	(25,3	(20,2	(16,2	(12,1	(10,1	(0, 10]	(0,0	(4,0	(2,4)	(1,2)	(0.0,1)	0,0.0	in ngo cu	Age Group		в.	(90,100]	(80,9	(70,8	(65,7	(60,6	(55,6	(50,55]	(45.5	(40.4	(35.4	C (2)	(22,02)	(16,2	(12,1	(10,1	(8,10	(6,8]	(4,6]	(2,4]	(1,2]	(0.5.1	(0.0)	Age group		A.	BEE. 1
			5 22		_	01 37								_	27			_			N	>	-	П				0] 682		5] 252							102 201		6] 227					54	3	11 18	-	N	п		nfant da
-	-	29	37	23		30		87	71	171	42	41	=		10	2 1	5 =	<u>+</u> -	(86)	-		14441	z	z			9 66			90	1 76					149	196			34	75	43	121	48	35	23	93	z	Ξ		ta fro
	75.25 2.87	68.05 1.64	50	58 18 140	53 16 157	47.19 127	42.92 1.33	38.10 1.41	33.18 1.34	27.90 1.46	23.41 1.40	18.5/ 0.83	14.4/ 1.33	11.12 0.61	3.13 0.64	19	0.14 0.34	2 00	8	0.00	0.21	4	mean «d	п	A	94.36 1.79	83.65 2.40	75.05 2.79	68.04 1.47	63.22 1.47	58.24 1.48	52.80 1.48	47.43 1.46	42.81 1.36	38 05 145	30 00 136		18.32		11.14 0.58	9.10 0.48	7.03 0.65	5.34 0.63	3.81 0.28	70	81.0 89.0	0.24 0.13	mean sd	п	A	om the litera
83.96 2.31	75.42 2.96	68.66 1.45	63.11 1.66	57 52 124	53 46 120	48 20 1.37	42.57 1.29	38.17 1.45	33.10 1.47	27.98 1.44	23.70 1.37	18.92 0.75	13.95 0.87	12 05 0.28	3.43 0.61	1.38 0.72	3.41 0.47	4.00 NA	0.32	_			mean sd	M	Age (y)	94.00 1.85	84.20 2.50	75.40 2.92	67.98 1.37	63.16 1.55	57.76 1.38	52.59 1.48	47.76 1.46	42.92 1.37	38 01 142	32 88 141	23.40 1.38	18.3/ 1.11	14.53 1.14	11.01 0.47	9.14 0.53	7.25 0.62	5.31 0.68	3.78 0.31	1.64 0.48	0 72 0 20	0.24 0.13	mean sd	M	Age (y)	BEE. *Infant data from the literature, males and females pooled. N values for infant BEE (0 to 2 years) indicate number of entries and (number
63.3 12.9	67.1 14.6		65.7 10.1	71.0 12 6		75.5 20.7	80.8 22.2	78.5 20.6	74.8 20.3	65.9 17.4	66.4 19.2	63./ 15.9	05.0 26.5	30.2 6.3	26.2 6.2	24.5 6.5	13.1 2.3	21.0 8.3	10.33	0.10	0.40	ηč	mean «d	П	Ma	158.0 9.1	157.5 7.2	159.4 6.7	161.4 6.7	161.5 7.1	163.6 6.2	163.5 5.9	164.6 6.1	163.7 7.2	164 2 6 5	164 5 8 2	16/ 1 2 9	163.9 7.4	160.6 8.4	148.5 8.0	133.5 9.3	122.5 10.2	112.7 6.7	101.2 4.6	82.3 5.0	69.1 4.3	59.7 4.6	mean sd	п	Heig	and females
	80.2 14.0	76.4 15.1		87 0 10 2	361 6 66	92 9 18 6	82.3 18.5	80.1 20.2	77.5 18.3	75.5 20.9	77.5 19.3	/4.8 12.5	44.0 14.0	45.3 13.9	0.00	24.1 4.6	19.9 3.7		173	777		_	mean sd	M	Mass (kg)	168.8 3.0	168.7 7.5	171.3 8.0	172.4 7.3	174.5 7.4	177.3 7.6	177.1 6.7	176.8 7.2	176.3 7.7	176 7 7 8	177 2 80	177 / 0.0	1/1.9 7.7	168.4 12.1	143.7 9.6	136.9 10.0	125.2 8.8	113.7 7.5	102.1 6.1	83.2 5.9	71846	60.4 5.4	mean sd	3	Height (cm)	pooled. N
