

Daily Energy Expenditure through the Human Life Course

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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 ~50% above adult values at ~1 yr, declines slowly
125 to adult levels by ~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 (*I*), which accounts for only a portion (usually ~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

142 increasing physical activity and age-related changes in tissue-specific metabolic rates are unclear
143 (12-16). Similarly, the decline in total expenditure beginning in older adults corresponds with
144 declines in fat free mass and physical activity but may also reflect age-related reductions in
145 organ metabolism (9, 17-19).

146 We investigated the effects of age, body composition, and sex on total expenditure using
147 a large (n = 6,421; 64% female), diverse (n = 29 countries) database of doubly labeled water
148 measurements for subjects aged eight days to 95 years (20), calculating total expenditure from
149 isotopic measurements using a single, validated equation for all subjects (21). Basal expenditure,
150 measured *via* indirect calorimetry, was available for n = 2,008 subjects, and we augmented the
151 dataset with additional published measures of basal expenditure in neonates and doubly labeled
152 water-measured 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 Neonates (0 to 1 y): 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 ~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 Adults (20 to 60 y): 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 expenditure fell at a similar rate (Figure 2, Figure S3, Text S1, Table
197 S4). For subjects 90+ y, adjusted total expenditure was ~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,
206 which is consistent with adjusted expenditures of neonates (both ~100%; Figure 2) in the first
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

209 critical period in early development in which growth often falters in nutritionally-stressed
210 populations (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 ~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).

227 We investigated the contributions of daily physical activity and changes in tissue-specific
228 metabolic rate to total and basal expenditure using a simple model with two components: activity
229 and basal expenditure (Figure 3; Methods). Activity expenditure was modeled as a function of
230 physical activity and body mass, assuming activity costs are proportional to weight, and could
231 either remain constant over the lifespan or follow the trajectory of daily physical activity

232 measured *via* accelerometry, peaking at 5 – 10 y and declining thereafter (12, 17, 18) (Figure 3).
233 Similarly, basal expenditure was modeled as a power function of fat free mass (consistent with
234 organ-based basal expenditure estimates; Methods) multiplied by a “tissue specific metabolism”
235 term, which could either remain constant at adult levels across the lifespan or follow the
236 trajectory observed in adjusted basal expenditure (Figure 2). For each scenario, total expenditure
237 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 relationships 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.

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263 **Conflict of interest**

