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► **To cite this version:**

Herman Pontzer, Yosuke Yamada, Hiroyuki Sagayama, Philip Ainslie, Lene Andersen, et al.. Daily energy expenditure through the human life course. *Science*, 2021, 373 (6556), pp.808-812. 10.1126/science.abe5017. hal-03364046

**HAL Id: hal-03364046**

**<https://hal.science/hal-03364046>**

Submitted on 4 Oct 2021

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1 **Published in "Science"**

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3 **Daily Energy Expenditure through the Human Life Course**

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27 # see supplementary materials

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121 **Abstract:** Total daily energy expenditure (“total expenditure”, MJ/d) reflects daily energy needs  
122 and is a critical variable in human health and physiology, yet it is unclear how daily expenditure  
123 changes over the life course. Here, we analyze a large, globally diverse database of total  
124 expenditure measured by the doubly labeled water method for males and females aged 8 days to  
125 95 yr. We show that total expenditure is strongly related to fat free mass in a power-law manner  
126 and identify four distinct metabolic life stages. Fat free mass-adjusted daily expenditure  
127 accelerates rapidly in neonates (0-1yr) to ~46% above adult values at ~1 yr, declines slowly  
128 throughout childhood and adolescence (1-20 yr) to adult levels at ~20 yr, remains stable in  
129 adulthood (20-60 yr) even during pregnancy, and declines in older adults (60+ yr). These  
130 changes in total expenditure shed new light on human development and aging and should help  
131 shape nutrition and health strategies across the lifespan.

132

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

135

136 **Main Text:** All of life’s essential tasks, from development and reproduction to maintenance and  
137 movement, require energy. Total expenditure is thus fundamental to understanding both daily  
138 nutritional requirements and the body’s investment among activities. Yet we know surprisingly  
139 little about the determinants of total expenditure in humans or how it changes over the lifespan.  
140 Most large ( $n > 1,000$ ) analyses of human energy expenditure have been limited to basal  
141 expenditure, the metabolic rate at rest ( $I$ ), which accounts for only a portion (usually ~50-70%)  
142 of total expenditure, or have estimated total expenditure from basal expenditure and daily  
143 physical activity (2-5). Measurements of total expenditure in humans during daily life, outside of

144 the laboratory, became possible in the 1980's with the advancement of the doubly labeled water  
145 method , but doubly labeled water studies to date have been limited in sample size (n < 600),  
146 geographic and socioeconomic representation, and/or age (6-9).

147         Body composition, size, and physical activity change over the life course, often in  
148 concert, making it difficult to parse the determinants of energy expenditure. Total expenditure  
149 increases with age as children grow (10), but the relative effects of increasing physical activity  
150 (11-13) and age-related changes in tissue-specific metabolic rates, as have been reported for the  
151 brain (14), are unclear. Total and basal expenditure increase from childhood through puberty, but  
152 much of this increase is attributable to increased fat free mass, and the role of endocrine or other  
153 effects is uncertain (15). The decline in total expenditure beginning in the sixth decade of life  
154 corresponds with a decline in fat free mass (9) and “physical activity level”, PAL (the ratio of  
155 total/basal expenditure), but may also reflect age-related reductions in organ metabolism.

156         We investigated the effects of age, body composition, and sex on total expenditure and its  
157 components, using a large (n = 6,421; 64% female), geographically and economical diverse (n =  
158 29 countries) database of doubly labeled water measurements for subjects aged eight days to 95  
159 years (16), calculating total expenditure from isotopic measurements using a single, validated  
160 equation for all subjects (17). Basal expenditure, measured *via* indirect calorimetry, was  
161 available for a n = 2,008 subjects, and we augmented the dataset with additional published  
162 measures of basal expenditure in neonates and doubly labeled water-measured total expenditure in  
163 pregnant and post-partum women (Methods; Table S1).

164         We found that both total and basal expenditure increased with fat free mass in a power-  
165 law manner ( $TEE = 0.677FFM^{0.708}$ ,  $r^2 = 0.83$  Figures 1, S1, S2, Table S1). Thus, body size,  
166 particularly fat free mass, accounted for most (83%) of the variation in daily expenditure,

167 requiring us to adjust for body size in subsequent analyses of expenditure across subjects and  
168 cohorts to isolate potential effects of age, sex, and other factors. Notably, analyses indicated an  
169 exponent  $<1$ , meaning that the ratio of energy expenditure/mass does not adequately control for  
170 body size because the ratio inherently trends lower for larger individuals (Figure S1 (18)).  
171 Instead, we used regression analysis to control for body size (18). A general linear model with  
172 *ln*-transformed values of energy expenditure (total or basal), fat free mass, and fat mass in adults  
173 20 – 60 y (Table S2) was used to calculate residual energy expenditures for each subject. We  
174 converted these residuals to “adjusted” expenditures for clarity in discussing age-related  
175 changes: 100% indicates an expenditure that matches the expected value given the subject’s fat  
176 free mass and fat mass, 120% indicates an expenditure 20% above expected, *etc.* (Methods).  
177 Using this approach, we also calculated the portion of adjusted total expenditure attributed to  
178 basal expenditure (Figure 2D; Methods). Segmented regression analysis of (Methods) revealed  
179 four distinct phases of adjusted (or residual) total and basal expenditure over the lifespan.

180 Neonates (0 to 1 y): Neonates in the first month of life had size-adjusted energy expenditures  
181 similar to adults, with adjusted total expenditure of  $99.0 \pm 17.2\%$  ( $n = 35$ ) and adjusted basal  
182 expenditure of  $78.1 \pm 15.0\%$  ( $n = 34$ ; Figure 2). Both measures increased rapidly in the first year.  
183 In segmented regression analysis, adjusted total expenditure rose  $84.7 \pm 7.2\%$  per year from birth  
184 to a break point at 0.7 years (95% CI: 0.6, 0.8); a similar rise ( $75.5 \pm 5.6\%$ ) and break point (1.0  
185 y, 95% CI: 0.9, 1.1) were evident in adjusted basal expenditure (Table S4). For subjects between  
186 9 and 15 months, adjusted total and basal expenditures were nearly ~50% elevated compared to  
187 adults (Figure 2).

188 Juveniles (1 to 20 y): Total and basal expenditure, along with fat free mass, continued to increase  
189 with age throughout childhood and adolescence (Figure 1), but body size-adjusted expenditures

190 steadily declined. Adjusted total expenditure declined at a rate of  $-2.8 \pm 0.1\%$  per year from  
191  $147.8 \pm 22.6\%$  for subjects 1 – 2 y (n = 102) to  $102.7 \pm 18.1\%$  for subjects 20 – 25 y (n = 314;  
192 Tables S2, S4). Segmented regression analysis identified a breakpoint in adjusted total  
193 expenditure at 20.5 y (95% CI: 19.8, 21.2), after which it plateaued at adult levels (Figure 2). A  
194 similar decline ( $-3.8 \pm 0.2\%$  per year) and break point (18.0 y, 95% CI: 16.8, 19.2) were evident  
195 in adjusted basal expenditure (Figure 2, Text S1, Table S4). No pubertal increases in adjusted  
196 total or basal expenditure were evident among subjects 10 – 15 y. In multivariate regression for  
197 subjects 1 to 20 y, males had a higher total expenditure and adjusted total expenditure (Tables  
198 S2, S3), but sex had no detectable effect on the rate of decline in adjusted total expenditure with  
199 age (sex:age interaction  $p=0.30$ ).

200 Adults (20 to 60 y): Total and basal expenditure and fat free mass were all stable from age 20 to  
201 60 (Figure 1, 2; Tables S1, S2; Text S1). Sex had no effect on total expenditure in multivariate  
202 models with fat free mass and fat mass, nor in analyses of adjusted total expenditure (Tables S2,  
203 S4). Adjusted total and basal expenditures were stable even during pregnancy, the elevation in  
204 unadjusted expenditures matching those expected from the gain in mothers' fat free mass and fat  
205 mass (Figure 2C). Segmented regression analysis identified a break point at 63.0 y (95% CI:  
206 60.1, 65.9), after which adjusted TEE begins to decline. This break point was somewhat earlier  
207 for adjusted basal expenditure (46.5, 95% CI: 40.6, 52.4), but the relatively small number of  
208 basal measures for 45 – 65 y (Figure 2D) reduces our precision in determining this break point.

209 Older adults (>60 y): At ~60 y, total and basal expenditure begin to decline, along with fat free  
210 mass and fat mass (Figures 1, S3, Table S1). Declines in expenditure are not only a function of  
211 reduced fat free mass and fat mass, however. Adjusted total expenditure declined by  $-0.7 \pm 0.1\%$



212 per year, and adjusted basal expenditure fell at a similar rates (Figure 2, Figure S3, Text S1, Table  
213 S4). For subjects in their nineties, adjusted TEE was ~26% below that of middle-aged adults.

214 In addition to providing empirical measures and predictive equations for total expenditure  
215 from infancy to old age (Tables S1, S2), our analyses bring to light major changes in metabolic  
216 rate across the life course. To begin, we can infer fetal metabolic rates from maternal measures  
217 during pregnancy: if body size-adjusted expenditures were elevated in the fetus, then adjusted  
218 expenditures for pregnant mothers, particularly late in pregnancy when the fetus accounts for a  
219 substantial portion of a mother's weight, would be likewise elevated. Instead, the stability of  
220 adjusted total and basal expenditures at ~100% during pregnancy (Figure 2B) indicates that the  
221 growing fetus maintains a fat free mass- and fat mass-adjusted metabolic rate similar to adults,  
222 which is consistent with adjusted expenditures of neonates (both ~100%; Figure 2) in the first  
223 weeks after birth. Total and basal expenditures, both absolute and size-adjusted values, then  
224 accelerate rapidly over the first year. This early period of metabolic acceleration corresponds to a  
225 critical period in early development in which growth often falters in nutritionally-stressed  
226 populations (19). Increasing energy demands could be a contributing factor.

227 After rapid acceleration in total and basal expenditure during the first year, adjusted  
228 expenditures progressively decline thereafter, reaching adult levels at ~20 yr. Elevated adjusted  
229 expenditures in this life stage may reflect the metabolic demands of growth and development.  
230 Adult expenditures, adjusted for body size and composition, are remarkably stable, even during  
231 pregnancy and post-partum. Declining metabolic rates in older adults could increase the risk of  
232 weight gain. However, neither fat mass nor percentage increased in this period (Figure S3),  
233 consistent with the hypothesis that energy intake is coupled to expenditure (20).

