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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

4 John R. Speakman^{1-4#*}, Jasper M.A. de Jong^{5,6*}, Srishti Sinha^{7,8*}, Klaas R. Westerterp^{9†*}, Yosuke
5 Yamada^{10,11†}, Hiroyuki Sagayama^{12†}, Philip N. Ainslie¹³, Liam J. Anderson¹⁴, Lenore Arab¹⁵,
6 Kweku Bedu-Addo¹⁶, Stephane Blanc^{17,18}, Alberto G. Bonomi¹⁹, Pascal Bovet²⁰, Soren Brage²¹,
7 Maciej S. Buchowski²², Nancy F. Butte²³, Stefan G.J.A. Camps⁹, Jamie A. Cooper^{17,24}, Richard
8 Cooper²⁵, Sai Krupa Das²⁶, Peter S.W. Davies²⁷, Lara R. Dugas^{25,28}, Ulf Ekelund²⁹, Sonja
9 Entringer^{30,31}, Terrence Forrester³², Barry W. Fudge³³, Melanie Gillingham³⁴, Santu Ghosh⁷,
10 Annelies H Goris⁹, Michael Gurven³⁵, Lewis G. Halsey³, Catherine Hambly², Hinke H. Haisma³⁷,
11 Daniel Hoffman³⁸, Sumei Hu^{39,1,3}, Annemiek M. Joosen⁹, Jennifer L. Kaplan⁵, Peter Katzmarzyk⁴⁰,
12 William E. Kraus⁴¹, Robert F. Kushner⁴², William R. Leonard⁴³, Marie Löf^{44,45}, Corby K. Martin⁴⁰,
13 Eric Matsiko⁴⁶, Anine C. Medin^{47,48}, Erwin P. Meijer⁹, Marian L. Neuhouser⁴⁹, Theresa A.
14 Nicklas²³, Robert M. Ojiambo^{50,51}, Kirsi H. Pietiläinen⁵², Jacob Plange-Rhule^{16**}, Guy Plasqui⁵³,
15 Ross L. Prentice⁴⁹, Susan B. Racette⁵⁴, David A. Raichlen⁵⁵, Eric Ravussin⁴⁰, Leanne M. Redman⁴⁰,
16 Susan B. Roberts²⁶, Michael C. Rudolph⁵⁶, Luis B. Sardinha⁵⁷, Albertine J. Schuit⁵⁸, Analiza M. de
17 Silva⁵⁷, Eric Stice⁵⁹, Samuel S. Urlacher^{60,61}, Giulio Valenti⁹, Ludo M. Van Etten⁹, Edgar A. Van
18 Mil⁶², Brian M. Wood^{63,64}, Jack A. Yanovski⁶⁵, Tsukasa Yoshida¹⁰, Xueying Zhang^{1,2}, Alexia J.
19 Murphy-Alford⁸, Cornelia U. Loechl⁸, Anura Kurpad^{7†}, Amy H Luke^{66†}, Herman Pontzer^{67,68†},
20 Matthew S. Rodeheffer^{5,69,70†}, Jennifer Rood^{40†}, Dale A. Schoeller^{71†}, William W. Wong^{23†} and
21 the IAEA DLW database group[%]

22 *equal contribution

23 † corresponding author

24 # lead corresponding author

25 ** deceased

26 % see supplementary materials

27

28 **Author affiliations**

- 29 1. Shenzhen key Laboratory of Metabolic Health, Center for Energy Metabolism and Reproduction,
30 Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, China
31 2. Institute of Biological and Environmental Sciences, University of Aberdeen, Aberdeen, UK
32 3. State Key Laboratory of Molecular Developmental Biology, Institute of Genetics and
33 Developmental Biology, Chinese Academy of Sciences, Beijing, China
34 4. CAS Center of Excellence in Animal Evolution and Genetics, Kunming, China.

- 35 5. Department of Comparative Medicine, Yale School of Medicine, New Haven, CT 06519, USA
- 36 6. Department of Molecular Biosciences, The Wenner-Gren Institute, Stockholm University, 106 91
37 Stockholm, Sweden
- 38 7. St Johns Medical college, Bengaluru, India
- 39 8. Nutritional and Health Related Environmental Studies Section, Division of Human Health,
40 International Atomic Energy Agency, Vienna, Austria.
- 41 9. School of Nutrition and Translational Research in Metabolism (NUTRIM), University of
42 Maastricht, Maastricht, The Netherlands.
- 43 10. National Institute of Health and Nutrition, National Institutes of Biomedical Innovation, Health
44 and Nutrition, Tokyo, Japan.
- 45 11. Institute for Active Health, Kyoto University of Advanced Science, Kyoto, Japan.
- 46 12. Faculty of Health and Sport Sciences, University of Tsukuba, Ibaraki, Japan.
- 47 13. Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool,
48 UK.
- 49 14. School of sport, exercise and rehabilitation sciences, University of Birmingham, Birmingham, UK
- 50 15. David Geffen School of Medicine, University of California, Los Angeles.
- 51 16. Department of Physiology, Kwame Nkrumah University of Science and Technology, Kumasi,
52 Ghana.
- 53 17. Nutritional Sciences, University of Wisconsin, Madison, WI, USA
- 54 18. Institut Pluridisciplinaire Hubert Curien. CNRS Université de Strasbourg, UMR7178, France.
- 55 19. Phillips Research, Eindhoven, The Netherlands.
- 56 20. University Center for Primary care and health (UNISANTE), Lausanne University Hospital,
57 Lausanne, Switzerland.
- 58 21. MRC Epidemiology Unit, University of Cambridge, UK
- 59 22. Division of Gastroenterology, Hepatology and Nutrition, Department of Medicine, Vanderbilt
60 University, Nashville, Tennessee, USA
- 61 23. Department of Pediatrics, Baylor College of Medicine, USDA/ARS Children's Nutrition Research
62 Center, Houston, Texas, USA.
- 63 24. Nutritional Sciences, University of Georgia, Athens, GA, USA
- 64 25. Department of Public Health Sciences, Parkinson School of Health Sciences and Public Health,
65 Loyola University, Maywood, IL, USA.
- 66
- 67 26. Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University. 711
68 Washington St. Boston MA USA
- 69 27. Child Health Research Centre, Centre for Children's Health Research, University of Queensland,
70 South Brisbane, Queensland
- 71 28. Division of Epidemiology and Biostatistics, School of Public Health and Family Medicine,
72 University of Cape Town, Cape Town, South Africa
- 73 29. Department of Sport Medicine, Norwegian School of Sport Sciences, Oslo, Norway.
- 74 30. Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-
75 Universität zu Berlin, and Berlin Institute of Health (BIH), Institute of Medical Psychology, Berlin,
76 Germany.
- 77 31. University of California Irvine, Irvine, California, USA.
- 78 32. Solutions for Developing Countries, University of the West Indies, Mona, Kingston, Jamaica.
- 79 33. University of Glasgow, Glasgow, UK.
- 80 34. Department of Molecular and Medical Genetics, Oregon Health & Science University, Portland,
81 Oregon

