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## **Total daily energy expenditure has declined over the past three decades due to declining basal expenditure, not reduced activity expenditure**

John Speakman, Jasper de Jong, Srishti Sinha, Klaas Westerterp, Yosuke Yamada, Hiroyuki Sagayama, Philip Ainslie, Liam Anderson, Lenore Arab, Kweku Bedu-Addo, et al.

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1 **Total daily energy expenditure has declined over the last 3 decades due to**  
2 **declining basal expenditure not reduced activity expenditure.**

3

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160 **Abstract**

161 Obesity is caused by prolonged positive energy balance<sup>1,2</sup>. Whether reduced energy  
162 expenditure stemming from reduced activity levels contributes, is debated<sup>3,4</sup>. Here we used the  
163 IAEA DLW database on energy expenditure of adults in the USA and Europe (n = 4799) to  
164 explore patterns in total (TEE: n=4799), basal (BEE: n = 1432) and physical activity energy  
165 expenditure (AEE: n = 1432) over time. In both sexes total energy expenditure (TEE) adjusted  
166 for body composition and age declined with time, while adjusted AEE increased over time. In  
167 males adjusted BEE decreased significantly, but in females this didn't reach significance. A  
168 larger dataset of basal metabolic rate (BMR equivalent to BEE) measurements of 9912 adults  
169 across 163 studies spanning 100 years replicated the decline in BEE in both sexes. Increasing  
170 obesity in the USA/Europe has probably not been fueled by reduced physical activity leading to  
171 lowered TEE. We identify here decline in adjusted BEE, as a previously unrecognized novel  
172 factor.

173

174 **Main text:** Obesity is a global health threat<sup>5</sup>. Although excess body fat is a result of prolonged  
175 positive energy balance<sup>1,2</sup>, the exact causes of this imbalance remain elusive. Two major  
176 potential factors have been suggested. First, food consumption (net energy consumption  
177 accounting for losses in feces) may have increased<sup>2</sup>. Alternatively, declines in energy  
178 expenditure, due to reduced work-time physical activity<sup>4</sup>, combined with increases in sedentary  
179 behavior, partly linked to elevated 'screen time' (TV, computer and phone use)<sup>6,7</sup> may be a key

180 driver. These may be linked in a vicious cycle<sup>8</sup>, where low activity leads to weight gain, which  
181 inhibits activity, leading to further weight gain.

182 Although there is direct evidence, that physical activity levels have declined and  
183 sedentary time has increased<sup>4,6,7,8</sup>, these changes do not necessarily translate into alterations in  
184 total energy expenditure (TEE). As individuals get larger the energy cost of movement also  
185 increases<sup>9</sup>. Thus, the same amount of energy may be utilized even though the actual time spent  
186 active has declined. Moreover, increases in one type of activity/behavior may be replaced by  
187 decreases in another behavior of equal cost. Consequently, apparently large behavior changes  
188 may result in only minor alterations in expenditure. Finally, it has been suggested that we may  
189 compensate for changes in physical activity by adjusting expenditure on other physiological  
190 tasks<sup>10,11</sup>. Although low TEE is repeatable, and having low TEE is not a risk factor for future  
191 weight gain over short timescales<sup>12</sup>, this does not negate a possible impact over longer periods.  
192 In the present paper we address the idea that reduced physical activity leading to reduced  
193 activity energy expenditure (AEE) may have fueled the epidemic.

194 The doubly-labelled water (DLW) method is a validated isotope based methodology for  
195 the measurement of free-living energy demands<sup>13</sup>. A previous analysis using this method  
196 suggested there had been no change in TEE between 1986 and 2005, calling into question the  
197 reduced physical activity hypothesis<sup>14</sup>. Nevertheless, these observations were based on a  
198 limited sample (n = 314) from a single European city over a restricted timespan of about 20  
199 years. Here we expanded this analysis using data for 4799 adults living across Europe and the  
200 USA drawn from the IAEA DLW database<sup>15</sup> for which we also had BEE measures in 1429

201 individuals. All estimates of TEE were recalculated using a common equation<sup>16</sup> that has been  
202 shown to perform best in validation studies<sup>16</sup>.

203 We split the data by sex, because this may affect the etiology of energy balance<sup>17,18</sup>. This  
204 resulted in 1672 measurements of males and 3127 measurements of females. In addition, for  
205 632 of the males and 800 of the females we also had measurements of basal energy  
206 expenditure (BEE) from which we derived activity energy expenditure (AEE) and physical  
207 activity level (PAL) – for calculations see methods. The data span a period of over 30 years with  
208 the first measurements in late 1981 and the latest measurements made in late 2017, with most  
209 data obtained between 1990 and 2017. The distribution of BMI in the sample for both males  
210 and females is shown in Supplementary Fig S1. Overall females had higher BMI than males. In  
211 the pooled sample the distribution was BMI < 18.5 = 2.3%, BMI 18.5 to 25 = 40.3%, BMI 25 to  
212 30 = 35.1% and BMI >30 = 22.2%. Combined overweight and obesity was 57.3%. In both males  
213 and females body weight increased over time (Figure S1) reflecting the secular trend in body  
214 weight over the same interval.

215 We first explored the changes in the unadjusted levels of TEE, BEE and AEE over time  
216 (Supplementary Fig S2: Table 1). In males there was no significant relationship between TEE and  
217 the date of measurement (date coded as months since Jan 1982) ( $r^2 = 0.0015$ ,  $p = 0.14$  (ns): Fig  
218 S2a) the least squares regression fit gave a gradient of +1.5 kJ/month (95%CI =  $\pm 2.06$   
219 kJ/month). This gradient leads to an estimated change in average TEE over 30 years of + 0.55  
220 MJ/day (95%CI =  $\pm 0.727$  MJ/day). Contrasting the lack of significant change in TEE, there was a  
221 significant decline in BEE over time (Fig S2b) ( $r^2 = 0.029$ ,  $p = 0.000018$ ). The gradient of decline  
222 (3.3 kJ/month, 95%CI =  $\pm 1.4$  kJ/month) was equivalent to an average fall in BEE by 1.19 MJ



223 (9.7%) over 30 years (95%CI =  $\pm 0.54$  MJ/day). As might be anticipated since  $TEE \times 0.9 = BEE +$   
224 AEE, the absence of a change in TEE and declining BEE was reflected by an increase in AEE over  
225 time, but this did not reach significance (Fig S2c) ( $r^2 = 0.003$ ,  $p = 0.16$ ). The gradient of the  
226 change in AEE (1.4 kJ/month, 95%CI =  $\pm 1.8$  kJ/month) was equivalent over 30 years to an  
227 increase by 0.50 MJ/day (95%CI =  $\pm 0.69$  MJ/day). In females, unadjusted levels of TEE, BEE and  
228 AEE did not change significantly over time (supplementary Fig S3, Table 1).

229 All the energy expenditure variables (TEE, BEE and AEE) in both sexes were dependent  
230 on body mass (BM) and BMI (illustrated for BMI in supplementary Fig 4). Because of these  
231 relationships it is necessary to adjust the raw expenditure data over time (Figs S2 and S3) to  
232 account for any changes in body composition over time that might generate a biased estimate  
233 of the change in expenditure variables. We adjusted the levels of log transformed TEE, BEE and  
234 AEE for body size and composition using residuals from general linear models with  $\log_e$  fat-free  
235 mass,  $\log_e$  fat mass and age as predictors. In this analysis the data were logged because the  
236 relationships between energy expenditure components and body composition follow power  
237 law relationships. In males, adjusted TEE significantly declined over the measurement period  
238 (Fig 2a:  $r^2 = 0.0103$ ,  $p < .0001$ ). The gradient of the fitted regression was -32.5 kJ/month (95%CI  
239 =  $\pm 1.20$  kJ/month) leading to an estimated average change over 30 years of -0.93 MJ/day in  
240 adjusted TEE (95%CI =  $\pm 0.465$  MJ/day), a decline on average of 7.7%. The adjusted BEE showed  
241 a highly significant decline over time (Fig 2b:  $r^2 = 0.064$ ,  $p < 10^{-9}$ ) with the gradient of 2.67  
242 kJ/month (95%CI =  $\pm 0.82$  kJ/month) being equivalent to an average fall in BEE of 0.96 MJ/day  
243 (14.7%) over 30 years (95%CI =  $\pm 0.15$  MJ/day). In contrast, the adjusted AEE increased over

244 time (Fig 2c:  $r^2 = 0.0221$ ,  $p < .0003$ ). The gradient of  $+2.8$  kJ/month (95%CI =  $\pm 1.4$  kJ/month)  
245 was equivalent to a rise of  $1.01$  MJ/day over 30 years (95%CI =  $\pm 0.53$  MJ/day).

246 In females as well, there was a significant decline in the adjusted TEE over time (Fig 3a:  
247  $r^2 = 0.006$ ,  $p < .00002$ ). The gradient of the effect  $1.42$  kJ/month was equivalent to a reduction  
248 in TEE over 30 years of  $0.51$  MJ (95%CI =  $\pm 0.22$  MJ/day) or 5.6%. This decline was paralleled by a  
249 reduction in adjusted BEE of 2.0% but this did not reach significance (Fig 3b:  $r^2 = 0.0015$ ,  
250  $p > .05$ ). The gradient of the fall in adjusted BEE was  $0.3$  kJ/month, equivalent to a reduction in  
251 adjusted BEE over 30 years of  $0.11$  MJ/day (95%CI =  $\pm 0.21$  MJ/day). In contrast, and again  
252 similarly to the males, adjusted AEE significantly increased over time (Fig 3c:  $r^2 = 0.0063$ ,  $p =$   
253  $0.026$ ). The gradient of increase in AEE of  $1.16$  kJ/month was equivalent to an increase in AEE of  
254  $0.42$  MJ/day over 30 years (95% CI =  $\pm 0.37$  MJ/day).

255 Because there was a small sample of measures in the early 1980s in males these may  
256 have exerted undue leverage in the regression models. We therefore repeated the analysis  
257 excluding these data. Their removal had no impact on the detected relationships  
258 (Supplementary Table S1). Since individual studies may also exert undue leverage we  
259 performed additional sensitivity analyses on the BEE effect (post 1987) where the data for each  
260 study was systematically removed and the regression recalculated. In males removal of no  
261 individual study resulted in the loss of significance (Supplementary Table S2). In females  
262 however, the absence of significance was due to inclusion of data from a single study  
263 (Supplementary Table S3). We have no reason to exclude these data, but their undue influence  
264 may explain the anomalous lack of decline in female BEE when TEE is declining and AEE is rising  
265 (Table 1 and fig 2).

266           Hence, in both males and females there was a decline in the adjusted TEE by 7.7 and  
267 5.6% respectively and in males in the adjusted BEE over time by 14.7% over 30 years (females  
268 declined by 2% which was not significant). In both sexes the confidence limits for the decline in  
269 adjusted TEE overlapped with the confidence limits for the decline in adjusted BEE, suggesting  
270 the decline in adjusted BEE could be sufficient to explain the reduction in adjusted TEE. In both  
271 sexes there was in contrast a significant increase over time in adjusted AEE. The comparable  
272 declines in adjusted TEE and BEE resulted in a significant increase in PAL (=TEE/BEE) in males  
273 (Males supplementary Fig S5a:  $r^2 = 0.0215$ ,  $p < .0003$ ) but in females the change in PAL over  
274 time was not significant (females supplementary Fig S5b:  $r^2 = 0.0037$ ,  $p = 0.085$ ).

275           To replicate and check our observation of decreasing BEE over time we systematically  
276 reviewed data from the literature on mean BMR over the last 100 years, restricted to studies in  
277 the USA and Europe, to match the restricted regions included in the time course from the IAEA  
278 database (Figs 1,2 and Table 1). For the distinction between BEE and BMR see the methods. The  
279 main effect on  $\text{Log}_e$  BMR was  $\text{Log}_e$  BM (Fig 3a), with additional effects of sex and age (total  $r^2 =$   
280 0.88). Including the date of measurement, sex, age and  $\text{log}_e$  body mass as predictors in a  
281 weighted regression analysis there was a significant negative effect of date of measurement ( $R^2$   
282 = 0.024,  $p = 0.022$ ) on the adjusted  $\text{log}_e$  BMR (Fig 3b). On average, BMR adjusted for BM, age  
283 and sex has declined by about 0.34 MJ/d over the last 100 years. This decline is consistent with,  
284 but at a lower rate, than the data from the IAEA database reported above (Table 1).

285           Basal metabolism may be influenced by many factors one of which is diet. Human  
286 dietary changes during the epidemic have included many things such as changes in the amounts  
287 of fiber and fat, and the types of fat consumed. Because evaluating the impacts of long-term

288 diets on human metabolism is difficult, we explored the potential impact of dietary fatty acids  
289 on metabolic rate using the mouse as a model. Working with mice has the advantage that diets  
290 can be rigorously controlled and maintained constant over protracted periods. We exposed  
291 adult male C57BL/6 mice to 12 diets (for details see supplementary Tables S2 and S3) that  
292 varied in their fatty acid composition for 4 weeks (equivalent to 3.5 years in a human). Mouse  
293 BMR (kJ/d) was strongly related to body weight (regression  $r^2 = 0.512$ ,  $p = 3 \times 10^{-11}$ ; Fig 4A). We  
294 included the total intake of different fatty acids (SAT: saturated fatty acids, MUFA: mono-  
295 unsaturated fatty acids and PUFA: poly-unsaturated fatty acids) with body weight into a general  
296 linear model. Only intake of saturated fatty acids was significant (SAT:  $F = 11.05$ ,  $p = 0.002$  (Fig  
297 4B); MUFA:  $F = 1.38$ ,  $p = 0.245$ ; PUFA:  $F = 0.17$ ,  $p = 0.686$ ) with higher levels of SAT linked to  
298 higher energy expenditure (Fig 4B).

299 Overall the data we present do not support the idea that lowered physical activity in  
300 general, leading to lowered energy expenditure, has contributed to the obesity epidemic during  
301 the last 30 years. Unadjusted AEE was higher in individuals with greater BMI (supplementary Fig  
302 S4). This is because, as shown previously, despite on average moving less, individuals with  
303 greater BMI have higher costs of movement<sup>9</sup>. Rather than adjusted AEE declining, it has  
304 significantly increased overtime in both sexes. Yet TEE (adjusted for age and body composition)  
305 has declined significantly in both males and females over the past 3 decades. Because adjusted  
306 AEE has increased at the same time that TEE has declined there has been a corresponding  
307 reduction in adjusted BEE (which only reached significance in males). The observation that  
308 adjusted AEE (and PAL in males) has significantly increased over time is counter intuitive given  
309 the patterns established in worktime physical activity and the suggested progressive increase in

310 sedentary behavior<sup>4,6-8</sup>. One possibility is that lowered work time physical activity may have  
311 been more than offset by increased engagement in leisure time physical activity. For example,  
312 sales of home gym equipment in the USA increased from 2.4 to 3.7 Bn US\$ between 1994 and  
313 2017<sup>19</sup>. Time spent in leisure time PA in the USA also increased between 1965 and 1995,<sup>20</sup>  
314 suggesting leisure time PA has replaced the decline in worktime PA levels<sup>20</sup>. Leisure time PA has  
315 also changed in other westernized populations<sup>21</sup>. Although time spent on computers has  
316 increased, much of the increase in this time has largely come at the expense of time spent  
317 watching TV. Since these activities have roughly equivalent energy costs<sup>22</sup> this change would  
318 not be apparent as a decline in overall adjusted AEE.

319         The reduction in adjusted BEE is less easily understood but is consistent with the recent  
320 observation that body temperatures have also declined over time<sup>23</sup>, over the same interval as  
321 the reduction of BMR in the wider data set we analysed (Fig 3b). The magnitude of secular  
322 change in BMR is consistent with studies measuring BMR and body temperature in several  
323 contexts, including calorie restriction, ovulation, and fever which show a 10-25% increase in  
324 BMR per 1°C increase in core temperature<sup>24,25</sup>. It was recently suggested that changes in both  
325 activity and basal metabolism may have contributed to the decline in body temperature ( $T_b$ )<sup>26</sup>,  
326 but our data suggest this is probably dominated by a BMR effect. The reduction in  $T_b$  has been  
327 speculated to be a consequence of a reduction in baseline immune function because we have  
328 greatly reduced our exposure to many pathogens. However, the links between immune  
329 function and metabolism are not straightforward. For example, artificial selection on metabolic  
330 rate leads to suppressed innate but not adaptive immune function<sup>27</sup>, and studies of birds point  
331 to no consistent relation between immune function and metabolism either within or between

332 subjects<sup>28</sup>. Experimental removal of parasites in Cape ground squirrels (*Xerus inauris*) led to  
333 elevated rather than reduced resting metabolic rate<sup>29</sup>. Nevertheless, some studies in forager-  
334 horticulturalist societies in South America have noted elevated BMR is linked to increased levels  
335 of circulating IgG<sup>30</sup> and cytokines<sup>31</sup>, supporting the view that a long term decline in BEE may be  
336 mediated by reduced immune function. Whether this has any relevance to changes in the  
337 USA/Europe in the past 30 years is unclear. It is also possible that the long-term reduction in  
338 BMR represents methodological artefacts. In the early years, measurements of BMR were often  
339 made using mouthpieces to collect respiratory gases, and recently such devices have been  
340 shown to elevate BMR by around 6%<sup>32</sup>. A second possibility is that early measurements paid  
341 less attention to controlling ambient temperature to ensure individuals were at thermoneutral  
342 temperatures<sup>33</sup>.