234           Following previous studies (21-25), we calculated the effect of organ size on basal  
235 expenditure over the lifespan (Methods). At rest, the tissue-specific metabolic rates (Watts/gram)  
236 of the heart, liver, brain, and kidneys are much greater than those of the muscles and other lean  
237 tissue or fat (21-25). Organs with a high tissue-specific metabolic rate, particularly the brain and  
238 liver, account for a greater proportion of fat free mass in young individuals, and thus organ-based  
239 basal expenditure, estimated from organ size and tissue-specific metabolic rate, follows a power-  
240 law relationship with fat free mass, roughly consistent with observed basal expenditures  
241 (Methods, Figure S6). Still, observed basal expenditure exceeded organ-based estimates by  
242 ~30% in early life (1 – 20 y) and was ~20% lower than organ-based estimates in subjects over 60  
243 y (Figure S6), consistent with previous work indicating that tissue-specific metabolic rates are  
244 elevated in children and adolescents (22, 24) and reduced in older adults (21, 23, 25).

245           We investigated the contributions of daily physical activity and changes in tissue-specific  
246 metabolic rate to total and basal expenditure using a simple model with two components: activity  
247 and basal expenditure (Figure 3; Methods). Activity expenditure was modeled as a function of  
248 physical activity and body mass, assuming activity costs are proportional to weight, and could  
249 either remain constant at adult levels over the lifespan or follow the trajectory of daily physical  
250 activity measured *via* accelerometry, peaking at 5 – 10 y and declining thereafter (11, 26, 27)  
251 (Figure 3). Similarly, basal expenditure was modeled as a power function of fat free mass  
252 (consistent with organ-based BEE estimates; Methods) multiplied by a “tissue specific  
253 metabolism” term, which could either remain constant at adult levels across the lifespan or  
254 follow the trajectory observed in adjusted basal expenditure (Figure 2). For each scenario, total  
255 expenditure was modeled as the sum of activity and basal expenditure (Methods).

256 Models that hold physical activity or tissue-specific metabolic rates constant over the  
257 lifespan do not reproduce the observed patterns of age-related change in absolute or adjusted  
258 measures of total or basal expenditure (Figure 3). Only when age-related changes in physical  
259 activity and tissue-specific metabolism are included does model output match observed  
260 expenditures, indicating that variation in both physical activity and tissue-specific metabolism  
261 contribute to total expenditure and its components across the lifespan. Elevated tissue-specific  
262 metabolism in early life may be related to growth or development (22, 24). Conversely, reduced  
263 expenditures in later life may reflect a decline in organ level metabolism (23, 25, 28).

264 Metabolic models of life history commonly assume continuity in tissue-specific  
265 metabolism over the life course, with cellular metabolic rates increasing in a power-law manner  
266 ( $\text{Energy} = a\text{Mass}^b$ ) and the energy available for growth during the juvenile period made available  
267 for reproduction in adults (29, 30). Measures of humans here challenge this view, with size  
268 adjusted metabolism elevated ~50% in childhood compared to adults (including pregnant  
269 females), and ~25% lower in the oldest subjects. It remains to be determined whether these  
270 fluctuations occur in other species. In addition to affecting energy balance, nutritional needs, and  
271 body weight, these metabolic changes present a potential target for clinical investigation into the  
272 kinetics of disease, pharmaceutical activity, and healing, processes intimately related to  
273 metabolic rate. Further, there is considerable metabolic variation among individuals, with TEE  
274 and its components varying more than  $\pm 20\%$  even when controlling for fat free mass, fat mass,  
275 sex, and age (Figure 1, 2, Table S2). Elucidating the processes underlying metabolic changes  
276 across the life course and variation among individuals may help reveal the roles of metabolic  
277 variation in health and disease.

278 **Acknowledgements**

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

285 **Conflict of interest**

286 The authors have no conflicts of interest to declare.

287 **Data Availability**

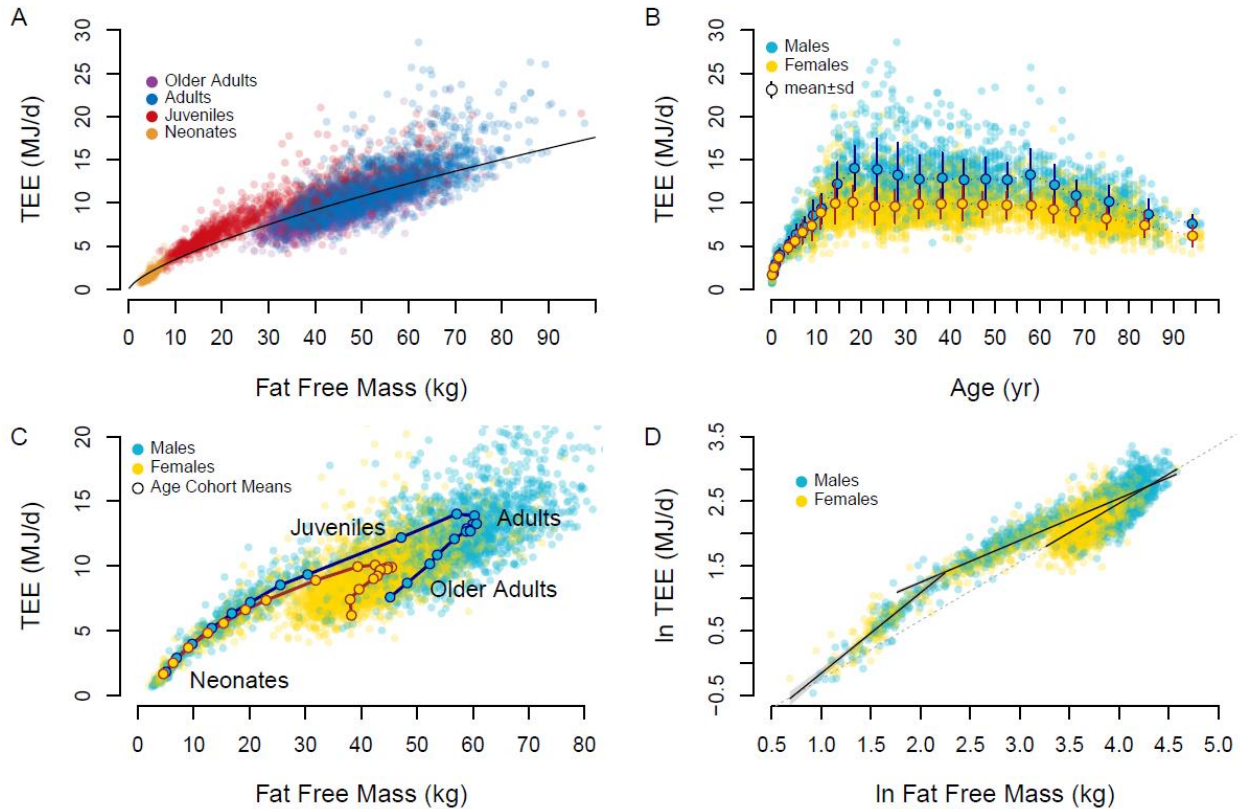
288 All data used in these analyses is freely available via the IAEA Doubly Labelled Water Database  
289 (<https://doubly-labelled-water-database.iaea.org/home> or <https://www.dlwdatabase.org/>).

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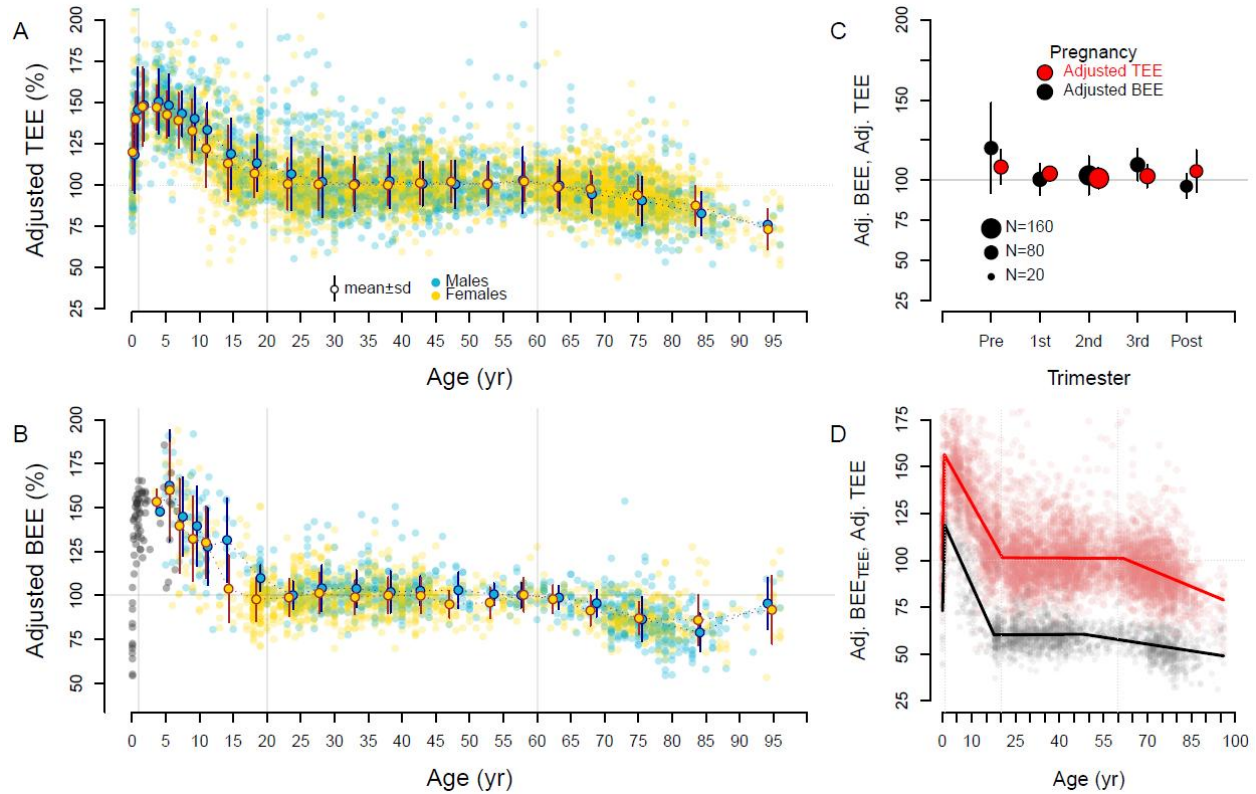
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408

409 **Figure 1. A.** Total expenditure (TEE) increases with fat free mass in a power-law manner, but age groups  
 410 cluster about the trend line differently. **B.** Total expenditure rises in childhood, is stable through  
 411 adulthood, and declines in older adults. Means $\pm$ sd for age-sex cohorts are shown. **C.** Age-sex cohort  
 412 means show a distinct progression of total expenditure and fat free mass over the life course. **D.** Neonate,  
 413 juveniles, and adults exhibit distinct relationships between fat free mass and expenditure. The dashed  
 414 line, extrapolated from the regression for adults, approximates the regression used to calculate adjusted  
 415 total expenditure.