82 35 Department of Anthropology, University of California Santa Barbara, Santa Barbara, CA, USA.
83 36 School of Life and Health Sciences, University of Roehampton, Holybourne Avenue, London, UK
84 37 Population Research Centre, University of Groningen, Groningen, Netherlands
85 38 Department of Nutritional Sciences, Program in International Nutrition, Rutgers University, New
86 Brunswick, NJ, USA
87 39 Beijing Advanced Innovation Center for Food Nutrition and Human Health, Beijing Engineering
88 and Technology Research Center of Food Additives, National Soybean Processing Industry
89 Technology Innovation Center, Beijing Technology and Business University, Beijing, China
90 40 Pennington Biomedical Research Center, Baton Rouge, Louisiana, USA.
91 41 Department of Medicine, Duke University, Durham, North Carolina, USA.
92 42 Northwestern University, Chicago, IL, USA.
93 43 Department of Anthropology, Northwestern University, Evanston, IL, USA.
94 44 Department of Biosciences and Nutrition, Karolinska Institute, Stockholm, Sweden
95 45 Department of Health, Medicine and Caring Sciences, Linköping University, 581 83 Linköping,
96 Sweden.
97 46 Department of Human Nutrition and Dietetics, University of Rwanda, Rwanda
98 47 Department of Nutrition and Public Health, Faculty of Health and Sport Sciences, University of
99 Agder, 4630 Kristiansand, Norway.
100 48 Department of Nutrition, Institute of Basic Medical Sciences, University of Oslo, 0317 Oslo,
101 Norway
102 49 Division of Public Health Sciences, Fred Hutchinson Cancer Research Center and School of Public
103 Health, University of Washington, Seattle, WA, USA.
104 50 Moi University, Eldoret, Kenya.
105 51 University of Global Health Equity, Kigali, Rwanda.
106 52 Helsinki University Central Hospital, Helsinki, Finland.
107 53 Department of Nutrition and Movement Sciences, Maastricht University, Maastricht, The
108 Netherlands.
109 54 Program in Physical Therapy and Department of Medicine, Washington University, School of
110 Medicine, St. Louis, Missouri, USA.
111 55 Biological Sciences and Anthropology, University of Southern California, California, USA.
112 56 Department of Physiology and Harold Hamm Diabetes Center, Oklahoma University Health
113 Sciences, Oklahoma City, OK, 73104, USA.
114 57 Exercise and Health Laboratory, CIPER, Faculdade de Motricidade Humana, Universidade de
115 Lisboa, Lisboa, Portugal
116 58 University of Tilburg, Tilburg, The Netherlands
117 59 Stanford University, Stanford CA, USA.
118 60 Department of Anthropology, Baylor University, Waco, TX, USA.
119 61 Child and brain development program, CIFAR, Toronto, Canada
120 62 Maastricht University, Maastricht and Lifestyle Medicine Center for Children, Jeroen Bosch
121 Hospital's-Hertogenbosch, The Netherlands.
122 63 University of California Los Angeles, Los Angeles, USA.
123 64 Max Planck Institute for Evolutionary Anthropology, Department of Human Behavior, Ecology,
124 and Culture.
125 65 Section on Growth and Obesity, Division of Intramural Research, *Eunice Kennedy*
126 *Shriver* National Institute of Child Health and Human Development, National Institutes of Health,
127 Bethesda, MD, USA.

128 66 Division of Epidemiology, Department of Public Health Sciences, Loyola University School of
129 Medicine, Maywood Illinois, USA.
130 67 Evolutionary Anthropology, Duke University, Durham NC, USA
131 68 Duke Global Health Institute, Duke University, Durham, NC, USA
132 69 Center of Molecular and Systems Metabolism, Yale University, New Haven, CT, 06519, USA
133 70 Department of Physiology, Yale University, New Haven, CT, 06511, USA.
134 71 Biotech Center and Nutritional Sciences University of Wisconsin, Madison, Wisconsin, USA.

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160 **Abstract**

161 Obesity is caused by prolonged positive energy balance^{1,2}. Whether reduced energy
162 expenditure stemming from reduced activity levels contributes, is debated^{3,4}. 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 threat⁵. Although excess body fat is a result of prolonged
175 positive energy balance^{1,2}, 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 increased². Alternatively, declines in energy
178 expenditure, due to reduced work-time physical activity⁴, combined with increases in sedentary
179 behavior, partly linked to elevated 'screen time' (TV, computer and phone use)^{6,7} may be a key

180 driver. These may be linked in a vicious cycle⁸, 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^{4,6,7,8}, 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 increases⁹. 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^{10,11}. Although low TEE is repeatable, and having low TEE is not a risk factor for future
191 weight gain over short timescales¹², 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 demands¹³. 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 hypothesis¹⁴. 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 database¹⁵ for which we also had BEE measures in 1429

201 individuals. All estimates of TEE were recalculated using a common equation¹⁶ that has been
202 shown to perform best in validation studies¹⁶.

203 We split the data by sex, because this may affect the etiology of energy balance^{17,18}. 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 = ± 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 = ± 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 = ± 1.4 kJ/month) was equivalent to an average fall in BEE by 1.19 MJ

223 (9.7%) over 30 years (95%CI = ± 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 = ± 1.8 kJ/month) was equivalent over 30 years to an
227 increase by 0.50 MJ/day (95%CI = ± 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 = ± 1.20 kJ/month) leading to an estimated average change over 30 years of -0.93 MJ/day in
240 adjusted TEE (95%CI = ± 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 = ± 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 = ± 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 = ± 1.4 kJ/month)
245 was equivalent to a rise of 1.01 MJ/day over 30 years (95%CI = ± 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 = ± 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 = ± 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 = ± 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 Log_e BMR was 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 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 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 movement⁹. 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^{4,6-8}. 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 2017¹⁹. Time spent in leisure time PA in the USA also increased between 1965 and 1995,²⁰
314 suggesting leisure time PA has replaced the decline in worktime PA levels²⁰. Leisure time PA has
315 also changed in other westernized populations²¹. 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 costs²² 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 time²³, 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^{24,25}. It was recently suggested that changes in both
325 activity and basal metabolism may have contributed to the decline in body temperature (T_b)²⁶,
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 function²⁷, and studies of birds point
331 to no consistent relation between immune function and metabolism either within or between

332 subjects²⁸. Experimental removal of parasites in Cape ground squirrels (*Xerus inauris*) led to
333 elevated rather than reduced resting metabolic rate²⁹. Nevertheless, some studies in forager-
334 horticulturalist societies in South America have noted elevated BMR is linked to increased levels
335 of circulating IgG³⁰ and cytokines³¹, 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%³². A second possibility is that early measurements paid
341 less attention to controlling ambient temperature to ensure individuals were at thermoneutral
342 temperatures³³.

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)³⁴. These changes have included
345 alterations in the intake of carbohydrates, fiber and fats, with % protein intake remaining
346 relatively constant³⁴. 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))³⁴. 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^{35,36}, although many studies suggest
357 no effect^{37,38}. 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^{39,40}.
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 years⁴¹
369 and has been shown in a randomized controlled trial to affect resting metabolic rate⁴².

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

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517

518 **Requests for materials**

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

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

525

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539 **Author contributions**

540 JRS, KRW and LH processed and analysed the IAEA data, JMAdJ, 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 and should be directed to the lead corresponding author j.speakman@abdn.ac.uk or Dr Alexia Alford at the (a.alford@iaea.org). The BMR data are available upon request to co-corresponding author Dr Anura Kurpad (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).