37.66 5.74	39.22 6.23	42.61 5.96	40.40 5.51	43 40 4 84	45 18 5 96	45.01 7.42	47.08 8.20	46.96 7.57	45.46 6.95	42.37 7.04	43.32 7.03	42.43 7.32	40.05 11.53	21.11 3.42		70.07 3.75	0 2 01 .CI	14.0/ 4.25	1.12	0.00	4.11		mean sd	п	Fat Free	58.98 12.81	63.61 12.29	68.50 14.42	73.67 15.55	76.21 18.34	75.35 17.07	79.37 19.42	73.18 17.40	74.23 18.78	75 50 17 68	73 30 17 78	67 00 10 73	64.31 16.34	56.72 14.67	45.15 11.65	33.62 11.50	27.62 8.49	20.41 3.86		6	8 54 140		mean sd	п	Mas	alues for int
	53.83 7.24	53.98 9.37	56.76 5.89	61 72 6 29	61 65 7 44	63 72 6 48	59.28 9.50	58.10 9.93	58.52 9.23	58.82 9.21	60.09 11.38	57.96 7.28	32.51 7.19	30.56 6.44	20.32 0.07	20.01 2.50	10.01 2.61	14.90 NA		11.10		not su	mean «d	M	Mass (kg)	62.60 3.47	72.76 13.80	77.19 14.92	78.50 16.64	82.34 17.11	87.53 13.91		83.74 15.81	82.12 15.90	81 55 19 88	70 14 19 56	78 66 10 51		61.73 18.36	44.91 13.45	35.76 13.69	25.71 5.49	21.74 5.73	17.38 3.03	11.69 1.65	9.17 133	6.12 1.52	mean sd	M	Mass (kg)	ant BEE (Ut
9	_		9 9	20 20	15.7	45			29.3 14.6	23.5 12.9	13.7	-	25.7 16.8	0.4 4.4	9.4 10.4	0.4 4.4	0.9 1.8	0./ 4.0	2.6	2.2	1.0	2	nean «d	F	Fat Ma	23.6 4.1	25.7 4.7	26.9 5.2	28.3 5.7	29.3 6.8	28.3 5.7	29.7 7.0	27.4 6.3	σ ω		20.2 0.0	24.0 6.4	23.9 5.8	21.9 4.8		18.2 4.5	18.0 3.9	16.0 2.0	15.9 1.7	16.3 1.0	17.8 2.1	6	nean sd n	п	BMI	o 2 years)
25 9 8 2	26.3 8.6	22.4 7.3	23.2 8.2	25.3 72	30 6 13 5	29.1 13.7	23.0 12.5	22.0 12.3	18.9 11.8	16.7 15.1	17.4 11.0	16.8 9.2	11.5 7.5	14./ 8.5	3.2 1.0	4.6 3.8	J. 1 1.5	J.U NA	0.63	0.53	0.00	000	nean «d	M	ss (kg)	22.0 3.4	25.5 4.2	26.2 4.2	26.2 4.5	27.2 4.5	27.8 3.7	28.4 4.8	27.2 4.3	26.4 4.3	26.0 5.4	24.3 4.0	24.14.3	23.5 4.9	21.5 5.6	21.2 4.4	18.4 4.8	16.2 2.4	16.6 2.9	16.6 2.4	16.8 1.0	17.7 13	16.4 1.9	lean sd	M	-	indicate
39 58 7 41	40.59 6.78	38.96 7.67	38.16 4.80	38 09 5 81	41 92 8 73	38 08 10.35	39.94 8.82	38.29 9.00	36.97 9.70	33.50 10.86	32.62 9.55	31.95 8.30	35.11 12.72	22.44 8.25	20.00 13.32	24.29 11.13	20.41 8.31	29.54 6.26		24.91	21.21		mean sd	п	Fa	38.26 8.50	38.02 5.22	39.62 5.65	42.20 5.85	42.92 6.83	43.42 6.06	44.66 6.51	44.02 6.44	44.76 7.56	45 47 6 82	45 20 6.01	43.20 6.97	42.49 7.26	39.37 7.27	31.85 6.35	22.96 5.01	19.28 3.97	15.34 2.31	12.51 1.85	9.04 1.32	6 32 0.91		mean sd	п	Fat Free	number of e
	32.14 6.27	28.78 5.58	28.22 6.25	28 68 5 83	31 98 7 19	29.89 8.78	26.35 9.81	25.86 8.49	23.09 8.65	20.50 8.21	21.25 8.61	21.65 8.25	24.17 8.02	29.96 10.88	22.20 13.20	77.41 10.59	10.04 4.77	16.91 NA		312	0.34	o o d	mean sd	M	Fat%	45.18 4.93	48.22 7.07	52.29 7.86	53.61 8.62	56.70 8.07	60.67 7.13	59.54 8.29	59.52 8.15	58.79 8.91	58 91 10 51	59 07 10 23	50 07 0 co	57.11 7.58	47.15 11.42	30.42 6.63	25.53 6.09	20.14 2.75	16.83 2.92	13.24 1.85	9.74 1.41		5.03 1.09	mean sd	M	Fat Free Mass (kg)	ntries and (r
