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Published in:
Nature Metabolism

DOI:
[10.1038/s42255-023-00782-2](https://doi.org/10.1038/s42255-023-00782-2)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2023

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Speakman, J. R., de Jong, J. M. A., Sinha, S., Westerterp, K. R., Yamada, Y., Sagayama, H., Ainslie, P. N., Anderson, L. J., Arab, L., Bedu-Addo, K., Blanc, S., Bonomi, A. G., Bovet, P., Brage, S., Buchowski, M. S., Butte, N. F., Camps, S. G. J. A., Cooper, J. A., Cooper, R., ... Wong, W. W. (2023). Total daily energy expenditure has declined over the past three decades due to declining basal expenditure, not reduced activity expenditure. *Nature Metabolism*, 5(4), 579-588. <https://doi.org/10.1038/s42255-023-00782-2>

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

Received: 26 October 2022

Accepted: 8 March 2023

Published online: 26 April 2023

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Obesity is caused by a prolonged positive energy balance^{1,2}. Whether reduced energy expenditure stemming from reduced activity levels contributes is debated^{3,4}. Here we show that in both sexes, total energy expenditure (TEE) adjusted for body composition and age declined since the late 1980s, while adjusted activity energy expenditure increased over time. We use the International Atomic Energy Agency Doubly Labelled Water database on energy expenditure of adults in the United States and Europe ($n = 4,799$) to explore patterns in total (TEE: $n = 4,799$), basal (BEE: $n = 1,432$) and physical activity energy expenditure ($n = 1,432$) over time. In males, adjusted BEE decreased significantly, but in females this did not reach significance. A larger dataset of basal metabolic rate (equivalent to BEE) measurements of 9,912 adults across 163 studies spanning 100 years replicates the decline in BEE in both sexes. We conclude that increasing obesity in the United States/Europe has probably not been fuelled by reduced physical activity leading to lowered TEE. We identify here a decline in adjusted BEE as a previously unrecognized factor.

Obesity is a global health threat⁵. Although excess body fat is a result of a prolonged positive energy balance^{1,2}, the exact causes of this imbalance remain elusive. Two major potential factors have been suggested. First, food consumption (net energy consumption accounting for losses in faeces) may have increased². Alternatively, declines in energy expenditure, due to reduced work-time physical activity (PA)⁴, combined with increases in sedentary behaviour, partly linked to elevated 'screen time' (TV, computer and phone use)^{6,7} may be a key driver. These may be linked in a vicious cycle⁸, where low activity leads to weight gain, which inhibits activity, leading to further weight gain.

Although there is direct evidence that PA has declined and sedentary time has increased^{4,6-8}, these changes do not necessarily translate into alterations in total energy expenditure (TEE). As individuals

get larger, the energy cost of movement also increases⁹. Thus, the same amount of energy may be utilized even though the actual time spent active has declined. Moreover, increases in one type of activity or behaviour may be replaced by decreases in another behaviour of equal cost. Consequently, apparently large behaviour changes may result in only minor alterations in expenditure. Finally, it has been suggested that we may compensate for changes in PA by adjusting expenditure on other physiological tasks^{10,11}. Although low TEE is repeatable, and having low TEE is not a risk factor for future weight gain over short timescales¹², this does not negate a possible impact over longer periods. Here we address the idea that reduced PA, leading to reduced activity energy expenditure (AEE), may have fuelled the epidemic.

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The doubly labelled water (DLW) method is a validated isotope-based methodology for the measurement of free-living energy demands¹³. A previous analysis using this method suggested there had been no change in TEE between 1986 and 2005, calling into question the reduced PA hypothesis¹⁴. However, these observations were based on a limited sample ($n = 314$) from a single European city over a restricted timespan of about 20 years. Here we expanded this analysis using data for 4,799 adults living across Europe and the United States drawn from the International Atomic Energy Agency (IAEA) DLW database¹⁵, for which we also had basal energy expenditure (BEE) measures in 1,432 individuals. All estimates of TEE were recalculated using a common equation¹⁶ that has been shown to perform best in validation studies¹⁶.

We split the data by sex, because this may affect the aetiology of energy balance^{17,18}. This resulted in 1,672 measurements of males and 3,127 measurements of females. In addition, for 632 of the males and 800 of the females, we also had measurements of BEE from which we derived AEE and physical activity level (PAL) (for calculations, see Methods). The data span a period of over 30 years, with the first measurements in late 1981 and the latest measurements made in late 2017, with most data obtained between 1990 and 2017. The distribution of body mass index (BMI) in the sample for both males and females is shown in Extended Data Fig. 1. Overall, females had higher BMI than males. In the pooled sample, the distribution was BMI <18.5 kg m⁻²: 2.3%; BMI 18.5–25 kg m⁻²: 40.3%; BMI 25–30 kg m⁻²: 35.1%; and BMI >30 kg m⁻²: 22.2%. Combined overweight and obesity was 57.3%. In both males and females, body weight increased over time (Extended Data Fig. 1), reflecting the secular trend in body weight over the same interval.

We first explored the changes in the unadjusted levels of TEE, BEE and AEE over time (Table 1 and Extended Data Fig. 2). In males, there was no significant relationship between TEE and the date of measurement (date coded as months since January 1982) ($r^2 = 0.0015$, $P = 0.14$ (not significant, NS); Extended Data Fig. 2a) the least squares regression fit gave a gradient of +1.5 kJ per month (95% confidence interval (CI) ± 2.06 kJ per month). This gradient leads to an estimated change in average TEE over 30 years of +0.55 MJ per day (95% CI ± 0.727 MJ per day). Contrasting the lack of significant change in TEE, there was a significant decline in BEE over time (Extended Data Fig. 2b) ($r^2 = 0.029$, $P = 0.000018$). The gradient of decline (3.3 kJ per month, 95% CI ± 1.4 kJ per month) was equivalent to an average fall in BEE by 1.19 MJ (9.7%) over 30 years (95% CI ± 0.54 MJ per day). As might be anticipated, since $TEE \times 0.9 = BEE + AEE$, the absence of a change in TEE and declining BEE was reflected by an increase in AEE over time, but this did not reach significance (Extended Data Fig. 2c) ($r^2 = 0.003$, $P = 0.16$). The gradient of the change in AEE (1.4 kJ per month, 95% CI ± 1.8 kJ per month) was equivalent over 30 years to an increase by 0.50 MJ per day (95% CI ± 0.69 MJ per day). In females, unadjusted levels of TEE, BEE and AEE did not change significantly over time (Table 1 and Extended Data Fig. 3).

All the energy expenditure variables (TEE, BEE and AEE) in both sexes were dependent on body mass (BM) and BMI (illustrated for BMI in Extended Data Fig. 4). Owing to these relationships, it is necessary to adjust the raw expenditure data over time (Extended Data Figs. 2 and 3) to account for any changes in body composition over time that might generate a biased estimate of the change in expenditure variables. We adjusted the levels of log-transformed TEE, BEE and AEE for body size and composition using residuals from general linear models with log_e fat-free mass (FFM), log_e fat mass (FM) and age as predictors. In this analysis, the data were logged because the relationships between energy expenditure components and body composition follow power law relationships. In males, adjusted TEE significantly declined over the measurement period (Fig. 1a: $r^2 = 0.0103$, $P < 0.0001$). The gradient of the fitted regression was -2.58 kJ per month (95% CI ± 1.20 kJ per month) leading to an estimated average change over 30 years of -0.93 MJ per day in adjusted TEE (95% CI ± 0.465 MJ per day), a decline, on average, of 7.7%. The adjusted BEE showed a highly significant decline over time (Fig. 1b: $r^2 = 0.064$, $P < 10^{-9}$) with the gradient of -2.67 kJ per month

Table 1 | Patterns of change in components of energy expenditure in males and females since the early 1990s

Males			
Unadjusted data			
Variable	Mean change over 30 years (MJ per day)	95% CI (\pm MJ per day)	Significance
TEE	+0.55	0.73	0.138 (NS)
BEE	-1.19	0.536	$P < 0.00002$
AEE	+0.50	0.695	0.159 (NS)
Adjusted data			
TEE	-0.93	0.46	$P < 0.0001$
BEE	-0.96	0.15	$P < 10^{-9}$
AEE	+1.01	0.53	$P < 0.0003$
Females			
Unadjusted data			
Variable	Mean change over 30 years (MJ per day)	95% CI	Significance
TEE	-0.16	0.360	0.405 (NS)
BEE	-0.32	0.352	0.071 (NS)
AEE	-0.18	0.452	0.448 (NS)
Adjusted data			
TEE	-0.51	0.26	$P < 0.00002$
BEE	-0.12	0.215	0.276 (NS)
AEE	+0.42	0.367	$P = 0.026$

Data are shown unadjusted and adjusted for body composition and age. The gradient of the least squared regression fitted relationships with time is translated to the overall change in expenditure (in megajoules) over 30 years with the 95% CIs for this change. $AEE = 0.9 \times TEE - BEE$. Significance of the relationships is also shown. $P > 0.05$ was considered NS. All tests were two sided.