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**

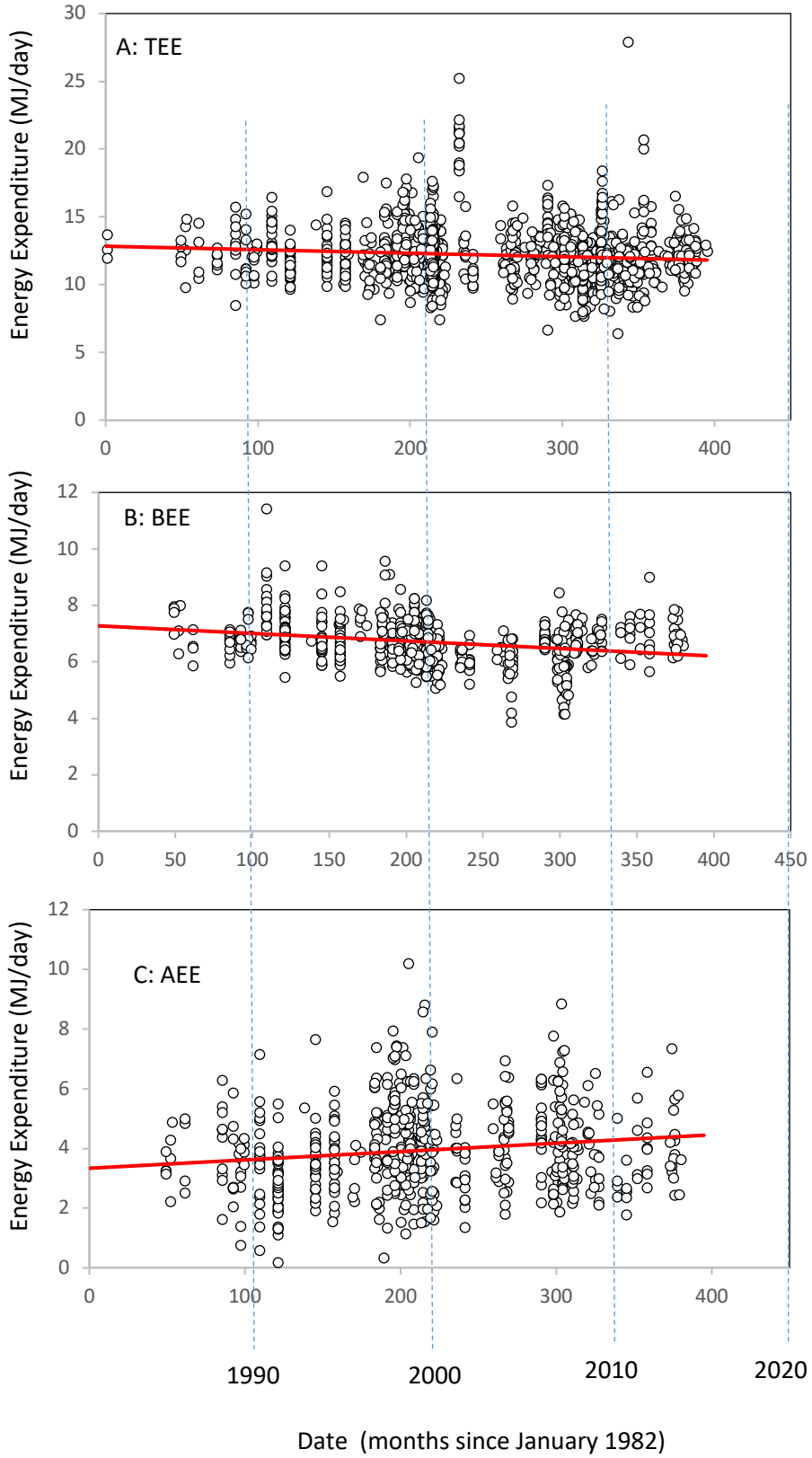
627 **Unadjusted data**

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

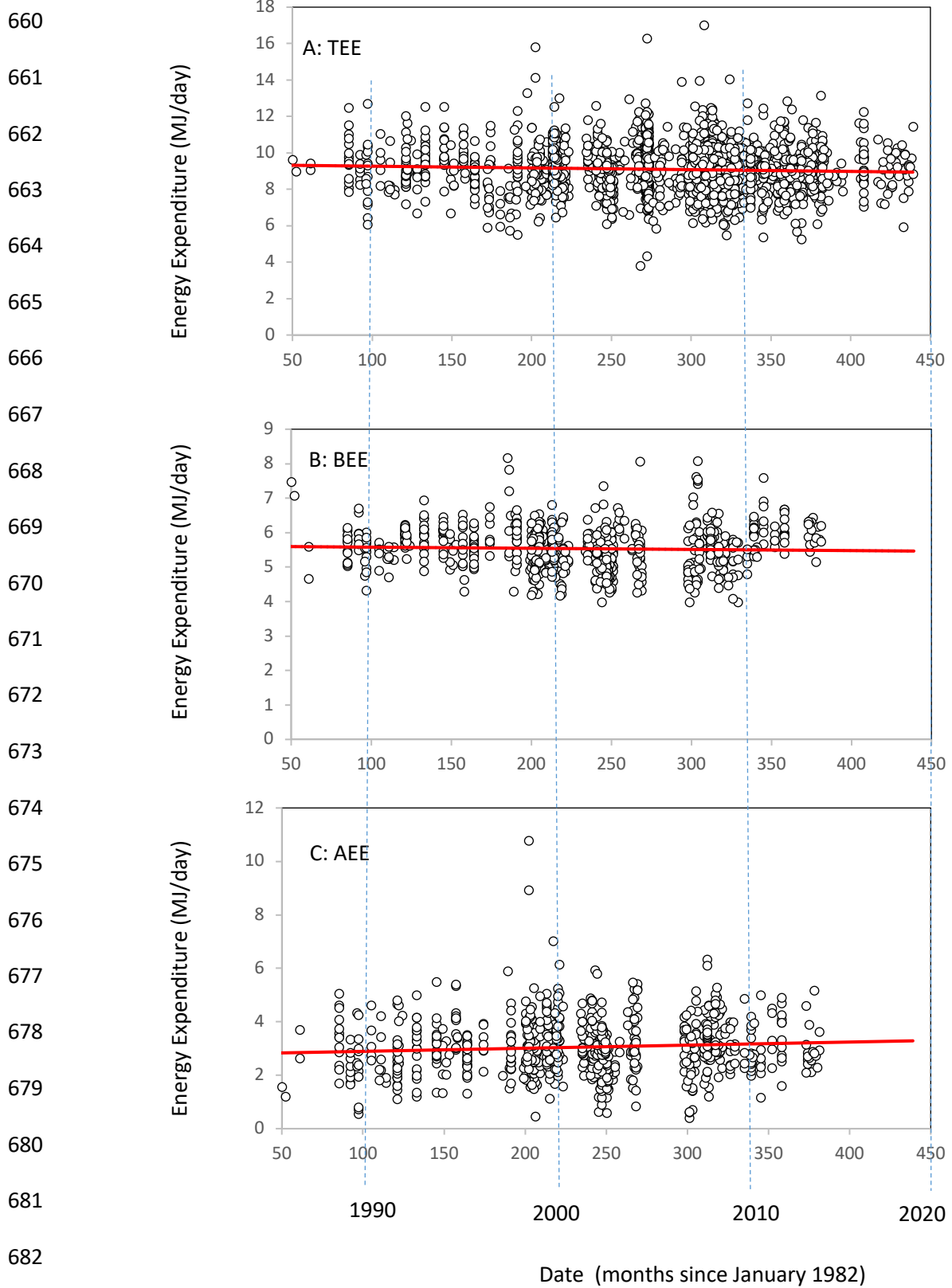
635 **Adjusted data**

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**

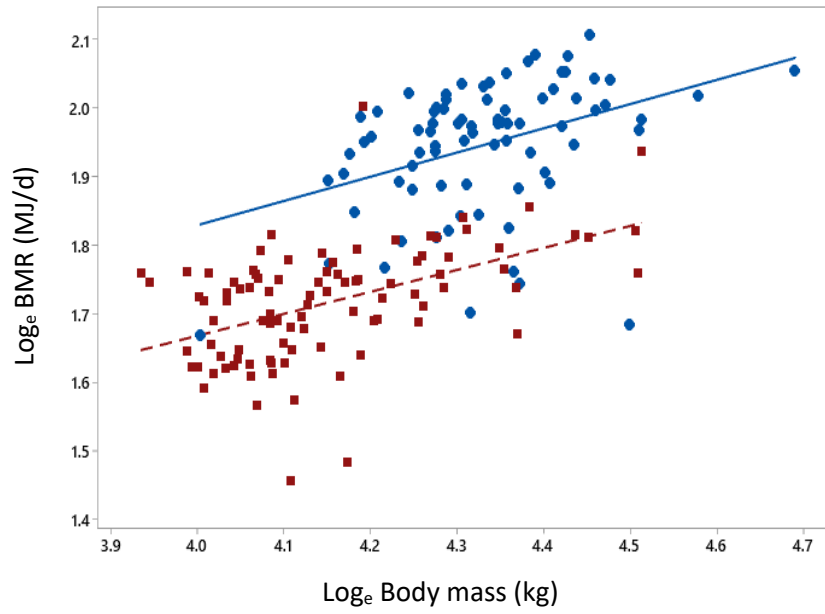


659 **Figure 2**

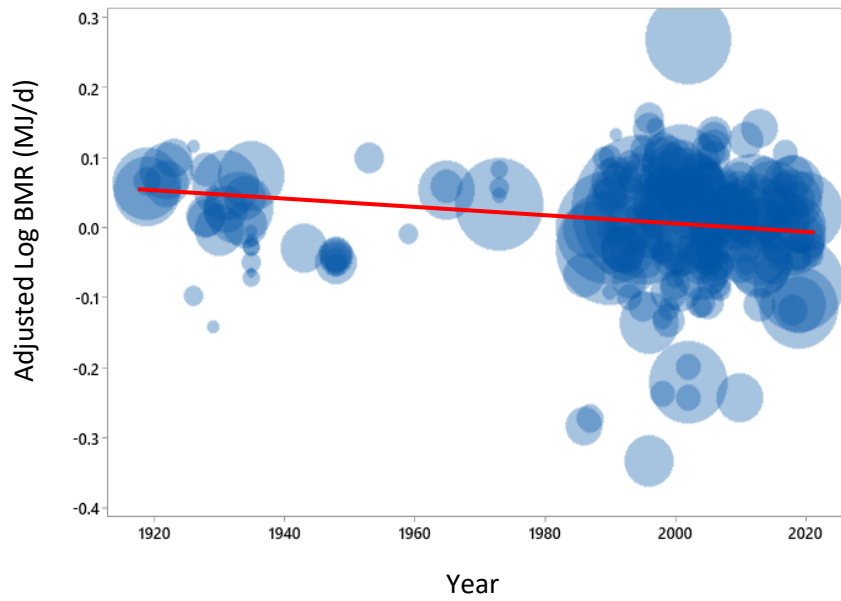


683 **Figure 3**

684 **A:**

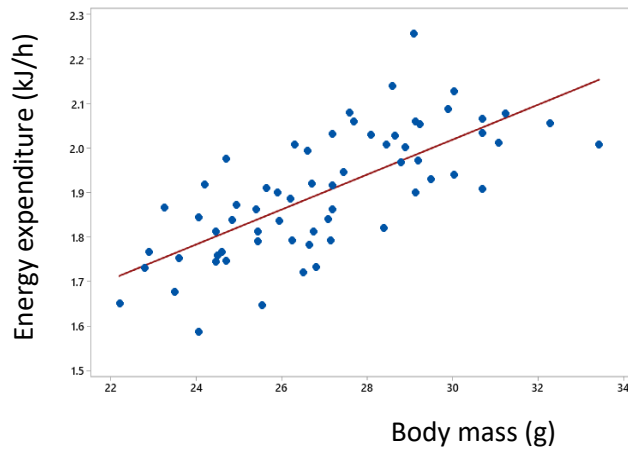


692 **B:**

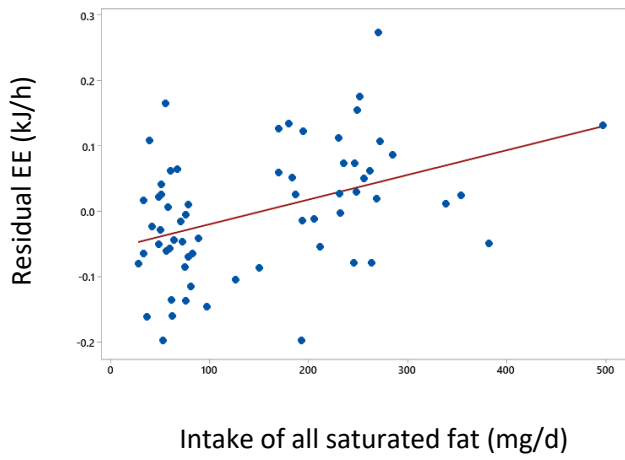


705 **Figure 4**

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) Database¹⁵, 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 equation¹⁶ 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)¹⁶. 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 BEE⁴³.

778
779 The DLW method is based on the differential elimination of isotopes of oxygen and hydrogen
780 introduced into the body water¹³. 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 CO₂ production using the technique¹⁶ and recalculated the entries in the
783 database using this common equation. These were then converted into energy expenditure
784 using the Weir equation⁴⁴ 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, date² and date³ 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 date² 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 date² and 663 for date³. 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

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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 (O₂) consumption (mL/h), carbon dioxide (CO₂) production (mL/h) and food intake (g) were
1315 recorded every 30 minutes. Energy expenditure (kJ/h) was calculated using the Weir Equation⁴⁴.
1316 Respiratory exchange ratio (RER) was calculated as $v\text{CO}_2/v\text{O}_2$.