4 55 0.81	76	30		99		73	24	22	6.03 0.94	5.83 0.87	17	5	3 8	44	10			4.07 0.67	2.44	2.11	1.14		mean sd	п	BEE	20.72 7.23	25.59 8.70	28.88 10.12	31.47 11.13	33.29 12.58	31.93 12.22	34.72 14.08	5	47			20.02 13.08	8 8	17.34 9.25	13.30 7.90	66	34	6	5	02	2 23 0.80		mean sd	п	Fat Mass	
5 10 0.85	5.91 1.00	6.53 0.93	7.02 0.79	7 56 0 72	7 64 0 96	7.99 1.16	7.50 1.09	7.32 1.17	7.47 1.09	7.50 1.17	7.34 1.24	7.86 0.90	6.10 1.08	5.66 0.65	0.00 0.00	4./1 0.59	4.09 1.05	3.93 NA	2.44 0.44	2.11 0.23	20.0		mean sd	M	(MJ/d)	17.42 6.93	24.53 8.24	24.90 8.74	24.89 9.55	25.64 10.52	26.86 9.42	28.84 10.08	24.21 9.91	23.33 9.98	20.01 12.10	20 07 12 18	18 58 17 54	17.25 12.26	14.58 10.95	14.50 8.25	10.23 8.76	5.57 3.62	4.91 3.55	4.14 1.69	1.96 0.76	2 23 0.65	1.09 0.66	mean sd	S	ass (kg)	of individuals). See Methods.
1 72 0.93	2.62 1.14	2.87 0.88	2.68 0.79	2 55 0 76	3 11 0 91	3 27 0 79	3.35 1.32	3.09 1.25	3.20 1.17	2.85 1.58	3.12 1.75	3.51 1.26	3.43 1.83	2.30 0.71	201 21.1	_		1.21 0.45					mean sd	п	AEE (I	34.7 7.9	39.3 7.0	41.1 6.7	41.6 7.2	42.5 6.7	41.0 7.7	42.2 7.8	38.3 8.3	_	_	_	3/ / 0.0	32.3 8.9	_	-	29.1 10.9	27.8 10.3	24.1 6.8	24.2 5.5	18.1 7.5	n i		ä.	п	Fat%	ee Methods
2 88 128	3.30 1.37	3.37 1.21	4.16 1.43	4 35 150	4 49 139	5 06 199	4.46 2.03	4.40 1.79	4.40 2.21	4.62 2.92	4.99 2.39	5./4 1.59	2.34 1.51	2.14 1.24	2.14 1.25	2.04 1.22	1.10 0.60	1.3/ NA					ä.	M	(MJ/d)	26.9 8.9	32.9 6.2	31.4 6.3	30.8 6.4	29.9 7.4	30.0 6.7	31.8 6.1	28.0 7.1	27.4 7.9	24.0 0.1 26.4 8.3	24.0 8.7	19.0 8.9			30.1 11.2	24.7 13.1	20.3 8.7	21.1 8.0	23.2 5.8	16.7 5.7	ωi	-	ä	M	1%	
								1.67 0.23	1.71 0.22	1.65 0.27													mean sd	п	PAL (TE	6.20 1.20	7.43 1.36	8.21 1.30	9.02 1.32	9.24 1.54					9 90 168				9.96 2.35	8.90 1.88	36			84				mean sd	п	TEE	
1.75 0.31	1.75 0.30	1.70 0.24	1.78 0.28	175 0.22	1 77 0 20	1.83 0.30	1.77 0.28	1.78 0.26	1.77 0.31	1.80 0.39	1.86 0.32	1.93 0.24	1.55 0.32	1.66 0.28	1.00 0.27	1.61 0.30	1.41 0.20	1.50 NA				incon so	mean «d	M	PAL (TEE/BEE)	7.60 1.03	8.69 1.70	10.17 1.80	10.86 1.79	12.09 2.36	13.27 2.97	12.69 2.03	12.77 2.47	12.68 2.39	12 90 2 92	12.24 3.13	13 04 3 36	14.02 2.59	12.20 2.53	9.35 1.68	8.54 1.77	7.20 1.13	6.35 1.18	5.21 0.89	3.99 0.74	2 90 0 78	1.83 0.58	mean sd	M	(MJ/d)	

Table S2. Model parameters Total Expenditure (TEE)	, ., _		-	s (0 - '				s (1 - 2				20 - 60	V)	Old	er Adu	lts (60	)+ v)
Model	Factors	ß		t-value	P	ß	std.err.	t-value	P P	ß		t-value	<u>p</u>	ß	std.err.		<u>P</u>
. TEE~Body Mass+Sex+Age	Intercept (MJ/d)	0.255	0.111	2.304	0.022	2.592		22.032	0.000	5.984	0.197	30.427	0.000			29.130	