416

417 **Figure 2.** Fat free mass- and fat mass-adjusted expenditures over the life course. Individual subjects and

418 age-sex cohort mean  $\pm$  SD are shown. For both total (Adj. TEE) (A) and basal (Adj. BEE) expenditure (B),

419 adjusted expenditures begin near adult levels (~100%) but quickly climb to ~150% in the first year.

420 Adjusted expenditures decline to adult levels ~20y, then decline again in older adults. Basal expenditures

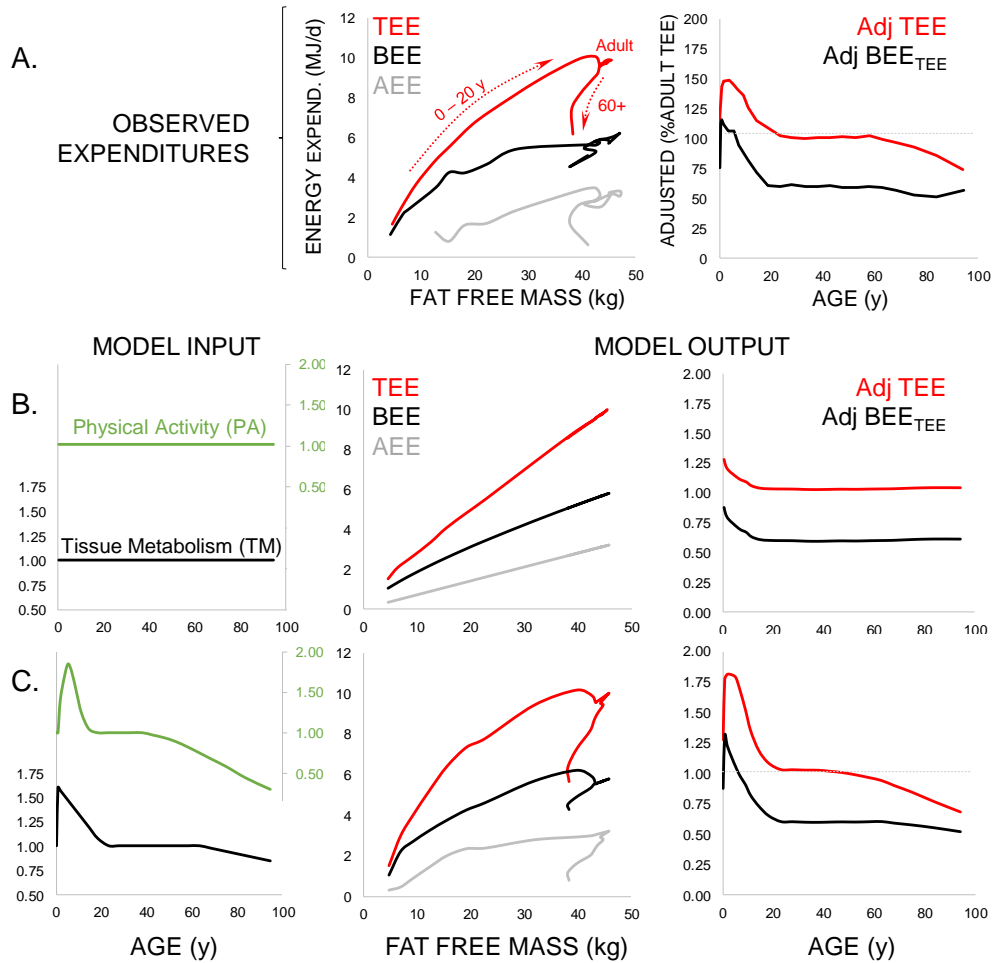
421 for infants and children not in the doubly labeled water database are shown in gray. C. Pregnant mothers

422 exhibit adjusted total and basal expenditures similar to non-reproducing adults (Pre: prior to pregnancy;

423 Post: 27 weeks post-partum). D. Segmented regression analysis of adjusted total (red) and adjusted

424 basal expenditure (calculated as a portion of total; Adj. BEE<sub>TEE</sub>; black) indicates a peak at ~1 y, adult

425 levels at ~20 y, and decline at ~60 y (see text).



426

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

435 **Supplementary Materials:**

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

437 **Contents:**

438 Materials and Methods

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  - 443 5. Segmented Regression Analysis
  - 444 6. Organ Size and BEE
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450 **Material and Methods**

451 1. Doubly Labeled Water Database

452 Data were taken from IAEA Doubly Labelled Water (DLW) Database, version 3.1,  
453 completed April, 2020 (16). This version of the database comprises 6,743 measurements of total  
454 expenditure using the doubly labeled water method. Of these, a total of 6,421 had valid data for  
455 total expenditure, fat free mass, fat mass, sex, and age. These 6,421 measurements were used in  
456 this analysis. This dataset was augmented with published basal expenditure measurements for  
457  $n=136$  neonates and infants (31-36) that included fat free mass and fat mass. Malnourished or

458 preterm infants were excluded. For sources that provided cohort means rather than individual  
459 subject measurements (33, 36) means were entered as single values into the dataset without  
460 reweighting to reflect sample size. This approach resulted in 77 measures of basal expenditure,  
461 fat free mass, and fat mass for n=136 subjects. We also added to the dataset published basal and  
462 total expenditure measurements of n=141 women before, during, and after pregnancy (37-39)  
463 that included fat free mass and fat mass. These measurements were grouped as pre-pregnancy, 1<sup>st</sup>  
464 trimester, 2<sup>nd</sup> trimester, 3<sup>rd</sup> trimester, and post-partum for analysis.

465 In the doubly labeled water method (5), subjects were administered a precisely measured  
466 dose of water enriched in  $^2\text{H}_2\text{O}$  and  $\text{H}_2^{18}\text{O}$ . The subject's body water pool is thus enriched in  
467 deuterium ( $^2\text{H}$ ) and  $^{18}\text{O}$ . The initial increase in body water enrichment from pre-dose values is  
468 used to calculate the size of the body water pool, measured as the dilution space for deuterium  
469 ( $N_d$ ) and  $^{18}\text{O}$  ( $N_o$ ). These isotopes are then depleted from the body water pool over time: both  
470 isotopes are depleted *via* water loss, whereas  $^{18}\text{O}$  is also lost *via* carbon dioxide production.  
471 Subtracting the rate (%/d) of deuterium depletion ( $k_d$ ) from the rate of  $^{18}\text{O}$  depletion ( $k_o$ ), and  
472 multiplying the size of the body water pool (derived from  $N_d$  and  $N_o$ ) provided the rate of carbon  
473 dioxide production,  $r\text{CO}_2$ . Entries in the DLW database include the original k and N values for  
474 each subject, which were then used to calculate  $\text{CO}_2$  using a common equation that has been  
475 validated in subjects across the lifespan (17). The rate of  $\text{CO}_2$  production, along with each  
476 subject's reported food quotient, was then used to calculate energy expenditure (MJ/d) using the  
477 Weir equation (40). We used the food quotients reported in the original studies to calculate total  
478 energy expenditure from  $r\text{CO}_2$  for each subject.

479 The size of the body water pool, determined from  $N_d$  and  $N_o$ , was used to establish FFM,  
480 using hydration constants for fat free mass taken from empirical studies. Other anthropometric

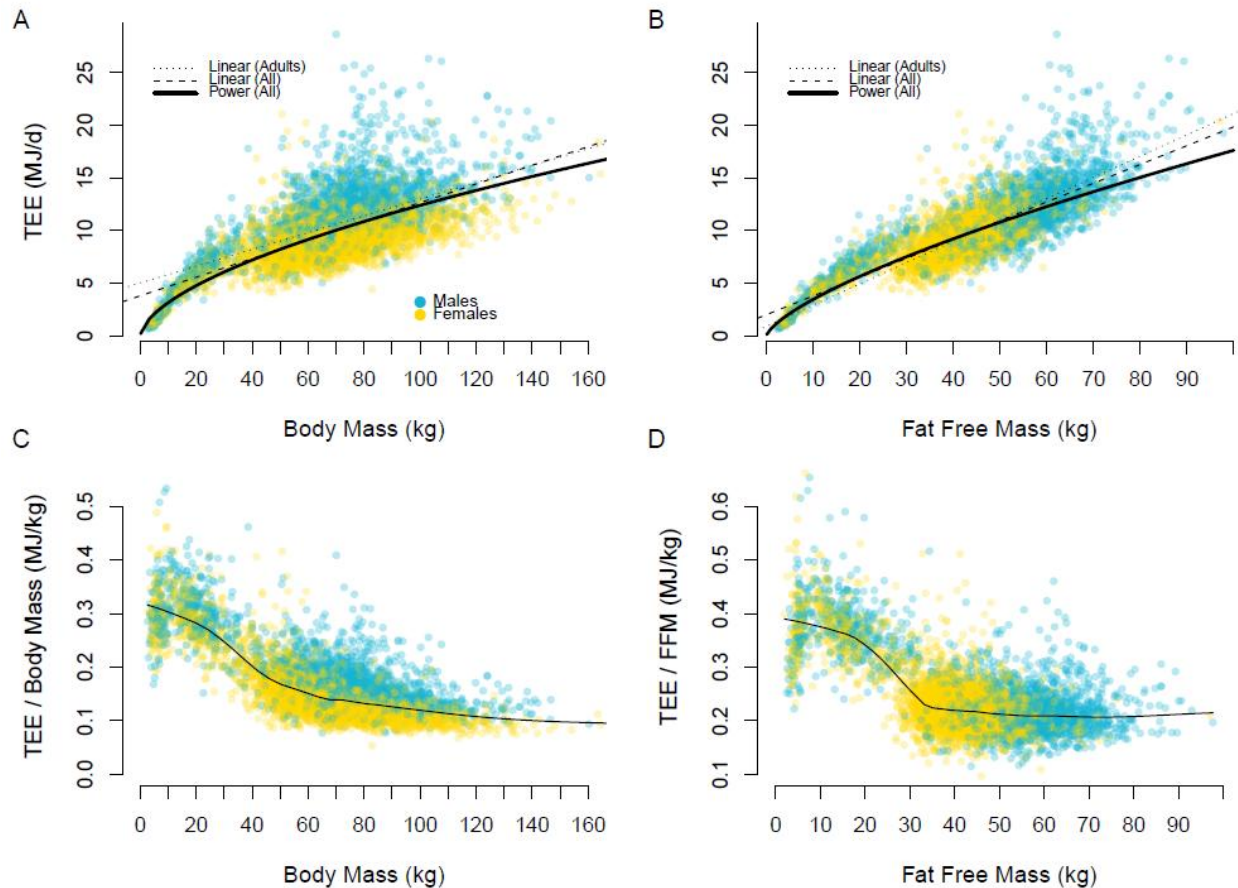
481 variables (age, height, body mass, sex) were measured using standard protocols. Fat mass was  
482 calculated as (body mass) – (fat free mass).