(95% CI ± 0.82 kJ per month) being equivalent to an average fall in BEE of 0.96 MJ per day (14.7%) over 30 years (95% CI ± 0.15 MJ per day). In contrast, the adjusted AEE increased over time (Fig. 1c: $r^2 = 0.0221$, $P < 0.0003$). The gradient of +2.8 kJ per month (95% CI ± 1.4 kJ per month) was equivalent to a rise of 1.01 MJ per day over 30 years (95% CI ± 0.53 MJ per day).

In females as well, there was a significant decline in the adjusted TEE over time (Fig. 2a: $r^2 = 0.006$, $P < 0.00002$). The gradient of the effect 1.42 kJ per month was equivalent to a reduction in TEE over 30 years of 0.51 MJ (95% CI ± 0.22 MJ per day) or 5.6%. This decline was paralleled by a reduction in adjusted BEE of 2.0%, but this did not reach significance (Fig. 2b: $r^2 = 0.0015$, $P = 0.071$). The gradient of the fall in adjusted BEE was 0.3 kJ per month, equivalent to a reduction in adjusted BEE over 30 years of 0.11 MJ per day (95% CI ± 0.21 MJ per day). In contrast, and again similarly to the males, adjusted AEE significantly increased over time (Fig. 2c: $r^2 = 0.0063$, $P = 0.026$). The gradient of increase in AEE of 1.16 kJ per month was equivalent to an increase in AEE of 0.42 MJ per day over 30 years (95% CI ± 0.37 MJ per day).

As there was a small sample of measures in the early 1980s in males, these may have exerted undue leverage in the regression models. We therefore repeated the analysis excluding these data. Their removal had no impact on the detected relationships (Supplementary Table 1). Since individual studies may also exert undue leverage, we performed additional sensitivity analyses on the BEE effect (post 1987) where the data for each study were systematically removed and the regression recalculated. In males, removal of no individual study resulted in the loss of significance (Supplementary Table 2). In females, however, the absence of significance was due to inclusion of data from a single study (Supplementary Table 3). We have no reason to exclude these data, but

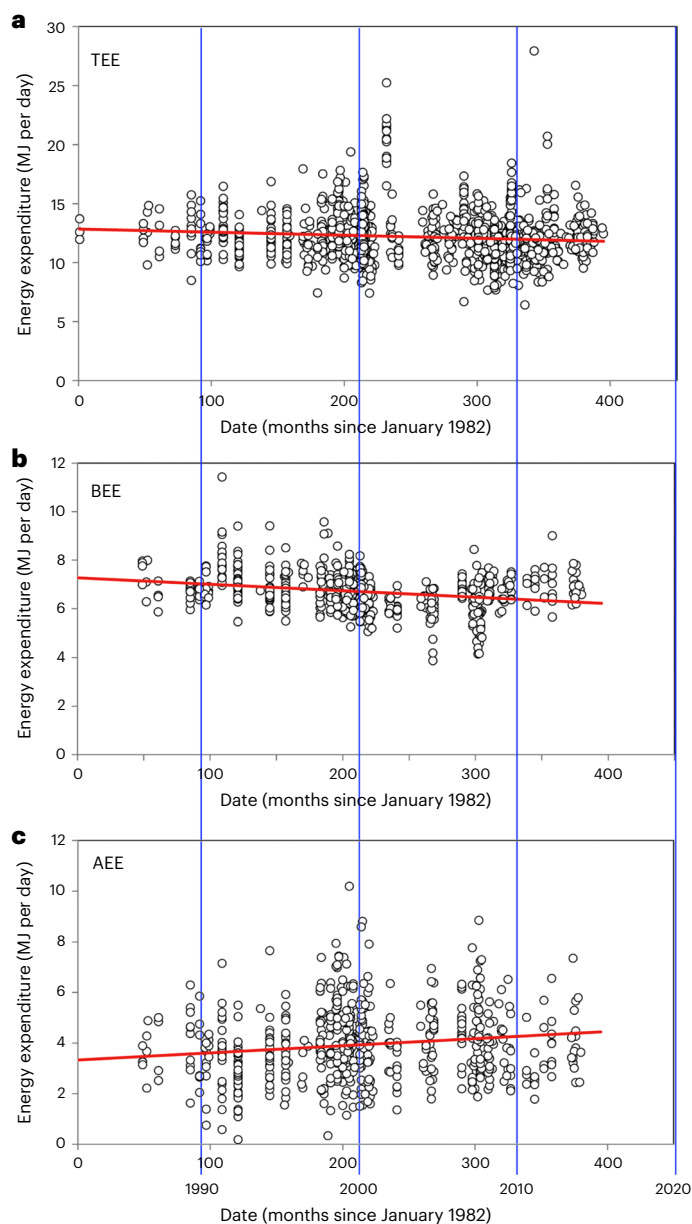


Fig. 1 | Trends over time for changes in energy expenditure components. **a–c**, Trends over time for males of adjusted TEE (**a**), adjusted BEE (**b**) and adjusted AEE (**c**). Adjustments were made for body composition (FM and FFM or BM, and age); for details, see Methods. All expenditures are in megajoules per day, and time is expressed in months since January 1982. Significant years are also indicated. Each data point is a different individual measurement of expenditure. The red lines are the fitted least squares regression fits. For regression details refer to the text and Table 1.

their undue influence may explain the anomalous lack of decline in female BEE when TEE is declining and AEE is rising (Table 1 and Fig. 2).

Hence, in both males and females there was a decline in the adjusted TEE by 7.7% and 5.6%, respectively, and in males in the adjusted BEE over time by 14.7% over 30 years (females declined by 2%, which was not significant). In both sexes, the confidence limits for the decline in adjusted TEE overlapped with the confidence limits for the decline in adjusted BEE, suggesting the decline in adjusted BEE could be sufficient to explain the reduction in adjusted TEE. In both sexes, there was in contrast a significant increase over time in adjusted AEE. The comparable declines in adjusted TEE and BEE resulted in a significant increase in PAL (TEE/BEE) in males (males, Extended Data Fig. 5a:

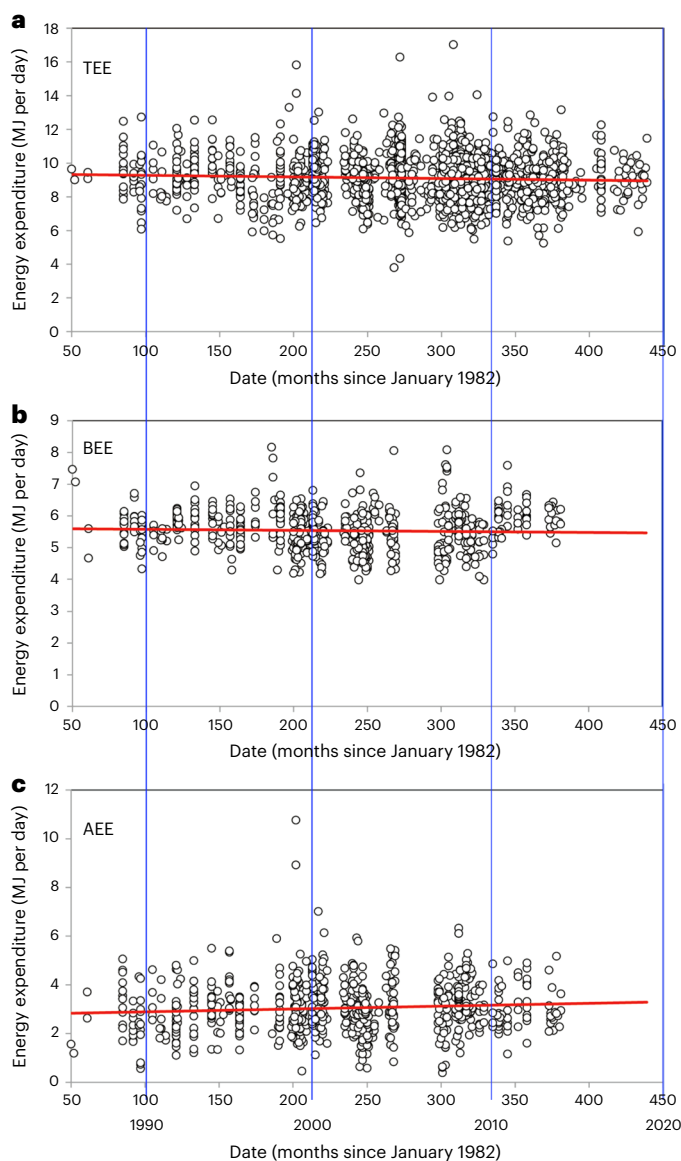


Fig. 2 | Trends over time for changes in energy expenditure components. **a–c**, Trends over time for females of adjusted TEE (**a**), adjusted BEE (**b**) and adjusted AEE (**c**). Adjustments were made for body composition (fat and lean mass, and age); for details, see Methods. Significant years are also indicated. All expenditures are in megajoules per day and time is expressed in months since January 1982. Each data point is a different individual measurement of expenditure. The red lines are the fitted least squares regression fits. For regression details refer to the text and Table 1.

$r^2 = 0.0215, P < 0.0003$), but in females, the change in PAL over time was not significant (females, Extended Data Fig. 5b: $r^2 = 0.0037, P = 0.085$).

To replicate and check our observation of decreasing BEE over time, we systematically reviewed data from the literature on mean basal metabolic rate (BMR) over the past 100 years, restricted to studies in the United States and Europe, to match the restricted regions included in the time course from the IAEA database (Figs. 1 and 2 and Table 1). For the distinction between BEE and BMR, see Methods. The main effect on \log_e BMR was \log_e BM (Fig. 3a), with additional effects of sex and age (total $r^2 = 0.88$). Including the date of measurement, sex, age and \log_e BM as predictors in a weighted regression analysis, there was a significant negative effect of date of measurement ($r^2 = 0.024, P = 0.022$) on the adjusted \log_e BMR (Fig. 3b). On average, BMR (in megajoules per day) adjusted for BM, age and sex has declined by about 0.34 MJ

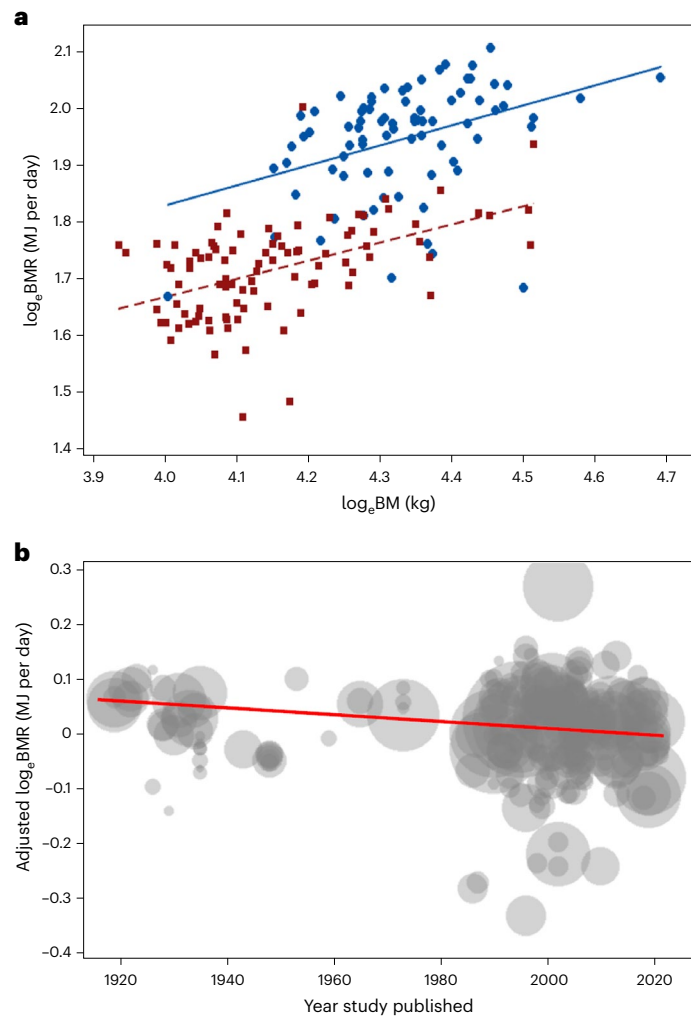


Fig. 3 | Trend in basal metabolic rate with body mass and over time. a, Effect of \log_{10} BM on the \log_{10} BMR in a systematic review of 165 studies dating back to the early 1900s (first study, 1919). Data for males in blue and for females in red. Studies with mixed male and female data are not illustrated. **b**, Bubble plot showing the residual \log_{10} basal metabolism derived from a weighted regression of \log_{10} BMR against sex, age and \log_{10} BM plotted against date of measurement in the same 165 studies. Bubbles represent the sample size of the studies. The red line is the fitted weighted regression.

over the past 100 years. This decline is consistent with, but at a lower rate, than the data from the IAEA database reported above (Table 1).

Basal metabolism may be influenced by many factors, one of which is diet. Human dietary changes during the obesity epidemic have included many things such as changes in the amounts of fibre and fat, as well as the types of fat consumed. As evaluating the impacts of long-term diets on human metabolism is difficult, we explored the potential impact of dietary fatty acids (FAs) on metabolic rate using the mouse as a model. Working with mice has the advantage that diets can be rigorously controlled and maintained constant over protracted periods. We exposed adult male C57BL/6 mice to 12 diets (for details, see Supplementary Table 4) that varied in their FA composition for 4 weeks (equivalent to 3.5 years in a human). Mouse BMR (kJ per day) was strongly related to body weight (regression $r^2 = 0.512$, $P = 3 \times 10^{-11}$; Fig. 4a). We included the total intake of different FAs (saturated FAs (SAT), mono-unsaturated FAs (MUFA) and poly-unsaturated FAs (PUFA)) with body weight into a general linear model. Only intake of saturated FAs was significant (SAT: $F = 11.05$, $P = 0.002$ (Fig. 4b); MUFA: $F = 1.38$, $P = 0.245$; PUFA: $F = 0.17$, $P = 0.686$) with higher levels of SAT linked to higher energy expenditure (Fig. 4b).