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 μL 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 described⁴⁷. 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 μL 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.

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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 $\mu\text{g}/\mu\text{L}$ of every FA was made in isooctane/ethyl acetate 3:1 v/v that
1331 was further diluted to 50 $\text{ng}/\mu\text{L}$, and stable isotope reference FA regression curves were
1332 prepared^{47,48}. For total FA composition, 500 ng of the blended internal reference standard was

1333 added to 50 μ L of total lipid extract, and samples were taken to dryness under N₂ gas. Dried
1334 samples were immediately resuspended in 500 μ L of 100% ethanol, saponified with 500 μ L of 1
1335 M NaOH at 90 °C for 45 min in Teflon capped tubes, and then acidified by addition of 525 μ L of 1
1336 M HCl. Saponified FA were re-extracted using 1 mL of isooctane (twice), dried under N₂ gas, and
1337 were derivatized as above. The pentafluorobenzyl FA esters were resuspended in 200 μ L of
1338 isooctane and diluted 1:10 into isooctane into GC/MS autosampler vials for injection. Analyte
1339 data were acquired in NICI 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^{47,48}. 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.

1372

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 ($F = 53.19$, $p < 10^{-14}$).

1379

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.

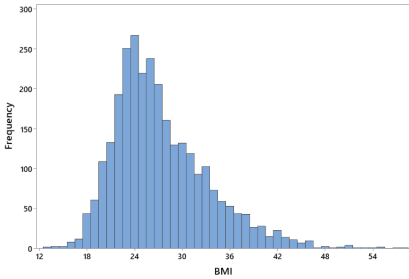
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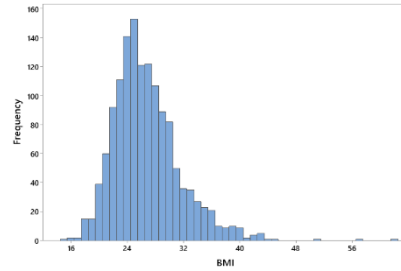
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1389 **Figure S1**