343         During the past century there have been enormous changes in the diets of US and  
344 European populations (USDA and FAO food supply data)<sup>34</sup>. These changes have included  
345 alterations in the intake of carbohydrates, fiber and fats, with % protein intake remaining  
346 relatively constant<sup>34</sup>. While intake of carbohydrates peaked in the late 1990s the intake of fat  
347 has increased almost linearly since the early part of the 1900s. Moreover, the fat composition  
348 has changed dramatically with large increases in soybean oil and seed oils from the 1930s  
349 onwards (dominated by the polyunsaturated 18:2 linoleic acid and other PUFAs) and reductions  
350 in animal fats (butter and lard) (dominated by saturated fatty acids palmitic (16:0) and stearic  
351 acid (18:0) and the mono-unsaturated oleic acid (18:1))<sup>34</sup>. The change has been dramatic, as  
352 animal fats comprised >90% of the fatty acid intake in 1910 but are currently less than 15%.  
353 Because linoleic acid is desaturated to form arachidonic acid (ARA) and ARA is linked to

354 endocannabinoids it has been speculated that expanding linoleic acid in the diet may be linked  
355 to various metabolic issues. Effects on basal metabolic rate however are disputed, and if  
356 anything, PUFAs lead to elevated not reduced metabolism<sup>35,36</sup>, although many studies suggest  
357 no effect<sup>37,38</sup>. This variation in outcome may reflect difficulties in controlling human diet over  
358 protracted periods necessary to generate robust changes in metabolism. In mice, where we can  
359 rigorously control the diet for prolonged periods (equivalent to many years of human life), we  
360 have shown here no effect of PUFAs on metabolic rate, but a clear impact of saturated fat, with  
361 greater intake of saturated fat leading to higher metabolic rate (adjusted for body mass). This  
362 finding is consistent with earlier reports of relationships between membrane lipids and  
363 elevated metabolic rate in mice, particularly a positive effect of palmitic and stearic acids<sup>39,40</sup>.  
364 This suggests that alterations in the intake of saturated relative to unsaturated fat over the last  
365 100 years may have contributed to the decline in BEE reported here, although clearly we should  
366 be cautious about extrapolations from males of a single inbred mouse strain and further studies  
367 in humans are required. Moreover, other aspects of the diet that impact metabolic rate may  
368 also have changed over time, for example intake of fiber which has declined in recent years<sup>41</sup>  
369 and has been shown in a randomized controlled trial to affect resting metabolic rate<sup>42</sup>.

### 370 **Strengths and limitations**

371 A strength of this study is the large sample of individuals over a restricted geographical  
372 area (US and Europe) measured using a complex methodology. This has allowed us to detect a  
373 small but nevertheless biologically meaningful signal. However, it is important to be aware that  
374 the studies were not designed with the current analysis in mind. Hence while we have adjusted  
375 for differences in age and body composition there may be other factors that differed over time

376 that we did not adjust for and that could explain the trends we found. Further, the participants  
377 recruited at different time points may not have been representative of the underlying  
378 populations, even though the overall distribution seems representative (Fig S1). The data are  
379 cross-sectional which limits the inferences that can be made regarding causality in the  
380 associations. Finally, while we have speculated on some potential factors that might have  
381 contributed to the reduction in BEE (i.e. immune function and diet), these factors were not  
382 quantified in most of the participants who had their TEE measured. The mouse work we  
383 performed showing potential links of diet to metabolism was only conducted in males of one  
384 strain and a single age and may not be more broadly applicable. These potential mechanisms  
385 therefore remain speculations until more direct data can be collected.

## 386 **Conclusion**

387 Overall our data show that there has been a significant reduction in adjusted TEE over  
388 the last three decades, which can be traced to a decline in BEE rather than any reduction in AEE  
389 linked to declining physical activity levels. Indeed, our data show that AEE has significantly  
390 increased over time. Reductions in BEE extend much further back in time (TEE data do not  
391 extend further back than 1981 as that was the first year the DLW technique was applied to  
392 humans), and mouse data indicated that one of many possible explanations is decreases in the  
393 intake of saturated relative to unsaturated fatty acids. If the decline in BEE over time has not  
394 been compensated for by a parallel reduction in net energy intake then the energy surplus  
395 resulting would be deposited as fat. This study therefore identifies a novel potential contributor  
396 to the obesity epidemic, that has not been previously recognized: a decline in adjusted BEE



397 linked to reduction in overall adjusted TEE. Further understanding the determinants of BEE and  
398 the cause of this decline over time, and if it can be reversed, are important future goals.

399

## 400 References

401

- 402 1. Hall, K.D., Heymsfield, S.B., Kemnitz, J., Klein, S., Schoeller, D.A. and Speakman, J.R. (2012)  
403 Energy balance and body weight regulation: a useful concept for understanding the obesity  
404 epidemic. *American Journal of Clinical Nutrition* **95**: 989-994
- 405 2. Hill, J.O., Wyatt, H.R. and Peters, J.C. (2012) Energy balance and obesity. *Circulation* **126**: 126-  
406 132.
- 407 3. Swinburn, B.A., Sacks, G., Hall, K.D., McPherson, K., Finegood, D.T., Moodie, M.L. and  
408 Gortmaker, S.L. (2011) Obesity 1: the global pandemic.: shaped by global drivers and local  
409 environments. *Lancet* **378**: 804-14.
- 410 4. Church, T.S., Thomas, D.M., Tudor-Locke, C., Katzmarzyk, P.T., Earnest, C.P., Rodarte, R.Q.,  
411 Martin, C.K., Blair, S.N., Bouchard, C. (2011) Trends over 5 decades in US occupation related  
412 physical activity and their associations with obesity. *Plos One* **6**: e19657.
- 413 5. Ezzati, M., Bentham, J., Di Ceare, M. et al (2017) Worldwide trends in body mass index,  
414 underweight, overweight and obesity from 1975 to 2016: a pooled analysis of 2416 population  
415 based measurement studies in 128.9 million children, adolescents and adults. *Lancet* **390**: 2627-  
416 2642.
- 417 6. Thorp, A.A., Owen, N., Neuhaus, M. and Dunstan, D.W. (2011) Sedentary behaviours and  
418 subsequent health outcomes in adults. A systematic review of longitudinal studies, 1996-2011.  
419 *Am. J. Preventative med.* **41**: 207-215.
- 420 7. Gordon-Larsen, P., Nelson, M.C. and Popkin, B.M. (2004) Longitudinal physical activity and  
421 sedentary behavior trends – adolescence to adulthood. *Am. J. Preventative med.* **27**: 277-283.
- 422 8. Pietilainen, K.H., Kaprio, J., Borg, P. et al (2008) Physical inactivity and obesity: a vicious circle.  
423 *Obesity* **16**: 409-414.
- 424 9. Muller, M., Enderle, J. and Bosy-Westphal, A. (2016) Changes in energy expenditure with weight  
425 gain and weight loss in humans. *Current obesity reports.* **5**: 413-423.
- 426 10. Pontzer, H. (2018) Energy Constraint as a Novel Mechanism Linking Exercise and health.  
427 *Physiology (Bethesda).* **33**:384-393.
- 428 11. Careau, V. et al (2021) Energy compensation, adiposity and aging in humans. *Current biology* **31**:  
429 4659+
- 430 12. Rimbach, R., et al (2022) Total energy expenditure is repeatable in adults but not associated  
431 with short-term changes in body composition. *Nature Communications* **13**: e99
- 432 13. Speakman, J.R. (1997) *Doubly-labelled water: theory and practice.* Springer New York.
- 433 14. Westerterp, K.R. and Speakman, J.R. (2008) Physical activity energy expenditure has not declined  
434 since the 1980s and matches energy expenditure of wild mammals. *International Journal of Obesity*  
435 **32**:1256-63
15. Speakman, J.R., Pontzer, H., Rood, J., Sagayama, H., Schoeller, D.A., Westerterp, K.R., Wong,  
W.W., Yamada, Y., Loechl, C. and Alford, A. (2019) The IAEA international doubly-labelled water  
database: aims, scope and procedures. *Annals of Nutrition and metabolism* **75**: 114-118.

- 436 16. Speakman, J.R., Yamada, Y., et al (2021) A standard calculation methodology for studies using  
437 doubly labeled water. *CELL reports medicine* **2**: e100203
- 438 17. Wardle, J., Waller, J. and Jarvis, M.J. (2002) Sex differences in the association of socioeconomic  
439 status with obesity. *American Journal of Public Health*. **92**: 1299-1304.
- 440 18. Lovejoy, J.C. and Sainsbury, A. (2009) Sex differences in obesity and the regulation of energy  
441 homeostasis. *Obesity reviews*. **10**: 154-167.
- 442 19. Statistics on sales of home gym equipment from [www.statista.com](http://www.statista.com) accessed Oct 2019.
- 443 20. Cutler, D. M., Glaeser, E.L. and Shapiro. J.M. (2003). Why Have Americans Become More Obese?  
444 *Journal of Economic Perspectives*, **17**: 93–118.
- 445 21. Chau, J., Chey, T., Burks-Young, S. and Bauman, A. (2017) Trends in prevalence of leisure time  
446 physical activity and inactivity: results from Australian National health surveys 1989 to 2011. *Aus*  
447 *NZ Journal of Public Health* **41**: 617-624.
- 448 22. Vaz, M., Karaolis, N., Draper, A. and Shetty, P. (2005) A compilation of energy costs of physical  
449 activities. *Public health nut.* **8**: 1153-1163.
- 450 23. Protsiv, M., Ley, C., Lankaster, J., Hastie, T. and Parsonnet, J. (2020) Decreasing human body  
451 temperature in the United States since the industrial revolution. *eLife* **9**: e49555
- 452 24. Zhang, S., et al (2020) Changes in sleeping energy metabolism and thermoregulation during  
453 menstrual cycle. *Physiological reports* **8**: e14353
- 454 25. Du Bois, E. F. (1921). The basal metabolism in fever. *JAMA*, **77**: 352–355
- 455 26. Yegian, A.K., Heymsfield, S.B. and Lieberman, D.E. (2021) Historical body temperature records as  
456 a population level thermometer of physical activity in the United states. *Current biology* **31**:  
457 R1375-1376.
- 458 27. Downs, C.J., Brown, J.L., Wone, B., et al (2013) Selection for increased mass independent  
459 maximal metabolic rate suppresses innate but not adaptive immune function. *Proceedings of*  
460 *the royal society* **280**: 20122636.
- 461 28. Buehler, D.M., Vezina, F., Goymann, W., Schwabl, I. et al (2012) Independence among  
462 physiological traits suggests flexibility in the face of ecological demands on phenotypes. *J. Evol.*  
463 *Biol.* **25**: 1600-1613.
- 464 29. Scantlebury, M., Waterman, J.M., Hillegass, M. et al (2007) Energetic costs of parasitism in Cape  
465 ground squirrel *Xerus inauris*. *Proc. Roy. Soc.* **274**: 2169-2177.
- 466 30. Urlacher, S.S., Snodgrass JJ, Dugas LR, Sugiyama LS, Liebert MA, Joyce CJ, Pontzer H. (2019)  
467 Constraint and tradeoffs regulate energy expenditure during childhood. *Science Advances*. **5**:  
468 eaax1065.
- 469 31. Gurven MD, Trumble BC, Stieglitz J, Cummings D, Blackwell A, Beheim BA, Kaplan H, Pontzer H.  
470 (2016) High resting metabolic rate among Amazonian forager-horticulturalists experiencing high  
471 pathogen burden. *Am J Phys Anthropol* **161** :414–25.
- 472 32. Roffey DM, Byrne NM, Hills AP. (2006) Day-to-day variance in measurement of resting metabolic  
473 rate using ventilated-hood and mouthpiece & nose-clip indirect calorimetry systems. *J Parent.*  
474 *Ent. Nutr* **30** :426-32.
- 475 33. Henry CJK. (2005) Basal metabolic rate studies in humans: measurement and development of  
476 new equations. *Public Health Nutr* **8** :1133-52.
- 477 34. Blasbalg, T.L. et al (2011) Changes in consumption of omega-3 and omega-6 fatty acids in the  
478 United States during the 20<sup>th</sup> century. *AJCN* **93**: 950-962.
- 479 35. Fan, R., Koehler, K and Chung, S. (2019) Adaptive thermogenesis by dietary n-3 polyunsaturated  
480 fatty acids: emerging evidence and mechanisms. *BBA – molecular and cell biology of lipids*.  
481 **1864**: 59-70

- 482 36. Van Marken Lichtenbelt, W.D., Mansink, R.P. and Westerterp, K.R. (1997) The effect of fat  
483 composition of the diet on energy metabolism. *Z. ernharnungs.* **36**: 303-305.
- 484 37. Katz, M. et al (2009) Dietary n-3-polyunsaturated fatty acids and energy balance in overweight  
485 or moderately obese men and women: a randomized controlled trial. *Nutr. and metab.* **6**: e24
- 486 38. De Meira, J.E.C., et al (2018) Unsaturated fatty acids do not have a favourable metabolic  
487 response in overweight subjects: results of a meta-analysis. *J. Functional foods.* **43**: 123-130.
- 488 39. Haggerty, C. et al (2008) Intra-specific variation in resting metabolic rate in MF1 mice is not  
489 associated with membrane lipid desaturation in the liver. *Mech Ag. Dev* **129**: 129-137.
- 490 40. Brzek et al. (2007) Anatomic and molecular correlates of divergent selection for basal metabolic  
491 rate in laboratory mice. *Physiological and Biochemical Zoology*, **80**: 491-99.
- 492 41. McGill, C.R. et al (2015) Ten-year trends in Fiber and whole grain intakes and food sources for  
493 the United states population: national health and nutrition examination survey 2001-2010.  
494 *Nutrients* **7**: 1119-1130.
- 495 42. Karl, J.P. et al (2017) Substituting whole grains for refined grains in a 6-wk randomized trial  
496 favorably affects energy-balance metrics in healthy men and postmenopausal women. *Am. J.*  
497 *Clin. Nut.* **105**: 589-599.

498  
499 *References only in the methods*

- 500 43. Speakman, J.R. and Pontzer, H. (2023: in review) Quantifying physical activity energy  
501 expenditure based on doubly-labelled water and basal metabolism calorimetry: what are we  
502 actually measuring? *Current opinion in clinical nutrition and metabolic care*
- 503 44. Weir, J.B. (1949) new methods for calculating metabolic rate with special reference to protein  
504 metabolism. *J. Physiol.* **109**: 1-9.
- 505 45. Wang, Z.M., Deurenberg, P., Wang, W., Pietrobielli, P., Baumgartner, R.N. and Heymsfield, S.B.  
506 (1999) Hydration of fat-free body mass: review and critique of a classic body composition  
507 constant. *Am J. Clin Nut.* **69**: 833-841.
- 508 46. Pontzer, H. et al (2021) Daily energy expenditure through the human life course. *Science* **373**:  
509 808+
- 510 47. Rudolph, M. C., Wellberg, E.A., Lewis, A.S., Terrell, K.L., Merz, A.L., Maluf, N.K., Serkova, N.J. and  
511 Anderson, S.M. (2014) Thyroid hormone responsive protein Spot14 enhances catalysis of fatty  
512 acid synthase in lactating mammary epithelium. *J Lipid Res* **55**: 1052-1065
- 513 48. Rudolph, M. C., Karl Maluf, N., Wellberg, E.A., Johnson, C.A., Murphy, R.C. and Anderson, S.M.  
514 (2012) Mammalian fatty acid synthase activity from crude tissue lysates tracing (1)(3)C-labeled  
515 substrates using gas chromatography-mass spectrometry. *Anal Biochem* **428**: 158-166

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518 **Requests for materials**

519 Correspondence should be directed to Dr John Speakman ([j.speakman@abdn.ac.uk](mailto:j.speakman@abdn.ac.uk)). Forms for  
520 requesting data from the IAEA DLW database can be found at [www.dlwdatabase.org](http://www.dlwdatabase.org) and should be  
521 directed to the lead corresponding author [j.speakman@abdn.ac.uk](mailto:j.speakman@abdn.ac.uk) or Dr Alexia Alford at the IAEA

522 ([a.alford@iaea.org](mailto:a.alford@iaea.org)). Requests for the reviewed BMR data should be directed to Dr Anura Kurpad  
523 ([a.kurpad@sjri.res.in](mailto:a.kurpad@sjri.res.in)). Requests for the mouse data should be directed to Dr Matthew Rodeheffer  
524 ([matthew.rodeheffer@yale.edu](mailto:matthew.rodeheffer@yale.edu)).

525

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538 no role in the content of this manuscript.

## 539 **Author contributions**

540 JRS, KRW and LH processed and analysed the IAEA data, JMAJ, JLK, and MCR collected, processed and  
541 analysed the mouse data, SS, SG, JRS and AK collected and analysed the retrospective BMR data from  
542 the literature. JRS, YY, HS, PNA, LFA, LJA, LA, IB, KBA, EEB, SB, AGB, CVCB, PB, MSB, NFB, SGJAC, GLC,  
543 JAC, RC, SKD, LRD, UE, SE, TF, BWF, AHG, MG, CH, AEH, MBH, SH, NJ, AMJ, PK, KPK, MK, WEK, RFK, EVL,  
544 AML, WRL, NL, CKM, ACM, EPM, JCM, JPM, MLN, TAN, RMO, HP, KHP, YPP, JPR, GP, RLP, RAR, SBR, DAR,  
545 ER, LMR, RMR, JR, SBR, MR, DAS, AJS, AMS, ES, SSU, GV, LMvE, EAvm, JCKW, GW, BMW, WWW, JAY, TY,  
546 XYZ contributed data to the database. JRS, YY, HS, SS, AJMM, CU, AHL, HP, JR, DAS and WWW created,  
547 curated and administered the database.

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**Conflict of interest**

The authors have no conflicts of interest to declare.

**Data Availability**

With respect to the IAEA database and the meta-analysis of BMR data this work comprises a secondary analysis of data that are mostly already published and available in the primary literature. These data have been compiled into a database, access to which is free. Forms for requesting data can be found at [www.dlwdatabase.org](http://www.dlwdatabase.org) and should be directed to the lead corresponding author [j.speakman@abdn.ac.uk](mailto:j.speakman@abdn.ac.uk) or Dr Alexia Alford at the ([a.alford@iaea.org](mailto:a.alford@iaea.org)). The BMR data are available upon request to co-corresponding author Dr Anura Kurpad ([a.kurpad@sjri.res.in](mailto:a.kurpad@sjri.res.in)). The mouse data described in the paper are available upon request to co-corresponding author Dr Matthew Rodeheffer ([matthew.rodeheffer@yale.edu](mailto:matthew.rodeheffer@yale.edu)).

573

574 **Figure legends**

575 **Figure 1:** Trends over time in a) adjusted total energy expenditure, b) adjusted basal energy  
576 expenditure, and c) adjusted activity energy expenditure for males. Adjustments were made for  
577 body composition (fat and fat-free mass or body mass, and age) – see methods for details. All  
578 expenditures are in MJ/d and time is expressed in months since January 1982. Significant years  
579 are also indicated. Each data point is a different measurement of expenditure. The red lines are  
580 the fitted least squares regression fits. For regression details refer to text and Table 1.

581 **Figure 2:** Trends over time in a) adjusted total energy expenditure, b) adjusted basal energy  
582 expenditure, and c) adjusted activity energy expenditure for females. Adjustments were made  
583 for body composition (fat and lean mass and age) – see methods for details. Significant years  
584 are also indicated. All expenditures are in MJ/d and time is expressed in months since January  
585 1982. Each data point is a different individual measurement of expenditure. The red lines are  
586 the fitted least squares regression fits. For regression details refer to text and Table 1.