Overall, the data we present do not support the idea that lowered PA in general, leading to lowered energy expenditure, has contributed to the obesity epidemic during the past 30 years. Unadjusted AEE was higher in individuals with higher BMI (Extended Data Fig. 4). This is because, as shown previously, despite moving less on average, individuals with higher BMI have higher costs of movement⁹. Rather than adjusted AEE declining, it has significantly increased over time in both sexes. Yet TEE (adjusted for age and body composition) has declined significantly in both males and females over the past three decades. As adjusted AEE has increased at the same time that TEE has declined, there has been a corresponding reduction in adjusted BEE (which only reached significance in males). The observation that adjusted AEE (and PAL in males) has significantly increased over time is counterintuitive given the patterns established in work-time PA and the suggested progressive increase in sedentary behaviour^{4,6-8}. One possibility is that lowered work-time PA may have been more than offset by increased engagement in leisure time PA. For example, sales of home gym equipment in the United States increased from US\$2.4 billion to US\$3.7 billion between 1994 and 2017 (ref. 19). Time spent in leisure time PA in the United States also increased between 1965 and 1995 (ref. 20), suggesting leisure time PA has replaced the decline in work-time PALs²⁰. Leisure time PA has also changed in other Westernized populations²¹. Although time spent on computers has increased, much of the increase in this time has largely come at the expense of time spent watching television. Since these activities have roughly equivalent energy costs²², this change would not be apparent as a decline in overall adjusted AEE.

The reduction in adjusted BEE is less easily understood but is consistent with the recent observation that body temperatures have also declined over time²³, over the same interval as the reduction of BMR in the wider dataset we analysed (Fig. 3b). The magnitude of secular change in BMR is consistent with studies measuring BMR and body temperature in several contexts, including calorie restriction, ovulation and fever, which show a 10–25% increase in BMR per 1 °C increase in core temperature^{24,25}. It was recently suggested that changes in both activity and basal metabolism may have contributed to the decline in body temperature²⁶, but our data suggest this is probably dominated by a BMR effect. The reduction in body temperature has been speculated to be a consequence of a reduction in baseline immune function, because we have greatly reduced our exposure to many pathogens. However, the links between immune function and metabolism are not straightforward. For example, artificial selection on metabolic rate leads to suppressed innate but not adaptive immune function²⁷, and studies of birds point to no consistent relation between immune function and metabolism, either within or between subjects²⁸. Experimental removal of parasites in Cape ground squirrels (*Xerus inauris*) led to elevated rather than reduced resting metabolic rate²⁹. Nevertheless, some studies in forager–horticulturalist societies in South America have noted elevated BMR is linked to increased levels of circulating immunoglobulin (Ig)G (ref. 30) and cytokines³¹, supporting the view that a long-term decline in BEE may be mediated by reduced immune function. Whether this has any relevance to changes in the United States and Europe in the past 30 years is unclear. It is also possible that the long-term reduction in BMR represents methodological artefacts. In the early years, measurements of BMR were often made using mouthpieces to collect respiratory gases, and recently such devices have been shown to elevate BMR by around 6% (ref. 32). A second possibility is that early measurements paid less attention to controlling ambient temperature to ensure individuals were at thermoneutral temperatures³³.

During the past century, there have been enormous changes in the diets of US and European populations (United States Department of Agriculture and Food and Agriculture Organization of the United Nations food supply data)³⁴. These changes have included alterations in the intake of carbohydrates, fibre and fats, with the per cent of protein intake remaining relatively constant³⁴. While intake of carbohydrates

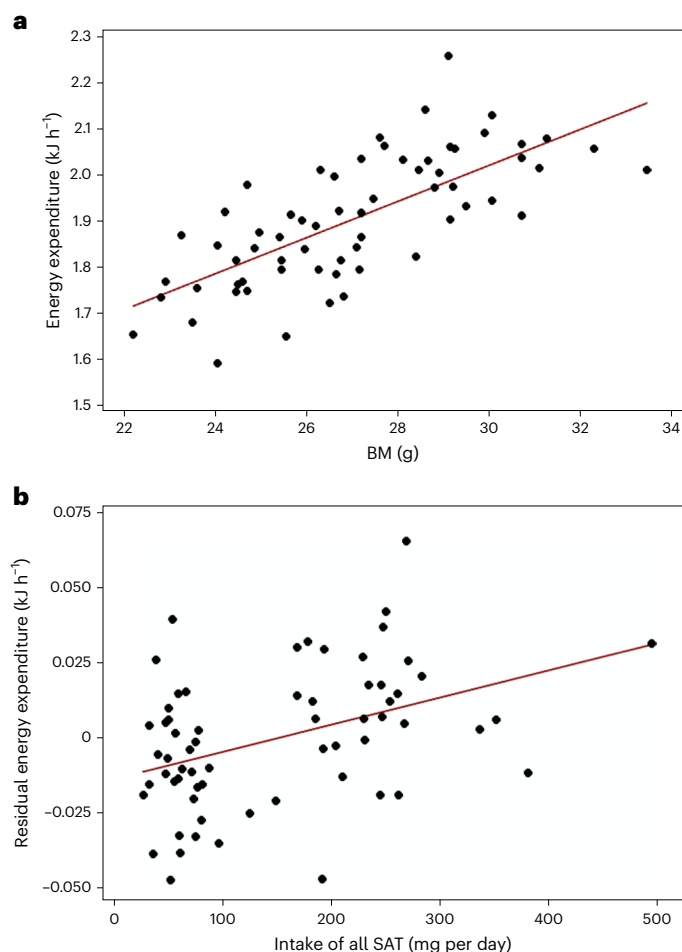


Fig. 4 | Effect of body weight and diet on mouse energy expenditure. **a**, The relationship between body weight and metabolic rate in the mice fed different diets with variable FA compositions. **b**, The effect of SAT intake on residual metabolic rate, corrected for body weight.

peaked in the late 1990s, the intake of fat has increased almost linearly since the early part of the 1900s. Moreover, the fat composition has changed dramatically, with large increases in soybean oil and seed oils from the 1930s onwards (dominated by the poly-unsaturated 18:2 linoleic acid and other PUFAs) and reductions in animal fats (butter and lard) (dominated by saturated fatty palmitic (16:0) and stearic (18:0) acids, and the mono-unsaturated oleic acid (18:1)) (ref. 34). The change has been dramatic, as animal fats accounted for >90% of the FA intake in 1910 but currently account for less than 15%. As linoleic acid is desaturated to form arachidonic acid and arachidonic acid is linked to endocannabinoids, it has been speculated that expanding linoleic acid in the diet may be linked to various metabolic issues. However, effects on BMR are disputed, and if anything, PUFAs lead to elevated not reduced metabolism^{35,36}, although many studies suggest no effect^{37,38}. This variation in outcome may reflect difficulties in controlling human diet over protracted periods necessary to generate robust changes in metabolism. In mice, where we can rigorously control the diet for prolonged periods (equivalent to many years of human life), we have shown here no effect of PUFAs on metabolic rate, but a clear impact of saturated fat, with higher intake of saturated fat leading to higher metabolic rate (adjusted for BM). This finding is consistent with earlier reports of relationships between membrane lipids and elevated metabolic rate in mice, particularly a positive effect of palmitic and stearic acids^{39,40}. This suggests that alterations in the intake of saturated relative to unsaturated fat over the past 100 years may have contributed to the decline in BEE reported here, although clearly we should be

cautious about extrapolations from males of a single inbred mouse strain and further studies in humans are required. Moreover, other aspects of the diet that impact metabolic rate may also have changed over time, for example, intake of fibre, which has declined in recent years⁴¹ and has been shown in a randomized controlled trial to affect resting metabolic rate⁴².

A strength of this study is the large sample of individuals over a restricted geographical area (the United States and Europe) measured using a complex methodology. This has allowed us to detect a small but nevertheless biologically meaningful signal. However, it is important to be aware that the studies were not designed with the current analysis in mind. Hence, while we have adjusted for differences in age and body composition, there may be other factors that differed over time that we did not adjust for and that could explain the trends we found. Further, the participants recruited at different timepoints may not have been representative of the underlying populations, even though the overall distribution seems representative (Extended Data Fig. 1). The data are cross-sectional, which limits the inferences that can be made regarding causality in the associations. Finally, while we have speculated on some potential factors that might have contributed to the reduction in BEE (that is, immune function and diet), these factors were not quantified in most of the participants who had their TEE measured. The mouse work we performed showing potential links of diet to metabolism was only conducted in males of one strain and a single age, and may not be more broadly applicable. These potential mechanisms, therefore, remain speculations until more direct data can be collected.