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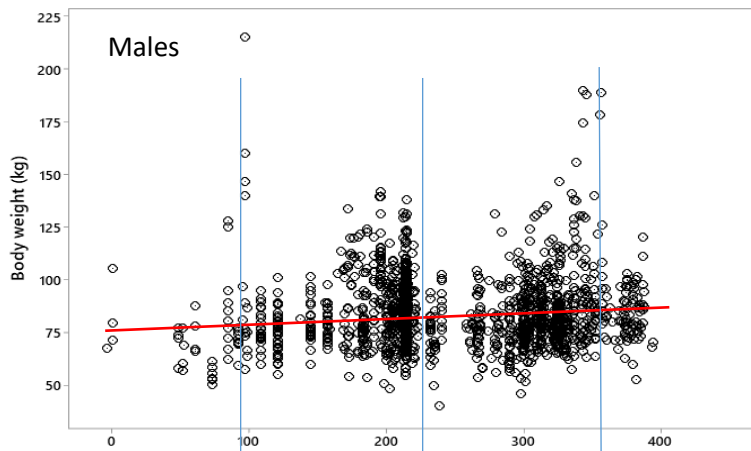
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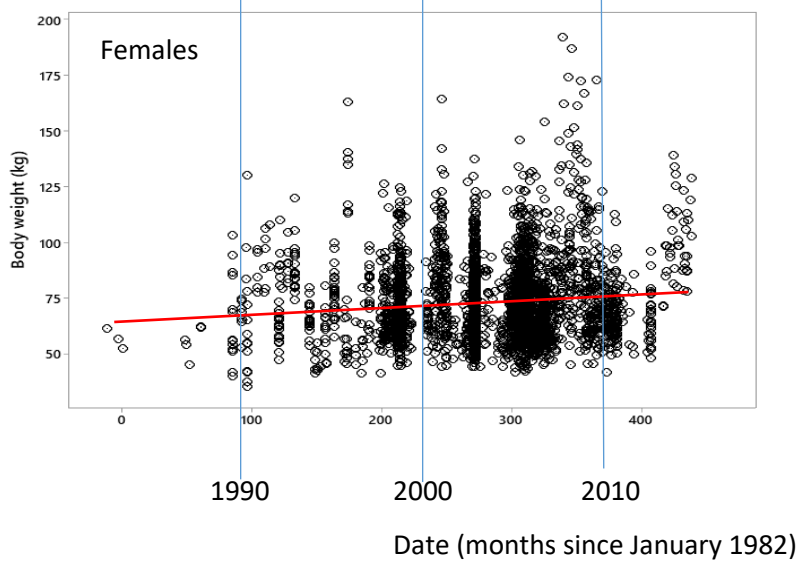
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1409 **Figure S2**

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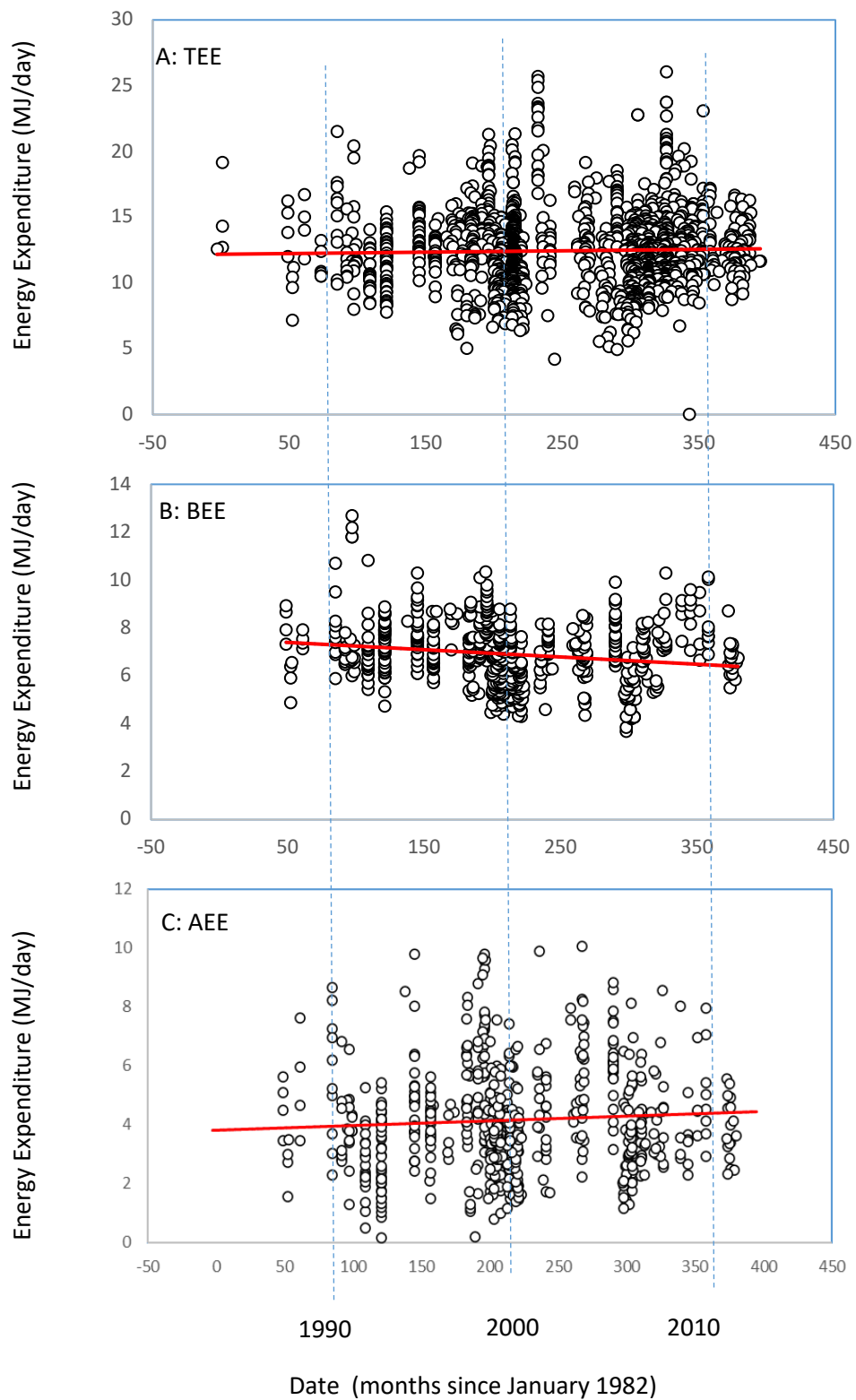
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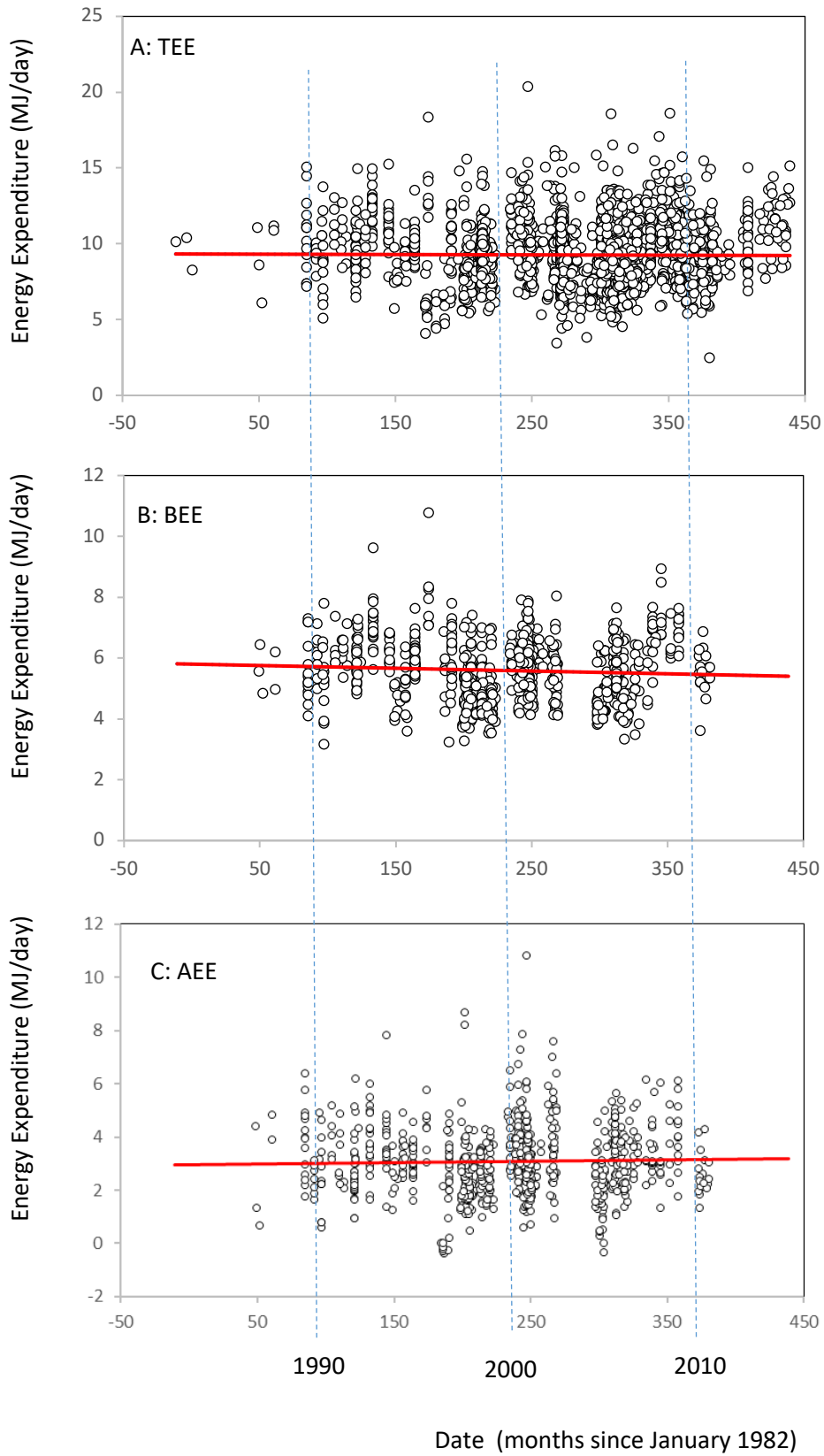
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1432 **Figure S3**