587 **Figure 3:** A: effect of  $\log_e$  body mass on the  $\log_e$  basal metabolic rate (BMR) in a systematic  
588 review of 165 studies dating back to the early 1900s (first study 1919). Data for males in blue  
589 and for females in red. Studies with mixed male and female data not illustrated. B: Bubble plot  
590 showing the Residual  $\log_e$  Basal metabolism derived from a weighted regression of  $\log_e$  BMR  
591 against sex, age and  $\log_e$  (body mass) plotted against date of measurement in the same 165  
592 studies. Bubbles represent the sample size of the studies. The red line is the fitted weighted  
593 regression.

594 **Figure 4:** A: the relationship between body weight and metabolic rate in the mice fed different  
595 diets with variable fatty acid compositions. B: the effect of saturated fatty acid intake on  
596 residual metabolic rate – corrected for body weight.

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606 **Table one:** Patterns of change in components of energy expenditure in males and females since  
 607 the early 1990s. Data are shown unadjusted and adjusted for body composition and age. The  
 608 gradient of the fitted relationships with time are translated to the overall change in expenditure  
 609 (MJ) over 30 years with the 95% confidence intervals (95%CI) for this change. TEE = total energy  
 610 expenditure, BEE = basal energy expenditure, AEE = activity energy expenditure (=0.9TEE-BEE).  
 611 Significance of the relationships is also shown.  $p > .01$  was considered not significant (ns).

612 **Males**

613 **Unadjusted data**

614 Variable	615 Mean change over 30 y (MJ/d)	616 95% CI ( $\pm$ MJ/d)	617 Significance
618 TEE	+0.55	0.73	ns
619 BEE	-1.19	0.536	$p < .00002$
620 AEE	+0.50	0.695	ns

621 **Adjusted data**

622 TEE	-0.93	0.46	$p < .0001$
623 BEE	-0.96	0.15	$p < 10^{-9}$
624 AEE	+1.01	0.53	$p < .0003$

625

626 **Females**

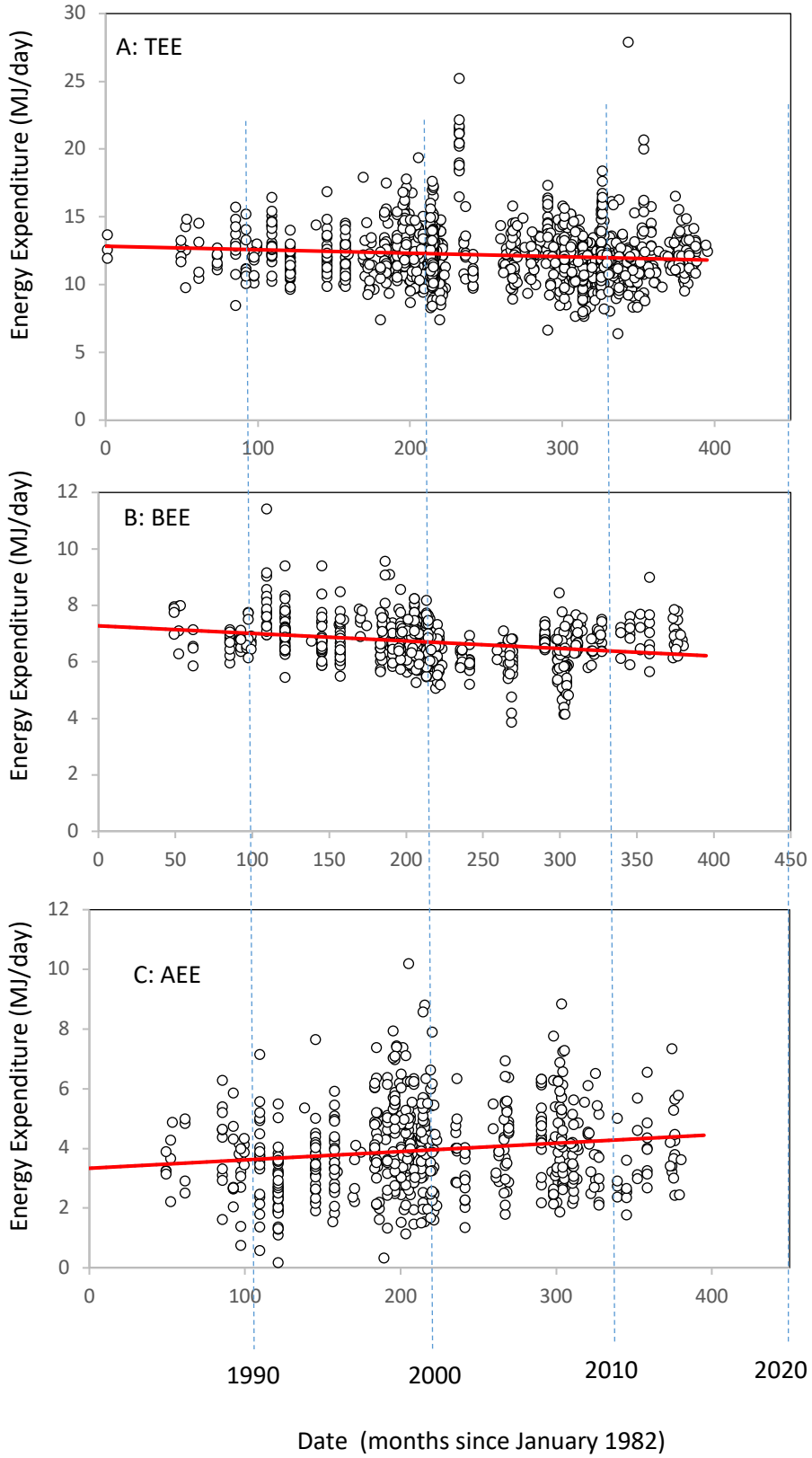
627 **Unadjusted data**

628 Variable	629 Mean change over 30 y (MJ/d)	630 95% CI	631 Significance
632 TEE	-0.16	0.360	ns
633 BEE	-0.32	0.352	ns
634 AEE	+0.18	0.452	ns

635 **Adjusted data**

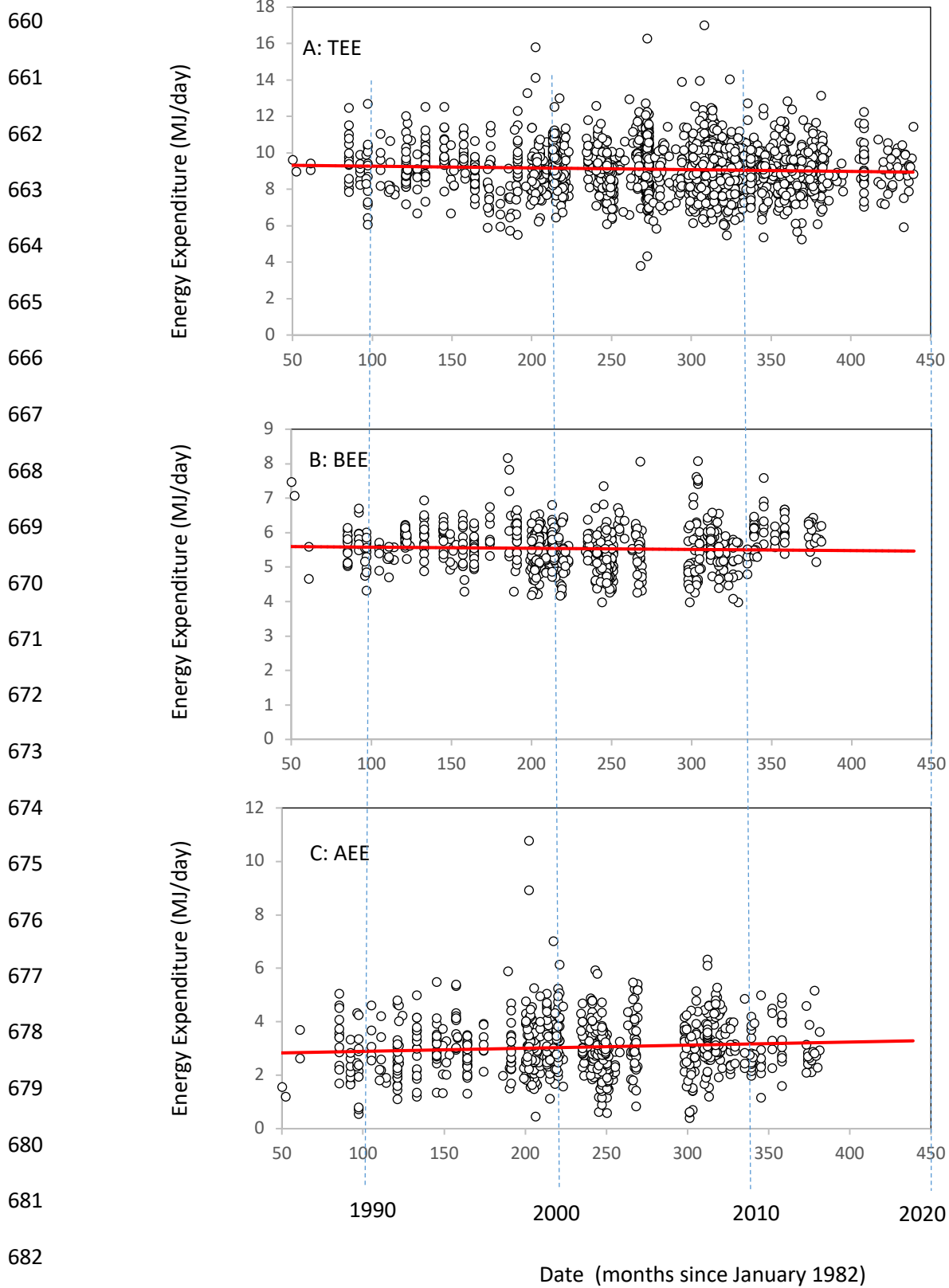
636 TEE	-0.51	0.26	$p < .00002$
637 BEE	-0.12	0.215	ns
638 AEE	+0.42	0.367	$p = 0.026$

635 **Figure 1**



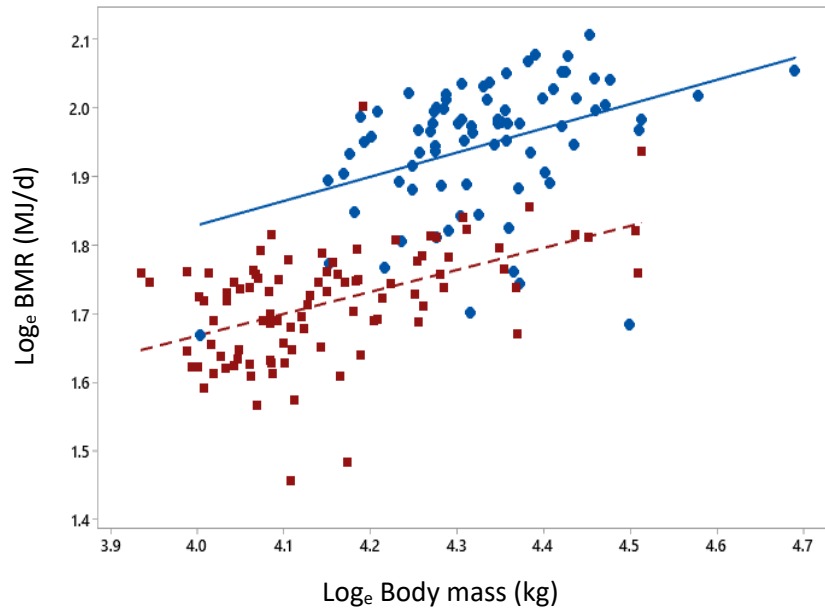


659 **Figure 2**

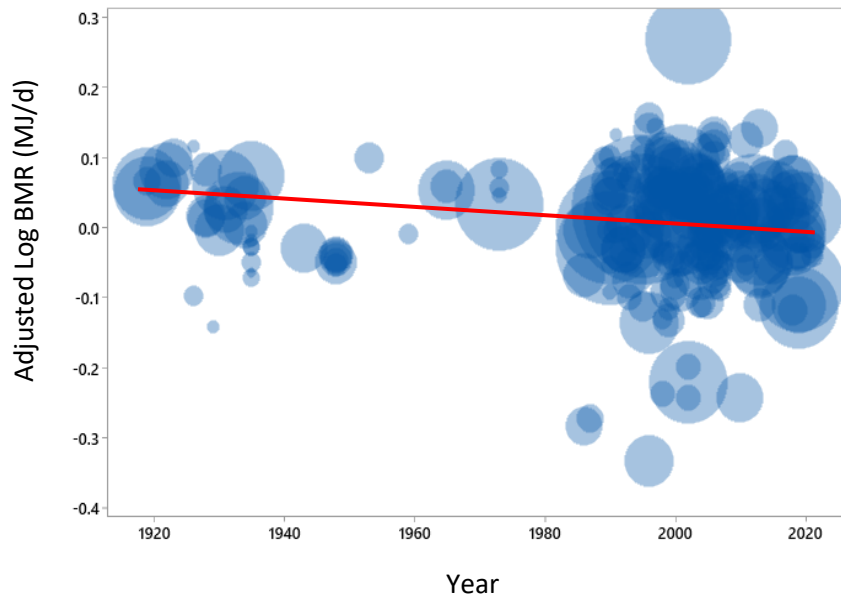


683 **Figure 3**

684 **A:**

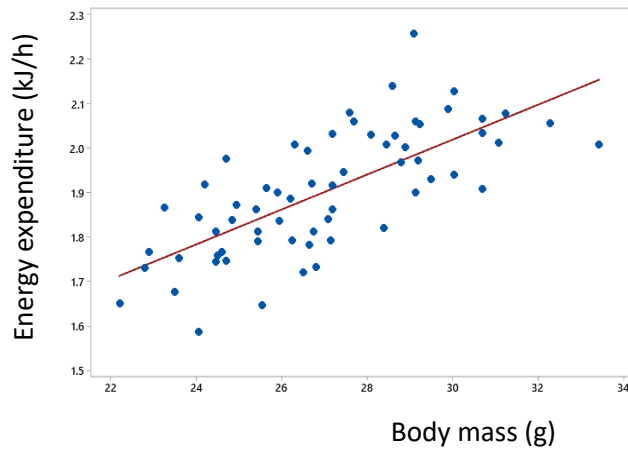


692 **B:**

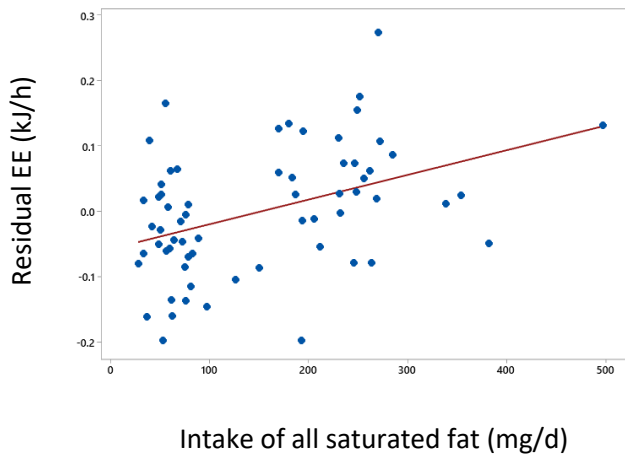


705 **Figure 4**

706 **A**



**B**



727 **Supplementary materials for**

728 Speakman et al *Total daily energy expenditure has declined over the last 4 decades due to*  
729 *declining basal expenditure not reduced activity expenditure.*

- 730 Contents      1. Materials and Methods  
731                    2, Supplementary figures  
732                    3. Supplementary tables  
733                    4. group authorship details.

734 **1. Materials and methods**

735 This study involves in part a retrospective analysis of data submitted to the IAEA DLW database  
736 (www.dlwdatabase.org). The data stretch back to the late 1980s, however, the clinical trials  
737 registry was only launched by the NIH in February 2000, hence, there was no possibility to pre-  
738 register the work before data collection started. Nevertheless, the analysis performed here was  
739 pre-registered on the IAEA DLW database website in 2020 ([https://doubly-labelled-water-](https://doubly-labelled-water-database.iaea.org/dataAnalysisPlanned)  
740 [database.iaea.org/dataAnalysisPlanned](https://doubly-labelled-water-database.iaea.org/dataAnalysisPlanned)).

741 **DLW database study**

742 Data were extracted from the IAEA Doubly Labeled Water (DLW) Database<sup>15</sup>, version 3.1.2,  
743 compiled in April, 2020, and then later while the manuscript was in review this was expanded  
744 to include additional data extracted from version 3.7.1. In total this latter version of the  
745 database comprises 8,313 measurements of TEE using the DLW method. We selected from the  
746 database measurements of adults aged >18 y, living in either Europe or the USA, that also had a  
747 record of age. We excluded individuals who were professional athletes, individuals engaged in  
748 unusual levels of activity (e.g. climbing mountains or participating in a long distance running

749 race), pregnant and lactating females and individuals with specific disease states. In total this  
750 resulted in 4799 measurements across both sexes. Submissions to the database did not reveal  
751 whether the sex was self-reported or assigned. Although an option was available to designate  
752 individuals as trans-sexual, none of the submitted data were identified as such. Gender was not  
753 available from the submitted data. Estimates of TEE were recalculated using a common  
754 equation<sup>16</sup> which has been shown to perform best in validation studies. The final data set  
755 included 1672 measurements of males and 3127 measurements of females.