Overall, our data show that there has been a significant reduction in adjusted TEE over the past three decades, which can be traced to a decline in BEE rather than any reduction in AEE linked to declining PALs. Indeed, our data show that AEE has significantly increased over time. Reductions in BEE extend much further back in time (TEE data do not extend further back than 1981 as that was the first year the DLW technique was applied to humans), and mouse data indicated that one of many possible explanations is decreases in the intake of saturated relative to unsaturated fats. If the decline in BEE over time has not been compensated for by a parallel reduction in net energy intake, then the energy surplus resulting would be deposited as fat. This study, therefore, identifies a novel potential contributor to the obesity epidemic that has not been previously recognized: a decline in adjusted BEE linked to reduction in overall adjusted TEE. Further understanding the determinants of BEE and the cause of this decline over time, and if it can be reversed, is an important future goal.

Methods

This study involves, in part, a retrospective analysis of data submitted to the IAEA DLW database (www.dlwdatabase.org). The data stretch back to the late 1980s. However, the clinical trials registry was only launched by the National Institutes of Health in February 2000; hence, there was no possibility to pre-register the work before data collection started. Nevertheless, the analysis performed here was pre-registered on the IAEA DLW database website in 2020 (<https://doubly-labelled-water-database.iaea.org/dataAnalysisPlanned>).

DLW database study

Data were extracted from the IAEA DLW database⁴⁵, version 3.1.2, compiled in April 2020, and then later, while the manuscript was in review, this was expanded to include additional data extracted from version 3.7.1. In total, this latter version of the database comprises 8,313 measurements of TEE using the DLW method. We selected from the database measurements of adults aged >18 years, living in either Europe or the United States that also had a record of age. We excluded individuals who were professional athletes, individuals engaged in unusual levels of activity (for example, climbing mountains or participating in a long distance running race), pregnant and lactating females, and individuals with specific disease states. In total, this resulted in 4,799

measurements across both sexes. Submissions to the database did not reveal whether the sex was self-reported or assigned. Although an option was available to designate individuals as trans-sexual, none of the submitted data was identified as such. Gender was not available from the submitted data. Estimates of TEE were recalculated using a common equation¹⁶ that has been shown to perform best in validation studies. The final dataset included 1,672 measurements of males and 3,127 measurements of females.

For 632 of the males and 800 of the females, we also had measurements of BMR measured by indirect calorimetry. BMR measurements were derived either from hood calorimetry or from minimal metabolic rate determined overnight during chamber calorimetry (strictly sleeping metabolic rates or SMR). We converted these BMR or SMR to estimates of BEE. BMR and SMR are measured for relatively short periods lasting 30 min to 1 h. BEE is a theoretical value for the energy expenditure that would pertain if this BMR/SMR measurement was sustained for 24 h. For those individuals with measurements of both BEE and TEE, we estimated AEE ($(0.9 \times \text{TEE}) - \text{BEE}$), and the PAL (TEE/BEE). The value 0.9 in the equation for AEE assumes the thermic effect of food (TEF) is 10% of the TEE. In practice, this varies between individuals and is dependent on the diet. Variation is introduced therefore by imprecision in this value. However, since the thermic effect of food is largely dependent on protein in the diet, and protein intakes have remained stable over the past 40 or so years, there is unlikely to be any systematic imprecision in the value that could affect the detected trends. It is important to note that TEE and BEE are both measured directly, while AEE is only inferred from the difference between the two. The accuracy and precision of TEE relative to chamber indirect calorimetry for the equation utilized here was estimated at 0.4% (accuracy) and 7.7% (precision)¹⁶. The accuracy and precision of estimates of BMRs of metabolism inferred by indirect calorimetry has been evaluated using alcohol burns and is estimated at around 1–2%. Error in the estimate of AEE by subtraction is considerably higher than the direct estimates of TEE and BEE⁴³.

The DLW method is on the basis of the differential elimination of isotopes of oxygen and hydrogen introduced into body water¹³. The details of the practical implementation of the method and its theoretical basis have been previously published. We recently derived a new equation for the calculation of CO₂ production using the technique¹⁶ and recalculated the entries in the database using this common equation. These were then converted into energy expenditure using the Weir equation⁴⁴ with food quotients derived from the original studies.

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

In the first set of analyses, we used the unadjusted measures of TEE, BEE and AEE as dependent variables in general linear models, with time since January 1982 as the predictor. Tests were two sided, and $P < 0.05$ was taken as significant. All analyses were performed using Minitab version 19. It is well established that TEE, BEE and AEE depend on body composition, as well as subject age. Patterns of variation in unadjusted values with time might then reflect biased population sampling with respect to these traits. For example, if more older subjects were sampled later in the time course, this might give a spurious indication that TEE was declining since all energy expenditure parameters decline after ~60 years (ref. 46). We adjusted (logarithmically) TEE, BEE and AEE using $\log_e \text{FFM}$, $\log_e \text{FM}$ and age as the predictor variables using general linear modelling. As analyses were run separately for each sex, no adjustment for sex was necessary. In both sexes, for $\log_e \text{BEE}$, the predictors age, $\log_e \text{FFM}$ and $\log_e \text{FM}$ were all significant but for $\log_e \text{TEE}$ and $\log_e \text{AEE}$, only age and $\log_e \text{FFM}$ were significant. In the latter cases,

we deleted the non-significant predictor and re-ran the analyses. Following the above procedure, we then calculated the residuals to the fitted models and added them back to the mean logged TEE, BEE and AEE across all measurements. These values were then converted back to measures of 'adjusted TEE', 'adjusted BEE' and 'adjusted AEE' by taking the exponent of the derived values. We then checked that the residuals were normally distributed and the adjusted variables were not significantly related to any of the predictor variables to ensure that the adjustment was adequate. Tests applied were two sided, and $P < 0.05$ was taken as significant. We then sought relationships between the adjusted variables and date of measurement using linear regression. The adjusted variables cover a narrower timespan from 1990 to 2017.

Sensitivity analyses

We performed several checks on the data to make sure the trends were not being driven by individual studies. First there were some small studies in males before 1987 that may have exerted undue leverage in the analysis. We therefore excluded these data and re-ran all the regressions (Supplementary Table 1). There were no significant changes in any of the parameters. Since the downward trend in BEE was the most important new finding, we directed particular attention to this trend.

To evaluate whether the male BEE data would be better fit by a more complex model than the linear model we used, we included higher-order terms of the date into a regression analysis. In this analysis, the r^2 explained by date, date² and date³ was increased relative to just including date alone. However, the variance inflation factors (VIFs) for these more complex models were enormous. When date and date² were included, the VIF for each variable was 28.9, and when all three were included, the VIF values were 438 for date, 2,084 for date² and 663 for date³. The usual VIF cut-off for deciding whether to include an extra term into a model is 5. In this case, it was clear that higher-order terms were not justified relative to a simple linear model.

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

Using the post-1987 data, we then systematically removed the data for each study and re-ran the analyses to see if any particular study exerted undue effects on the regression. The analyses are summarized in Supplementary Table 2. This analysis showed that no individual study was responsible for the negative relationship. In all cases, the relationship between BMR and time remained negative and highly significant. A single study (number 23 in 1991) involved relatively high BMR values, and so omitting it reduced the coefficient and the significance. However, the P value for the regression when omitting these data was still highly significant $P < 10^{-5}$, and the coefficient was still strongly negative and biologically important.

