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The Oxford Brookes basal metabolic rate database – a reanalysis

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Abstract

Objective: To produce prediction equations for basal metabolic rate (BMR) derived from weight and height covering the age range from birth to old age.
Design: Cross-sectional data on BMR, sex, age, weight, height, ethnicity and measurement technique from the Oxford Brookes BMR database.
Setting: Worldwide.
Subjects: Data for 13 910 men, women and children from 174 papers published between 1914 and 2001.
Results: Absolute and proportional regression models were developed for each sex, showing a steep rise in predicted BMR with age until 15 years, more pronounced in males than females, then a gradual fall through adulthood. Predicted BMR increased by 6% and 1.4%, respectively, per standard deviation increase in weight and height. Predicted BMR in Caucasians was 4% higher than in non-Caucasians, though the effect size was sensitive to the inclusion or exclusion of data from certain influential publications. The effect of measurement technique on BMR, closed-circuit versus open-circuit, was small, near 1%.
Conclusions: It is possible to develop prediction equations that avoid splitting the data into arbitrary age groups. Heterogeneity between publications is greater than might be expected by chance, probably due to undocumented differences in technique.

Keywords
Basal metabolic rate
Ethnicity
Multiple regression model

Introduction

The Oxford Brookes database consists of 13 910 measurements of basal metabolic rate (BMR) in men, women and children assembled from 174 papers published between 1914 and 2001. The database includes information on the ethnicity, sex, age, weight and height of each subject, plus the year of the paper's publication and a flag distinguishing between BMR measured by open-circuit and closed-circuit calorimetry. The purpose of this analysis is to produce a set of prediction equations for BMR, which can be applied to individuals worldwide.

The age range of the subjects in the database is 0–106 years. Previously published equations have applied to particular age groups, e.g. females age 3–10 or males age 30–60. But this leads to discontinuities at the boundaries between age groups, so that for example a girl aged 2.99 has a materially different predicted BMR than for an otherwise similar girl aged 3.01. In addition, splitting the data into age groups reduces the sample size and makes individual research papers, focusing on particular ages, more influential than they would otherwise be.

The philosophy of the analysis here is to derive 'seamless' sex-specific equations which cover infancy to old age while avoiding discontinuities between age groups, and which also make use of the entire dataset.

Statistical methods

Seamless analysis

The main implication of this 'seamless' approach is that the analysis should combine data for children and adults, which has not previously been done. It poses a significant technical problem in that BMR, plus the two important covariates of body size and shape, weight and height, change rapidly with age during childhood, but are relatively insensitive to age once adulthood is reached.

The approach used here is to first standardise all three measurements – BMR, weight and height – for age, and then to relate age-standardised BMR to age-standardised weight and age-standardised height. It is then straightforward to quantify the effects of ethnicity and measurement technique across the lifespan.

The process of standardising weight and height for age in childhood is well understood, and many growth references exist which allow their conversion to reference centiles and Z-scores. Converting a measurement to a Z-score involves subtracting a mean value for the individual's age and sex, and dividing by an age-sex-specific standard deviation (SD):

$$Z\text{-score} = \frac{\text{Measurement} - \text{Mean for age and sex}}{\text{SD for age and sex}} \qquad (1)$$

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The reference used here is the British 1990 reference[1], though it needs to be emphasised that any other reference could be used, and the conclusions reached would be broadly the same. The advantages of the British reference are that it is soundly statistically based, using the LMS (lambda, mu, sigma) method[2], and it is available in computerised form. The LMS method uses the coefficient of variation (CV = SD/mean) of the measurement rather than the SD, and extends the *Z*-score calculation to include a skewness adjustment, but the principle is the same.

To ensure a unified treatment across the lifespan, adult weight and height need to be converted to *Z*-scores as well. The British reference extends only to age 23, so for simplicity adult weight and height *Z*-scores are calculated here assuming an adult age of 20 years. Again this assumption is not critical, as a later stage of the analysis provides a further opportunity for age adjustment during adulthood.