756

757 For 632 of the males and 800 of the females we also had measurements of basal metabolic rate  
758 (BMR) measured by indirect calorimetry. BMR measurements were derived either from hood  
759 calorimetry or from minimal metabolic rate determined overnight during chamber calorimetry  
760 (strictly sleeping metabolic rates or SMR). We converted these BMR or SMR to estimates of  
761 basal energy expenditure (BEE). BMR and SMR are measured for relatively short periods lasting  
762 30 minutes to an hour. BEE is a theoretical value for the energy expenditure that would pertain  
763 if this BMR/SMR measurement was sustained for 24h. For those individuals with measurements  
764 of both BEE and TEE we estimated activity energy expenditure ( $AEE = (0.9 * TEE) - BEE$ ), and the  
765 physical activity level ( $PAL = TEE / BEE$ ). The value 0.9 in the equation for AEE assumes the  
766 thermic effect of food (TEF) is 10% of the total energy expenditure. In practice this varies  
767 between individuals and is dependent on the diet. Variation is introduced therefore by  
768 imprecision in this value. However, since the TEF is largely dependent on protein in the diet,  
769 and protein intakes have remained stable over the last 40 or so years there is unlikely to be any  
770 systematic imprecision in the value that could affect the detected trends. It is important to

771 note that TEE and BEE are both measured directly, while AEE is only inferred from the  
772 difference between the two. The accuracy and precision of TEE relative to chamber indirect  
773 calorimetry for the equation utilized here was estimated at 0.4% (accuracy) and 7.7%  
774 (precision)<sup>16</sup>. The accuracy and precision of estimates of basal metabolic rates of metabolism  
775 inferred by indirect calorimetry has been evaluated using alcohol burns and is estimated at  
776 around 1-2%. Error in the estimate of AEE by subtraction is considerably higher than the direct  
777 estimates of TEE and BEE<sup>43</sup>.

778  
779 The DLW method is based on the differential elimination of isotopes of oxygen and hydrogen  
780 introduced into the body water<sup>13</sup>. The details of the practical implementation of the method  
781 and its theoretical basis have been previously published. We recently derived a new equation  
782 for the calculation of CO<sub>2</sub> production using the technique<sup>16</sup> and recalculated the entries in the  
783 database using this common equation. These were then converted into energy expenditure  
784 using the Weir equation<sup>44</sup> with food quotients derived from the original studies.

785  
786 Additional characteristics of the subjects (body mass (BM), age, and sex) were measured using  
787 standard protocols. We estimated the fat-free mass (FFM) of individuals using the estimated  
788 total body water and an assumed hydration constant for lean tissue of 0.73 (ref 45) and then  
789 calculated fat mass by difference (FM = BM-FFM). The date of the measurement was expressed  
790 in months relative to January 1982 which was the first year that the DLW method was applied  
791 to human subjects.

792

793 In the first set of analyses we used the unadjusted measures of TEE, BEE and AEE as dependent  
794 variables in general linear models with time since January 1982 as the predictor. Tests were  
795 two-sided and  $p < .05$  was taken as significant. All analyses were performed using Minitab v19.  
796 It is well established that TEE, BEE and AEE depend on body composition, as well as subject age.  
797 Patterns of variation in unadjusted values with time might then reflect biased population  
798 sampling with respect to these traits. For example, if more older subjects were sampled later in  
799 the time course this might give a spurious indication that TEE was declining since all EE  
800 parameters decline after  $\sim 60y^{46}$ . We adjusted (logarithmically) TEE, BEE and AEE using  $\log_e$  FFM,  
801  $\log_e$  FM and age as the predictor variables using general linear modelling. Analyses were run  
802 separately for each sex therefore no adjustment for sex was necessary. In both sexes, for  $\log_e$   
803 BEE, the predictors age,  $\log_e$  FFM and  $\log_e$  FM were all significant but for  $\log_e$  TEE and  $\log_e$  AEE,  
804 only age and  $\log_e$  FFM were significant. In the latter cases we deleted the non-significant  
805 predictor and re-ran the analyses. Following the above procedure we then calculated the  
806 residuals to the fitted models and added them back to the mean logged TEE, BEE and AEE  
807 across all measurements. These values were then converted back to measures of 'adjusted  
808 TEE', 'adjusted BEE' and 'adjusted AEE' by taking the exponent of the derived values. We then  
809 checked that the residuals were normally distributed and the adjusted variables were not  
810 significantly related to any of the predictor variables to ensure that the adjustment was  
811 adequate. Tests applied were two-sided and  $p < .05$  was taken as significant. We then sought  
812 relationships between the adjusted variables and date of measurement using linear regression.  
813 The adjusted variables cover a narrower time span from 1990 to 2017.

814

## 815 **Sensitivity analyses**

816 We performed several checks on the data to make sure the trends were not being driven by  
817 individual studies. First there were some small studies in males prior to 1987 that may have  
818 exerted undue leverage in the analysis. We therefore excluded these data and reran all the  
819 regressions (Table S1). There were no significant changes in any of the parameters. Since the  
820 downward trend in BEE was the most important new finding we directed particular attention to  
821 this trend.

822 To evaluate if the male BEE data would be better fit by a more complex model than the linear  
823 model we used, we included higher order terms of the date into a regression analysis. In this  
824 analysis the  $r^2$  explained by date, date<sup>2</sup> and date<sup>3</sup> was increased relative to just including date  
825 alone. However, the variance inflation factors (VIF) for these more complex models were  
826 enormous. When date and date<sup>2</sup> were included the VIF for each variable was 28.9, and when all  
827 3 were included the VIF values were 438 for date, 2084 for date<sup>2</sup> and 663 for date<sup>3</sup>. The usual  
828 VIF cut-off for deciding whether to include an extra term into a model is 5. In this case it was  
829 clear that higher order terms were not justified relative to a simple linear model.

830 We performed a general linear model analysis with date as a covariate and study as a factor in  
831 the model. In males when we used such a model there was indeed a large study effect (F =  
832 12.97,  $p < 10^{-15}$ ) but the effect of date remained highly significant (F= 22.87,  $P < 10^{-8}$ ) and  
833 strongly negative (coefficient = -1.85 MJ/d over 30 years), exceeding that in the original  
834 analysis. In females there was also a strong study effect (F = 9.54,  $P < 10^{-12}$ ) but the effect of  
835 date remained non-significant (F = 12.9,  $P = 0.256$ ).



836 Using the post 1987 data we then systematically removed the data for each study and reran the  
837 analyses to see if any particular study exerted undue effects on the regression. The analyses are  
838 summarized in Table S2. This analysis showed that no individual study was responsible for the  
839 negative relationship. In all cases the relationship between BMR and time remained negative  
840 and highly significant. A single study (number 23 in 1991) involved relatively high BMR values  
841 and so omitting it reduced the coefficient and the significance. But the p value for the  
842 regression when omitting these data was still highly significant  $P < 10^{-5}$ , and the coefficient still  
843 strongly negative and biologically important.

844 We then turned our attention to the female data for BEE against date to see if the absence of a  
845 relationship there might be because of inclusion of any particular study. We used the same  
846 leave one out procedure as used for the males. The results are shown in Table S3. In this case  
847 the pattern was very different in that the relationship was always not significant ( $P > 0.1$ ),  
848 except when a single study (study 65) was removed from the analysis, and in that case the  
849 relationship became significant ( $P = 0.001$ ) and the negative gradient (extrapolated to over 30  
850 years) increased to  $-0.39$  MJ/day. Omitting a second study ( $n = 69$ ) has a smaller effect that also  
851 resulted in the relationship becoming marginally significant ( $p = 0.037$ ). If both studies 65 and  
852 69 were omitted (not shown in table) the p value for the relationship fell to  $P < 10^{-5}$  and the  
853 gradient was  $-0.59$  MJ/d. Study 65 was a study of overweight individuals by Camps et al (2013).

854 We have no objective reason to reject these data but it is interesting that the anomalous  
855 absence of a negative relationship of BMR to time in the females is dependent only on inclusion  
856 of this one study. It is worth noting that excluding this study from the male data strengthened  
857 the relationship for males (Table S2).

## 858 **Systematic review of BMR trends**

859 This systematic review was registered at PROSPERO, 2021 (CRD42021270242) and executed per  
860 PRISMA guidelines (see supplementary Fig S6). The details of search strategy, data extraction and  
861 analysis were as follows.

### 862 *Search Strategy*

863 A literature search was carried out on PubMed using the following keywords: “Basal  
864 metabolic rate”, “BMR”, “basal energy expenditure”, “BEE”, “resting metabolic rate”, “RMR”,  
865 “resting energy expenditure”, “REE”, “Indirect calorimetry”, “open circuit indirect calorimetry”,  
866 “ventilated hood indirect calorimetry”, “healthy”, “apparently healthy”. Papers published in  
867 English from 1900 to 2021 were considered. Cross-references from these papers were also  
868 evaluated.

### 869 *Eligibility and study selection*

870 Papers reporting the measurement of BMR (or BEE) or resting metabolic rate (RMR) on  
871 healthy male and female adults, aged 18-65 years, across different body mass index (BMI) were  
872 included. Additionally, only studies on either the American or European population were  
873 considered. Data were abstracted from cross-sectional studies as well as randomized controlled  
874 trials (RCTs). For RCTs, the data collected for control group, which met our inclusion criteria, were  
875 included. Studies on infants, children, adolescents, elderly, moderate or heavy activity workers,  
876 soldiers and athletes were excluded. The study selection was carried out in two levels: first,  
877 articles were included based on their title and abstract; second, the included articles were again  
878 filtered based on a reading of their full text. Finally, 163 studies were included into the analysis,  
879 as listed in the references below.

### 880 *Data Extraction*

881 From the selected articles, data on age, sex, geography, population/ethnicity, sample size,  
882 weight, height, body mass index, physical activity level, fat mass, fat free mass, method of  
883 measuring BMR or RMR, measured value for BMR or RMR, and the instrument error or intra-

884 individual variability were extracted where available. When raw data were available in some  
885 papers, the individual data was included in the analysis. When BMR or RMR was reported as kcal  
886 or KJ per day, it was converted to MJ per day. When the BMR or RMR data was provided as per  
887 kg body weight or fat free mass (FFM) or per square meters surface area, then it was converted  
888 to MJ per day by multiplying the respective body weight, FFM or surface area. Finally, assuming  
889 that RMR is 10% higher than BMR, any reported RMR data were converted to BMR as  $0.9 \times \text{RMR}$ .  
890 Where mean for age and weight was not provided in the paper [11,21,23,75,80,93,146,154], but  
891 range or dispersion indicators of age and weight (minimum/maximum or 95% CI or IQR) were  
892 provided, the middle values of these were transformed to obtain the mean values. In some  
893 papers, rather than body weight, FFM and fat mass (FM) values were reported; here, these were  
894 added to obtain the body weight [47,84,93,151,159]. When SD or SE of weight was provided,  
895 these were converted to 95% CI. If FFM and body weight were reported, the FM was calculated  
896 as a difference between body weight and FFM.

897 The data were extracted, sorted, coded and entered into an Excel workbook; statistical analyses  
898 were carried out on R version 4.1.0 (R Core Team, 2021, Vienna, Austria). A weighted regression  
899 analysis of  $\log_e$  BMR (MJ) on time was performed where  $\log_e$  (body weight), age and sex were  
900 considered as covariates along with regression weights assigned to studies based on their study  
901 size (n).

902

### 903 **References for studies included in the systematic review**

- 904 1. Benedict FG, Miles WR, Roth P, Smith HM. Human vitality and efficiency under prolonged restricted  
905 diets. Washington DC: Carnegie Institute 1919; Publication no. 280, pp 701.
- 906 2. Harris JA, Benedict FG. A biometric study of basal metabolism in man. Washington DC: Carnegie  
907 Institute 1919; Publication no. 279, pp 266.
- 908 3. Boothby WM, Sandiford I. Summary of the basal metabolism data on 8614 subjects with special  
909 reference to the normal standards for the estimation of the basal metabolic rate. J Biol Chem  
910 1922;54:783-803.
- 911 4. Hobson FG. A comparative study of basal metabolism in normal men. Quart J Med 1923;16:363-389.
- 912 5. Hafkesbring R, Borgstrom P. Studies on basal metabolism in New Orleans. Am J Physiol 1926-  
913 27;79:221-228.

- 914 6. Benedict FG. Basal metabolism data on normal men and women (series II) with some considerations  
915 on the use of prediction standards. *Am J Physiol* 1928;85:607-620.
- 916 7. Griffiths Jr FR, Pucher GW, Bronwell KA, Klein JD, Carmer MF. Studies in human physiology: the  
917 metabolism and body temperature (oral) under basal conditions. *Am J Physiol* 1928-29;87:602-603.
- 918 8. Gustafson FL, Benedict FG. The seasonal variation in basal metabolism. *Am J Physiol* 1928;86:43-58.
- 919 9. Tilt J. The basal metabolism of young college women in Florida. *J Biol Chem* 1930;86:635-641.
- 920 10. Remington RE, Culp FB. Basal metabolic rate of medical students and nurses in training at Charleston,  
921 SC. *Archs Int Med* 1931;47:366-375.
- 922 11. Stark ME. Standards for predicting basal metabolism I Prediction for girls from 17-21. *J Nutr*  
923 1933;6:11-35.
- 924 12. Mason ED. The basal metabolism of European women in South India and the effect of change of  
925 climate on European and South Indian women. *J Nutr* 1934;8:695-713.
- 926 13. Wising PJ. The basal metabolism of healthy subjects in Sweden. *Acta Med Scand* 1934;81:487-510.
- 927 14. McKittrick EJ. Basal metabolism of Wyoming University women. *J Nutr* 1935;11:319-325.
- 928 15. Tilt J, Walters CF. The basal metabolism and diet of normal young college women in Florida. *J Nutr*  
929 1935;9:109-117.
- 930 16. Lewis RC, Iloff A, Duval AM. Further considerations of the effect of altitude on basal metabolism: A  
931 study of young women residents of Denver. *J Nutr* 1943;26:175-185.
- 932 17. Thompson EM, Cox EW, Ridgeway AM. The basal metabolism of two hundred and eighteen girls and  
933 young women of Southern Arizona, fourteen to twenty one years of age, inclusive. *J Nutr*  
934 1948;36:507-517.
- 935 18. Munro AF. Basal metabolic rates and physical fitness scores of British and Indian males in the tropics.  
936 *J Physiol* 1950;110:356-366.
- 937 19. Wedgewood RJ, Bass DE, Klimas JA, Kleeman CR, Quinn M. Relationship of body composition to basal  
938 metabolic rate in normal men. *J Appl Physiol* 1953;6:317-334.
- 939 20. Thompson EM, Staley MG, Kight MA, Mayfield ME. The effect of high environmental temperature on  
940 basal metabolism and serum ascorbic acid concentration of women. *J Nutr* 1959;68:35-47.
- 941 21. Gill MB, Pugh LGCE. Basal metabolism and respiration in men living at 5800 M (19000 FT). *J App*  
942 *Physiol* 1964;19:949-954.
- 943 22. Mason ED, Jacob M, Balakrishnan V. Racial group differences in the basal metabolism and body  
944 composition of Indian and European women in Bombay. *Hum Biol* 1964;36:374-396.
- 945 23. Hamberger L, Lundgren O. Basal metabolic rate in a group of young medical students with note on  
946 body surface area formulas. *Scand J Clin Lab Invest* 1965;17:281-286.
- 947 24. Bailey D, Harry D, Johnson RE, Kupprat I. Oscillations in oxygen consumption of man at rest. *J Appl*  
948 *Physiol* 1973;34:467-470.
- 949 25. Hannon JP, Sundman DM. Basal metabolic and cardiovascular function of women during altitude  
950 acclimatization. *J App Physiol* 1973;34:471-477.
- 951 26. Keys A, Taylor HL, Grande F. Basal metabolism and age of adult man. *Metabolism* 1973;22:579-587.
- 952 27. Owen OE, Kavle E, Owen RS, Polansky M, Caprio S, Mozzoli MA, Kendrick ZV, Bushman MC, Boden G.  
953 A reappraisal of caloric requirements in healthy women. *Am J Clin Nutr.* 1986;44(1):1-19.

- 954 28. McAnena OJ, Harvey LP, Katzeff HL, Daly JM. Indirect calorimetry: comparison of hood and mask  
955 systems for measuring resting energy expenditure in healthy volunteers. *JPEN J Parenter Enteral*  
956 *Nutr.* 1986;10(6):555-7.
- 957 29. Leff ML, Hill JO, Yates AA, Cotsonis GA, Heymsfield SB. Resting metabolic rate: measurement  
958 reliability. *JPEN J Parenter Enteral Nutr.* 1987;11(4):354-9.
- 959 30. Owen OE, Holup JL, D'Alessio DA, Craig ES, Polansky M, Smalley KJ, Kavle EC, Bushman MC, Owen LR,  
960 Mozzoli MA. A reappraisal of the caloric requirements of men. *Am J Clin Nutr.* 1987;46(6):875-85.
- 961 31. Raurich JM, Ibanez J, Marse P. Validation of a new closed circuit indirect calorimetry method  
962 compared with the open Douglas bag method. *Intensive Care Med.* 1989;15(4):274-8.
- 963 32. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting  
964 energy expenditure in healthy individuals. *Am J Clin Nutr.* 1990;51(2):241-7.
- 965 33. Welle S, Nair KS. Relationship of resting metabolic rate to body composition and protein turnover.  
966 *Am J Physiol.* 1990;258(6 Pt 1):E990-8.
- 967 34. Merli M, Riggio O, Romiti A, Ariosto F, Mango L, Pinto G, Savioli M, Capocaccia L. Basal energy  
968 production rate and substrate use in stable cirrhotic patients. *Hepatology.* 1990;12(1):106-12.
- 969 35. Thorne A, Wahren J. Diminished meal-induced thermogenesis in elderly man. *Clin Physiol.*  
970 1990;10(5):427-37.
- 971 36. Hommes MJ, Romijn JA, Godfried MH, Schattenkerk JK, Buurman WA, Endert E, Sauerwein HP.  
972 Increased resting energy expenditure in human immunodeficiency virus-infected men. *Metabolism.*  
973 1990;39(11):1186-90.
- 974 37. Spicher V, Roulet M, Schutz Y. Assessment of total energy expenditure in free-living patients with  
975 cystic fibrosis. *J Pediatr.* 1991;118(6):865-72.
- 976 38. Vermeij CG, Feenstra BW, Oomen AM, de Graaf EJ, Zillikens MC, Swart GR, Bruining HA. Assessment  
977 of energy expenditure by indirect calorimetry in healthy subjects and patients with liver cirrhosis.  
978 *JPEN J Parenter Enteral Nutr.* 1991;15(4):421-5.
- 979 39. Hommes MJ, Romijn JA, Endert E, Sauerwein HP. Resting energy expenditure and substrate oxidation  
980 in human immunodeficiency virus (HIV)-infected asymptomatic men: HIV affects host metabolism in  
981 the early asymptomatic stage. *Am J Clin Nutr.* 1991;54(2):311-5.
- 982 40. Roberts SB, Heyman MB, Evans WJ, Fuss P, Tsay R, Young VR. Dietary energy requirements of young  
983 adult men, determined by using the doubly labeled water method. *Am J Clin Nutr.* 1991;54(3):499-  
984 505.
- 985 41. Schols AM, Schoffelen PF, Ceulemans H, Wouters EF, Saris WH. Measurement of resting energy  
986 expenditure in patients with chronic obstructive pulmonary disease in a clinical setting. *JPEN J*  
987 *Parenter Enteral Nutr.* 1992;16(4):364-8.
- 988 42. Thorne A, Johansson U, Wahren J, Eriksson S. Thermogenic response to intravenous nutrition in  
989 patients with cirrhosis. *J Hepatol.* 1992;16(1-2):145-52.
- 990 43. Franssila-Kallunki A, Groop L. Factors associated with basal metabolic rate in patients with type 2  
991 (non-insulin-dependent) diabetes mellitus. *Diabetologia.* 1992;35(10):962-6.
- 992 44. Leenen R, van der Kooy K, Deurenberg P, Seidell JC, Weststrate JA, Schouten FJ, Hautvast JG. Visceral  
993 fat accumulation in obese subjects: relation to energy expenditure and response to weight loss. *Am*  
994 *J Physiol.* 1992;263(5 Pt 1):E913-9.