## 483 2. Basal Expenditure, Activity Expenditure, and Physical Activity Level (PAL)

484 A total of 2,008 subjects in the database had associated basal expenditure, measured *via*  
485 respirometry. For these subjects, we analyzed basal expenditure, activity expenditure, and  
486 “physical activity level” (PAL). Activity expenditure was calculated as  $[0.9(\text{total expenditure}) -$   
487  $(\text{basal expenditure})]$  which subtracts basal expenditure and the assumed thermic effect of food  
488  $[\text{estimated at } 0.1(\text{total expenditure})]$  from total expenditure. The PAL ratio was calculated as  
489  $(\text{total expenditure})/(\text{basal expenditure})$ . As noted above, the basal expenditure dataset was  
490 augmented with measurements from neonates and infants, but these additional measures do not  
491 have associated total expenditure and could not be used to calculate activity expenditure or PAL.

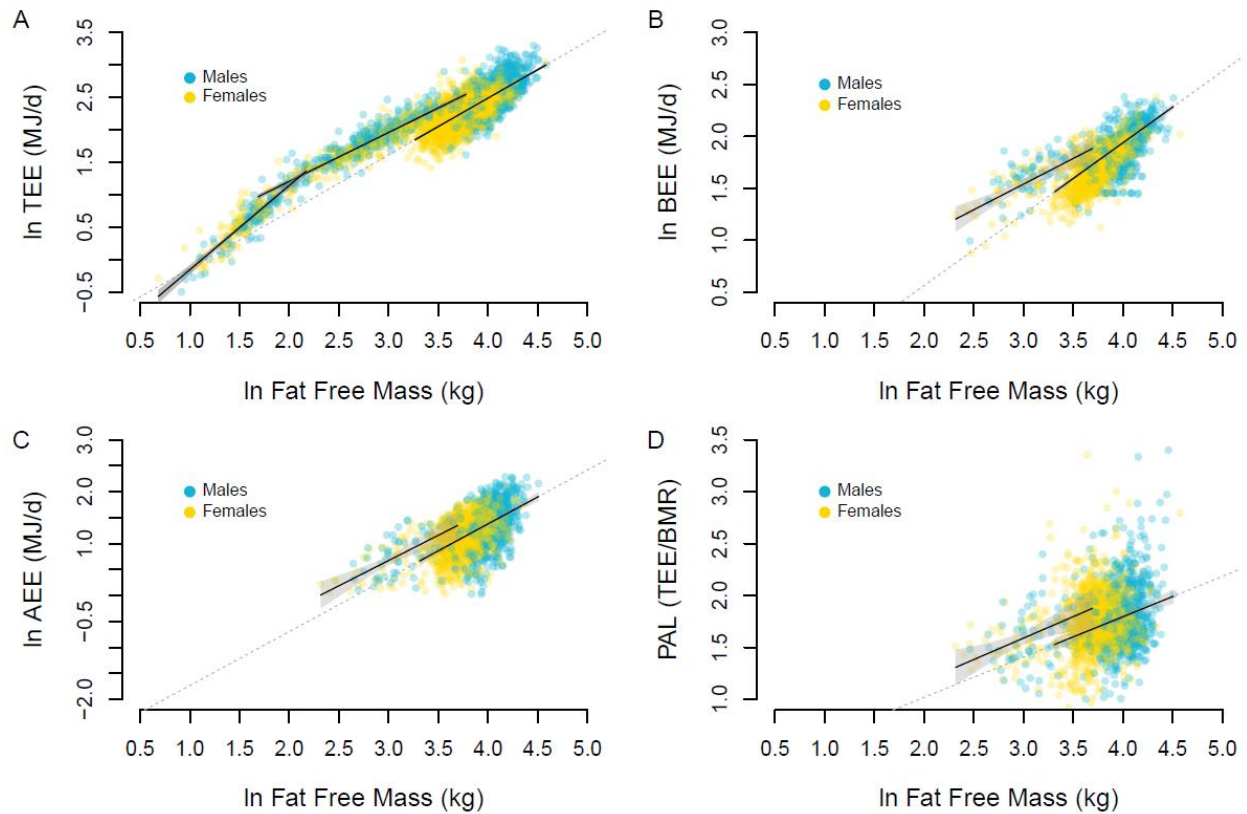
## 492 3. Predictive Models for Total, Basal, and Activity Expenditures and PAL

493 We used general linear models to regress measures of energy expenditure against  
494 anthropometric variables. We used the base package in R version 4.0.3 (41) for all analyses.  
495 General linear models were implemented using the `lm` function. These models were used to  
496 develop predictive equations for total expenditure for clinical and research applications, and to  
497 determine the relative contribution of different variables to total expenditure and its components.  
498 Given the marked changes in metabolic rate over the lifespan (Figure 1, Figure 2) we calculated  
499 these models separately for each life history stage: infants (0 – 1 y), juveniles (1 – 20 y), adults  
500 (20 – 60 y), and older adults (60+ y). These age ranges were identified using segmented  
501 regression analysis. Results of these models are shown in Table S2.



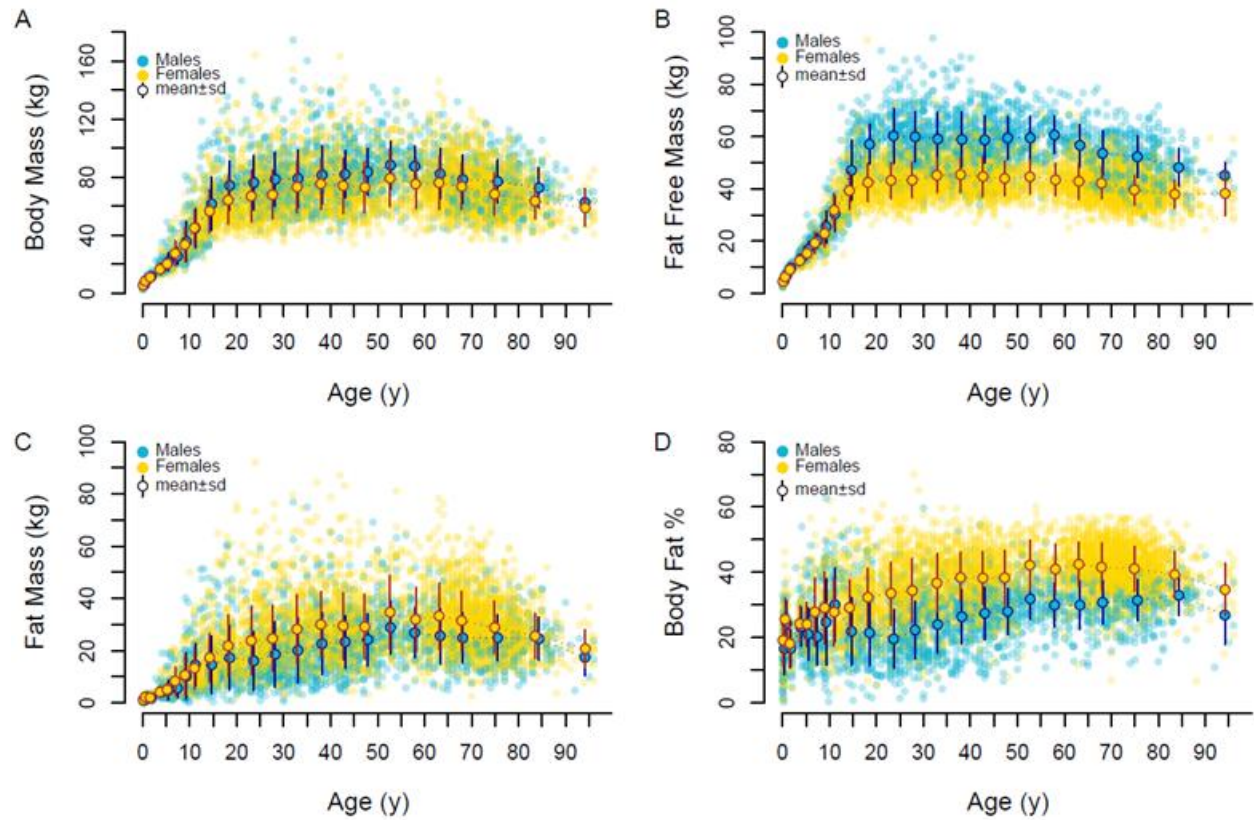
502

503 **Figure S1.** Total expenditure (TEE) increases with body size in a power-law manner. For the entire  
 504 dataset ( $n = 6,407$ ): **A.** the power-law regression for total body mass ( $\ln TEE = 0.593 \pm 0.004 \ln Mass -$   
 505  $0.214 \pm 0.018$ ,  $p < 0.001$ , adj.  $r^2 = 0.73$ , model std. err. = 0.223,  $df = 6419$ ) is less predictive than the  
 506 regression for **B.** fat free mass ( $\ln TEE = 0.708 \pm 0.004 \ln FFM - 0.391 \pm 0.015$ ,  $p < 0.001$ , adj.  $r^2 = 0.83$ ,  
 507 model std. err. = 0.176,  $df = 6419$ ). For both body mass and fat free mass regressions, power-law  
 508 regressions outperform linear models, particularly at the smallest body sizes. For all models, for both  
 509 body mass and fat free mass, children have elevated total expenditure, clustering above the trend line.  
 510 Children also exhibit elevated basal and activity expenditures (Figure S2). Power-law regressions have  
 511 an exponent  $< 1.0$ , and linear regressions (dashed: linear regression through all data; dotted: linear  
 512 regression through adults only) have a positive intercept, indicating that simple ratios of **C.** (total  
 513 expenditure)/(body mass) or **D.** (total expenditure)/(fat free mass) do not adequately control for  
 514 differences in body size (18) as smaller individuals will tend to have higher ratios. Lines in **C** and **D**  
 515 are lowess with span 1/6. In body mass regressions (panel **A**, power and linear models) and the ratio of (total  
 516 expenditure)/(body mass) (**C**), adult males cluster above the trend line while females cluster below due to  
 517 sex differences in body composition. In contrast, males and females fit the fat free mass regressions (**B**)  
 518 and ratio (**D**) equally well.