264 The authors have no conflicts of interest to declare.

265 **Data Availability**

266 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**

- 274 1. C. J. Henry, Basal metabolic rate studies in humans: measurement and development of new
 275 equations. *Public Health Nutr* **8**, 1133-1152 (2005).
- 276 2. FAO, Human energy requirements: report of a joint FAO/ WHO/UNU Expert Consultation. *Food*
 277 *Nutr Bull* **26**, 166 (2005).
- 278 3. K. R. Westerterp, J. O. de Boer, W. H. M. Saris, P. F. M. Schoffelen, F. ten Hoor, Measurement of
 279 energy expenditure using doubly labelled water. *Int J Sport Med* **5**, S74-75 (1984).
- 280 4. P. D. Klein *et al.*, Calorimetric validation of the doubly-labelled water method for determination
 281 of 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).
- 283 6. A. E. Black, W. A. Coward, T. J. Cole, A. M. Prentice, Human energy expenditure in affluent
 284 societies: an analysis of 574 doubly-labelled water measurements. *Eur J Clin Nutr* **50**, 72-92
 285 (1996).
- 286 7. L. R. Dugas *et al.*, Energy expenditure in adults living in developing compared with industrialized
 287 countries: a meta-analysis of doubly labeled water studies. *Am J Clin Nutr* **93**, 427-441 (2011).
- 288 8. H. Pontzer *et al.*, Constrained Total Energy Expenditure and Metabolic Adaptation to Physical
 289 Activity in Adult Humans. *Curr Biol* **26**, 410-417 (2016).
- 290 9. J. R. Speakman, K. R. Westerterp, Associations between energy demands, physical activity, and
 291 body composition in adult humans between 18 and 96 y of age. *Am J Clin Nutr* **92**, 826-834
 292 (2010).
- 293 10. N. F. Butte, Fat intake of children in relation to energy requirements. *Am J Clin Nutr* **72**, 1246s-
 294 1252s (2000).
- 295 11. H. L. Cheng, M. Amatory, K. Steinbeck, Energy expenditure and intake during puberty in
 296 healthy nonobese adolescents: a systematic review. *Am J Clin Nutr* **104**, 1061-1074 (2016).
- 297 12. D. L. Wolff-Hughes, D. R. Bassett, E. C. Fitzhugh, Population-referenced percentiles for waist-
 298 worn accelerometer-derived total activity counts in U.S. youth: 2003 - 2006 NHANES. *PLoS One*
 299 **9**, e115915 (2014).
- 300 13. E. A. Schmutz *et al.*, Physical activity and sedentary behavior in preschoolers: a longitudinal
 301 assessment of trajectories and determinants. *Int J Behav Nutr Phys Act* **15**, 35 (2018).
- 302 14. J. A. Hnatiuk, K. E. Lamb, N. D. Ridgers, J. Salmon, K. D. Hesketh, Changes in volume and bouts of
 303 physical activity and sedentary time across early childhood: a longitudinal study. *Int J Behav Nutr*
 304 *Phys Act* **16**, 42 (2019).
- 305 15. A. Hsu *et al.*, Larger mass of high-metabolic-rate organs does not explain higher resting energy
 306 expenditure in children. *Am J Clin Nutr* **77**, 1506-1511 (2003).
- 307 16. Z. Wang *et al.*, A cellular level approach to predicting resting energy expenditure: Evaluation of
 308 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**,
 311 447-453 (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).
- 315 19. D. Gallagher, A. Allen, Z. Wang, S. B. Heymsfield, N. Krasnow, Smaller organ tissue mass in the
 316 elderly fails to explain lower resting metabolic rate. *Ann N Y Acad Sci* **904**, 449-455 (2000).
- 317 20. J. R. Speakman *et al.*, The International Atomic Energy Agency International Doubly Labelled
 318 Water Database: Aims, Scope and Procedures. *Ann Nutr Metab* **75**, 114-118 (2019).
- 319 21. J. R. Speakman *et al.*, A standard calculation methodology for human doubly labeled water
 320 studies. *Cell Rep Med* **2**, 100203 (2021).