- 995 45. Bullough RC, Melby CL. Effect of inpatient versus outpatient measurement protocol on resting  
996 metabolic rate and respiratory exchange ratio. *Ann Nutr Metab.* 1993;37(1):24-32.
- 997 46. Schneeweiss B, Pammer J, Ratheiser K, Schneider B, Madl C, Kramer L, Kranz A, Ferenci P, Druml W,  
998 Grimm G, et al. Energy metabolism in acute hepatic failure. *Gastroenterology.* 1993;105(5):1515-21.
- 999 47. Svendsen OL, Hassager C, Christiansen C. Impact of regional and total body composition and  
1000 hormones on resting energy expenditure in overweight postmenopausal women. *Metabolism.*  
1001 1993;42(12):1588-91.
- 1002 48. Hugli O, Frascarolo P, Schutz Y, Jequier E, Leuenberger P, Fitting JW. Diet-induced thermogenesis in  
1003 chronic obstructive pulmonary disease. *Am Rev Respir Dis.* 1993;148(6 Pt 1):1479-83.
- 1004 49. Mathieu RL, Casez JP, Jaeger P, Montandon A, Peheim E, Horber FF. Altered body composition and  
1005 fuel metabolism in stable kidney transplant patients on immuno-suppressive monotherapy with  
1006 cyclosporine A. *Eur J Clin Invest.* 1994;24(3):195-200.
- 1007 50. Roubenoff R, Roubenoff RA, Cannon JG, Kehayias JJ, Zhuang H, Dawson-Hughes B, Dinarello CA,  
1008 Rosenberg IH. Rheumatoid cachexia: cytokine-driven hypermetabolism accompanying reduced body  
1009 cell mass in chronic inflammation. *J Clin Invest.* 1994;93(6):2379-86.
- 1010 51. Platte P, Pirke KM, Trimborn P, Pietsch K, Krieg JC, Fichter MM. Resting metabolic rate and total  
1011 energy expenditure in acute and weight recovered patients with anorexia nervosa and in healthy  
1012 young women. *Int J Eat Disord.* 1994;16(1):45-52.
- 1013 52. Goran MI, Calles-Escandon J, Poehlman ET, O'Connell M, Danforth E Jr. Effects of increased energy  
1014 intake and/or physical activity on energy expenditure in young healthy men. *J Appl Physiol* (1985).  
1015 1994;77(1):366-72.
- 1016 53. Koot P, Deurenberg P. Comparison of changes in energy expenditure and body temperatures after  
1017 caffeine consumption. *Ann Nutr Metab.* 1995;39(3):135-42.
- 1018 54. Lyon X, Schutz Y, Buclin T, Jequier E, Deriaz O. Inhibition of Na(+)-K(+)-ATPase by digoxin and its  
1019 relation with energy expenditure and nutrient oxidation rate. *Am J Physiol.* 1995;268(6 Pt 1):E1051-  
1020 6.
- 1021 55. Wigmore SJ, Falconer JS, Plester CE, Ross JA, Maingay JP, Carter DC, Fearon KC. Ibuprofen reduces  
1022 energy expenditure and acute-phase protein production compared with placebo in pancreatic cancer  
1023 patients. *Br J Cancer.* 1995;72(1):185-8.
- 1024 56. Jensen EX, Fusch C, Jaeger P, Peheim E, Horber FF. Impact of chronic cigarette smoking on body  
1025 composition and fuel metabolism. *J Clin Endocrinol Metab.* 1995;80(7):2181-5.
- 1026 57. Poehlman ET, Toth MJ, Bunyard LB, Gardner AW, Donaldson KE, Colman E, Fonong T, Ades PA.  
1027 Physiological predictors of increasing total and central adiposity in aging men and women. *Arch*  
1028 *Intern Med.* 1995;155(22):2443-8.
- 1029 58. Mingrone G, Greco AV, Benedetti G, Capristo E, Semeraro R, Zoli G, Gasbarrini G. Increased resting  
1030 lipid oxidation in Crohn's disease. *Dig Dis Sci.* 1996;41(1):72-6.
- 1031 59. Wolf M, Weigert A, Kreymann G. Body composition and energy expenditure in thyroidectomized  
1032 patients during short-term hypothyroidism and thyrotropin-suppressive thyroxine therapy. *Eur J*  
1033 *Endocrinol.* 1996;134(2):168-73.
- 1034 60. Buchowski MS, Sun M. Energy expenditure, television viewing and obesity. *Int J Obes Relat Metab*  
1035 *Disord.* 1996;20(3):236-44.

- 1036 61. Horber FF, Kohler SA, Lippuner K, Jaeger P. Effect of regular physical training on age-associated  
1037 alteration of body composition in men. *Eur J Clin Invest.* 1996;26(4):279-85.
- 1038 62. Waluga M, Zahorska-Markiewicz B, Janusz M, Stabiak Z, Chelmicka A. Resting energy expenditure in  
1039 patients with cirrhosis of the liver measured by indirect calorimetry, anthropometry and bioelectrical  
1040 impedance analysis. *Experientia.* 1996;52(6):591-6.
- 1041 63. Schwenk A, Hoffer-Belitz E, Jung B, Kremer G, Burger B, Salzberger B, Diehl V, Schrappe M. Resting  
1042 energy expenditure, weight loss, and altered body composition in HIV infection. *Nutrition.*  
1043 1996;12(9):595-601.
- 1044 64. Couet C, Delarue J, Ritz P, Antoine JM, Lamisse F. Effect of dietary fish oil on body fat mass and basal  
1045 fat oxidation in healthy adults. *Int J Obes Relat Metab Disord.* 1997;21(8):637-43.
- 1046 65. Capristo E, Mingrone G, Addolorato G, Greco AV, Corazza GR, Gasbarrini G. Differences in metabolic  
1047 variables between adult coeliac patients at diagnosis and patients on a gluten-free diet. *Scand J*  
1048 *Gastroenterol.* 1997;32(12):1222-9.
- 1049 66. Greco AV, Mingrone G, Benedetti G, Capristo E, Tataranni PA, Gasbarrini G. Daily energy and  
1050 substrate metabolism in patients with cirrhosis. *Hepatology.* 1998;27(2):346-50.
- 1051 67. De Lorenzo A, Candeloro N, Bertini I, Talluri T, Pierangeli L. Total body capacity correlated with basal  
1052 metabolic rate. *Appl Radiat Isot.* 1998;49(5-6):493-4.
- 1053 68. McCrory MA, Kim HR, Wright NC, Lovelady CA, Aitkens S, Kilmer DD. Energy expenditure, physical  
1054 activity, and body composition of ambulatory adults with hereditary neuromuscular disease. *Am J*  
1055 *Clin Nutr.* 1998;67(6):1162-9.
- 1056 69. Capristo E, Mingrone G, Addolorato G, Greco AV, Gasbarrini G. Metabolic features of inflammatory  
1057 bowel disease in a remission phase of the disease activity. *J Intern Med.* 1998;243(5):339-47.
- 1058 70. Grinspoon S, Corcoran C, Miller K, Wang E, Hubbard J, Schoenfeld D, Anderson E, Basgoz N, Klibanski  
1059 A. Determinants of increased energy expenditure in HIV-infected women. *Am J Clin Nutr.*  
1060 1998;68(3):720-5.
- 1061 71. Ritz P, Acheson KJ, Gachon P, Vico L, Bernard JJ, Alexandre C, Beaufriere B. Energy and substrate  
1062 metabolism during a 42-day bed-rest in a head-down tilt position in humans. *Eur J Appl Physiol Occup*  
1063 *Physiol.* 1998;78(4):308-14.
- 1064 72. Jimenez-Exposito MJ, Garcia-Lorda P, Alonso-Villaverde C, de VÃrgala CM, SolÃ R, Masana L, Arijia V,  
1065 Izquierdo V, Salas-Salvado J. Effect of malabsorption on nutritional status and resting energy  
1066 expenditure in HIV-infected patients. *AIDS.* 1998;12(15):1965-72.
- 1067 73. Addolorato G, Capristo E, Greco AV, Stefanini GF, Gasbarrini G. Influence of chronic alcohol abuse on  
1068 body weight and energy metabolism: is excess ethanol consumption a risk factor for obesity or  
1069 malnutrition? *J Intern Med.* 1998;244(5):387-95.
- 1070 74. Hansen DL, Toubro S, Stock MJ, Macdonald IA, Astrup A. Thermogenic effects of sibutramine in  
1071 humans. *Am J Clin Nutr.* 1998;68(6):1180-6.
- 1072 75. Capristo E, Addolorato G, Mingrone G, Greco AV, Gasbarrini G. Effect of disease localization on the  
1073 anthropometric and metabolic features of Crohn's disease. *Am J Gastroenterol.* 1998;93(12):2411-9.
- 1074 76. Capristo E, Mingrone G, Addolorato G, Greco AV, Gasbarrini G. Glucose metabolism and insulin  
1075 sensitivity in inactive inflammatory bowel disease. *Aliment Pharmacol Ther.* 1999;13(2):209-17.

- 1076 77. Schneeweiss B, Lochs H, Zauner C, Fischer M, Wyatt J, Maier-Dobersberger T, Schneider B. Energy  
1077 and substrate metabolism in patients with active Crohn's disease. *J Nutr.* 1999;129(4):844-8.
- 1078 78. Vinken AG, Bathalon GP, Sawaya AL, Dallal GE, Tucker KL, Roberts SB. Equations for predicting the  
1079 energy requirements of healthy adults aged 18-81 y. *Am J Clin Nutr.* 1999;69(5):920-6.
- 1080 79. Addolorato G, Capristo E, Caputo F, Greco AV, Ceccanti M, Stefanini GF, Gasbarrini G. Nutritional  
1081 status and body fluid distribution in chronic alcoholics compared with controls. *Alcohol Clin Exp Res.*  
1082 1999;23(7):1232-7.
- 1083 80. Madden AM, Morgan MY. Resting energy expenditure should be measured in patients with cirrhosis,  
1084 not predicted. *Hepatology.* 1999;30(3):655-64.
- 1085 81. Pernerstorfer-Schoen H, Schindler K, Parschalk B, Schindl A, Thoeny-Lampert S, Wunderer K, Elmadfa  
1086 I, Tschachler E, Jilma B. Beneficial effects of protease inhibitors on body composition and energy  
1087 expenditure: a comparison between HIV-infected and AIDS patients. *AIDS.* 1999;13(17):2389-96.
- 1088 82. Al-Jaouni R, HÄ©buterne X, Pouget I, Rampal P. Energy metabolism and substrate oxidation in  
1089 patients with Crohn's disease. *Nutrition.* 2000;16(3):173-8.
- 1090 83. Barber MD, McMillan DC, Preston T, Ross JA, Fearon KC. Metabolic response to feeding in weight-  
1091 losing pancreatic cancer patients and its modulation by a fish-oil-enriched nutritional supplement.  
1092 *Clin Sci (Lond).* 2000;98(4):389-99.
- 1093 84. Nielsen S, Hensrud DD, Romanski S, Levine JA, Burguera B, Jensen MD. Body composition and resting  
1094 energy expenditure in humans: role of fat, fat-free mass and extracellular fluid. *Int J Obes Relat Metab*  
1095 *Disord.* 2000;24(9):1153-7.
- 1096 85. Paton NI, Angus B, Chaowagul W, Simpson AJ, Suputtamongkol Y, Elia M, Calder G, Milne E, White  
1097 NJ, Griffin GE. Protein and energy metabolism in chronic bacterial infection: studies in melioidosis.  
1098 *Clin Sci (Lond).* 2001;100(1):101-10.
- 1099 86. Zauner C, Rabitsch W, Schneeweiss B, Schiefermeier M, Greinix HT, Keil F, Ratheiser K, Kalhs P. Energy  
1100 and substrate metabolism in patients with chronic extensive graft-versus-host disease.  
1101 *Transplantation.* 2001;71(4):524-8.
- 1102 87. De Lorenzo A, Tagliabue A, Andreoli A, Testolin G, Comelli M, Deurenberg P. Measured and predicted  
1103 resting metabolic rate in Italian males and females, aged 18-59 y. *Eur J Clin Nutr.* 2001;55(3):208-14.
- 1104 88. Boirie Y, Beaufrere B, Ritz P. Energetic cost of protein turnover in healthy elderly humans. *Int J Obes*  
1105 *Relat Metab Disord.* 2001;25(5):601-5.
- 1106 89. van Pelt RE, Dinneno FA, Seals DR, Jones PP. Age-related decline in RMR in physically active men:  
1107 relation to exercise volume and energy intake. *Am J Physiol Endocrinol Metab.* 2001;281(3):E633-9.
- 1108 90. Muller MJ, Illner K, Bosy-Westphal A, Brinkmann G, Heller M. Regional lean body mass and resting  
1109 energy expenditure in non-obese adults. *Eur J Nutr.* 2001;40(3):93-7.
- 1110 91. Heymsfield SB, Gallagher D, Kotler DP, Wang Z, Allison DB, Heshka S. Body-size dependence of resting  
1111 energy expenditure can be attributed to nonenergetic homogeneity of fat-free mass. *Am J Physiol*  
1112 *Endocrinol Metab.* 2002;282(1):E132-8.
- 1113 92. Buchholz AC, Rafii M, Pencharz PB. Is resting metabolic rate different between men and women? *Br*  
1114 *J Nutr.* 2001;86(6):641-6.



- 1115 93. Topp H, Armbrust S, Lengger C, Schoch G, Davies J, Stichler W, Manz F, Fusch C. Renal excretion of 8-  
1116 oxo-7,8-dihydro-2(')-deoxyguanosine: degradation rates of RNA and metabolic rate in humans. Arch  
1117 Biochem Biophys. 2002;402(1):31-7.
- 1118 94. Calsbeek DJ, Thompson TL, Dahl JA, Stob NR, Brozinick JT Jr, Hill JO, Hickey MS. Metabolic and  
1119 anthropometric factors related to skeletal muscle UCP3 gene expression in healthy human adults.  
1120 Am J Physiol Endocrinol Metab. 2002;283(4):E631-7.
- 1121 95. Asbeck I, Mast M, Bierwag A, Westenhofer J, Acheson KJ, Muller MJ. Severe underreporting of energy  
1122 intake in normal weight subjects: use of an appropriate standard and relation to restrained eating.  
1123 Public Health Nutr. 2002;5(5):683-90.
- 1124 96. Buchholz AC, McGillivray CF, Pencharz PB. Differences in resting metabolic rate between paraplegic  
1125 and able-bodied subjects are explained by differences in body composition. Am J Clin Nutr.  
1126 2003;77(2):371-8.
- 1127 97. Kosmiski LA, Kuritzkes DR, Sharp TA, Hamilton JT, Lichtenstein KA, Mosca CL, Grunwald GK, Eckel RH,  
1128 Hill JO. Total energy expenditure and carbohydrate oxidation are increased in the human  
1129 immunodeficiency virus lipodystrophy syndrome. Metabolism. 2003;52(5):620-5.
- 1130 98. Bosity-Westphal A, Eichhorn C, Kutzner D, Illner K, Heller M, Muller MJ. The age-related decline in  
1131 resting energy expenditure in humans is due to the loss of fat-free mass and to alterations in its  
1132 metabolically active components. J Nutr. 2003;133(7):2356-62.
- 1133 99. Riggio O, Angeloni S, Ciuffa L, Nicolini G, Attili AF, Albanese C, Merli M. Malnutrition is not related to  
1134 alterations in energy balance in patients with stable liver cirrhosis. Clin Nutr. 2003;22(6):553-9.
- 1135 100. Bosity-Westphal A, Reinecke U, Schlorke T, Illner K, Kutzner D, Heller M, Muller MJ. Effect of organ and  
1136 tissue masses on resting energy expenditure in underweight, normal weight and obese adults. Int J  
1137 Obes Relat Metab Disord. 2004;28(1):72-9.
- 1138 101. Lof M, Hannestad U, Forsum E. Comparison of commonly used procedures, including the doubly-  
1139 labelled water technique, in the estimation of total energy expenditure of women with special  
1140 reference to the significance of body fatness. Br J Nutr. 2003;90(5):961-8.
- 1141 102. Paul DR, Novotny JA, Rumpler WV. Effects of the interaction of sex and food intake on the relation  
1142 between energy expenditure and body composition. Am J Clin Nutr. 2004;79(3):385-9.
- 1143 103. Alfonso-Gonzalez G, Doucet E, Almeras N, Bouchard C, Tremblay A. Estimation of daily energy needs  
1144 with the FAO/WHO/UNU 1985 procedures in adults: comparison to whole-body indirect calorimetry  
1145 measurements. Eur J Clin Nutr. 2004;58(8):1125-31.
- 1146 104. St-Onge MP, Rubiano F, Jones A Jr, Heymsfield SB. A new hand-held indirect calorimeter to measure  
1147 postprandial energy expenditure. Obes Res. 2004;12(4):704-9.
- 1148 105. Marra M, Scalfi L, Contaldo F, Pasanisi F. Fasting respiratory quotient as a predictor of long-term  
1149 weight changes in non-obese women. Ann Nutr Metab. 2004;48(3):189-92.
- 1150 106. Crenn P, Rakotoanbinina B, Raynaud JJ, Thuillier F, Messing B, Melchior JC. Hyperphagia contributes  
1151 to the normal body composition and protein-energy balance in HIV-infected asymptomatic men. J  
1152 Nutr. 2004;134(9):2301-6.
- 1153 107. St-Pierre DH, Karelis AD, Cianflone K, Conus F, Mignault D, Rabasa-Lhoret R, St-Onge M, Tremblay-  
1154 Lebeau A, Poehlman ET. Relationship between ghrelin and energy expenditure in healthy young  
1155 women. J Clin Endocrinol Metab. 2004;89(12):5993-7.