519

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



530

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

532 and **D.** Body fat percentage.



533 4. Adjusted Expenditures

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

538 We used models 2 and 5 in Table S2, which have the form  $\ln(\text{Expenditure}) \sim \ln(\text{FFM}) +$   
539  $\ln(\text{Fat Mass})$  and were implemented using the `lm` function in base R version 4.0.3 (41). We  
540 used  $\ln$ -transformed variables due to the inherent power-law relationship between body size and  
541 both total and basal expenditure (ref. 2; see Figure 1, Figure S1). Predicted values for each  
542 subject, given their fat free mass and fat mass, were calculated from the model using the  
543 `pred()` function; these  $\ln$ -transformed values were converted back into MJ as  $\exp(\text{Predicted})$ .  
544 Residuals for each subject were calculated as (Observed – Predicted) expenditure, and were then  
545 used to calculate adjusted expenditures as:

$$546 \quad \text{Adjusted Expenditure} = 1 + \text{Residual} / \text{Predicted} \quad [1]$$

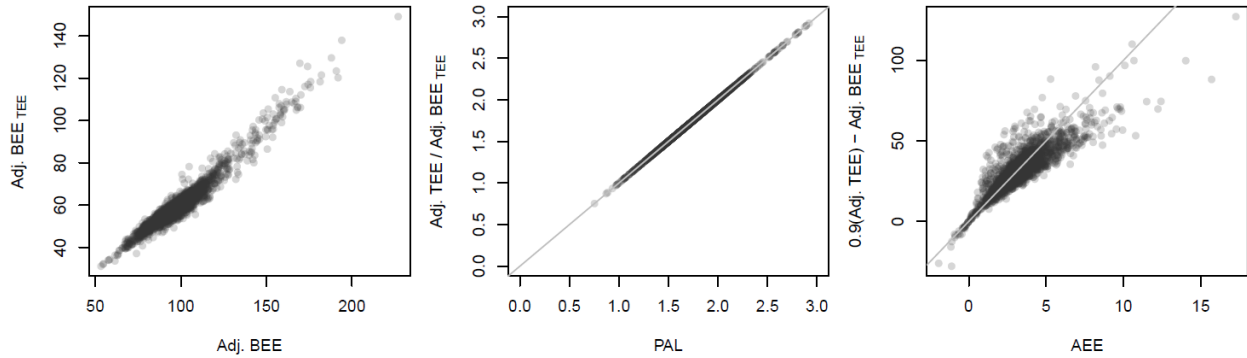
547 The advantage of expressing residuals as a percentage of the predicted value is that it allows us  
548 to compare residuals across the range of age and body size in the dataset. Raw residuals (MJ) do  
549 not permit direct comparison because the relationship between size and expenditure is  
550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

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

562 This same approach was used to calculate adjusted basal expenditure as a proportion of  
563 total expenditure (Figure 2D), hereafter termed adjusted  $BEE_{TEE}$ .  $Residual_{BEE-TEE}$ , the deviation  
564 of observed basal expenditure from the adult total expenditure regression (eq. 2 in Table S2),  
565 was calculated as (Observed Basal Expenditure – Predicted Total Expenditure) and then used to  
566 calculate adjusted  $BEE_{TEE}$  as

$$567 \quad \text{Adjusted } BEE_{TEE} = 1 + \text{Residual}_{BEE-TEE} / \text{Predicted Total Expenditure} \quad [2]$$

568 When adjusted  $BEE_{TEE} = 80\%$ , observed basal expenditure is equal to 80% of predicted total  
569 expenditure given the subject's fat free mass and fat mass. Adjusted  $BEE_{TEE}$  is equivalent to  
570 adjusted basal expenditure (Figure S4) but provides some analytical advantages. The derivation  
571 of adjusted  $BEE_{TEE}$  approach applies identical manipulations to observed total expenditure and  
572 observed basal expenditure and therefore maintains them in directly comparable units. The ratio  
573 of (adjusted total expenditure)/(adjusted basal expenditure) is identical to the PAL ratio of (total  
574 expenditure)/(basal expenditure), and the difference (0.9adjusted total expenditure– adjusted  
575 basal expenditure) is proportional to activity expenditure (Figure S4). Plotting adjusted total  
576 expenditure and adjusted  $BEE_{TEE}$  over the lifespan (Figure 2D) therefore shows both the relative  
577 magnitudes of total and basal expenditure and their relationship to one another in comparable  
578 units.



579

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

#### 584 5. Segmented Regression Analysis

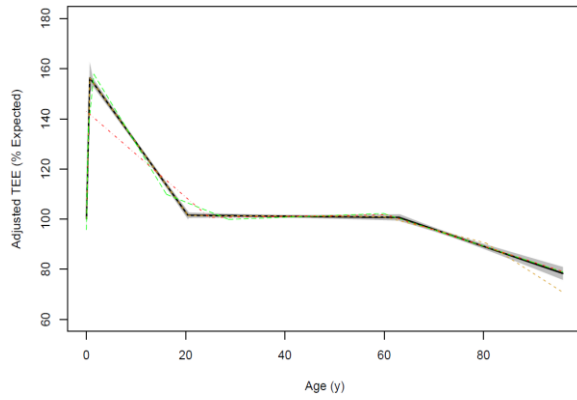
585 We used segmented regression analysis to determine the change points in the relationship  
 586 between adjusted expenditure and age. We used the Segmented (version 1.1-0) package in R  
 587 (42). For adjusted total expenditure, we examined a range of models with 0 to 5 change points,  
 588 using the `npsi=` term in the `segmented()` function. This approach does not specify the  
 589 location or value of change points, only the number of them. Each increase in the number of  
 590 change points from 0 to 3 improved the model adj.  $R^2$  and standard error considerably.  
 591 Increasing the number of change points further to 4 or 5 did not improve the model, and the  
 592 additional change points identified by the `segmented()` function fell near the change points for  
 593 the 3-change point model. We therefore selected the 3-change point model as the best fit for  
 594 adjusted total expenditure in this dataset. Segmented regression results are shown in Table S4. A  
 595 similar 3-change point segmented regression approach was conducted for adjusted basal  
 596 expenditure (Figure S4) and adjusted BEE<sub>TEE</sub> (Figure 2D). We note that the decline in adjusted  
 597 basal expenditure and adjusted BEE<sub>TEE</sub> in older adults begins earlier (as identified by segmented

598 regression analysis) than does the decline in adjusted total expenditure among older adults.  
599 However, this difference may reflect the relative paucity of basal expenditure measurements for  
600 subjects 40 – 60 y. Additional measurements are needed to determine whether the decline in  
601 basal expenditure does in fact begin earlier than the decline in total expenditure. Here, we view  
602 the timing as essentially coincident and interpret the change point in adjusted total expenditure  
603 (~60 y), which is determined with a greater number of measurements, as more accurate and  
604 reliable.

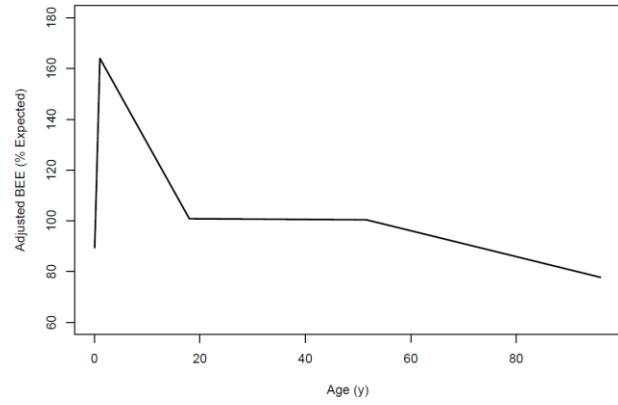
605         Having established that 3 break points provided the best fit for this dataset, we examined  
606 whether changes in the age range used to calculate adjusted total energy expenditure affected the  
607 age break-points identified by segmented regression. When the age range used to calculate  
608 adjusted expenditure was set at 20 – 60 y, the set of break point (95% CI) was: 0.69 (0.61-0.76),  
609 20.46 (19.77-21.15), 62.99 (60.14-65.85). When the age range was expanded to 15 – 70 y, break  
610 points determined through segmented regression were effectively unchanged: 0.69 (0.62 – 0.76),  
611 21.40 (20.60-22.19), 61.32 (58.60-64.03). Break points were also unchanged when the initial age  
612 range for adjusted expenditure was limited to 30 – 50 y: 0.69 (0.62-0.77), 20.56 (19.84-21.27),  
613 62.85 (59.97-65.74).

614

**A**



**B**



615

616 **Figure S5.** Segmented regression analysis of adjusted TEE (**A**) and adjusted BEE (**B**). In both panels,  
617 the black line and gray shaded confidence region depicts the 3 change-point regression. For adjusted  
618 TEE, segmented regressions are also shown for 2 change points (red), 4 change points (yellow), and 5  
619 change points (green). Segmented regression statistics are given in Table S4.