We then turned our attention to the female data for BEE against date to see if the absence of a relationship there might be due to inclusion of any particular study. We used the same leave-one-out procedure as used for the males. The results are presented in Supplementary Table 3. In this case, the pattern was very different in that the relationship was always not significant ($P > 0.1$), except when a single study (study 65) was removed from the analysis, and in that case the relationship became significant ($P = 0.001$) and the negative gradient (extrapolated to over 30 years) increased to -0.39 MJ per day. Omitting a second study (study 69) had a smaller effect that also resulted in the relationship becoming marginally significant ($P = 0.037$). If both studies 65 and 69 were omitted, the P value for the relationship fell to $P < 10^{-5}$ and the gradient was -0.59 MJ per day. Study 65 was a study of overweight individuals⁴⁷. We have no objective reason to reject these data, but it is interesting that

the anomalous absence of a negative relationship of BMR to time in the females is dependent only on inclusion of this one study. It is worth noting that excluding this study from the male data strengthened the relationship for males (Supplementary Table 2).

Mouse indirect calorimetry measurements

All mouse studies followed the guidelines issued by Yale University's Institutional Animal Care and Use Committee. Male C57BL/6J mice (Jackson Laboratories, stock no. 000664) arrived at the facility at 5 weeks of age and were kept on a 12 h/12 h light/dark cycle and had free access to water and chow diet (Envigo Teklad, 2018S). At 6 weeks of age, mice were switched to one of the different high-fat diets (HFDs) (Research Diets Inc., Supplementary Table 4). The HFD contained 20% protein, 35% carbohydrates and 45% fat by energy with the fat being derived from different sources (listed in Supplementary Table 5). After 4 weeks of HFD feeding, mice were housed in a TSE PhenoMaster system for 4 days. Data from the final 72 h were used for calculations. O₂ consumption (ml h⁻¹), CO₂ production (ml h⁻¹) and food intake (g) were recorded every 30 min. Energy expenditure (kJ h⁻¹) was calculated using the Weir equation⁴⁴. The respiratory exchange ratio was calculated as vol CO₂/vol O₂.

Preparation of samples for GC–MS

For mouse diets, approximately 40–50 mg of pulverized diet was weighed and dissolved in 0.5 ml of pure water, acidified with 10 µl of 1 M HCl, and 1 ml of 100% methanol was added. Diet samples were mechanically homogenized to a uniform slurry. Total lipid extraction was performed on all samples as previously described⁴⁸. Isooctane/ethyl acetate 3:1 vol/vol (1.5 ml) was added and vortexed vigorously, then the organic phase was collected and this step was repeated. The two volumes of organic phase were combined and taken to dryness by evaporation under nitrogen gas at 40 °C. Samples were resuspended in 300 µl of isooctane/ethyl acetate 3:1 vol/vol. The diet samples were subsequently diluted 1:200 into isooctane/ethyl acetate 3:1 vol/vol.

FA quantification by GC–MS

Individual stable isotope FA stock solutions were made in isooctane/ethyl acetate 3:1 vol/vol, a mixture containing 1.0 µg µl⁻¹ of every FA was made in isooctane/ethyl acetate 3:1 vol/vol that was further diluted to 50 ng µl⁻¹, and stable isotope reference FA regression curves were prepared^{47,48}. For total FA composition, 500 ng of the blended internal reference standard was added to 50 µl of total lipid extract, and samples were taken to dryness under N₂ gas. Dried samples were immediately resuspended in 500 µl of 100% ethanol, saponified with 500 µl of 1 M NaOH at 90 °C for 45 min in Teflon capped tubes, and then acidified by addition of 525 µl of 1 M HCl. Saponified FA were re-extracted using 1 ml of isooctane (twice), dried under N₂ gas and were derivatized as above. The pentafluorobenzyl FA esters were resuspended in 200 µl of isooctane and diluted 1:10 into isooctane into gas chromatography–mass spectrometry (GC–MS) autosampler vials for injection. Analyte data were acquired in negative-ion chemical ionization full scan, the FA analyte peak area ratio to that of its corresponding stable isotope reference FA was calculated for each analyte, and ratios were converted to absolute amounts relative to regression curves for each chain length and saturation^{48,49}. Total SFA, MUFA and PUFA was the quantitative sum of the nmoles of the class of FA measured. Quantitative FA data were normalized to the total mass of diet input to the lipid extraction (that is, milligrams FA per gram diet). Dietary FA amounts are listed in Supplementary Table 4. Dietary FA intake (in mg) was calculated by multiplying dietary FA amounts (mg g⁻¹) by the amount of diet consumed (g).

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

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 A.J.M.-A. at a.alford@iaea.org. The BMR data are available upon request to co-corresponding author A.K. (a.kurpad@sjri.res.in). The mouse data described in the paper are available upon request to co-corresponding author M.S.R. (matthew.rodeheffer@yale.edu).

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Acknowledgements

The authors gratefully acknowledge funding to directly support this work as well as funding for the original studies that contributed to the database that are not listed individually here. In particular, direct support grants CAS 153E11KY5B20190045 from the Chinese Academy of Sciences to J.R.S. and grant BCS-1824466 from the National Science Foundation of the United States to H.P. are gratefully acknowledged. The mouse work was supported by grants from the Swedish Research Council International Postdoctoral Fellowship (VR 2018-06735) to J.M.A.J., National Institutes of Health grants K01DK109079 and R03DK122189 to M.C.R. and grants R01DK090489 and R01DK126447 to M.S.R. A.K. is supported by the IA/CRC/19/1/610006 grant from the DBT-Wellcome Trust India Alliance. We are grateful to T. Goodrich for comments on earlier drafts of the manuscript. The DLW database, which can be found at <https://www.dlwdatabase.org/>, is also generously supported by the IAEA, Taiyo Nippon Sanso and SERCON. We are grateful to these companies for their support and especially to T. Oono of Taiyo Nippon Sanso. The funders played no role in the content of this manuscript. Individuals who submitted data to the database that were not used in the analysis in this paper are listed in Supplementary Information (part 3). We are grateful for their contribution to the database.

Author contributions

J.R.S., K.R.W. and L.G.H. processed and analysed the IAEA data. J.M.A.d.J., J.L.K. and M.C.R. collected, processed and analysed the mouse data. S.S., S.G., J.R.S. and A.K. collected and analysed the retrospective BMR data from the literature. J.R.S., K.R.W., Y.Y., H.S., P.N.A., L.J.A., L.A., K.B.-A., S. Blanc, A.G.B., P.B., S. Brage, M.S.B., N.F.B., S.G.J.A.C., J.A.C., R.C., S.K.D., L.R.D., P.S.W.D., U.E., S.E., T.F., B.W.F., M. Gillingham, A.H.G., M. Gurven, C.H., H.H.H., D.H., S.H., A.M.J., P.K., W.E.K., R.F.K., W.R.L., M.L., A.H.L., C.K.M., E.M., A.C.M., E.P.M., J.C.M., J.P.M., M.L.N., T.A.N., R.M.O., H.P., K.H.P., J.P.-R., G.P., R.L.P., S.B. Racette, D.A.R., E.R., L.M.R., J.R., S.B. Roberts, L.B.S., D.A.S., A.J.S., A.M.S., E.S., S.S.U., G.V., L.M.v.E., E.A.v.M., B.M.W., W.W.W., J.A.Y.,

T.Y. and X.Z. contributed data to the database. J.R.S., Y.Y., H.S., S.S., A.J.M.-A., C.U., A.H.L., H.P., J.R., D.A.S. and W.W.W. created, curated and administered the database.

Competing interests

The authors have no conflicts of interest to declare.

Additional information

Extended data is available for this paper at <https://doi.org/10.1038/s42255-023-00782-2>.

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s42255-023-00782-2>.

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Peer review information *Nature Metabolism* thanks the anonymous reviewers for their contribution to the peer review of this work. Primary Handling Editor: Isabella Samuelson, in collaboration with the *Nature Metabolism* team.