No references exist to convert BMR to *Z*-scores, and in any case the current analysis is intended to provide such a reference. For *Z*-scores to be calculated, reference values for the mean and SD of BMR need to be derived, consisting of smooth curves by sex plotted against age.

The mean curve rises steeply during childhood, reflecting the concurrent increase in body size, it peaks at some age in early adulthood, and subsequently stays fairly flat, possibly with a slight falling trend. This form of curve is difficult to estimate using conventional regression analysis, as it combines a steeply rising early region with an essentially flat later region, and a fairly abrupt joining point. It can be estimated using a cubic smoothing spline curve (which is the basis of the LMS method that was used for the British 1990 weight and height references), or it can be made by ‘gluing together’ a polynomial curve for childhood and a polynomial curve for adulthood. Both approaches are used here.

In the same way a smooth curve can be derived for the SD of BMR versus age. Like the mean, the SD depends strongly on age, being far less in young children (when mean BMR is relatively small) than say in young adults where mean BMR is at a maximum. If this age dependence of the SD is ignored the regression analysis focuses only on the data where the variability is greatest, i.e. in adulthood, and it broadly ignores the childhood data. To avoid this two approaches are possible: (1) weighted regression analysis to take the varying SD into account, or (2) unweighted regression analysis assuming that the SD is proportional to the mean, so that the ratio of the two, i.e. the CV, remains constant. This is explained further below.

The LMS method

The BMR data were first analysed using the LMS method[2]. This analysis ignored height, weight and the other factors, and was purely to explore age changes in the distribution of BMR. The LMS method derives the mean and SD of BMR by age, after choosing a suitable power transformation to make the data closer to normally distributed. The three quantities – mean, proportional SD (or CV), and power transform – are summarised as smooth curves plotted against age.

The preliminary analysis led to three conclusions:

- The best power transformation was somewhere between a log transform and no transform, so either could be used;
- The shape of the mean curve was too complex to model adequately with a cubic smoothing spline, with a steep rise up to age 17 then a gradual fall through adulthood. But the partially smoothed curve was useful for assessing the fit of the regression models developed later;
- The CV was fairly constant across the age range, between 12% and 16%. This means that the SD of BMR is about one-seventh (14%) of mean BMR at all ages.

Absolute and proportional effects

The usual regression model developed to predict BMR assumes absolute effects. To show what this means, take the regression coefficient of BMR on weight *Z*-score. This coefficient is the change in BMR associated with a unit change in weight *Z*-score (i.e. one weight SD) – it represents an absolute effect on BMR and is in units of MJ day^{-1} per weight SD.

But BMR can also be modelled assuming proportional effects. The coefficient of weight *Z*-score then reflects the *proportional* change in BMR, measured say in percentage units, per weight SD.

For an adult population the two forms of regression model give similar results, but with a mixed adult-child population the absolute and proportional models can be very different. Consider the regression coefficient of weight *Z*-score: with the absolute model it is the average difference in BMR between individuals whose weights differ by 1 SD. But this depends on age, as BMR is relatively small in childhood and the effect of weight *Z*-score must be similarly small. In crude terms the weight effect is likely to change with age in line with mean BMR. But the absolute model assumes erroneously that the effect is constant with age.

By contrast the regression coefficient of weight *Z*-score in the proportional model is less affected by age. It measures the mean *percentage* difference in BMR between individuals differing by 1 weight SD. This is broadly independent of mean BMR, and so is not directly related to age. The proportional effect may well be fairly constant, e.g. a regression coefficient of 6% indicating that an increase of 1 weight SD corresponds to a 6% increase in BMR at all ages.

The way to carry out these two analyses is as follows: the absolute approach uses BMR as the dependent variable ($y = \text{BMR}$), while the proportional approach uses 100 times the natural logarithm of BMR as dependent variable

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($y = 100\log_e$ BMR). This latter transformation converts the regression coefficients to percentage effects on BMR[3], and the SD of 100 $\log_e$ BMR is essentially the same as the CV of BMR (in % units). Both approaches are investigated here.