- 321 22. D. B. Allison, F. Paultre, M. I. Goran, E. T. Poehlman, S. B. Heymsfield, Statistical considerations
322 regarding the use of ratios to adjust data. *Int J Obes Relat Metab Disord* **19**, 644-652 (1995).
- 323 23. H. Alderman, D. Headey, The timing of growth faltering has important implications for
324 observational analyses of the underlying determinants of nutrition outcomes. *PLoS One* **13**,
325 e0195904 (2018).
- 326 24. J. E. Blundell *et al.*, The drive to eat in homo sapiens: Energy expenditure drives energy intake.
327 *Physiol Behav* **219**, 112846 (2020).
- 328 25. Z. Wang *et al.*, Specific metabolic rates of major organs and tissues across adulthood: evaluation
329 by mechanistic model of resting energy expenditure. *Am J Clin Nutr* **92**, 1369-1377 (2010).
- 330 26. Z. Wang, S. Heshka, S. B. Heymsfield, W. Shen, D. Gallagher, A cellular-level approach to
331 predicting resting energy expenditure across the adult years. *Am J Clin Nutr* **81**, 799-806 (2005).
- 332 27. Y. Yamada *et al.*, Extracellular water may mask actual muscle atrophy during aging. *J Gerontol A*
333 *Biol Sci Med Sci* **65**, 510-516 (2010).
- 334 28. G. B. West, J. H. Brown, B. J. Enquist, A general model for ontogenetic growth. *Nature* **413**, 628-
335 631 (2001).
- 336 29. J. H. Brown, J. F. Gillooly, A. P. Allen, V. M. Savage, G. B. West, Toward a metabolic theory of
337 ecology. *Ecology* **85**, 1771-1789 (2004).
- 338 30. R. D. Montgomery, Changes in the basal metabolic rate of the malnourished infant and their
339 relation to body composition. *J Clin Invest* **41**, 1653-1663 (1962).
- 340 31. O. G. Brooke, T. Cocks, Resting metabolic rate in malnourished babies in relation to total body
341 potassium. *Acta Paediatr Scand* **63**, 817-825 (1974).
- 342 32. N. F. Butte *et al.*, Energy requirements derived from total energy expenditure and energy
343 deposition during the first 2 y of life. *Am J Clin Nutr* **72**, 1558-1569 (2000).
- 344 33. M. Hernández-Triana *et al.*, Total energy expenditure by the doubly-labeled water method in
345 rural preschool children in Cuba. *Food Nutr Bull* **23**, 76-81 (2002).
- 346 34. S. S. Summer, J. M. Pratt, E. A. Koch, J. B. Anderson, Testing a novel method for measuring
347 sleeping metabolic rate in neonates. *Respir Care* **59**, 1095-1100 (2014).
- 348 35. N. F. Butte *et al.*, Energy expenditure and deposition of breast-fed and formula-fed infants
349 during early infancy. *Pediatr Res* **28**, 631-640 (1990).
- 350 36. L. A. Gilmore *et al.*, Energy Intake and Energy Expenditure for Determining Excess Weight Gain in
351 Pregnant Women. *Obstet Gynecol* **127**, 884-892 (2016).
- 352 37. G. R. Goldberg *et al.*, Longitudinal assessment of energy expenditure in pregnancy by the doubly
353 labeled water method. *Am J Clin Nutr* **57**, 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* **79**, 1078-
356 1087 (2004).
- 357 39. J. B. Weir, New methods for calculating metabolic rate with special reference to protein
358 metabolism. *J Physiol* **109**, 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 *Physiology, Stress, and Malnutrition*, 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 gestation and early infancy. *Pediatrics* **47**, Suppl 2:169+ (1971).

- 369 45. D. K. Molina *et al.*, Organ Weight Reference Ranges for Ages 0 to 12 Years. *Am J Forensic Med*
370 *Pathol* **40**, 318-328 (2019).
- 371 46. M. Sawabe *et al.*, Standard organ weights among elderly Japanese who died in hospital,
372 including 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).
- 375 48. E. R. Hager *et al.*, Toddler physical activity study: laboratory and community studies to evaluate
376 accelerometer validity and correlates. *BMC Public Health* **16**, 936 (2016).
- 377 49. P. Silva *et al.*, Lifespan snapshot of physical activity assessed by accelerometry in Porto. *J Phys*
378 *Act Health* **8**, 352-360 (2011).
- 379 50. A. Doherty *et al.*, Large Scale Population Assessment of Physical Activity Using Wrist Worn
380 Accelerometers: The UK Biobank Study. *PLoS One* **12**, e0169649 (2017).
- 381 51. P. S. Blair *et al.*, Childhood sleep duration and associated demographic characteristics in an
382 English cohort. *Sleep* **35**, 353-360 (2012).
- 383 52. J. Kohyama, J. A. Mindell, A. Sadeh, Sleep characteristics of young children in Japan: internet
384 study 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).
- 387 54. P. Brambilla *et al.*, Sleep habits and pattern in 1-14 years old children and relationship with
388 video devices use and evening and night child activities. *Ital J Pediatr* **43**, 7 (2017).

389 **Figure Legends**

390 **Figure 1. A.** Total expenditure (TEE) increases with fat free mass in a power-law manner (black line: $TEE =$
391 $0.677FFM^{0.708}$, $r^2=0.83$, $p<0.0001$; Table S2) but age groups cluster about the trend line differently. **B.** Total
392 expenditure rises in childhood, is stable through adulthood, and declines in older adults. Means \pm sd for age-
393 sex cohorts are shown. **C.** Age-sex cohort means show a distinct progression of total expenditure and fat
394 free mass over the life course. **D.** Neonate, juveniles, and adults exhibit distinct relationships between fat
395 free mass and expenditure. The dashed line, extrapolated from the regression for adults, approximates the
396 regression used to calculate adjusted total expenditure.

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

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