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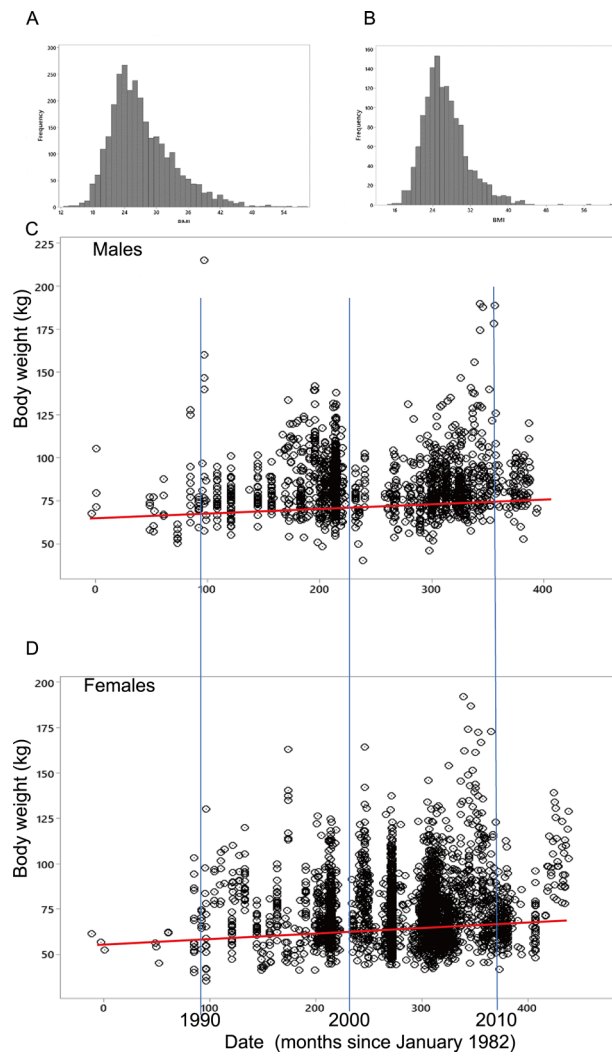
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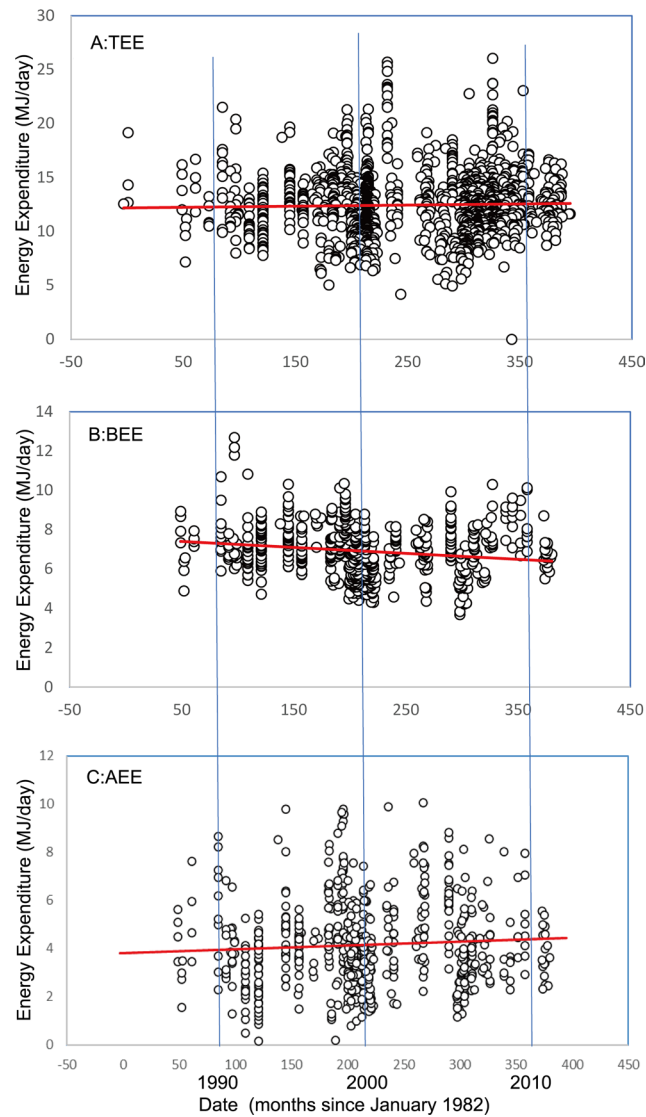
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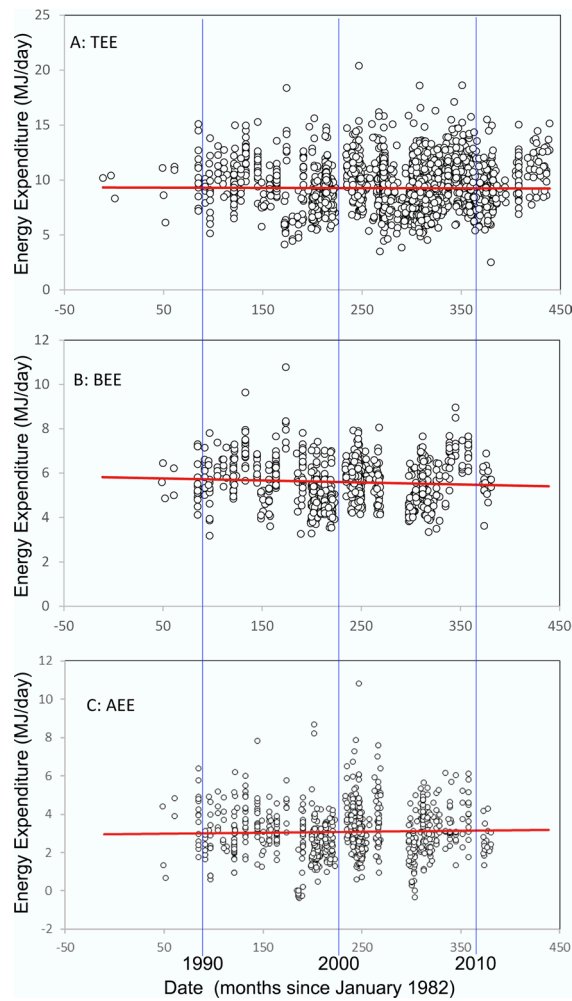
Extended Data Fig. 1 | Representativeness of the IAEA database dataset included in the analysis. Distribution of BMI in the sample data for a) females and b) males. Trends in body weight over the interval from 1982 to 2017 for c) males and d) females. There was a significant increase in weight over time in

both sexes. For males (gradient = 0.015 kg/month $F = 7.04$, $p = 0.009$) reflecting an average weight increase of 5.4 kg over 30 years, and for females (gradient = 0.023 kg/month $F = 20.84$, $p = 0.000005$) reflecting an average increase of 8.3 kg over 30 years.



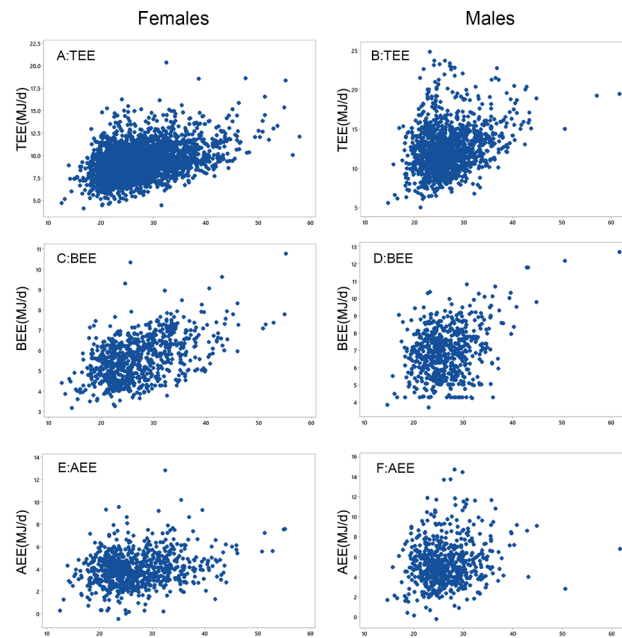
Extended Data Fig. 2 | Trends over time in unadjusted total, basal and activity energy expenditure in males. Trends over time in a) unadjusted total energy expenditure, b) unadjusted basal energy expenditure, and c) unadjusted activity energy expenditure for males. All expenditures are in MJ/d and time is expressed

in months since January 1982. Significant years are also indicated. Each data point is a different measurement of expenditure. The red lines are the fitted least squares regression fits. For regression details refer to text and Table 1.