	Body Mass (kg) Sex(M)	0.205	0.025	8.061 1.953	0.000	0.080	0.004		0.000	0.065 2.669	0.002	30.274 33.036	0.000	0.048	0.002	24.701 23.672	0.00
	Age (y)	0.951	0.205	4.632	0.000	0.183	0.015		0.000	-0.025	0.004	-6.635	0.000	-0.080		-18.451	0.0
	model	N	SEE	df	adjR2	N	SEE	df	adjR2	N	SEE	df	adjR2	N	SEE	df	adjl
		235 β	0.343 std.err.	231 t-value	0.733	1403 β	1.719 std.err.	1399 t-value	0.726	2805 β	2.032 std.err.	2801 t-value	0.482	1978 ß	1.311 std.err.	1974 t-value	0.5
2. In(TEE)~In(FFM)+In(FM)	Intercept (MJ/d)	-1.270	0.074	-17.130	<u>p</u> 0.000	-0.121	0.028		<u>p</u> 0.000	-1.102	0.050	-22.038	<u>p</u> 0.000	<u>β</u> -0.773	0.062	-12.403	0.0
	In(Fat Free Mass; kg)	1.163	0.046		0.000	0.696	0.011		0.000	0.916		71.248	0.000	0.797	0.018	44.723	0.0
	In(Fat Mass; kg)	0.053	0.014	3.862	0.000	-0.041	0.007	-5.714	0.000	-0.030	0.005	-5.986	0.000	-0.016	0.009	-1.828	0.0
	model	N 235	SEE 0.160	df 232	adjR2 0.796	N 1403	SEE 0.154	<i>df</i> 1400	adjR2 0.842	N 2805	SEE 0.142	df 2802	adjR2 0.646	N 1978	SEE 0.139	df 1975	adjF 0.5
		β	std.err.	t-value	p	β	std.err.		P	β	std.err.	t-value	p	β	std.err.	t-value	p
3. In(TEE)~In(FFM)+In(FM)+Sex+A		-1.122	0.089	-12.619	0.000	-0.348	0.044		0.000	-1.118	0.069	-16.129	0.000	0.092	0.089	1.032	0.3
	In(Fat Free Mass; kg) In(Fat Mass; kg)	1.025 0.034	0.067	15.215 2.294	0.000	0.784	0.021	38.119	0.000	0.920	0.020	45.942 -5.149	0.000	0.736	0.025	29.883 -3.118	0.0
	Sex(M)	-0.014	0.021	-0.644	0.520	0.067	0.009	7.592	0.000	-0.002	0.009	-0.249	0.803	0.011	0.010	1.042	0.2
	Age (y)	0.254	0.082	3.104	0.002	-0.012	0.002		0.000	0.000	0.000	0.765	0.444	-0.008	0.000	-19.038	
	model	N 235	SEE 0.157	df 230	adjR2 0.804	N 1403	SEE 0.147	df 1398	adjR2 0.857	N 2805	SEE 0.142	<i>df</i> 2800	adjR2 0.646	N 1978	SEE 0.128	df 1973	adjF 0.6
		235	0.157	230	0.004	1403	0.147	1390	0.007	2005	0.142	2000	0.040	1970	0.120	1973	0.0
Basal Expenditure (BEE)								s (1 - 2				20 - 60				lts (60	_
<u>Model</u> 4. BEE~Body Mass+Sex+Age				ntercep	Factors	<u>β</u> 2.965	std.err. 0.158	t-value 18.785	<u>p</u> 0.000	<u>β</u> 3.649	std.err. 0.104	t-value 34.943	<u>p</u> 0.000	<u>β</u> 5.905	std.err. 0.379	t-value 15.571	0.0
T. DEL DOUY MASS OUXTAUE				Body Ma		0.034	0.156		0.000	0.036	0.104	32.494	0.000	0.031	0.002	14.277	0.0
					Sex(M)	1.185	0.101	11.733	0.000	1.263	0.045	27.915	0.000	0.724	0.066	10.939	0.0
					Age (y)	0.033 N	0.015 SEE	2.212 df	0.028	-0.008 N	0.002 SEE	-3.487	0.001	-0.041 N	0.004 SEE	-9.501 df	0.0
					model	345	0.848	341	adjR2 0.581	1036	0.694	df 1032	adjR2 0.682	621	0.761	617	adjF 0.5