1458 **Figure S4**

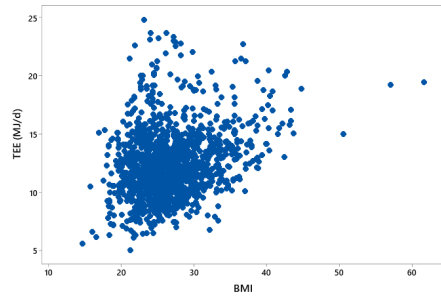
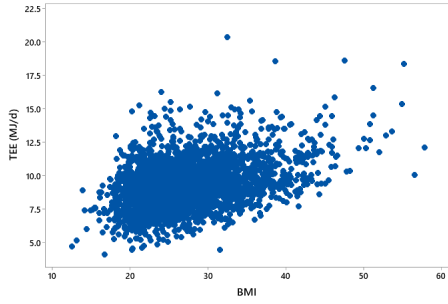
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Females

Males

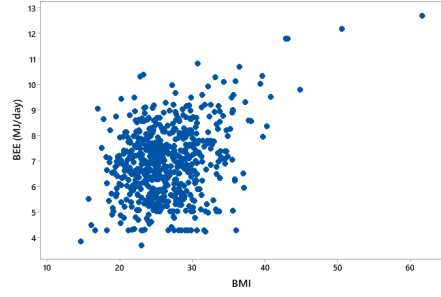
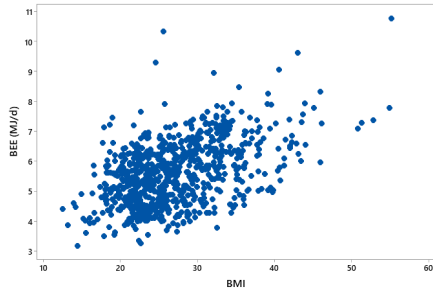
A:TEE

B:TEE



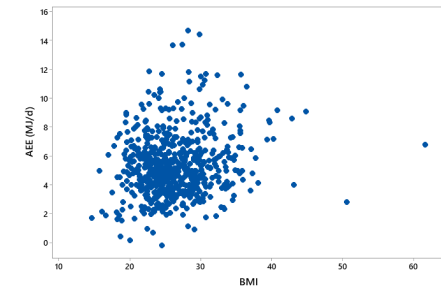
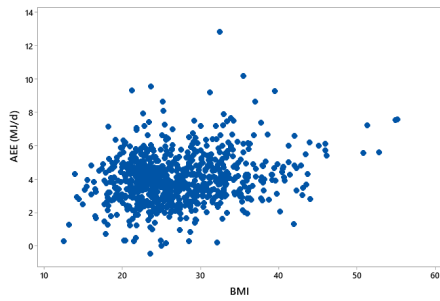
C: BEE