Constant coefficient of variation

The LMS method analysis shows that the CV can be assumed constant across the age range, and this greatly simplifies the subsequent analysis. For the absolute analysis where weighted regression is used, the more variable points are down weighted compared to the less variable points. It can be shown that to mimic a constant CV, the regression of BMR requires each BMR to be weighted inversely as the square of the subject's expected BMR derived from the regression equation. This ensures that for young children, where expected BMR for age is small, the weighting is large, whereas for adults, with a large expected BMR, the weighting is relatively small. The end result is that all subjects, irrespective of their age, have an equal impact on the analysis in the sense that the weighted residuals are equally variable at all ages.

By contrast the proportional analysis minimises the SD of 100 log BMR which is also the CV of BMR. So in this case unweighted regression is appropriate.

To summarise, the analyses are multiple regressions of BMR on age, weight Z-score, height Z-score, ethnicity and measurement technique. Within this there are two specific analyses: (1) absolute, the weighted regression of BMR (in units of MJ day^{-1}) and (2) proportional, the unweighted regression of 100 log BMR (in percentage units).

Modelling age

The trends in age through childhood and adulthood are modelled as two separate fractional polynomial curves (described below) which are 'joined together' at age 15. This age emerges from two separate analyses. The LMS analyses used to obtain smooth estimates of mean BMR versus age show that peak BMR occurs in both sexes at age 17. There is a sharp discontinuity in the curve at this age, rising steeply beforehand and falling slightly afterwards, particularly in males. Subsequently in the regression analysis this age is optimised, and a slightly better fit is obtained with age 15 than 17.

To include both child and adult curves in the model, interaction terms of age with a dummy variable called '*adult*' are included, where '*adult*' is 1 for age 15+ and 0 for age < 15. So for each age term the main effect applies to children and adults, while the interaction with '*adult*' applies only to adults. The interaction term is set to 0 at age 15 by defining it as follows:

$$adult \times \left[f(age) - f(15)\right] \quad (2)$$

where $f(.)$ indicates a fractional polynomial function in age. This ensures that the main effect and interaction join smoothly at the transitional age of 15. A dummy variable '*child*' is also used, where $child = 1 - adult$. Interactions of *child* with functions of age are calculated in the same way as for *adult* (Equation 2), and allow the child section of the curve to vary in shape independently of the adult section.

Fractional polynomials of age are the usual integer powers of age (i.e. age and age^2) plus extra fractional and inverse terms such as $\sqrt{}$age, log age and 1/age. Combined in the model they provide a rich family of curves, which have better properties than conventional polynomials (e.g. cubic or quartic curves) which tend to fit poorly at the extremes of age. The advantage of fractional polynomials interacting with adult is that a complex curve shape can be fitted for the child region along with a simpler curve in adulthood.

To handle fractional and/or inverse powers which require age > 0, an offset of 0.1 is added to age, chosen by inspection to optimise the fit. The regressions for males involve an interaction of age^6 or age^8 with *child*, i.e. applying only to the child section of the curve. These high powers of age are necessary to model the sharp rise in BMR leading up to age 15.

Modelling weight and height

The simplest model includes weight and height as Z-scores based on the British 1990 reference. In the absolute analysis the regression coefficient for weight depends on age, being small at birth, increasing through childhood and stabilising in adulthood. This pattern is modelled seamlessly by including interactions of weight Z-score with fractional polynomials of age and their adult interactions. This leads to second order interaction terms in the model, e.g. weight Z-score by age by adult. The net effect is that the coefficient of weight Z-score changes smoothly with age, in the same way that mean BMR itself does.

The analysis assumes a linear additive relationship between BMR, weight Z-score and height Z-score. This may fail in either of two ways – the relationship is curvilinear not linear, and the weight and height effects may interact with each other. The first effect is tested for by including squared terms in the model for weight Z-score and height Z-score, and the second by adding the product of weight Z-score and height Z-score. If they are not significant then the assumptions of linearity and additivity are justified.