- 1156 108. Brehm BJ, Spang SE, Lattin BL, Seeley RJ, Daniels SR, D'Alessio DA. The role of energy expenditure in  
1157 the differential weight loss in obese women on low-fat and low-carbohydrate diets. *J Clin Endocrinol*  
1158 *Metab.* 2005;90(3):1475-82.
- 1159 109. Day DS, Gozansky WS, Van Pelt RE, Schwartz RS, Kohrt WM. Sex hormone suppression reduces resting  
1160 energy expenditure and  $\beta$ -adrenergic support of resting energy expenditure. *J Clin Endocrinol*  
1161 *Metab.* 2005;90(6):3312-7.
- 1162 110. Reeves MM, Capra S, Bauer J, Davies PS, Battistutta D. Clinical accuracy of the MedGem indirect  
1163 calorimeter for measuring resting energy expenditure in cancer patients. *Eur J Clin Nutr.*  
1164 2005;59(4):603-10.
- 1165 111. Gonzalez-Bermejo J, Lofaso F, Falaize L, Lejaille M, Raphael JC, Similowski T, Melchior JC. Resting  
1166 energy expenditure in Duchenne patients using home mechanical ventilation. *Eur Respir J.*  
1167 2005;25(4):682-7.
- 1168 112. Wang Z, Heshka S, Heymsfield SB, Shen W, Gallagher D. A cellular-level approach to predicting resting  
1169 energy expenditure across the adult years. *Am J Clin Nutr.* 2005;81(4):799-806.
- 1170 113. Coin A, Sergi G, Enzi G, Busetto L, Pigozzo S, Lupoli L, Strater D, Peruzza S, Inelmen EM. Total and  
1171 regional body composition and energy expenditure in multiple symmetric lipomatosis. *Clin Nutr.*  
1172 2005;24(3):367-74.
- 1173 114. Capristo E, Farnetti S, Mingrone G, Certo M, Greco AV, Addolorato G, Gasbarrini G. Reduced plasma  
1174 ghrelin concentration in celiac disease after gluten-free diet treatment. *Scand J Gastroenterol.*  
1175 2005;40(4):430-6.
- 1176 115. Joosen AM, Bakker AH, Westerterp KR. Metabolic efficiency and energy expenditure during short-  
1177 term overfeeding. *Physiol Behav.* 2005;85(5):593-7.
- 1178 116. Gougeon R, Harrigan K, Tremblay JF, Hedrei P, Lamarche M, Morais JA. Increase in the thermic effect  
1179 of food in women by adrenergic amines extracted from citrus aurantium. *Obes Res.* 2005;13(7):1187-  
1180 94.
- 1181 117. Bader N, Bosy-Westphal A, Dilba B, Muller MJ. Intra- and interindividual variability of resting energy  
1182 expenditure in healthy male subjects -- biological and methodological variability of resting energy  
1183 expenditure. *Br J Nutr.* 2005;94(5):843-9.
- 1184 118. Johnstone AM, Murison SD, Duncan JS, Rance KA, Speakman JR. Factors influencing variation in  
1185 basal metabolic rate include fat-free mass, fat mass, age, and circulating thyroxine but not sex,  
1186 circulating leptin, or triiodothyronine. *Am J Clin Nutr.* 2005;82: 941– 8.
- 1187 119. Lof M, Forsum E. Activity pattern and energy expenditure due to physical activity before and during  
1188 pregnancy in healthy Swedish women. *Br J Nutr.* 2006;95(2):296-302.
- 1189 120. Bertoli S, Battezzati A, Merati G, Margonato V, Maggioni M, Testolin G, Veicsteinas A. Nutritional  
1190 status and dietary patterns in disabled people. *Nutr Metab Cardiovasc Dis.* 2006;16(2):100-12.
- 1191 121. Rubenbauer JR, Johannsen DL, Baier SM, Litchfield R, Flakoll PJ. The use of a handheld calorimetry  
1192 unit to estimate energy expenditure during different physiological conditions. *JPEN J Parenter Enteral*  
1193 *Nutr.* 2006;30(3):246-50.
- 1194 122. Harris AM, Jensen MD, Levine JA. Weekly changes in basal metabolic rate with eight weeks of  
1195 overfeeding. *Obesity (Silver Spring).* 2006;14(4):690-5.

- 1196 123. Lowe JC, Yellin J, Honeyman-Lowe G. Female fibromyalgia patients: lower resting metabolic rates  
1197 than matched healthy controls. *Med Sci Monit.* 2006;12(7):CR282-9.
- 1198 124. Battezzati A, Bertoli S, San Romerio A, Testolin G. Body composition: an important determinant of  
1199 homocysteine and methionine concentrations in healthy individuals. *Nutr Metab Cardiovasc Dis.*  
1200 2007;17(7):525-34.
- 1201 125. Di Renzo L, Del Gobbo V, Bigioni M, Premrov MG, Cianci R, De Lorenzo A. Body composition analyses  
1202 in normal weight obese women. *Eur Rev Med Pharmacol Sci.* 2006;10(4):191-6.
- 1203 126. De Lorenzo A, Martinoli R, Vaia F, Di Renzo L. Normal weight obese (NWO) women: an evaluation of  
1204 a candidate new syndrome. *Nutr Metab Cardiovasc Dis.* 2006;16(8):513-23. Epub 2006 Mar 3.
- 1205 127. Harris AM, Lanningham-Foster LM, McCrady SK, Levine JA. Nonexercise movement in elderly  
1206 compared with young people. *Am J Physiol Endocrinol Metab.* 2007;292(4):E1207-12.
- 1207 128. Buscemi S, Verga S, Caimi G, Cerasola G. A low resting metabolic rate is associated with metabolic  
1208 syndrome. *Clin Nutr.* 2007;26(6):806-9.
- 1209 129. Metsios GS, Stavropoulos-Kalinoglou A, Douglas KM, Koutedakis Y, Nevill AM, Panoulas VF, Kita M,  
1210 Kitas GD. Blockade of tumour necrosis factor-alpha in rheumatoid arthritis: effects on components  
1211 of rheumatoid cachexia. *Rheumatology (Oxford).* 2007;46(12):1824-7.
- 1212 130. Johannsen DL, Welk GJ, Sharp RL, Flakoll PJ. Differences in daily energy expenditure in lean and obese  
1213 women: the role of posture allocation. *Obesity (Silver Spring).* 2008;16(1):34-9.
- 1214 131. Johannsen DL, DeLany JP, Frisard MI, Welsch MA, Rowley CK, Fang X, Jazwinski SM, Ravussin E;  
1215 Louisiana Healthy Aging Study. Physical activity in aging: comparison among young, aged, and  
1216 nonagenarian individuals. *J Appl Physiol (1985).* 2008;105(2):495-501.
- 1217 132. Later W, Bosy-Westphal A, Hitze B, Kossel E, Gluer CC, Heller M, Muller MJ. No evidence of mass  
1218 dependency of specific organ metabolic rate in healthy humans. *Am J Clin Nutr.* 2008;88(4):1004-9.
- 1219 133. Dellava JE, Hoffman DJ. Validity of resting energy expenditure estimated by an activity monitor  
1220 compared to indirect calorimetry. *Br J Nutr.* 2009;102(1):155-9.
- 1221 134. Leone A, Pencharz PB. Resting energy expenditure in stroke patients who are dependent on tube  
1222 feeding: a pilot study. *Clin Nutr.* 2010;29(3):370-2.
- 1223 135. Galgani JE, Ravussin E. Effect of dihydrocapsiate on resting metabolic rate in humans. *Am J Clin Nutr.*  
1224 2010;92(5):1089-93.
- 1225 136. Li AC, Tereszowski CM, Edwards AM, Simpson JA, Buchholz AC. Published predictive equations  
1226 overestimate measured resting metabolic rate in young, healthy females. *J Am Coll Nutr.*  
1227 2010;29(3):222-7.
- 1228 137. de la Torre CL, Ramirez-Marrero FA, Martinez LR, Nevarez C. Predicting resting energy expenditure  
1229 in healthy Puerto Rican adults. *J Am Diet Assoc.* 2010;110(10):1523-6.
- 1230 138. Wang Z, Ying Z, Bosy-Westphal A, Zhang J, Schautz B, Later W, Heymsfield SB, Muller MJ. Specific  
1231 metabolic rates of major organs and tissues across adulthood: evaluation by mechanistic model of  
1232 resting energy expenditure. *Am J Clin Nutr.* 2010;92(6):1369-77.
- 1233 139. Hronek M, Klemra P, Tosner J, Hrnčiarikova D, Zadák Z. Anthropometric measured fat-free mass as  
1234 essential determinant of resting energy expenditure for pregnant and non-pregnant women.  
1235 *Nutrition.* 2011;27(9):885-90.

- 1236 140. Kao CC, Hsu JW, Bandi V, Hanania NA, Kheradmand F, Jahoor F. Resting energy expenditure and  
1237 protein turnover are increased in patients with severe chronic obstructive pulmonary disease.  
1238 *Metabolism*. 2011;60(10):1449-55.
- 1239 141. Muller MJ, Langemann D, Gehrke I, Later W, Heller M, Gluer CC, Heymsfield SB, Bosy-Westphal A.  
1240 Effect of constitution on mass of individual organs and their association with metabolic rate in  
1241 humans--a detailed view on allometric scaling. *PLoS One*. 2011;6(7):e22732.
- 1242 142. Frankenfield DC. Bias and accuracy of resting metabolic rate equations in non-obese and obese  
1243 adults. *Clin Nutr*. 2013;32(6):976-82.
- 1244 143. Kosmiski L, Schmiege SJ, Mascolo M, Gaudiani J, Mehler PS. Chronic starvation secondary to anorexia  
1245 nervosa is associated with an adaptive suppression of resting energy expenditure. *J Clin Endocrinol*  
1246 *Metab*. 2014;99(3):908-14.
- 1247 144. Snell B, Fullmer S, Eggett DL. Reading and listening to music increase resting energy expenditure  
1248 during an indirect calorimetry test. *J Acad Nutr Diet*. 2014;114(12):1939-42.
- 1249 145. Larsson I, Hulthen L, Landen M, Palsson E, Janson P, Stener-Victorin E. Dietary intake, resting energy  
1250 expenditure, and eating behavior in women with and without polycystic ovary syndrome. *Clin Nutr*.  
1251 2016;35(1):213-218.
- 1252 146. Sondergaard E, Nellemann B, Sørensen LP, Christensen B, Gormsen LC, Nielsen S. Lean body mass,  
1253 not FFA, predicts VLDL-TG secretion rate in healthy men. *Obesity (Silver Spring)*. 2015;23(7):1379-85.
- 1254 147. Horner KM, Byrne NM, Cleghorn GJ, King NA. Influence of habitual physical activity on gastric  
1255 emptying in healthy males and relationships with body composition and energy expenditure. *Br J*  
1256 *Nutr*. 2015;114(3):489-96.
- 1257 148. Jacques MF, Orme P, Smith J, Morse CI. Resting Energy Expenditure in Adults with Becker's Muscular  
1258 Dystrophy. *PLoS One*. 2017;12(1):e0169848.
- 1259 149. Irving CJ, Eggett DL, Fullmer S. Comparing Steady State to Time Interval and Non-Steady State  
1260 Measurements of Resting Metabolic Rate. *Nutr Clin Pract*. 2017;32(1):77-83.
- 1261 150. Chiurazzi C, Cioffi I, De Caprio C, De Filippo E, Marra M, Sammarco R, Di Guglielmo ML, Contaldo F,  
1262 Pasanisi F. Adequacy of nutrient intake in women with restrictive anorexia nervosa. *Nutrition*.  
1263 2017;38:80-84.
- 1264 151. Schiavo L, Scalera G, Pilone V, De Sena G, Iannelli A, Barbarisi A. Fat mass, fat-free mass, and resting  
1265 metabolic rate in weight-stable sleeve gastrectomy patients compared with weight-stable  
1266 nonoperated patients. *Surg Obes Relat Dis*. 2017;13(10):1692-1699.
- 1267 152. Geisler C, Hubers M, Granert O, Muller MJ. Contribution of structural brain phenotypes to the  
1268 variance in resting energy expenditure in healthy Caucasian subjects. *J Appl Physiol (1985)*.  
1269 2018;125(2):320-327.
- 1270 153. Mathisen TF, Engen KM, Sundgot-Borgen J, Stensrud T. Evaluation of a short protocol for indirect  
1271 calorimetry in females with eating disorders and healthy controls. *Clin Nutr ESPEN*. 2017;22:28-35.
- 1272 154. Patkova A, Juskova V, Havel E, Najpaverova S, Uramova D, Kovarik M, Zadak Z, Hronek M. Prognostic  
1273 value of respiratory quotients in severe polytrauma patients with nutritional support. *Nutrition*.  
1274 2018;49:90-95.

- 1275 155. Alcantara JMA, Sanchez-Delgado G, Martinez-Tellez B, Merchan-Ramirez E, Labayen I, Ruiz JR.  
1276 Congruent validity and inter-day reliability of two breath by breath metabolic carts to measure  
1277 resting metabolic rate in young adults. *Nutr Metab Cardiovasc Dis*. 2018;28(9):929-936.
- 1278 156. Roh E, Kim KM, Park KS, Kim YJ, Chun EJ, Choi SH, Park KS, Jang HC, Lim S. Comparison of pancreatic  
1279 volume and fat amount linked with glucose homeostasis between healthy Caucasians and Koreans.  
1280 *Diabetes Obes Metab*. 2018;20(11):2642-2652.
- 1281 157. Armbruster M, Rist M, Seifert S, Frommherz L, Weinert C, Mack C, Roth A, Merz B, Bunzel D, Krager  
1282 R, Kulling S, Watzl B, Bub A. Metabolite profiles evaluated, according to sex, do not predict resting  
1283 energy expenditure and lean body mass in healthy non-obese subjects. *Eur J Nutr*. 2019;58(6):2207-  
1284 2217.
- 1285 158. Deng Y, Liu NY, Tsow F, Xian X, Krajmalnik-Brown R, Tao N, Forzani E. Tracking Personal Health-  
1286 Environment Interaction with Novel Mobile Sensing Devices. *Sensors (Basel)*. 2018;18(8). pii: E2670.
- 1287 159. Mele C, Tagliaferri MA, Saraceno G, Mai S, Vietti R, Zavattaro M, Aimaretti G, Scacchi M, Marzullo P.  
1288 Serum uric acid potentially links metabolic health to measures of fuel use in lean and obese  
1289 individuals. *Nutr Metab Cardiovasc Dis*. 2018;28(10):1029-1035.
- 1290 160. Amaro-Gahete FJ, Sanchez-Delgado G, Alcantara JMA, Martinez-Tellez B, Munoz-Hernandez V,  
1291 Merchan-Ramirez E, Lof M, Labayen I, Ruiz JR. Congruent Validity of Resting Energy Expenditure  
1292 Predictive Equations in Young Adults. *Nutrients*. 2019;11(2). pii: E223.
- 1293 161. Martin CK, Johnson WD, Myers CA, Apolzan JW, Earnest CP, Thomas DM, Rood JC, Johannsen NM,  
1294 Tudor-Locke C, Harris M, Hsia DS, Church TS. Effect of different doses of supervised exercise on food  
1295 intake, metabolism, and non-exercise physical activity: The E-MECHANIC randomized controlled trial.  
1296 *Am J Clin Nutr*. 2019;110(3):583-592.
- 1297 162. Thom G, Gerasimidis K, Rizou E, Alfheaid H, Barwell N, Manthou E, Fatima S, Gill JMR, Lean MEJ,  
1298 Malkova D. Validity of predictive equations to estimate RMR in females with varying BMI. *J Nutr Sci*.  
1299 2020 May 26;9:e17. Erratum in: *J Nutr Sci*. 2020 Jun 18;9:e22.
- 1300 163. Mey JT, Matuska B, Peterson L, Wyszynski P, Koo M, Sharp J, Pennington E, McCarroll S, Micklewright  
1301 S, Zhang P, Aronica M, Hoddy KK, Champagne CM, Heymsfield SB, Comhair SAA, Kirwan JP, Erzurum  
1302 SC, Mulya A. Resting Energy Expenditure Is Elevated in Asthma. *Nutrients*. 2021;13(4). pii: 1065.

1303  
1304

### 1305 **Mouse indirect calorimetry measurements**

1306 All mouse studies followed the guidelines issued by Yale University's Institutional Animal Care  
1307 and Use Committee (IACUC). Male C57BL/6J mice (Jackson Laboratories, stock # 000664) arrived  
1308 at the facility at 5 weeks of age and were kept on a 12h/12h light/dark cycle and had free access  
1309 to water and chow diet (Envigo Teklad, 2018S). At 6 weeks of age, mice were switched to one of  
1310 the different high-fat diets (Research Diets Inc., Table S4). The high-fat diets (HFD) contained 20%

1311 protein, 35% carbohydrates and 45% fat by energy with the fat being derived from different  
1312 sources (listed in Table S5). After 4 weeks of HFD feeding, mice were housed in a TSE  
1313 PhenoMaster system for 4 days. Data from the final 72 hours were used for calculations. Oxygen  
1314 ( $O_2$ ) consumption (mL/h), carbon dioxide ( $CO_2$ ) production (mL/h) and food intake (g) were  
1315 recorded every 30 minutes. Energy expenditure (kJ/h) was calculated using the Weir Equation<sup>44</sup>.  
1316 Respiratory exchange ratio (RER) was calculated as  $vCO_2/vO_2$ .

1317

### 1318 **Preparation of samples for GCMS**

1319 For mouse diets, approximately 40-50 mg of pulverized diet was weighed and dissolved in 0.5 mL  
1320 of pure water, acidified with 10  $\mu$ L of 1 M HCl, and 1 mL of 100% methanol was added. Diet  
1321 samples were mechanically homogenized to a uniform slurry. Total lipid extraction was  
1322 performed on all samples as previously described<sup>47</sup>. 1.5 mL of isooctane/ethyl acetate 3:1 v/v  
1323 was added, vortexed vigorously, the organic phase was collected, and this step was repeated.  
1324 The two volumes of organic phase were combined and taken to dryness by evaporation under  
1325 nitrogen gas at 40°C. Samples were resuspended in 300  $\mu$ L of isooctane/ethyl acetate 3:1 v/v.  
1326 The diet samples were subsequently diluted 1:200 into isooctane/ethyl acetate 3:1 v/v.