						β	std.err.		р	β	std.err.		p	β	std.err.	t-value	p
5. In(BEE)~In(FFM)+In(FM)				ntercep		0.055	0.078		0.480	-0.954		-16.176		-0.923	0.099	-9.350	0.0
				Free Ma n(Fat Ma		0.535	0.028		0.000	0.707	0.016	45.353 3.408	0.000	0.656	0.027	24.640 1.819	0.0
					model	N	SEE	df	adjR2	N	SEE	df	adjR2	N	SEE	df	adjl
						345	0.153	342	0.573	1036	0.103	1033	0.688	621	0.135	618	0.5
						β	std.err.		р	β	std.err.	t-value	<u>p</u>	β	std.err.	t-value	p
<ol><li>In(BEE)~In(FFM)+In(FM)+Sex+A</li></ol>				ntercep Free Ma		-0.270 0.663	0.100	-2.704 15.167	0.007	-0.497 0.561	0.079	-6.281 24.008	0.000	-0.089 0.549	0.151 0.040	-0.587 13.663	0.5
				n(Fat Ma		-0.054	0.014	-4.005	0.000	0.054	0.007	7.809	0.000	0.042	0.016	2.619	0.0
				ļ.	Sex(M)	0.090	0.019		0.000	0.086	0.010	8.297	0.000	0.037	0.016	2.288	0.0
					Age (y)	-0.018	0.003 SEE	-5.102 df	0.000	-0.001	0.000 SEE	-2.124 df	0.034	-0.006	0.001 SEE	-8.814	0.00
					model	N 345	0.137	340	adjR2 0.658	N 1036	0.100	1031	adjR2 0.708	N 621	0.128	<i>df</i> 616	adjF 0.58
Activity Expenditure (AEE) Model					Factors	β	std.err.	s (1 - 2	Dy)	β	std.err.	20 - 60 t-value	<b>עו</b>	β	std.err.	Its (60	р <b>+ у)</b>
7. AEE~Body Mass+Sex+Age			1	ntercep		-0.481	0.237	-2.030	0.043	1.822	0.252	7.231	0.000	5.835	0.604	9.663	0.00
			E	Body Ma		0.032	0.005		0.000	0.023	0.003	8.870	0.000	0.014	0.003	4.111	0.00
					Sex(M) Age (y)	0.999	0.152		0.000	1.308 -0.012	0.109	11.983 -2.216	0.000	0.661	0.105	6.264 -8.354	0.00
					model	N	SEE	df	adjR2	N	SEE	df	adjR2	N	SEE	df	adjR
						345	1.275	341	0.476	1036	1.675	1032	0.201	621	1.212	617	0.21
				ntoroon	+ /N/I/a)	<u>β</u> -3.330	std.err. 0.231	<u>t-value</u> -14.447	<u>p</u> 0.000	<u>β</u> -4.124	std.err. 0.248	t-value -16.627	<u>p</u> 0.000	<u>β</u> -2.556	std.err. 0.401	t-value -6.381	<u>p</u> 0.00
8. In(AEE)~In(FFM)+In(FM)				ntercep Free Ma		1.301	0.231		0.000	1.476	0.240	22.614	0.000	0.952	0.401	8.807	0.00
				n(Fat Ma		-0.099	0.041	-2.414	0.016	-0.142	0.023	-6.130	0.000	-0.042	0.062	-0.685	0.49
					model	N	SEE	df	adjR2	N	SEE	df	adjR2	N	SEE	df	adjF
						338 β	0.445 std.err.	335 t-value	0.550 p	1023 β	0.423 std.err.	1020 t-value	0.333 n	612 β	0.546 std.err.	609 t-value	0.11
9. In(AEE)~In(FFM)+In(FM)+Sex+A			1	ntercep	t (MJ/d)		0.332			-5.194		-15.187	<u>p</u> 0.000	0.222	0.625	0.355	<u>p</u> 0.72
			In(Fat	Free Ma	ass; kg)	1.349	0.145	9.295	0.000	1.816	0.100	18.079	0.000	0.674	0.165	4.088	0.00
			lr	n(Fat Ma		-0.093 0.006	0.044		0.037	-0.221 -0.198	0.029	-7.598 -4.480	0.000	-0.010 0.079	0.066	-0.151 1.181	0.88
					Sex(M) Age (y)	-0.005	0.062	-0.474	0.928	0.002	0.044	-4.480	0.000	-0.025	0.067	-7.852	0.2