## 620 6. Organ Size and Basal Expenditure

621 Measuring the metabolic rate of individual organs is notoriously challenging, and the  
622 available data come from only a small number of studies. The available data indicate that organs  
623 differ markedly in their mass-specific metabolic rates at rest (43). The heart ( $1848 \text{ kJ kg}^{-1} \text{ d}^{-1}$ ),  
624 liver ( $840 \text{ kJ kg}^{-1} \text{ d}^{-1}$ ), brain ( $1008 \text{ kJ kg}^{-1} \text{ d}^{-1}$ ), and kidneys ( $1848 \text{ kJ kg}^{-1} \text{ d}^{-1}$ ) have much greater  
625 mass-specific metabolic rates at rest than do muscle ( $55 \text{ kJ kg}^{-1} \text{ d}^{-1}$ ), other lean tissue ( $50 \text{ kJ kg}^{-1}$   
626  $\text{d}^{-1}$ ), and fat ( $19 \text{ kJ kg}^{-1} \text{ d}^{-1}$ ). Consequently, the heart, liver, brain, and kidneys combined account  
627 for ~60% of basal expenditure in adults (21, 22, 44, 45). In infants and children, these  
628 metabolically active organs constitute a larger proportion of body mass. The whole body mass-  
629 specific basal expenditure [i.e., (basal expenditure)/(body mass), or (basal expenditure)/(fat free  
630 mass)] for infants and children is therefore expected to be greater than adults' due to the greater  
631 proportion of metabolically active organs early in life adults (21, 22, 44, 45). Similarly, reduced  
632 organ sizes in elderly subjects may result in declining basal expenditure (21).

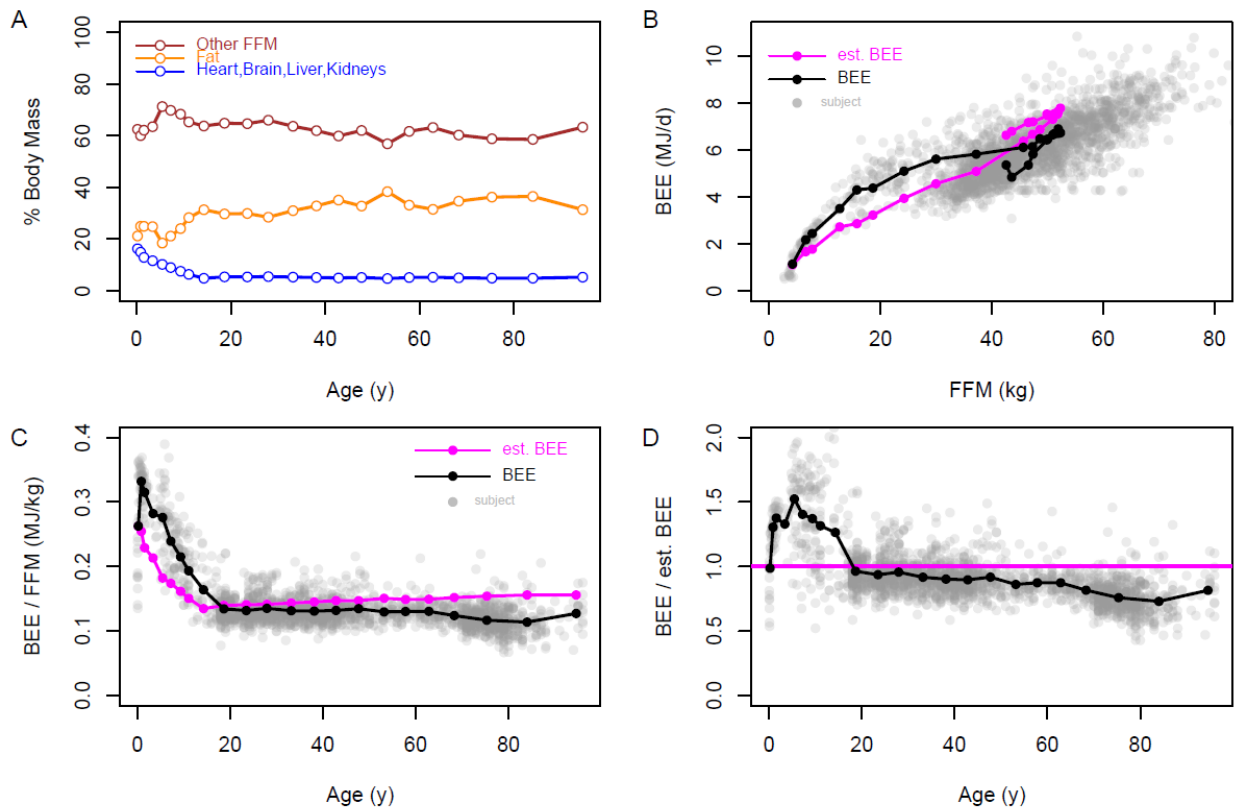
633 To examine this effect of organ size on basal expenditure in our dataset, we used  
634 published references for organ size to determine the mass of the metabolically active organs  
635 (heart, liver, brain, and kidneys) as a percentage of body mass or fat free mass for subjects 0 – 12  
636 y (22, 44-46), 15 to 60 y (21, 22), and 60 to 100 y (21, 47). We used these relationships to  
637 estimate the combined mass of the metabolically active organs (heart, liver, brain, kidneys) for  
638 each subject in our dataset. We then subtracted the mass of the metabolically active organs from  
639 measured fat free mass to calculate the mass of “other fat free mass”. These two measures, along  
640 with measured fat mass, provided a three-compartment model for each subject: metabolically  
641 active organs, other fat free mass, and fat (Figure S6A).

642           Following previous studies (21-25), we assigned mass-specific metabolic rates to each  
643 compartment and estimated basal expenditure for each subject. We used reported mass-specific  
644 metabolic rates for the heart, liver, brain, and kidneys (see above; (43)) and age-related changes  
645 in the proportions of these organs for subjects 0 – 12 y (22, 46), 15 to 60 y (21-25), and 60 to 100  
646 y (21, 23, 25, 47) to calculate an age-based weighted mass-specific metabolic rate for the  
647 metabolically active organ compartment. We averaged the mass-specific metabolic rates of  
648 resting muscle and other lean tissue (see above; (21, 22)) and assigned a value of 52.5 kJ kg<sup>-1</sup> d<sup>-1</sup>  
649 to “other fat free mass”, and we used a mass-specific metabolic rate of 19 kJ kg<sup>-1</sup> d<sup>-1</sup> for fat.

650           Results are shown in Figure S6. Due to the greater proportion of metabolically active  
651 organs in early life, the estimated basal expenditure from the three-compartment model follows a  
652 power-law relationship with FFM (using age cohort means, BEE= 0.38 FFM<sup>0.75</sup>; Figure S6B)  
653 that is similar to that calculated from observed basal expenditure in our dataset (see Table S2 and  
654 *7. Modeling the Effects of Physical Activity and Tissue Specific Metabolism*, below). Estimated  
655 BEE from the three-compartment model produced mass-specific metabolic rates that are  
656 considerably higher for infants and children than for adults and roughly consistent with observed  
657 age-related changes in (basal expenditure)/(fat free mass) (Figure S6C). Thus, changes in organ  
658 size can account for much of the variation in basal expenditure across the lifespan observed in  
659 our dataset.

660           Nonetheless, observed basal expenditure was ~30% greater early in life, and ~20% lower  
661 in older adults, than estimated basal expenditure from the three-compartment model (Figure  
662 S6D). The departures from estimated basal expenditure suggest that the mass-specific metabolic  
663 rates of one or more organ compartments are considerably higher early in life, and lower late in  
664 life, than they are in middle-aged adults, consistent with previous assessments (21-25). It is

665 notable, in this context, that observed basal expenditure for neonates is nearly identical to basal  
 666 expenditure estimated from the three-compartment model, which assumes adult-like tissue  
 667 metabolic rates (Figure S6B,C,D). Observed basal expenditure for neonates is thus consistent  
 668 with the hypothesis that the mass-specific metabolic rates of their organs are similar to those of  
 669 other adults, specifically the mother.



670  
 671 **Figure S6. Organ sizes and BEE.** **A.** The relative proportions of metabolically active organs (heart,  
 672 brain, liver, kidneys), other fat free mass (FFM), and fat changes over the life course. Age cohort means  
 673 are shown. **B.** Consequently, estimated basal expenditure (BEE) from the three-compartment model  
 674 increases with fat free mass (FFM) in a manner similar to observed basal expenditure, with **C.** greater  
 675 whole body mass-specific basal expenditure (BEE/FFM) early in life. **D.** Observed basal expenditure is  
 676 ~30% greater early in life, and ~20% lower after age 60 y, than estimated basal expenditure from the  
 677 three-compartment model (shown as the ratio of BEE/est.BEE). In panels **B**, **C**, and **D**, age-cohort means  
 678 for observed (black) and estimated (magenta) basal expenditure are shown.



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

680 We constructed two simple models to examine the contributions of physical activity and  
681 variation in tissue metabolic rate to total and basal expenditure. In the simplest version, we used  
682 the observed relationship between basal expenditure and fat free mass for all adults 20 – 60 y  
683 determined from linear regression of  $\ln(\text{basal expenditure})$  and  $\ln(\text{fat free mass})$  (untransformed  
684 regression equation:  $\text{basal expenditure} = 0.32 (\text{fat free mass})^{0.75}$ ,  $\text{adj. } r^2 = 0.60$ ,  $\text{df} = 1684$ ,  $p <$   
685  $0.0001$ ) to model basal expenditure as

$$686 \quad \text{Basal expenditure} = 0.32 \text{ TM}_{\text{age}} (\text{fat free mass})^{0.75} \quad [3]$$

687 The  $\text{TM}_{\text{age}}$  term is tissue metabolic rate, a multiplier between 0 and 2 reflecting a relative  
688 increase ( $\text{TM}_{\text{age}} > 1.0$ ) or decrease ( $\text{TM}_{\text{age}} < 1.0$ ) in organ metabolic rate relative that expected  
689 from the power-law regression for adults. Note that, even when  $\text{TM}_{\text{age}} = 1.0$ , smaller individuals  
690 are expected to exhibit greater mass-specific basal expenditure (that is, a greater basal  
691 expenditure per kg body weight) due to the power-law relationship between basal expenditure  
692 and fat free mass. Further, we note that the power-law relationship between basal expenditure  
693 and fat free mass for adults is similar to that produced when estimating basal expenditure from  
694 organ sizes (see *Organ Size and Basal Expenditure*, above). Thus, variation in  $\text{TM}_{\text{age}}$  reflects  
695 modeled changes in tissue metabolic rate *in addition* to power-law scaling effects, and also, in  
696 effect, in addition to changes in basal expenditure due to age-related changes in organ size and  
697 proportion. To model variation in organ activity over the lifespan, we either 1) maintained  $\text{TM}_{\text{age}}$   
698 at adult levels ( $\text{TM}_{\text{age}} = 1.0$ ) over the entire lifespan, or 2) had  $\text{TM}_{\text{age}}$  follow the trajectory of  
699 adjusted basal expenditure with age (Figure S8).