D:BEE



E: AEE

F:AEE



1486 **Figure S5**

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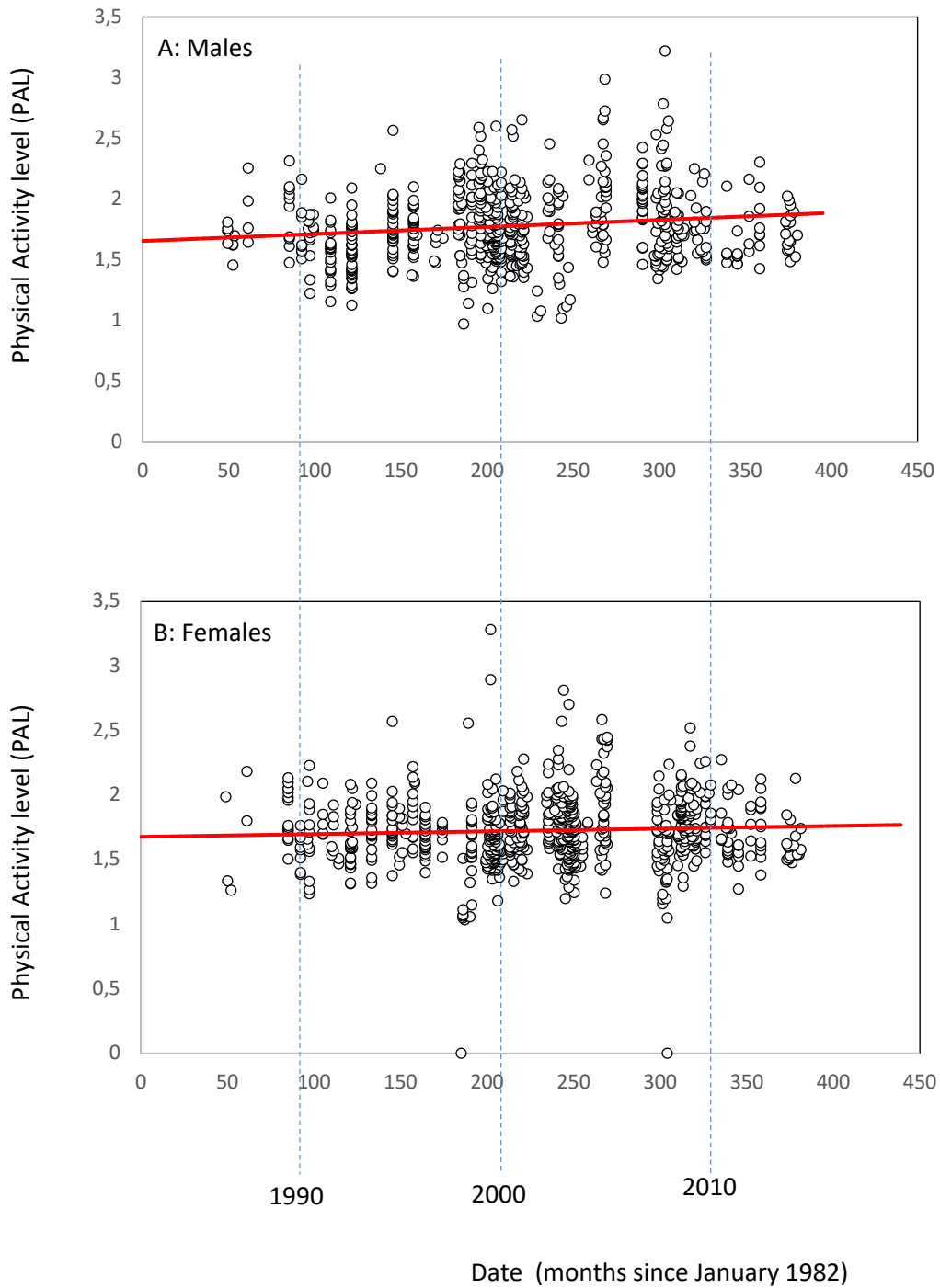
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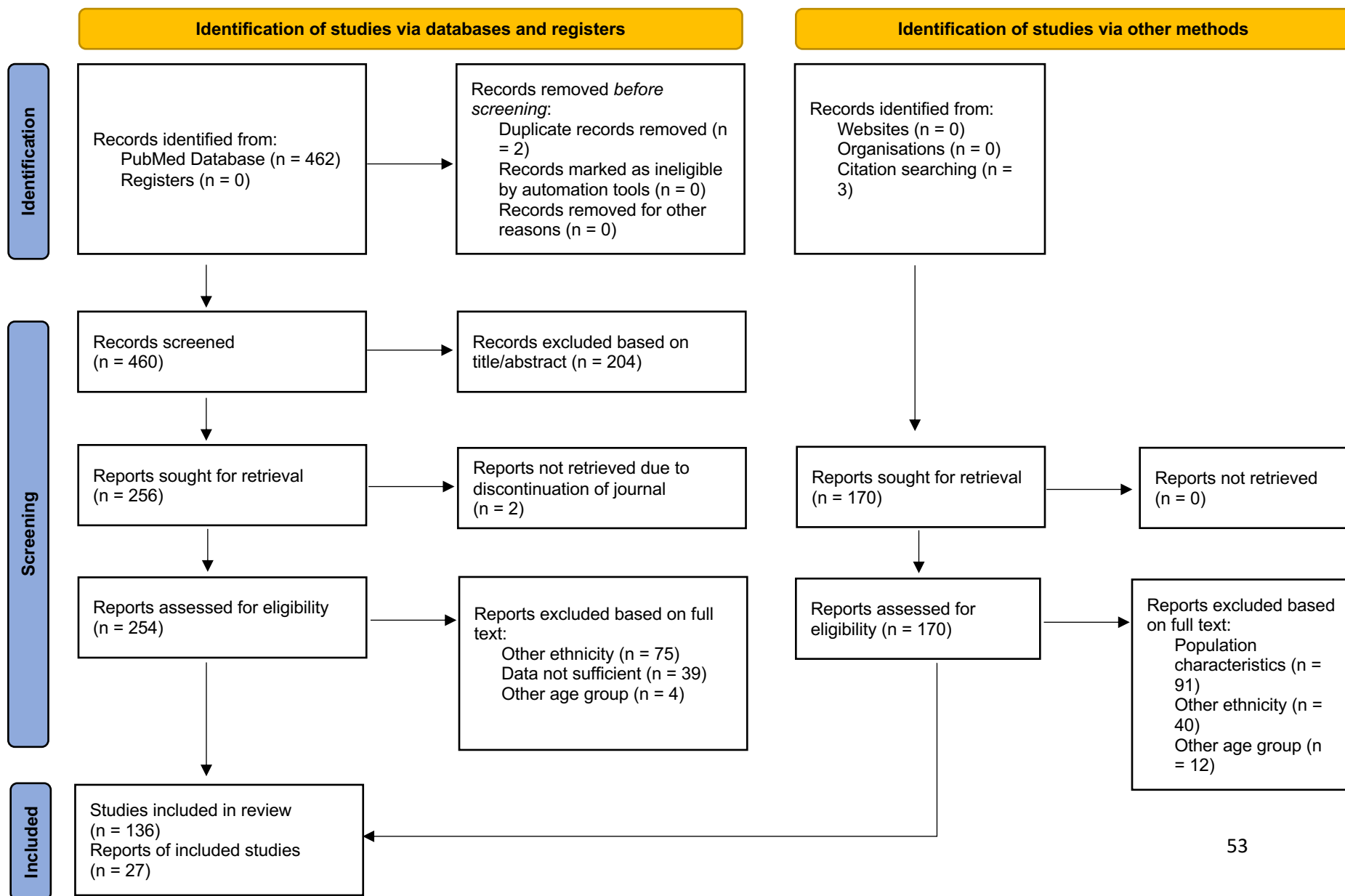
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1509 **Figure S6**

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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 ⁻⁹	-0.91	p < 10 ⁻⁸
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 R²x100 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 ² x100	F	p
None	0		-0.912	5.47	35.3	< 10 ⁻⁸
10	12	191	-0.918	5.57	35.2	< 10 ⁻⁸
13	4	61	-0.952	5.81	37.3	< 10 ⁻⁸
17	4	97	-0.886	4.90	32.7	< 10 ⁻⁸
20	10	85	-0.964	5.82	37.0	< 10 ⁻⁸
22	8	92	-0.942	5.63	35.9	< 10 ⁻⁸
23	21	109	-0.653	3.02	18.4	< 10 ⁻⁵
24	10	96-99	-0.966	5.88	37.4	< 10 ⁻⁸
31	38	121	-0.794	3.96	23.6	< 10 ⁻⁶
32	26	145	-0.912	5.47	35.3	< 10 ⁻⁸
35	12	157	-0.960	6.07	38.6	< 10 ⁻⁸
36	10	138-171	-0.886	5.19	32.9	< 10 ⁻⁸
37	10	157	-0.892	5.29	33.5	< 10 ⁻⁸
40	19	183-185	-0.937	5.82	36.5	< 10 ⁻⁸
41	4	184	-0.901	5.38	34.5	< 10 ⁻⁸
43	30	193-197	-0.908	5.39	34.6	< 10 ⁻⁸
46	7	185-190	-0.875	5.36	34.1	< 10 ⁻⁸
49	30	205-214	-0.888	5.54	33.6	< 10 ⁻⁸
51	9	199-200	-0.905	5.42	34.4	< 10 ⁻⁸
55	10	235-236	-0.902	5.40	34.3	< 10 ⁻⁸
57	10	259-269	-0.906	5.40	34.3	< 10 ⁻⁸
59	12	241	-0.892	5.34	33.7	< 10 ⁻⁸
60	24	290	-0.972	6.03	37.6	< 10 ⁻⁸
62	18	191-314	-0.982	6.12	38.6	< 10 ⁻⁸
65	22	339-358	-1.140	7.79	49.7	< 10 ⁻¹²
69	18	373-380	-1.135	7.32	47.9	< 10 ⁻¹²
72	14	322-327	-0.998	6.28	39.9	< 10 ⁻¹⁰
74	190	199-305	-0.577	3.05	13.4	< 10 ⁻⁴
79	11	302-321	-0.925	5.52	34.9	< 10 ⁻⁸
129	25	266-269	-0.813	4.63	28.4	< 10 ⁻⁷

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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	r ² x100	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	-0.393	1.53	0.001
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 ₂ 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	0
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	0
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	0
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	0
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	0
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	0
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	0
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	0
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	0
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	0
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	0
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	0

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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.