					model	Ν	SEE	df	adjR2	N	SEE	df	adjR2	N	SEE	df	adjR
						338	0.446	333	0.547	1023	0.420	1018	0.345	612	0.521	607	0.19
PAL (TEE/BEE)						Ju	venile	s (1 - 2	0y)	A	dults (	20 - 60	y)	Old	er Adu	lts (60	)+ y)
Model					actors	β	std.err.	t-value	p	β	std.err.	t-value	p	β	std.err.	t-value	P
10. PAL~Body Mass+Sex+Age				ntercep Body Ma		1.290 0.002	0.048	26.913 2.093	0.000	1.668 0.001	0.041	40.739 2.058	0.000	2.209	0.144 0.001	15.348 -0.239	0.00
				JULY IVIE	Sex(M)	0.002	0.001	1.641	0.102	0.001	0.000	5.312	0.040	0.000	0.001	2.298	0.02
					Age (y)	0.022	0.004	4.933	0.000	-0.001	0.001	-1.260	0.208	-0.007	0.002	-4.142	0.00
					model	N 345	SEE 0.258	df 3/11	adjR2	N 1036	SEE 0.272	df 1032	adjR2	N 621	SEE 0.280	df 617	adjF
						345 β	0.258 std.err.		0.234	1036 <u>β</u>	0.272 std.err.	1032 <u>t-value</u>	0.032	621 β	0.289 std.err.	617 <u>t-value</u>	0.03
				ntercep	t (MJ/d)		0.129		<u>p</u> 0.001	<u>P</u> 0.174	0.148	1.178	<u>p</u> 0.239	<u>P</u> 1.215	0.212	5.736	<u>p</u> 0.00
11. PAL~In(FFM)+In(FM)						0.386	0.046	8.348	0.000	0.477	0.039	12.221	0.000	0.201	0.057	3.524	0.00
11. PAL~in(FFM)+in(FM)			In(Fat						0.415	-0.098						-2.605	0.00
11. PAL~In(FFM)+In(FM)			In(Fat	Free Ma n(Fat Ma	ass; kg)		0.023				0.014	-6.999	0.000 adiR2	-0.085	0.033		
11. PAL~In(FFM)+In(FM)			In(Fat			N	SEE	df	adjR2	N	SEE	df	adjR2	N	SEE	df	
11. PAL~In(FFM)+In(FM)			In(Fat		ass; kg)			df 342	<i>adjR2</i> 0.263	N 1036			<i>adjR2</i> 0.137				0.02
			In(Fat Ir	n(Fat Ma	ass; kg) model t (MJ/d)	Ν 345 <u>β</u> 0.528	SEE 0.253 std.err. 0.185	df           342           t-value           2.860	adjR2 0.263 <u>p</u> 0.005	Ν 1036 <u>β</u> -0.744	SEE 0.257 <u>std.err.</u> 0.200	<i>df</i> 1033 <u>t-value</u> -3.714	adjR2 0.137 <u>p</u> 0.000	Ν 621 <u>β</u> 1.841	SEE 0.291 std.err. 0.340	<i>df</i> 618 <u>t-value</u> 5.417	0.02 <u>p</u> 0.00
			In(Fat Ir In(Fat	n(Fat Ma ntercep Free Ma	ass; kg) model t (MJ/d) ass; kg)	Ν 345 <u>β</u> 0.528 0.338	SEE 0.253 std.err. 0.185 0.081	df           342           t-value           2.860           4.179	adjR2 0.263 <u>p</u> 0.005 0.000	Ν 1036 <u>β</u> -0.744 0.777	SEE 0.257 std.err. 0.200 0.059	<i>df</i> 1033 <u>t-value</u> -3.714 13.140	adjR2 0.137 <u>p</u> 0.000 0.000	Ν 621 <u>β</u> 1.841 0.164	SEE 0.291 <u>std.err.</u> 0.340 0.090	<i>df</i> 618 <u>t-value</u> 5.417 1.814	0.02 <u>p</u> 0.00 0.07