700 To incorporate effects of fat mass into the model, we constructed a second version of the  
701 model in which basal expenditure was modeled following the observed relationship with FFM  
702 and fat mass for adults 20 – 60 y,

$$703 \quad \text{Basal expenditure} = 0.32 \text{ TM}_{\text{age}} (\text{fat free mass})^{0.7544} (\text{fat mass})^{0.0003} \quad [4]$$

704 As with the fat free mass model (eq. 3), we either maintained  $\text{TM}_{\text{age}}$  at 1.0 over the life span or  
705 modeled it using the trajectory of adjusted basal expenditure.

706 Activity expenditure was modeled as a function of physical activity and body mass  
707 assuming larger individuals expend more energy during activity. We began with activity  
708 expenditure, calculated as  $[0.9(\text{total expenditure}) - (\text{basal expenditure})]$  as described above. The  
709 observed ratio of  $(\text{activity expenditure})/(\text{fat free mass})$  for adults 20 – 60 y was  $0.07 \text{ MJ d}^{-1} \text{ kg}^{-1}$ .  
710 We therefore modeled activity expenditure as

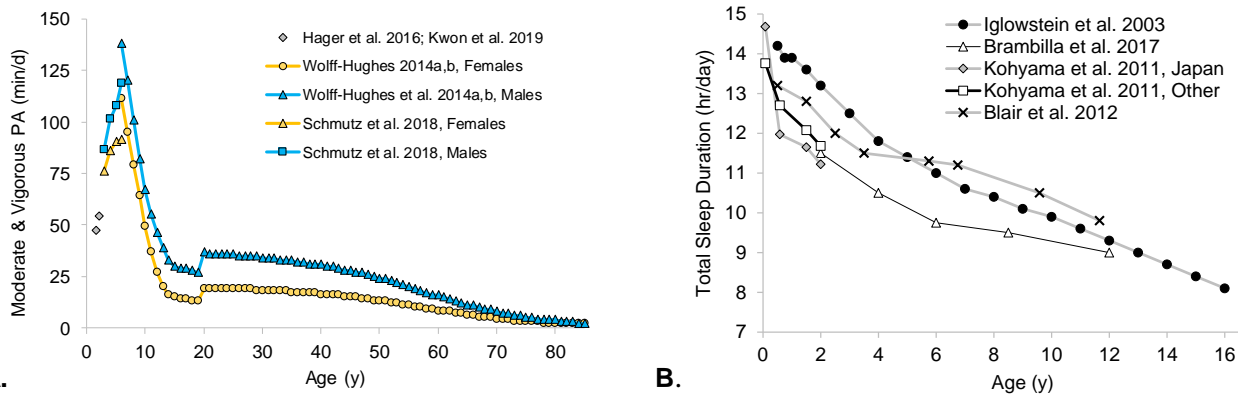
$$711 \quad \text{Activity expenditure} = 0.07 \text{ PA}_{\text{age}} (\text{fat free mass}) \quad [5]$$

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

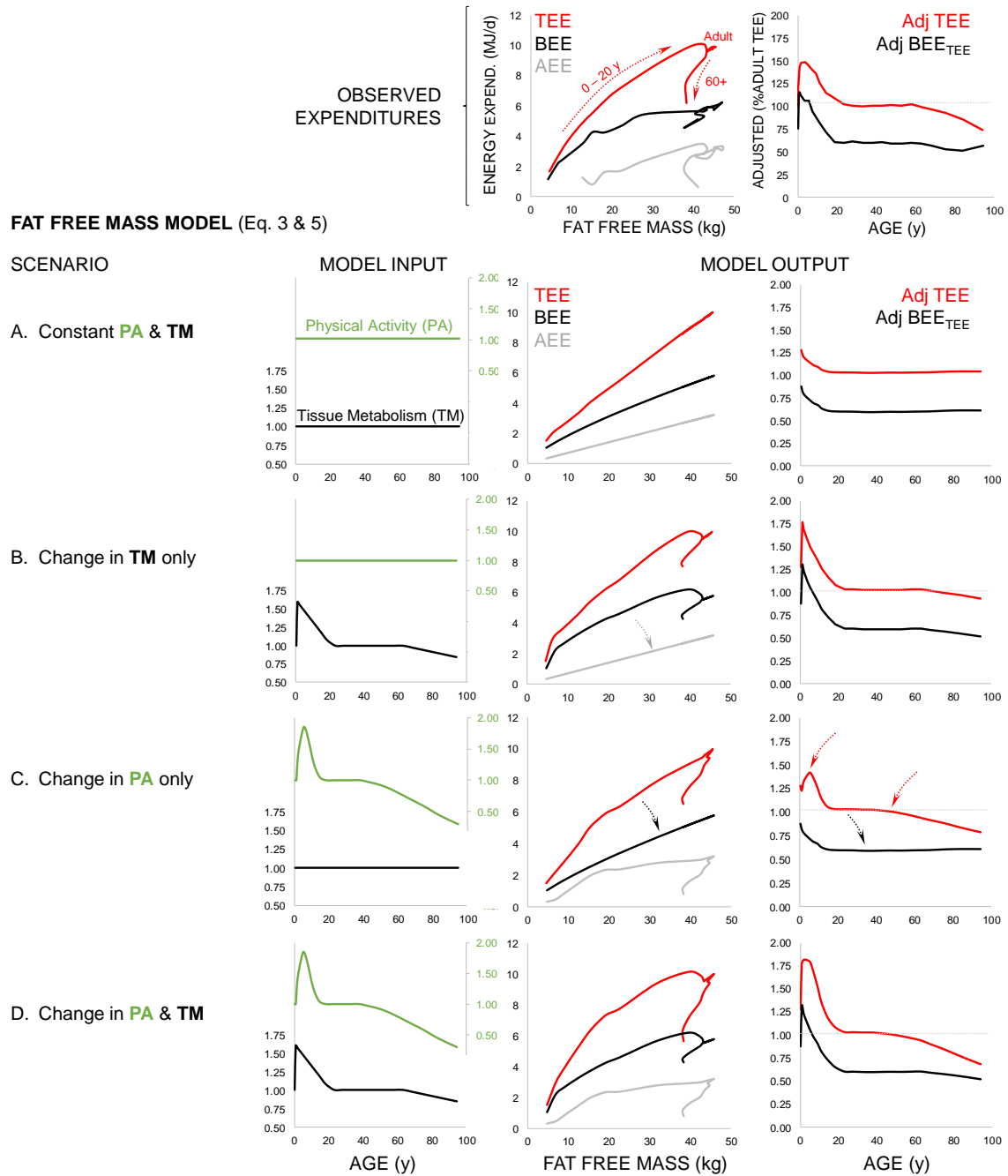
$$714 \quad \text{Activity expenditure} = 0.04 \text{ PA}_{\text{age}} (\text{body weight}) \quad [6]$$

715 In both equations,  $\text{PA}_{\text{age}}$  represents the level of physical activity relative to the mean value for 20  
716 – 60 y adults.  $\text{PA}_{\text{age}}$  could either remain constant at adult levels ( $\text{PA}_{\text{age}}=1.0$ ) over the lifespan or  
717 follow the trajectory of physical activity measured *via* accelerometry, which peaks between 5 –  
718 10 y, declines rapidly through adolescence, and then declines more slowly beginning at ~40 y  
719 (11-13, 26, 27, 48-51). Different measures of physical activity (*e.g.*, moderate and vigorous PA,  
720 mean counts per min., total accelerometry counts) exhibit somewhat different trajectories over  
721 the lifespan, but the patterns are strongly correlated; all measures show the greatest activity at 5-  
722 10 y and declining activity in older adults (Figure S7). We chose total accelerometry counts (11,

723 26), which sum all movement per 24-hour period, to model age-related changes in  $PA_{age}$ . We  
 724 chose total counts because activity energy expenditure should reflect the summed cost of all  
 725 activity, not only activity at moderate and vigorous intensities. Further, the amplitude of change  
 726 in moderate and vigorous activity over the lifespan is considerably larger than the observed  
 727 changes in adjusted total expenditure or adjusted activity expenditure (Figure S10). Determining  
 728 the relative contributions of different measures of physical activity to total expenditure is beyond  
 729 the scope of the simple modeling approach here and remains an important task for future  
 730 research.  
 731