1698

1699 **Dr Helidoro Aleman-Mateo**

1700 Centro de Investigación en Alimentación y Desarrollo, A.C.

1701

1702 **Dr Lene F. Andersen**

1703 University of Oslo, Norway

1704

1705 **Dr Isaad Baddou**

1706 Unité Mixte de Recherche en Nutrition et Alimentation, CNESTEN- Université Ibn Tofail URAC39

1707

1708 **Dr Linda Bandini,**

1709 University of Massachusetts Chan Medical School

1710

1711 **Dr Ellen E Blaak**

1712 Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht University Medical Centre,
1713 Maastricht, Netherlands.

1714

1715 **Dr Carlinjn V.C. Bouten,**

1716 Department of Biomedical Engineering and Institute for Complex Molecular Systems, Eindhoven
1717 University of Technology, Eindhoven, The Netherlands

1718

1719 **Dr Stefan Branth**

1720 University of Uppsala, Uppsala, Sweden

1721

1722 **Dr Niels C. De Bruin**

1723 Erasmus University, Rotterdam, The Netherlands

1724

1725 **Dr Graeme L. Close**

1726 Liverpool John Moores University

1727

1728 **Dr Lisa H. Colbert**

1729 Kinesiology, University of Wisconsin, Madison, WI,

1730

1731 **Dr Dan Cummings**

1732

1733 **Dr Prasangi Debare**

1734 Department of Physiotherapy, Faculty of Allied Health Sciences, General Sir John Kotelawala Defence
1735 University, Sri Lanka
1736
1737 **Dr William Dietz**
1738 George Washington University, Washington DC, USA
1739
1740 **Dr Alice E. Dutman**
1741 TNO Quality of Life, Zeist, The Netherlands
1742
1743 **Dr Simon D Eaton**
1744 UCL, Great Ormond Street Institute of Child Health, London, UK
1745
1746 **Dr Cara Ebbeling**
1747 Boston Children's Hospital, Boston, Massachusetts, USA.
1748
1749 **Dr Asmaa El Hamdouchi**
1750 Unité Mixte de Recherche en Nutrition et Alimentation, CNESTEN- Université Ibn Tofail URAC39
1751
1752 **Dr Sölve Elmståhl**
1753 Lund University, Lund, Sweden
1754
1755 **Dr Mikael Fogelholm**
1756 Dept of Food and Nutrition, Helsinki, Finland
1757
1758 **Dr Tamara Harris**
1759 Aging, NIH, Bethesda, MD,
1760
1761 **Dr Marije B. Hoos**
1762 Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht University Medical Centre,
1763 Maastricht, Netherlands.
1764
1765 **Dr Rik Heijligenberg**
1766 Academic Medical Center of Amsterdam University, Amsterdam, The Netherlands
1767
1768 **Dr Hans U. Jorgensen**
1769 Bispebjerg Hospital, Copenhagen, Denmark
1770
1771 **Dr Noorjean Joonas**
1772 Central health Laboratory, Ministry of Health and Wellness, Mauritius
1773
1774 **Dr Kitty P. Kempen**
1775 Maastricht University, Maastricht, The Netherlands
1776
1777 **Dr Misaka Kimura**
1778 Institute for Active Health, Kyoto University of Advanced Science, Kyoto, Japan
1779
1780 **Dr Wantanee Kriengsinyous**

1781 Institute of Nutrition, Mahidol University, Thailand
1782
1783 **Dr Rebecca Kuriyan**
1784 Division of Nutrition, St. John's Research Institute, Bangalore, India
1785
1786 **Dr Estelle V. Lambert**
1787 Health through Physical Activity, Lifestyle and Sport Research Centre, Division of Exercise Science and
1788 Sports Medicine (ESSM), FIMS International Collaborating Centre of Sports Medicine, Department of
1789 Human Biology, Faculty of Health Sciences, University of Cape Town
1790
1791 **Dr Pulani Lanerolle**
1792 Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Colombo, Sri
1793 Lanka
1794
1795 **Dr Chystel L. Larsson**
1796 University of Gothenburg, Gothenburg, Sweden
1797
1798 **Dr Nader Lessan**
1799 Imperial College London Diabetes Centre, Abu Dhabi, United Arab Emirates and Imperial College
1800 London, London, United Kingdom
1801
1802 **Dr David S. Ludwig**
1803 Boston Children's Hospital, Boston, Massachusetts, USA.
1804
1805 **Dr Margaret McCloskey**
1806 Royal Belfast Hospital for Sick Children, Belfast, Northern Ireland
1807
1808 **Dr Alida Melse-Boonstra**
1809 Wageningen University, Wageningen, Netherlands
1810
1811 **Dr Gerwin A. Meijer**
1812 Maastricht University, Maastricht, The Netherlands
1813
1814 **Dr James C. Morehen**
1815 Research Institute for Sport and Exercise, Liverpool John Moores University, Liverpool, UK.
1816
1817 **Dr James P Morton**
1818 Research Institute for Sport and Exercise, Liverpool John Moores University, Liverpool, UK.
1819
1820 **Dr Aviva Must**
1821 Tufts University School of Medicine, Boston, USA
1822
1823 **Dr Christine D. Nystrom**
1824 Department of Biosciences and Nutrition, Karolinska Institute, Stockholm, Sweden
1825
1826 **Dr Daphne L. Pannemans**
1827 Maastricht University, Maastricht, The Netherlands

1828
1829 **Dr Renaat M. Philippaerts**
1830 Catholic University Leuven, Leuven, Belgium
1831
1832 **Dr Yannis P. Pitsiladis**
1833 University of Brighton, Eastbourne, UK
1834
1835 **Dr Roberto A. Rabinovich**
1836 Centre for Cardiovascular Sciences, Queen's Medical Research Institute, University of Edinburgh,
1837 Edinburgh, UK
1838
1839 **Dr John J. Reilly**
1840 University of Strathclyde, Glasgow, UK
1841
1842 **Dr Rebecca M. Reynolds**
1843 Centre for Cardiovascular Sciences, Queen's Medical Research Institute, University of Edinburgh,
1844 Edinburgh, UK
1845
1846 **Dr Elisabet M. Rothenberg**
1847 Göteborg University, Göteborg, Sweden
1848
1849 **Dr Dulani Samaranayakem**
1850
1851 **Dr Sabine Schulz**
1852 University of Maastricht, Maastricht, The Netherlands
1853
1854 **Dr Anders M. Sjödin**
1855 Department of Nutrition, Exercise and Sports, Copenhagen University, Copenhagen, Denmark.
1856
1857 **Dr Amy Subar**
1858 Epidemiology and Genomics, Division of Cancer Control, NIH, Bethesda, MD,
1859
1860 **Dr Minna Tanskanen**
1861 University of Jyväskylä, Jyväskylä, Finland
1862
1863 **Dr Ricardo Uauy**
1864 Institute of Nutrition and Food Technology (INTA), University of Chile, Santiago Chile.
1865
1866 **Dr Mauro E. Valencia**
1867 Centro de Investigación en Alimentación y Desarrollo, A.C.
1868
1869 **Dr Rita Van den Berg-Emons**
1870 Maastricht University, Maastricht, The Netherlands
1871
1872 **Dr Wim G. Van Gemert**
1873 Maastricht University, Maastricht, The Netherlands
1874

- 1875 **Dr Erica J. Velthuis-te Wierik**
1876 TNO Nutrition and Food Research Institute, Zeist, The Netherlands
1877
- 1878 **Dr Wilhelmine W. Verboeket-van de Venne**
1879 Maastricht University, Maastricht, The Netherlands
1880
- 1881 **Dr Jeanine A. Verbunt**
1882 Maastricht University, Maastricht, The Netherlands
1883
- 1884 **Dr Jonathan C.K. Wells**
1885 Population, Policy and Practice Research and Teaching Department, UCL Great Ormond Street Institute
1886 of Child Health, London, UK
1887
- 1888 **Dr George Wilson**
1889 Research Institute for Sport and Exercise, Liverpool John Moores University, Liverpool, UK