11. PAL~In(FFM)+In(FM) 12. PAL~In(FFM)+In(FM)+Sex+Age			In(Fat Ir In(Fat	n(Fat Ma ntercep Free Ma n(Fat Ma	ass; kg) model t (MJ/d) ass; kg) ass; kg)	N 345 <u>β</u> 0.528 0.338 -0.026	SEE 0.253 std.err. 0.185 0.081 0.025	df           342           t-value           2.860           4.179           -1.034	adjR2 0.263 <u>p</u> 0.005 0.000 0.302	Ν 1036 <u>β</u> -0.744 0.777 -0.164	SEE 0.257 std.err. 0.200 0.059 0.017	<i>df</i> 1033 <u>t-value</u> -3.714 13.140 -9.442	adjR2 0.137 <u>p</u> 0.000 0.000 0.000	Ν 621 <u>β</u> 1.841 0.164 -0.087	SEE 0.291 <u>std.err.</u> 0.340 0.090 0.036	<i>df</i> 618 <u>t-value</u> 5.417 1.814 -2.405	0.00 0.07 0.01
			In(Fat Ir In(Fat	n(Fat Ma ntercep Free Ma n(Fat Ma	ass; kg) model t (MJ/d) ass; kg) ass; kg) Sex(M)	Ν 345 <u>β</u> 0.528 0.338	SEE 0.253 std.err. 0.185 0.081	df           342           t-value           2.860           4.179           -1.034           -0.250	adjR2 0.263 <u>p</u> 0.005 0.000	Ν 1036 <u>β</u> -0.744 0.777	SEE 0.257 std.err. 0.200 0.059	<i>df</i> 1033 <u>t-value</u> -3.714 13.140	adjR2 0.137 <u>p</u> 0.000 0.000	Ν 621 <u>β</u> 1.841 0.164	SEE 0.291 <u>std.err.</u> 0.340 0.090	<i>df</i> 618 <u>t-value</u> 5.417 1.814	0.02 <u>p</u> 0.00 0.07
			In(Fat Ir In(Fat	n(Fat Ma ntercep Free Ma n(Fat Ma	ass; kg) model t (MJ/d) ass; kg) ass; kg)	N 345 <u>β</u> 0.528 0.338 -0.026 -0.009	SEE 0.253 std.err. 0.185 0.081 0.025 0.035	df           342           t-value           2.860           4.179           -1.034           -0.250	adjR2 0.263 <u>P</u> 0.005 0.000 0.302 0.803	N 1036 <u>β</u> -0.744 0.777 -0.164 -0.174	SEE 0.257 std.err. 0.200 0.059 0.017 0.026	<i>df</i> 1033 <u>t-value</u> -3.714 13.140 -9.442 -6.645	adjR2 0.137 <u>p</u> 0.000 0.000 0.000 0.000	N 621 <u>β</u> 1.841 0.164 -0.087 0.000	SEE 0.291 std.err. 0.340 0.090 0.036 0.037	<i>df</i> 618 <u>t-value</u> 5.417 1.814 -2.405 0.007	0.02 <u>p</u> 0.00 0.07 0.01 0.99

		Adjust	ed TEI	E - Fer	nale &	Male	Cohort	s				Adjust	ted BE	E and A	Adjuste	d BE	ETEE			
						Adjus	ted TEE					-	Adjuste	ed BEE	-		Ad	justeo	BEE <sub>TE</sub>	E
Age		N	mear	n Age	F		1	M	N		mean	Age		F	М		F		M	
Cohort	F	М	F	М	mean	sd	mean	sd	F	М	F	М	mean	sd	mean	sd	mean	sd	mean	sd
(0,0.5]	103	93	0.2	0.2	120.0	23.2	118.4	23.2	22 (11	1)*	0.	2		100.47	33.89		ε	36.03	28.9	
(0.5,1]	18	23	0.7	0.7	139.8	17.0	145.5	25.7	20 (8	8)*	0.	9		142.89	11.62		1:	15.47	9.2	
(1,2]	33	35	1.7	1.6	147.4	23.9	148.2	21.6	18 (8	6)*	1.	6		142.02	13.52		1:	11.94	9.6	
(2,4]	54	48	3.8	3.8	147.0	13.4	150.3	19.6	3	1	3.8	4.0	150.2	6.0	144.3	NA	108.6	7.4	100.7	NA
(4,6]	99	121	5.3	5.3	142.5	14.0	148.2	18.5	9	5	5.7	5.4	156.4	26.3	158.8	30.9	110.1	19.9	108.1	19.9
(6,8]	42	42	7.0	7.2	139.2	16.7	143.2	13.6	18	12	7.2	7.4	136.9	25.8	141.9	21.8	94.6	17.7	94.6	15.1
(8,10]	79	75	9.1	9.1	132.8	19.2	140.2	18.7	22	16	9.2	9.5	130.0	23.4	137.3	21.8	87.2	15.2	88.8	14.2