Ethnicity

Ethnicity is important in the prediction of BMR. Several ethnic groups are represented in the database, with up to 23 distinct categories coded, but for most the sample size is small. In addition there has been some controversy within the largest ethnic group, Caucasians, since a large number come from a few Italian pre-World War II papers, and their results appear to be anomalous. So 'ethnicity' actually covers two separate concerns, differences between racial

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groups and a potential imbalance in the data due to one racial group.

The approach taken here is to identify just two ethnic groups, white Caucasians (who make up 69% of the total) and everyone else. It would be entirely possible to subdivide the groups further, but the uncertainties within the Caucasian group make this of limited value, at least initially. The variable '*Caucasian*' is a binary dummy variable taking the value 1 for Caucasian subjects and 0 for non-Caucasians. Its regression coefficient corresponds to a constant increment in absolute or percentage BMR at all ages. Interactions of '*Caucasian*' with age are also used to explore age-specific changes in the effect of ethnicity on BMR.

Measurement technique

Many different techniques have been used to measure BMR, but for simplicity they are coded in the database as either open-circuit or closed-circuit calorimetry. To test for differences attributable to the measurement technique a dummy variable '*Closed*', taking the value 1 for closed-circuit and 0 for open-circuit, is included in all the models. This assumes the same absolute or percentage effect at all ages.

The multiple regression model

Absolute effect model

For the absolute effect model, the fractional polynomials in age and their various interactions can be represented as follows:

$$\begin{aligned} \mathrm{BMR} &= f(age) + \mathrm{Weight}\,Z \times g(age) + \mathrm{Height}\,Z \times h(age) \\ &\quad + \mathrm{Caucasian} \times j(age) + \mathrm{Closed} \times k(age) \end{aligned} \tag{3}$$

where $f(age)$, $g(age)$, $h(age)$, $j(age)$ and $k(age)$ are smooth curves. The curve $f(age)$ is mean predicted BMR plotted against age, for an individual of mean weight and height for age (i.e. Z-score $= 0$), ethnic non-Caucasian measured by open-circuit. The other curves, which represent age-specific regression coefficients for each independent variable, are simpler in form and in the simplest case are the same at all ages.

The absolute regression is weighted so that the variance for an individual is proportional to the square of their predicted BMR. This requires some iteration: the regression analysis is initially unweighted, and the predicted BMRs from the model are used to calculate the weights for each subject and the model is revised using weighted regression. The new predicted BMRs are used to update the weights and revise the model a second time. Repeating this process two to three times leads to a stable model where each subject's sample weight is equal to his or her squared predicted BMR. The residual 'SD' from this model is the residual CV, due to the weighted analysis.

Proportional effect model

The proportional effect model is similar except for the dependent variable:

$$\begin{aligned} 100\log\mathrm{BMR} &= f(age) + \mathrm{Weight}Z \times g(age) + \mathrm{Height}Z \times h(age) \\ &\quad + \mathrm{Caucasian} \times j(age) + \mathrm{Closed} \times k(age) \end{aligned} \tag{4}$$

Here $f(age)$ needs back-transforming to $\exp(f(age)/100)$ to give predicted BMR by age. The other terms have similar meanings to their counterparts in Equation 3, except that they now represent proportional not absolute effects on BMR, i.e. the percentage change in BMR associated with a unit change in each variable.

Unlike the absolute model, this regression analysis is unweighted. But like the absolute model the residual SD (RSD) is the residual CV, and the CVs for the two models can be compared directly.

Model building

The process of developing the regression model, in particular the fractional polynomial $f(age)$, is sequential. Firstly weight and height Z-scores are included in the model, plus age raised to some power and the interaction of this age term with 'adult'. The power of the age term is varied to identify the optimum value, as judged by the minimum residual CV.