1327

### 1328 **Fatty acid quantification by GCMS**

1329 Individual stable isotope fatty acid (FA) stock solutions were made in isooctane/ethyl acetate 3:1  
1330 v/v, a mixture containing 1.0  $\mu$ g/ $\mu$ L of every FA was made in isooctane/ethyl acetate 3:1 v/v that  
1331 was further diluted to 50 ng/ $\mu$ L, and stable isotope reference FA regression curves were  
1332 prepared<sup>47,48</sup>. For total FA composition, 500 ng of the blended internal reference standard was

1333 added to 50  $\mu$ L of total lipid extract, and samples were taken to dryness under  $N_2$  gas. Dried  
1334 samples were immediately resuspended in 500  $\mu$ L of 100% ethanol, saponified with 500  $\mu$ L of 1  
1335 M NaOH at 90  $^{\circ}$ C for 45 min in Teflon capped tubes, and then acidified by addition of 525  $\mu$ L of 1  
1336 M HCl. Saponified FA were re-extracted using 1 mL of isooctane (twice), dried under  $N_2$  gas, and  
1337 were derivatized as above. The pentafluorobenzyl FA esters were resuspended in 200  $\mu$ L of  
1338 isooctane and diluted 1:10 into isooctane into GC/MS autosampler vials for injection. Analyte  
1339 data were acquired in NCI full scan, the FA-analyte peak area ratio to that of its corresponding  
1340 stable isotope reference FA was calculated for each analyte, and ratios were converted to  
1341 absolute amounts relative to regression curves for each chain length and saturation<sup>47,48</sup>. Total  
1342 SFA, MUFA and PUFA was the quantitative sum of the nmoles of the class of fatty acid measured.  
1343 Quantitative FA data were normalized to the total mass of diet input to the lipid extraction (i.e.  
1344 mg FA / g diet). Dietary FA amounts are listed in Table S4. Dietary FA intake (in mg) was calculated  
1345 by multiplying dietary FA amounts (mg/g) by the amount of diet consumed (g).

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1355 **2. Supplementary figures**

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1357 **Figure S1:** Distribution of BMI in the sample data for a) females and b) males. Trends in body  
1358 weight over the interval from 1982 to 2017 for c) males and d) females. There was a significant  
1359 increase in weight over time in both sexes. For males (gradient = 0.015 kg/month  $F = 7.04$ ,  $p =$   
1360 0.009) reflecting an average weight increase of 5.4 kg over 30 years, and for females (gradient =  
1361 0.023 kg/month  $F = 20.84$ ,  $p = 0.000005$ ) reflecting an average increase of 8.3 kg over 30 years

1362 **Figure S2:** Trends over time in a) unadjusted total energy expenditure, b) unadjusted basal  
1363 energy expenditure, and c) unadjusted activity energy expenditure for males. All expenditures  
1364 are in MJ/d and time is expressed in months since January 1982. Significant years are also  
1365 indicated. Each data point is a different measurement of expenditure. The red lines are the  
1366 fitted least squares regression fits. For regression details refer to text and Table 1.

1367 **Figure S3:** Trends over time in a) unadjusted total energy expenditure, b) unadjusted basal  
1368 energy expenditure, and c) unadjusted activity energy expenditure for females. All expenditures  
1369 are in MJ/d and time is expressed in months since January 1982. Significant years are also  
1370 indicated. Each data point is a different measurement of expenditure. The red lines are the  
1371 fitted least squares regression fits. For regression details refer to text and Table 1.

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1373 **Figure S4:** Relationships between energy expenditure parameters and Body mass index (BMI).  
1374 In females the relationships were: for TEE vs BMI ( $F = 559.3$ ,  $p < 10^{-16}$ ), TEE vs BM ( $F = 1163$ ,  $p <$   
1375  $10^{-16}$ ), BEE vs BMI ( $F = 242.6$ ,  $p < 10^{-16}$ ) BEE vs BM ( $F = 341.1$ ,  $p < 10^{-16}$ ), AEE vs BMI ( $F = 45.13$ ,  
1376  $p < 10^{-10}$ ) and AEE vs BM ( $F = 91.08$ ,  $p < 10^{-16}$ ). For males the relationships were: for TEE vs BMI  
1377 ( $F = 114.6$ ,  $p < 10^{-16}$ ), TEE vs BM ( $F = 302.3$ ,  $p < 10^{-16}$ ), BEE vs BMI ( $F = 79.4$ ,  $p < 10^{-16}$ ) BEE vs BM  
1378 ( $F = 341.1$ ,  $p < 10^{-16}$ ), AEE vs BMI ( $F = 16.28$ ,  $p = 6 \times 10^{-5}$ ) and AEE vs BM ( $F = 53.19$ ,  $p < 10^{-14}$ ).

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1380 **Figure S5:** Trends over time in Physical Activity Level (PAL = TEE/BEE). PAL is dimensionless and  
1381 time is expressed in months since January 1982. Significant years are also indicated. Upper plot  
1382 is for males and lower is for females. The red lines are the fitted least squares regression fits.  
1383 For regression details refer to text.

1384 **Figure S6:** Systematic review strategy. Flow diagram for selection of studies according to  
1385 PRISMA guidelines.

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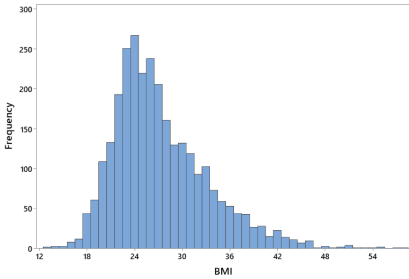


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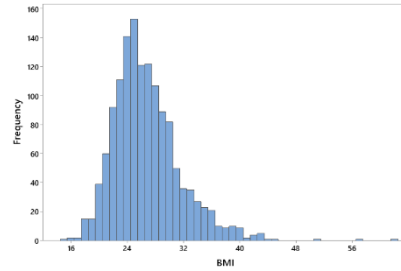
1389 **Figure S1**

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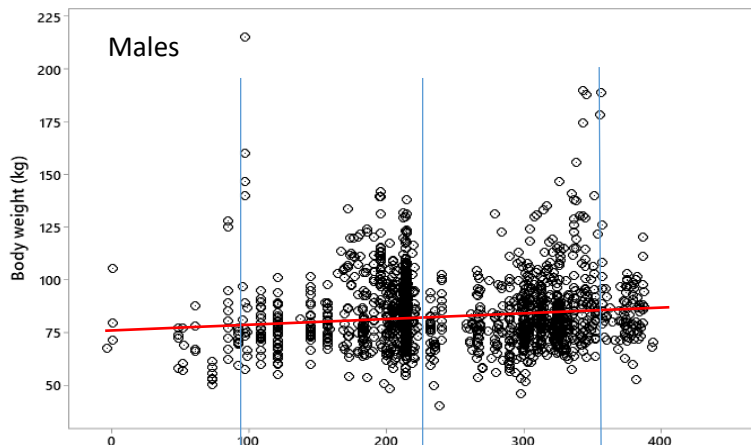
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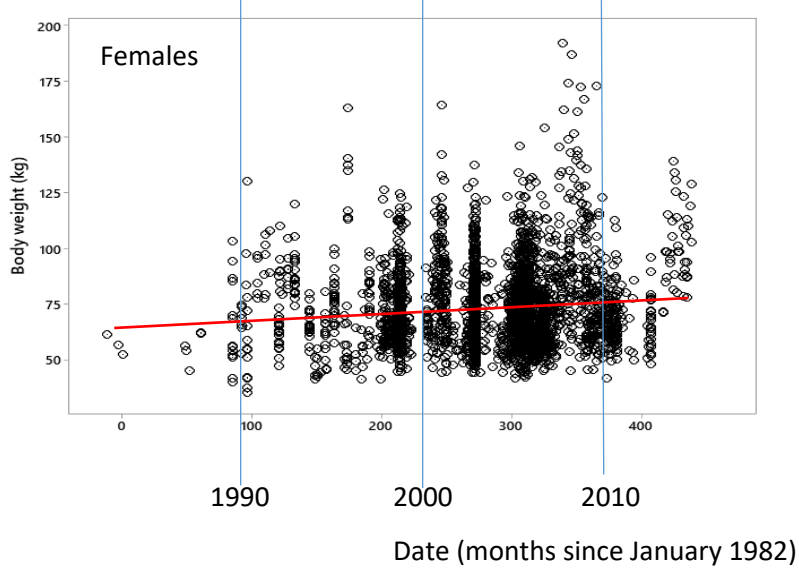
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1409 **Figure S2**

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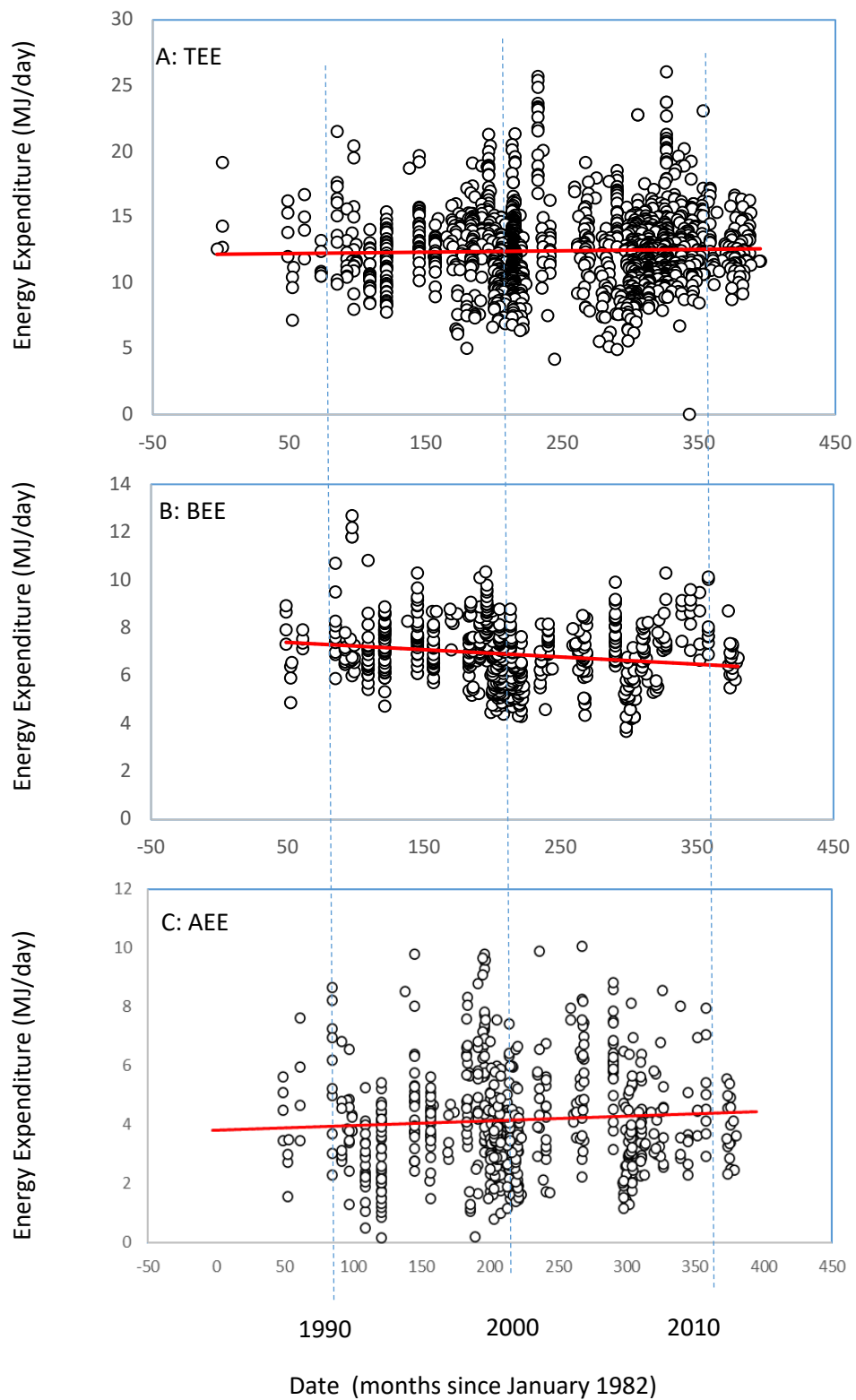
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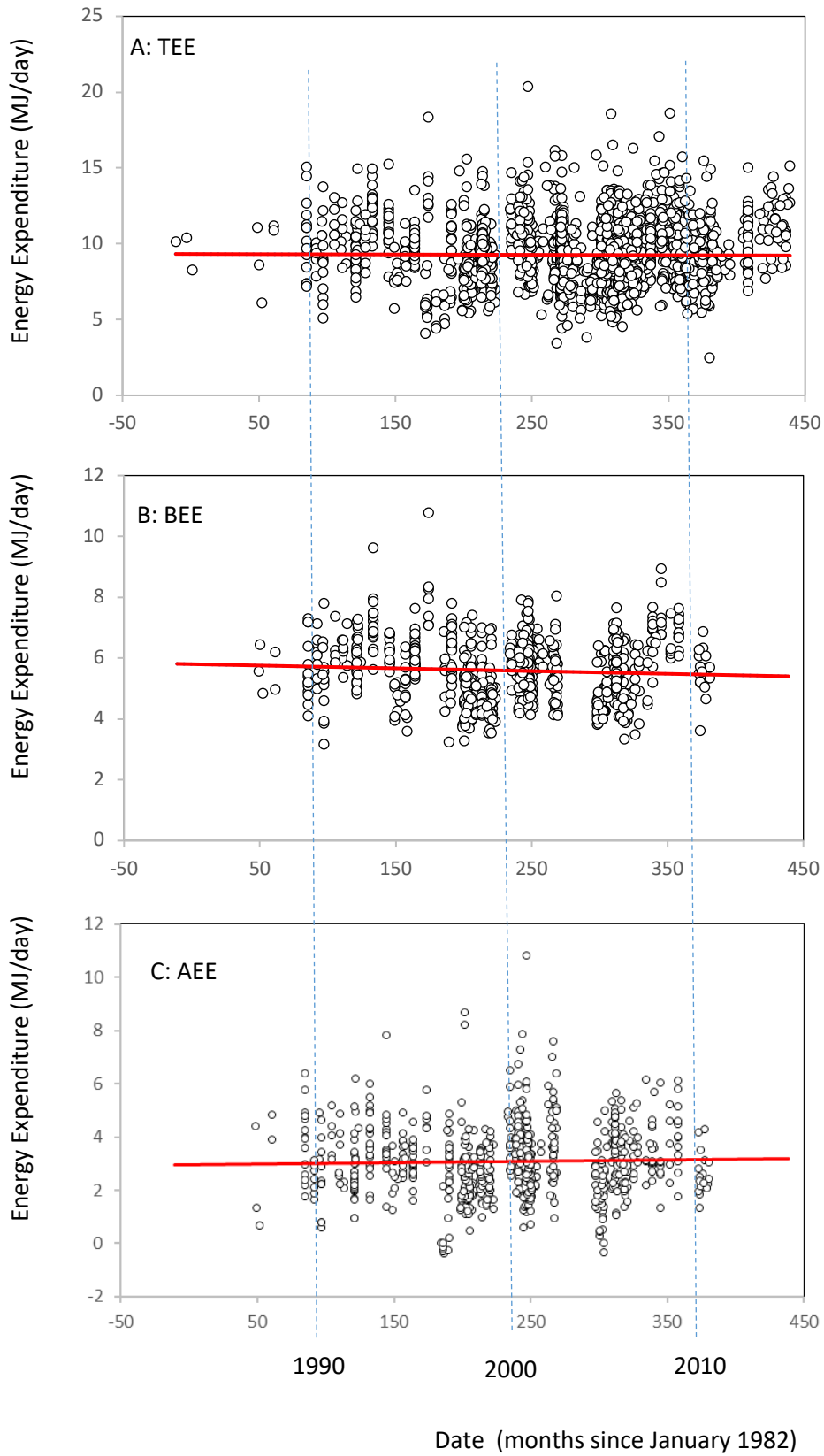
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1432 **Figure S3**



1458 **Figure S4**

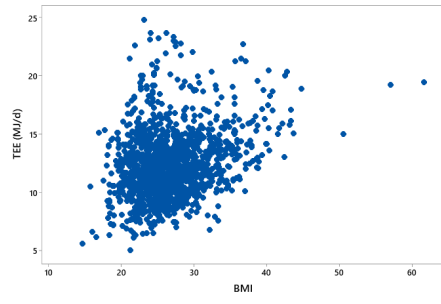
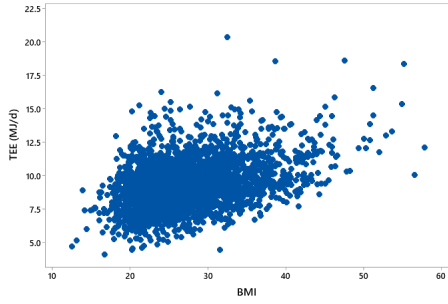
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Females

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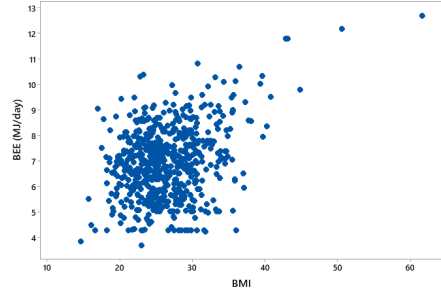
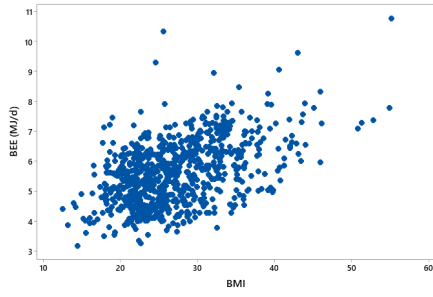
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B:TEE



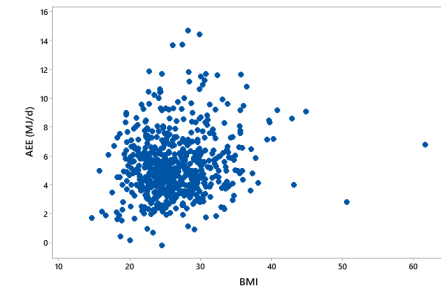
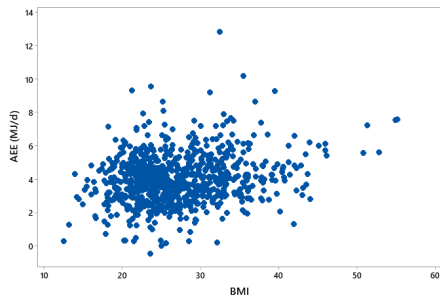
C: BEE