(10,12]	68	34	11.1	11.0	122.0	23.4	133.4	16.3	5	5	11.1	11.1	128.3	19.9	126.3	21.2	82.6	12.3	81.8	15.0
(12,16]	229	128	14.4	14.5	113.1	22.9	118.9	21.4	18	16	14.4	13.9	103.1	18.6	130.0	23.3	64.9	12.2	82.4	15.7
(16,20]	209	103	18.3	18.4	107.1	14.4	113.3	17.1	155	148	18.5	18.9	97.5	12.9	109.3	7.5	60.2	8.1	62.9	5.3
(20,25]	252	123	23.2	23.5	100.6	15.5	106.7	21.9	135	116	23.4	23.8	98.3	10.5	99.6	8.1	60.6	7.1	57.0	5.2
(25,30]	280	182	27.8	28.0	100.5	15.3	102.0	21.2	115	104	27.9	27.9	100.8	11.5	104.0	13.4	62.5	7.8	59.6	8.3
(30,35]	235	146	33.0	32.8	100.0	11.9	100.7	16.5	96	94	33.2	33.1	98.7	9.7	103.3	10.4	60.9	6.3	59.7	7.0
(35,40]	231	165	38.0	38.0	100.0	11.9	102.3	16.3	112	110	38.1	38.2	99.7	10.2	101.6	11.7	61.4	6.9	59.1	7.2
(40,45]	301	165	42.8	42.9	101.3	12.6	100.8	13.2	100	96	42.9	42.6	99.8	10.4	102.9	9.1	61.6	6.9	59.7	6.1
(45,50]	171	144	47.4	47.8	102.0	12.4	100.5	14.3	42	41	47.3	48.1	99.0	14.7	108.1	14.6	61.4	9.6	62.7	8.9
(50,55]	105	93	52.8	52.6	100.5	11.4	100.8	13.2	33	33	53.1	53.4	96.1	9.1	103.1	9.2	59.8	5.5	60.3	5.9
(55,60]	111	76	58.2	57.8	102.2	11.7	102.9	20.0	23	23	58.1	57.5	100.3	9.5	100.0	7.1	62.5	6.1	57.9	4.5
(60,65]	252	90	63.2	63.2	98.8	12.4	99.8	15.3	23	21	62.4	63.1	99.5	12.8	99.2	8.5	62.6	8.3	58.3	5.2
(65,70]	387	90	68.0	68.0	97.6	10.9	94.4	11.1	40	40	68.0	68.7	91.0	8.6	95.2	7.6	56.9	5.9	56.4	4.8
(70,80]	681	232	75.1	75.4	93.9	12.1	90.6	14.6	188	173	75.2	75.4	86.8	9.9	86.4	12.9	55.2	6.6	51.5	8.0
(80,90]	149	66	83.6	84.2	87.6	12.2	82.8	13.0	47	38	84.1	84.0	86.5	16.0	78.6	10.8	55.3	10.8	47.6	6.8
(90,100]	22	8	94.4	94.0	73.2	12.4	76.0	9.6	14	5	94.9	94.0	91.2	19.1	94.8	14.6	57.1	12.9	57.3	8.6

**Table S3.** Adjusted total expenditure (TEE), Adjusted basal expenditure (BEE), and Adjusted BEE<sub>TEE</sub>. \*Infant data from the literature, males and females pooled. N values for infant BEE (0 to 2 years) indicate number of entries and (number of individuals).

# **Table S4.** Segmented Regression Analyses

adjTEE	Segme	nts			Break Poir	Break Points										
	beta	SE	CI_lower	Cl_upper	Estimate	CI_lower	Cl_upper									
	84.70	7.15	70.69	98.71	0.69	0.61	0.76									
	-2.77	0.07	-2.91	-2.63	20.46	19.77	21.15									
	-0.02	0.02	-0.07	0.03	62.99	60.13	65.85									
	-0.68	0.06	-0.79	-0.57												
adjBEE	Segme	nts			Break Poir	nts										
	beta	SE	CI_lower	Cl_upper	Estimate	CI_lower	Cl_upper									
	75.51	5.59	64.55	86.46	1.04	0.94	1.14									
	-3.75	0.22	-4.17	-3.33	18.00	16.82	19.18									
	0.02	0.05	-0.07	0.12	46.46	40.57	52.35									
	-0.45	0.04	-0.53	-0.37												