The process of varying the age power, and indeed optimising other variables in the model like the transitional age of 15, uses what is known as a 'Slider' variable in the statistical software package Data Desk version 6.1 (Data Description Inc, Cornell, USA). This is a scale on which the value of a variable is changed by dragging the cursor from side to side, and the value (i.e. the power transformation here) corresponds to the position of the cursor. The regression model is continuously refitted as the power changes, so that the power is estimated on a continuous rather than a discrete scale.

The first age term fitted to the model focuses on childhood, where the age trend is most marked, and the inclusion of the interaction allows the adult section of the curve to vary relatively independently. For example as an extreme case, the adult interaction coefficient could be exactly equal and opposite to the child (main effect) coefficient, so that the effect in adulthood of the two terms combined would exactly cancel out.

Once the optimal childhood power transformation has been found, it is rounded to a suitable number (i.e. an integer in the range -2 to $+8$, or ± 0.5). The power of the interaction term is optimised in the same way, and retained in the model if it is sufficiently significant.

The process is then repeated as many times as necessary, optimising the power of a new age term and then the corresponding interaction in the expanded model, and retaining them if significant. Once the new term ceases to be significant the process stops.

This same process is then used to build up the fractional polynomial $g(age)$ representing the weight Z-score coefficient, except that now each age term and interaction are multiplied by weight Z-score. This turns out to be more important for the absolute than the proportional analysis.

Similar processes are used for height Z-score and ethnicity. The regression coefficient for measurement technique proves to be too small for age trends to be fitted and is assumed constant across age.

Model testing

The size of the database, with BMRs for over 5000 females and 8000 males, means that the regression model has considerable power to detect significant factors. Significance by itself is unhelpful due to the large sample size, because a variable may be highly significant and yet explain only a minute fraction of the variability in BMR. For this reason variables are included in the model only if their t-statistic exceeds 3 or 4, corresponding to a significance level $P < 0.0001$. In most cases the t-statistics are considerably larger than this.

Once the model has been fitted, each subject's BMR can be expressed as a standardised residual similar to the Equation 1:

$$\frac{\mathrm{BMR} - \mathrm{predicted\ BMR}}{\mathrm{RSD} \times \mathrm{BMR}} \qquad (5)$$

where the predicted value comes from the model and the RSD is actually the residual CV. This equation takes slightly different forms for the absolute and proportional models due to the differing dependent variables.

Several regression diagnostics are used to test the model's validity. The diagnostics are applied to the standardised residuals, to take into account the weighted analysis where appropriate. The distribution of the standardised residuals is tested with a probability plot, the standardised residuals are plotted against their expected values (which identifies extreme outliers), and the leverage is tested with a probability plot to identify unduly influential points.

Methodological differences between publications

The structure of the BMR database is hierarchical, consisting of a series of publications each of which provides data for a group of subjects. One way to analyse such data is with a multilevel model, which estimates separate error variance terms for each level of the hierarchy, i.e. publications at the upper level and subjects within publications at the lower level. The differences between publications, after adjusting for the covariates in the model, are summarised as a *random effect*, i.e. the variance of mean BMR across publications. Instead a simpler approach has been used here, *fixed effects* rather than random effects, where a separate mean is fitted for each publication.

The regression models described so far ignore heterogeneity between publications, and an important part of testing the model fit is to seek outliers among them. For this the mean standardised residual for each publication is calculated. Assuming no heterogeneity this is distributed with mean 0 and approximate variance $1/n$, where n is the number of subjects from the publication. The mean for each publication can be plotted against n, allowing outlying publications to be identified where the mean exceeds $\pm 3/\sqrt{n}$ (i.e. outside the 99.8% confidence interval). Outliers, where the mean BMR is systematically larger or smaller than for other publications, indicate important biases due to some aspect of the methodology.

Outlying publications can be handled in either of two ways: their data can be excluded from the analysis, or a dummy variable identifying cases from the publication can be added to the model to adjust for the non-zero mean. The first approach wastes data and may introduce other biases, while the second removes the between-publication bias while retaining within-publication information. The latter approach is used here.