Extended Data Fig. 3 | Trends over time in unadjusted total, basal and activity energy expenditure in females. Trends over time in a) unadjusted total energy expenditure, b) unadjusted basal energy expenditure, and c) unadjusted activity energy expenditure for females. All expenditures are in MJ/d and time is

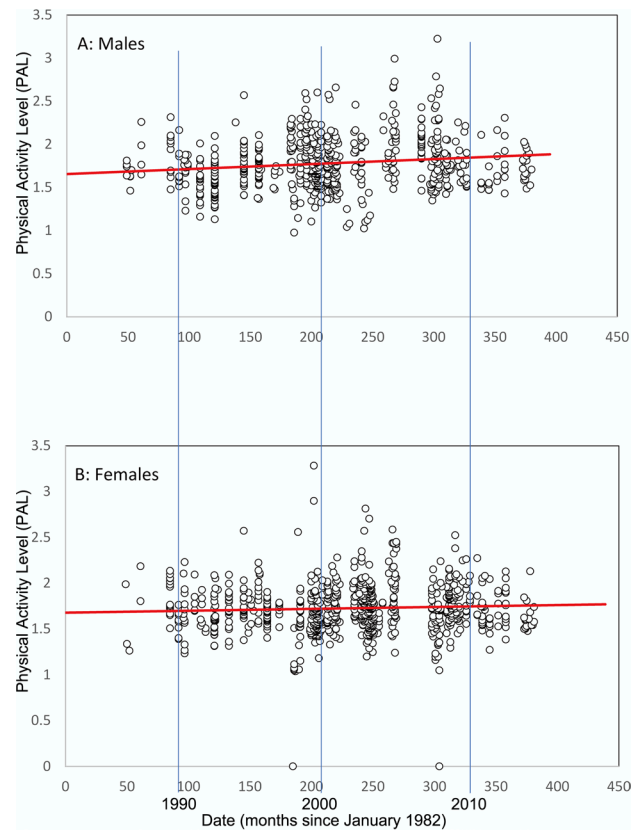
expressed in months since January 1982. Significant years are also indicated. Each data point is a different measurement of expenditure. The red lines are the fitted least squares regression fits. For regression details refer to text and Table 1.



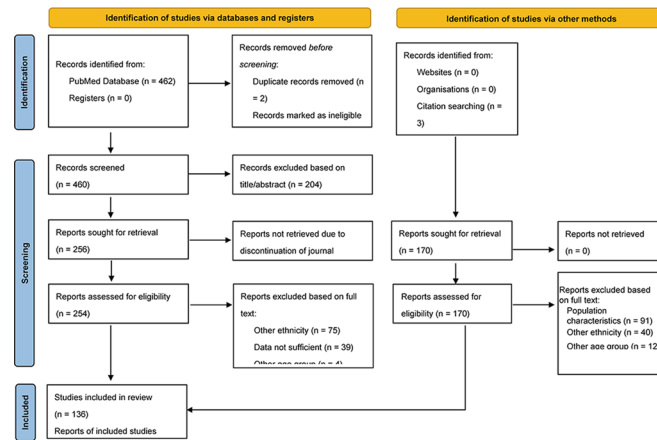
Extended Data Fig. 4 | Relationships of unadjusted total, basal and activity energy expenditure to body mass index in both males and females.

Relationships between energy expenditure parameters and Body mass index (BMI). In females the relationships were: a) for TEE vs BMI ($F = 559.3, p < 10^{-16}$),

c) BEE vs BMI ($F = 242.6, p < 10^{-16}$), e) AEE vs BMI ($F = 45.13, p < 10^{-10}$). For males the relationships were: b) for TEE vs BMI ($F = 114.6, p < 10^{-16}$), d) BEE vs BMI ($F = 79.4, p < 10^{-16}$), f) AEE vs BMI ($F = 16.28, p = 6 \times 10^{-5}$).



Extended Data Fig. 5 | Trends over time in physical activity level in both males and females. Trends over time in Physical Activity Level (PAL = TEE/BEE). PAL is dimensionless and time is expressed in months since January 1982. Significant years are also indicated. a) is for males and b) is for females. The red lines are the fitted least squares regression fits. For regression details refer to text.



Extended Data Fig. 6 | Search strategy for systematic review. Systematic review strategy. Flow diagram for selection of studies according to PRISMA guidelines.

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This study comprised three parts. A retrospective analysis of data compiled into an international database, a systematic review and an animal study. With respect to the first two, this was a secondary analysis of data that are already published and available in the primary literature. We compiled these data into a database sponsored by the International Atomic Energy Agency (IAEA). The IAEA DLW database is publicly accessible and free to access via submission of a data analysis request. Please see www.dlwdatabase.org for the appropriate forms to make a request. As with previous publications from the database the specific data published in the present study will be made available after publication to anyone requesting it, without the need to submit an analysis request for approval. Details of how to make such a request are available on the database website listed above. The data used for the systematic review are available on request to Dr Anura Kurpad, and the mouse data are available on request to dr Matthew Rodeheffer.

Human research participants

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Reporting on sex and gender

Data were analysed separately based on self reported sex of the participants. In total there were data available for 1672 males and 3127 females for total energy expenditure. For basal and activity energy expenditure we had available 632 measures for males and 800 for females. The option was available for declaration of non-binary gender and other gender types but these options were never selected by the persons submitting the data.

Population characteristics

Adult humans aged > 18 years old of both sexes, free of disease and living in Europe and North America.

Recruitment

Different studies employed different recruitment criteria. This recruitment information was not compiled when the study data were entered into the IAEA DLW database and hence it is not possible to share it. In general however the criteria were to recruit both sexes of adults aged >18 years old, free from obvious disease and not engaged in exceptional physical activity.

Ethics oversight

The component studies were each ethically approved at the component sites where the studies were performed.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

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Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size

This was a retrospective analysis of a convenience sample of data compiled across >100 component studies. The data were compiled into the IAEA DLW database. There was no pre-determined sample size because the data were collected before the idea to perform the analysis was formulated. This intention to perform the analysis was pre-registered on the IAEA DLW website.

Data exclusions

Data were excluded from children (aged <18 y), professional and amateur athletes and non-athletes engaged in exceptional physical activities (eg long distance running). Also individuals with identified chronic illness were excluded.

Replication

We found BMR declined over time in the component measures of individuals in the database. Since this was a unique database the finding could not be experimentally replicated. To replicate the finding we surveyed the literature via a registered systematic review (PROSPERO) to assess if the finding was replicated more generally in data pertaining to the USA and Europe dating back to the 1920s. This replication was successful.

Randomization

This was an observational study not an experiment. Accordingly there was no experimental allocation and hence no randomisation involved.

Blinding

There were no group allocations to be blinded against.

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<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
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Methods

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<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Animals and other research organisms

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Laboratory animals	male C57BL/6 mice aged 6 weeks at the start and 10 weeks at the end of the dietary intervention. The housing temperature averaged 21.3 oC and the relative humidity was set at 50% but was not monitored.
Wild animals	No wild animals were used in the study
Reporting on sex	The measurements were only made on males. The aim of this part of the study was to demonstrate only proof of principle that diet differences can impact metabolism.
Field-collected samples	No field collected samples were used in the study
Ethics oversight	Yale University Institutional Animal Care and Use committee (IACUC)

Note that full information on the approval of the study protocol must also be provided in the manuscript.