732 **A.** **Figure S7.** Modeling physical activity across the lifespan. **A.** Across studies and countries,  
 733 accelerometer-measured physical activity rises through infancy and early childhood, peaking between 5  
 734 and 10y before declining to adult levels in the teenage years (11-13, 26, 27, 48-51). Physical activity  
 735 declines again, more slowly, in older adults. The onset of decline in older adults varies somewhat across  
 736 studies, beginning between ~40 y and ~60 y. Here, physical activity is shown as minutes/day of moderate  
 737 and vigorous physical activity. Other measures (e.g., total accelerometer counts; mean counts/min, vector  
 738 magnitude) follow a similar pattern of physical activity over the life span (11, 26). **B.** The increase in  
 739 physical activity from 0 to ~10 y is mirrored by the steady decline in total daily sleep duration during this  
 740 period (52-55).  
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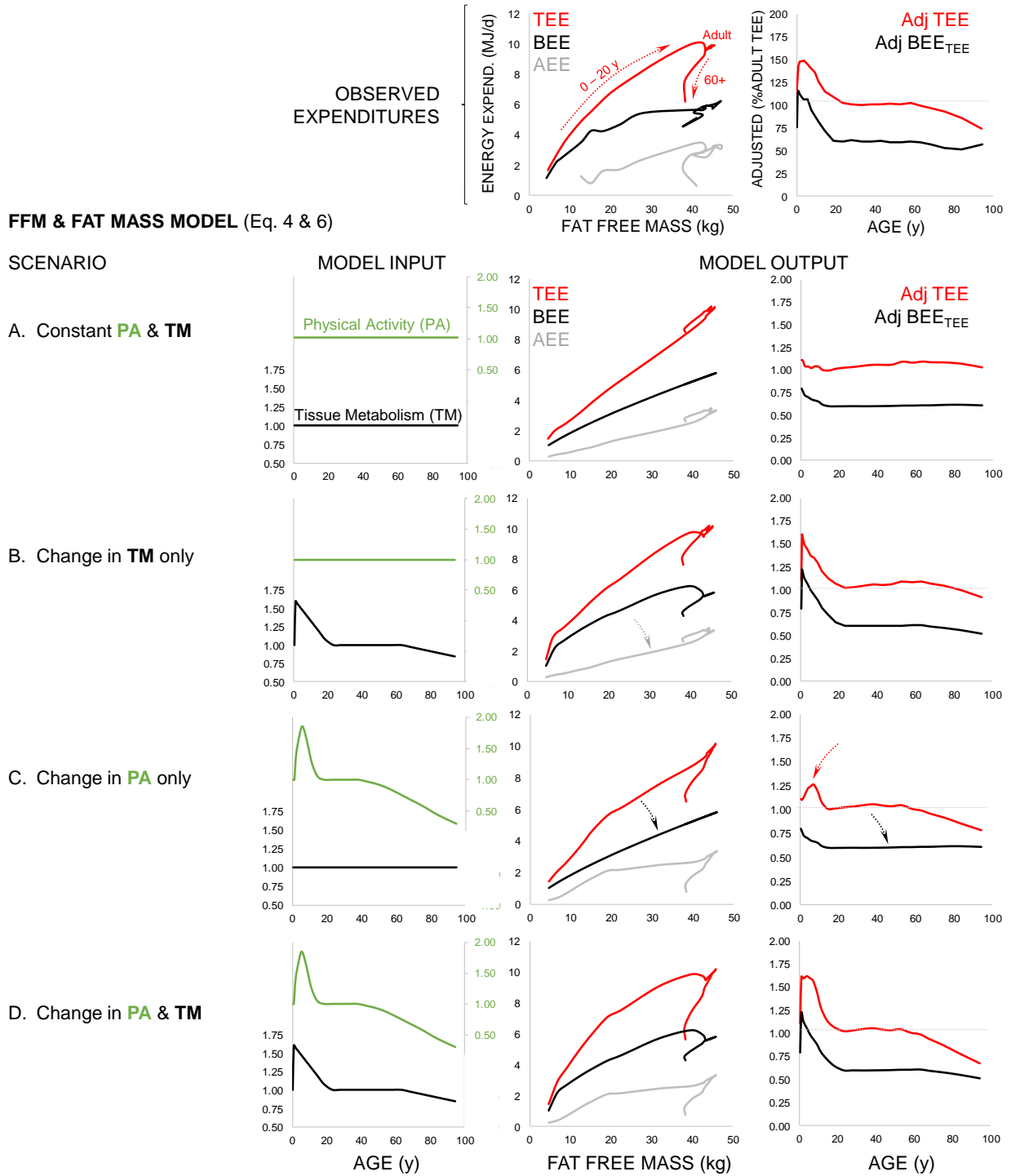
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**Figure S8.** Results of the fat free mass model. Observed expenditures exhibit a marked age effect on the relationship between expenditure and fat free mass that is evident in both absolute (Figure 1C) and adjusted (Figure 2D) measures. **A.** If physical activity (PA) and cellular metabolism (TM) remain constant at adult levels, age effects do not emerge from the model. **B.** When only TM varies, age effects emerge for total expenditure (TEE) and basal expenditure (BEE), but not activity expenditure (AEE; gray arrow). **C.** Conversely, if only physical activity varies age effects emerge for AEE and TEE but not BEE (black arrows). Adjusted TEE also peaks later in childhood and declines earlier in adulthood (red arrows) than observed. **D.** Varying both PA and TM gives model outputs similar to observed expenditures.



751

752 **Figure S9.** Results of the fat free mass and fat mass model. Model outputs are similar to those of the fat

753 free mass model (Figure S8). The scenario that best matches the observed relationships between fat free

754 mass, age, and expenditure is D, in which AEE is influenced by age-related variation in both physical

755 activity and cellular metabolism. Abbreviations as in Fig S8.

## 756 8. Physical Activity, Activity Expenditure and PAL

757           To further interrogate our simple model of expenditure and the contribution of physical  
758 activity, we examined the agreement between accelerometry-measured physical activity,  
759 adjusted activity expenditure, and modeled PAL over the lifespan. First, as noted in our  
760 discussion of the simple expenditure model (see above; Figures 3, S8, S9), moderate and  
761 vigorous physical activity and total accelerometry counts show a similar shape profile when  
762 plotted against age, but moderate and vigorous physical activity shows a greater amplitude of  
763 change over the lifespan (Figure S10). Moderate and vigorous physical activity reach a peak ~4-  
764 times greater than the mean values observed for 20 – 30 y men and women, far greater than the  
765 amplitude of change in adjusted total expenditure.

766           We used adjusted total and basal expenditures to model activity expenditure and PAL  
767 over the lifespan for comparison with published accelerometry measures of physical activity.  
768 Modeling activity expenditure and PAL was preferable because our dataset has no subjects less  
769 than 3 y with measures of both total and basal expenditure, and only 4 subjects under the age of 6  
770 y with both measures (Table S1). Using values of adjusted total expenditure and adjusted  
771  $BEE_{TEE}$  (basal expenditure expressed as a percentage of total expenditure) for age cohorts from  
772 Table S3 enabled us to model activity expenditure and PAL for this critical early period of  
773 development, in which both physical activity and expenditure change substantially. We modeled  
774 adjusted activity expenditure as  $[(\text{adjusted total expenditure}) - (\text{adjusted } BEE_{TEE})]$  and PAL as  
775  $[(\text{adjusted total expenditure}) / (\text{adjusted } BEE_{TEE})]$ , which as we show in Figure S4 correlate  
776 strongly with unadjusted measures of activity expenditure and PAL, respectively.

777           Modeled adjusted activity expenditure and PAL showed a somewhat different pattern of  
778 change over the lifecourse than either total counts or moderate and vigorous activity measured via

779 accelerometry (Figure S10). Modeled activity expenditure was most similar to total counts, rising  
780 through childhood, peaking between 10 and 20 y before falling to a stable adult level; the adult  
781 level was stable from ~30 – 75 y before declining (Figure S10). Modeled PAL rose unevenly  
782 from birth through age 20, then remained largely stable thereafter.

783           The agreement, and lack thereof, between the pattern of accelerometry-measured physical  
784 activity and modeled activity expenditure and PAL must be assessed with caution. These  
785 measures are from different samples; we do not have paired accelerometry and energy  
786 expenditure measures in the present dataset. The life course pattern of accelerometry-measured  
787 physical activity, particularly total counts, is broadly consistent with that of modeled activity  
788 expenditure. However, more work is clearly needed to determine the effects of physical activity  
789 and other factors to variation in activity expenditure and PAL over the lifecourse.

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802 **9.IAEA DLW database consortium**

803 This group authorship contains the names of people whose data were contributed into the  
804 database by the analysis laboratory but they later could not be traced, or they did not respond to  
805 emails to assent inclusion among the authorship. The list also includes some researchers who did  
806 not assent inclusion because they felt their contribution was not sufficient to merit authorship

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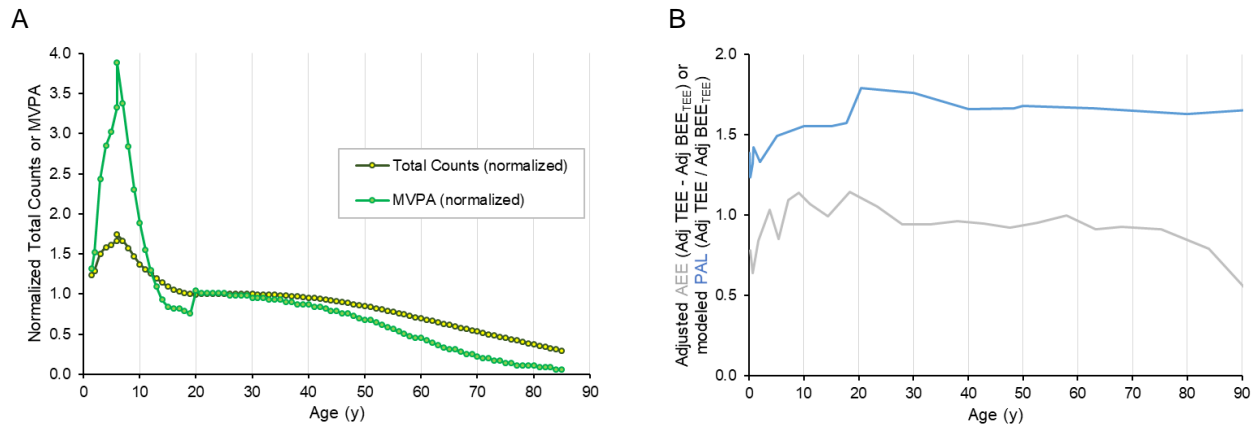
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**Figure S10. A.** Physical activity measured via accelerometry from published analyses (11-13, 26, 27, 48-51) and **B.** modeled activity expenditure and PAL calculated from cohort means for adjusted total expenditure and adjusted BEE<sub>TEE</sub> in Table S3. Accelerometry measures and modeled activity expenditure are normalized to mean values for 20 – 30 y subjects.





**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).

		Adjusted TEE - Female & Male Cohorts								Adjusted BEE and Adjusted BEE <sub>TEE</sub>											
		N		mean Age		Adjusted TEE				N		mean Age		Adjusted BEE				Adjusted BEE <sub>TEE</sub>			
Age						F		M		F	M			F		M		F		M	
Cohort	F	M	F	M	mean	sd	mean	sd	F	M	F	M	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 (111)*		0.2		100.47	33.89			86.03	28.9			
(0.5,1]	18	23	0.7	0.7	139.8	17.0	145.5	25.7	20 (88)*		0.9		142.89	11.62			115.47	9.2			
(1,2]	33	35	1.7	1.6	147.4	23.9	148.2	21.6	18 (86)*		1.6		142.02	13.52			111.94	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	

906 **Table S4.** Segmented Regression Analyses

<b>adjTEE</b>	<b>Segments</b>				<b>Break Points</b>		
	<i>beta</i>	<i>SE</i>	<i>CI_lower</i>	<i>CI_upper</i>	<i>Estimate</i>	<i>CI_lower</i>	<i>CI_upper</i>
	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			

<b>adjBEE</b>	<b>Segments</b>				<b>Break Points</b>		
	<i>beta</i>	<i>SE</i>	<i>CI_lower</i>	<i>CI_upper</i>	<i>Estimate</i>	<i>CI_lower</i>	<i>CI_upper</i>
	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			

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