D:BEE



E: AEE

F:AEE



1486 **Figure S5**

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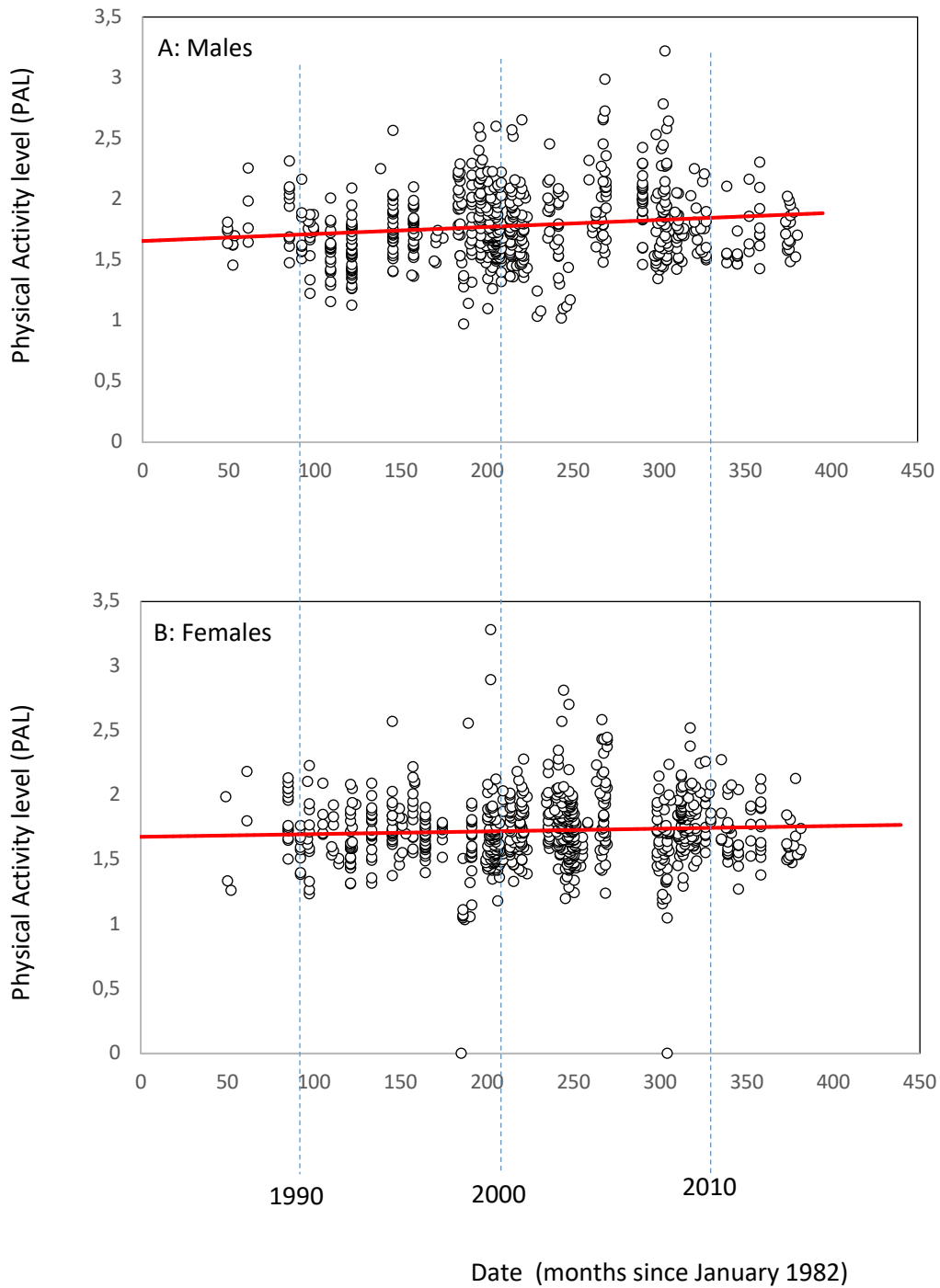
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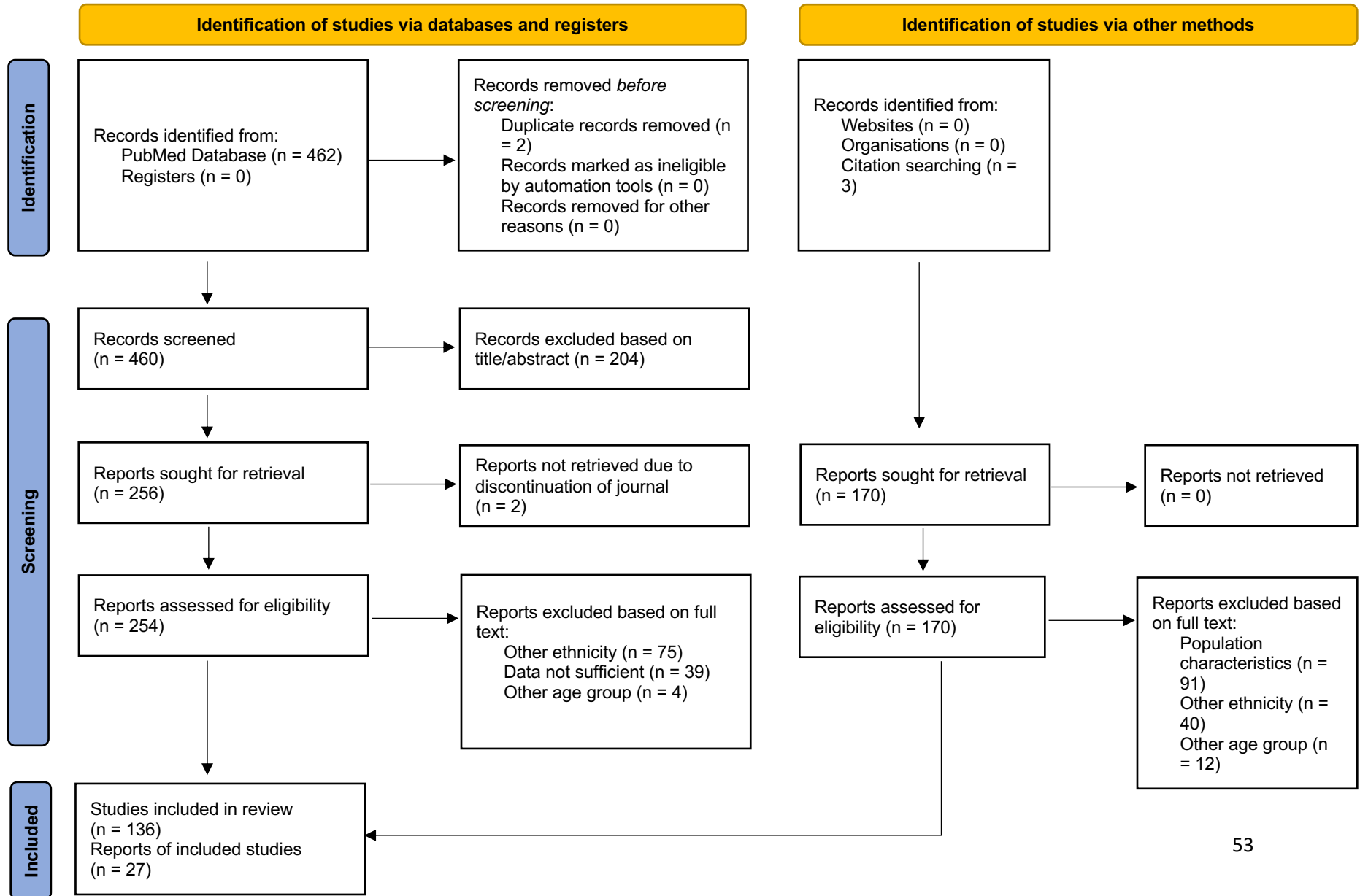
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1509 **Figure S6**

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1541 **3. Supplementary tables**

1542 **Table S1.** Patterns in change of metabolic rate of males over the last 35 to 40 years including  
1543 or excluding data prior to 1987. Values show the change in MJ/day over 30 years and the  
1544 associated p value. ns = not significant. None of the patterns or interpretations are changed  
1545 by the omission of the early data.

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		Including		Excluding		
1547						
1548	Unadjusted	TEE	+0.55	p > .05, ns	+0.60	p > .05, ns
1549		BEE	-1.19	p < 0.00002	-1.16	p < 0.00002
1550		AEE	+0.50	p > .05, ns	+0.54	p > .05, ns
1551	Adjusted	TEE	-0.93	p < 0.0001	-0.94	p < 0.0002
1552		BEE	-0.96	p < 10 <sup>-9</sup>	-0.91	p < 10 <sup>-8</sup>
1553		AEE	+1.01	p < 0.0003	+1.02	p > 0.0003

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1567 **Table S2:** Impact of removing individual studies on the relationship between male BEE and date.  
 1568 Individual studies are identified by the code for the study is that in the database. N is the number of  
 1569 samples omitted. Dates covered are the months since jan-82 that were involved in the particular data  
 1570 set. Coefficient is the fitted linear regression coefficient converted to the change in MJ/d over 30 years.  
 1571 R<sup>2</sup>x100 is the explained variation (%) by time since 1987. And F and p are the regression statistics for the  
 1572 time effect.

Study omitted	n	dates covered	coefficient	r <sup>2</sup> x100	F	p
None	0		-0.912	5.47	35.3	< 10 <sup>-8</sup>
10	12	191	-0.918	5.57	35.2	< 10 <sup>-8</sup>
13	4	61	-0.952	5.81	37.3	< 10 <sup>-8</sup>
17	4	97	-0.886	4.90	32.7	< 10 <sup>-8</sup>
20	10	85	-0.964	5.82	37.0	< 10 <sup>-8</sup>
22	8	92	-0.942	5.63	35.9	< 10 <sup>-8</sup>
23	21	109	<b>-0.653</b>	3.02	18.4	< 10 <sup>-5</sup>
24	10	96-99	-0.966	5.88	37.4	< 10 <sup>-8</sup>
31	38	121	-0.794	3.96	23.6	< 10 <sup>-6</sup>
32	26	145	-0.912	5.47	35.3	< 10 <sup>-8</sup>
35	12	157	-0.960	6.07	38.6	< 10 <sup>-8</sup>
36	10	138-171	-0.886	5.19	32.9	< 10 <sup>-8</sup>
37	10	157	-0.892	5.29	33.5	< 10 <sup>-8</sup>
40	19	183-185	-0.937	5.82	36.5	< 10 <sup>-8</sup>
41	4	184	-0.901	5.38	34.5	< 10 <sup>-8</sup>
43	30	193-197	-0.908	5.39	34.6	< 10 <sup>-8</sup>
46	7	185-190	-0.875	5.36	34.1	< 10 <sup>-8</sup>
49	30	205-214	-0.888	5.54	33.6	< 10 <sup>-8</sup>
51	9	199-200	-0.905	5.42	34.4	< 10 <sup>-8</sup>
55	10	235-236	-0.902	5.40	34.3	< 10 <sup>-8</sup>
57	10	259-269	-0.906	5.40	34.3	< 10 <sup>-8</sup>
59	12	241	-0.892	5.34	33.7	< 10 <sup>-8</sup>
60	24	290	-0.972	6.03	37.6	< 10 <sup>-8</sup>
62	18	191-314	-0.982	6.12	38.6	< 10 <sup>-8</sup>
65	22	339-358	-1.140	7.79	49.7	< 10 <sup>-12</sup>
69	18	373-380	-1.135	7.32	47.9	< 10 <sup>-12</sup>
72	14	322-327	-0.998	6.28	39.9	< 10 <sup>-10</sup>
74	190	199-305	-0.577	3.05	13.4	< 10 <sup>-4</sup>
79	11	302-321	-0.925	5.52	34.9	< 10 <sup>-8</sup>
129	25	266-269	-0.813	4.63	28.4	< 10 <sup>-7</sup>

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**Table S3:** Impact of removing individual studies on the relationship between female BEE and date. Individual studies are identified by the code for the study is that in the database. N is the number of samples omitted. Dates covered are the months since jan-82 that were involved in the particular data set. Coefficient is the fitted linear regression coefficient converted to the change in MJ/d over 30 years. r2x100 is the explained variation (%) by time since 1987. F and p are the regression statistics for the time effect. ns is P > 0.1. when P < 0.1 the exact p is quoted.

Study omitted	n	dates covered	coefficient	r2x100	p
None	0		-0.119	0.11	ns
10	16	191	-0.099	0.10	ns
13	2	61	-0.134	0.15	ns
14	3	92	-0.133	0.18	ns
15	3	85	-0.092	0.09	ns
20	11	85	-0.117	0.14	ns
22	5	92	-0.105	0.11	ns
30	20	133	-0.053	0.03	ns
31	21	121	-0.009	0.01	ns
33	11	149-158	-0.141	0.21	ns
34	17	145	-0.065	0.04	ns
37	11	157	-0.107	0.12	ns
42	7	174	-0.103	0.16	ns
46	12	185-191	-0.082	0.11	ns
49	28	205-217	-0.091	0.07	ns
51	4	200-201	-0.115	0.14	ns
55	15	235-236	-0.120	0.15	ns
57	24	254-268	-0.140	0.21	ns
59	6	241	-0.117	0.15	ns
62	12	310-314	-0.166	0.29	ns
65	33	339-358	<b>-0.393</b>	1.53	<b>0.001</b>
69	18	373-381	-0.248	0.59	0.032
73	6	199-233	-0.108	0.17	ns
74	184	199-233	-0.170	0.40	ns
75	34	314-341	-0.050	0.03	ns
79	45	305-321	-0.083	0.07	ns
85	2	50-52	-0.065	0.04	ns
86	9	97	-0.148	0.22	ns
93	23	93-124	-0.151	0.26	ns
118	147	234-251	-0.047	0.03	ns
129	25	266-269	-0.095	0.10	ns
135	22	312	-0.135	0.18	ns

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1659 **Table S4** Mouse diet details.

1660 Ingredients of 45% kcal high-fat diets. All diets were modeled after Research Diets D12451.

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	Mouse high-fat diets		
		grams	kcal (%)
	Protein	24	20
	Carbohydrate	41	35
	Fat	24	45
	Total		100
	Caloric density (kcal/g)	4.7	
Macronutrient	Ingredient	grams	kcal
Protein	Casein, 80 Mesh	200	800
	L-Cystine	3	12
Carbohydrate	Corn Starch	72.8	291
	Maltodextrin 10	100	400
	Sucrose	172.8	691
Filler	Cellulose BW200	50	0
Vitamins and Minerals	Mineral Mix S10026	10	0
	DiCalcium Phosphate	13	0
	Calcium Carbonate	5.5	0
	Potassium Citrate, 1 H <sub>2</sub> O	16.5	0
	Vitamin Mix V10001	10	40
	Choline Bitartrate	2	0
Fat	Soybean oil	25	225
	Dietary Fat Source	177.5	1598

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1673 **Table S5** Mouse diet details. Dietary fat composition of 45% kcal high-fat diets. Amounts are  
 1674 listed as percentages of weight and kilocalories. Note that each diet contains 5.5 kcal% soybean  
 1675 oil (providing essential fatty acids).

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Diet	Catalog #	Amount	Butter	Cocoa butter	Coconut oil	Fish oil	High oleic Safflower oil	High oleic Sunflower oil	Lard	Olive oil	Palm oil	Peanut oil	Safflower oil	Soybean oil
Butter	D06022405	gram	20.7	0	0	0	0	0	0	0	0	0	0	2.9
		kcal	39.4	0	0	0	0	0	0	0	0	0	0	5.5
Cocoa butter	D11112703	gram	0	20.7	0	0	0	0	0	0	0	0	0	2.9
		kcal	0	39.4	0	0	0	0	0	0	0	0	0	5.5
Coconut oil	D05122301	gram	0	0	20.7	0	0	0	0	0	0	0	0	2.9
		kcal	0	0	39.4	0	0	0	0	0	0	0	0	5.5
Fish oil	D03022403	gram	0	0	0	20.7	0	0	0	0	0	0	0	2.9
		kcal	0	0	0	39.4	0	0	0	0	0	0	0	5.5
High oleic Safflower oil	D05122103	gram	0	0	0	0	20.7	0	0	0	0	0	0	2.9
		kcal	0	0	0	0	39.4	0	0	0	0	0	0	5.5
High oleic Sunflower oil	D07062503	gram	0	0	0	0	0	20.7	0	0	0	0	0	2.9
		kcal	0	0	0	0	0	39.4	0	0	0	0	0	5.5
Lard	D12451	gram	0	0	0	0	0	0	20.7	0	0	0	0	2.9
		kcal	0	0	0	0	0	0	39.4	0	0	0	0	5.5
Olive oil	D06022403	gram	0	0	0	0	0	0	0	20.7	0	0	0	2.9
		kcal	0	0	0	0	0	0	0	39.4	0	0	0	5.5
Palm oil	D07081501	gram	0	0	0	0	0	0	0	0	20.7	0	0	2.9
		kcal	0	0	0	0	0	0	0	0	39.4	0	0	5.5
Peanut oil	D16010705	gram	0	0	0	0	0	0	0	0	0	20.7	0	2.9
		kcal	0	0	0	0	0	0	0	0	0	39.4	0	5.5
Safflower oil	D02062102	gram	0	0	0	0	0	0	0	0	0	0	20.7	2.9
		kcal	0	0	0	0	0	0	0	0	0	0	39.4	5.5
Soybean oil	D05042003	gram	0	0	0	0	0	0	0	0	0	0	0	23.6
		kcal	0	0	0	0	0	0	0	0	0	0	0	44.9

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#### 1691 **4. Group authorship details**

1692 This group authorship contains the names researchers who submitted data to the database or did not  
1693 assent inclusion to the main authorship because they felt their contribution was not sufficient to merit  
1694 authorship, or their specific data was not used in the present analysis (eg pediatric data). It also includes  
1695 some people whose data were contributed into the IAEA DLW database by the analysis laboratory but  
1696 they later could not be traced, or they did not respond to emails to assent inclusion among the  
1697 authorship.

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