The models described so far can be extended by fitting fixed effects for each publication, in addition to the other covariates. This has the effect of adjusting out all differences between publications. As a result the model cannot test for the effect of closed-circuit calorimetry as it is confounded with publication – each publication uses one particular technique, so once the differences between publications have been adjusted out there is no within-publication information on which to base a closed-circuit effect. But all the other terms in the model, for age, weight, height and ethnicity, can still be estimated, and the differences in coefficients with and without the publication adjustment provide insight to the robustness of the regression equation.

The 'zero age' problem

More than 96% of subjects in the database have age recorded to a whole year, including most children and many infants. There are 293 infants with age coded as 0, yet many of them are clearly too large to be neonates. Due to the rapid growth rate in infancy some have pathologically large Z-scores, over 15 for height and over 12 for weight. These data are clearly very influential, so all the models have been developed while testing for the effect of including or excluding them. The conclusion is that they are too influential to include, so all points with age coded as precisely 0 have been excluded. However the 89 points with a decimal age between 0 and 1 are retained.

Of the 1598 children aged 1–10 years only 11 have non-integral ages, so biases in the Z-scores arise here as well. But as the growth rate is slower the biases are smaller and have been ignored in the analysis.

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Results

Age trends

Figure 1 shows smoothed age trends in BMR from infancy to old age, by sex. They are cubic spline curves fitted by the LMS method ignoring all covariates except age. Both curves start with a low value in infancy and rise steeply to peak at age 17, and then decline steadily to old age. The age trend in childhood is more complex for boys than girls, with a steeper rise during puberty.

Absolute regression model

Males

Table 1 gives the weighted regression model for males of BMR on age, weight *Z*-score, height *Z*-score, ethnic Caucasian and closed-circuit. It involves 8390 measurements on subjects from 0.03 to 101 years, weighted inversely as the square of each subject's predicted BMR. The model explains 92% of the variance in BMR and the residual CV is 0.102 or 10.2%.

The fitted trends for age and weight *Z*-score each involve four terms, while there is a single coefficient for height *Z*-score. Figure 2 shows the three age trends ($f(age)$, $g(age)$ and $h(age)$ in Equation 3), with the latter two multiplied by 10 for clarity.

The upper curve in Fig. 2 shows predicted BMR as a function of age, for a subject of average weight and height, ethnically non-Caucasian and measured by open-circuit. The age trend in predicted BMR is clearly similar in shape, particularly during childhood, to the unadjusted curve in Fig. 1. This is achieved by including a term in age^8 for the child part of the regression model, which rises almost vertically just before the 'adult' age of 15.

The weight coefficient also changes appreciably with age, being smallest in infancy and largest in early adult life (Fig. 2, middle curve). In broad terms it follows the shape of the predicted BMR. The meaning of the weight coefficient is as follows: at age 15 for example it takes the value 0.5 (remembering to divide by 10 in Fig. 2) – this means that a change of 1 SD in weight at age 15 predicts a change of 0.5 MJ day^{-1} in BMR. At birth the coefficient is far smaller at 10.040, and similar to the height coefficient of 0.043 (Table 1 and Fig. 2, lower curve). This means that a 1 SD change in weight or length in infancy predicts a change of 0.04 MJ day^{-1} in BMR.

Table 1 also shows that on average BMR is 0.39 MJ day^{-1} larger in Caucasians than non-Caucasians, and 0.12 MJ day^{-1} larger measured by closed-circuit than by open-circuit calorimetry.

Biases between publications are discussed more fully with the proportional model, but to give a flavour here the mean BMR for publication 205 ($n = 571$ subjects) is 0.45 MJ day^{-1} greater than predicted by the model, while for publication 155 ($n = 130$) it is 0.80 MJ day^{-1} less than predicted. Both these biases are very highly significant.

Females

Table 2 gives the weighted regression model for females of BMR on age, weight *Z*-score, height *Z*-score, ethnicity and measurement technique. It involves 5191 measurements on subjects from 0.03 to 106 years. The model explains 94.6% of the variance in BMR and the residual CV is 0.102 or 10.2%, the same as for males.

The model is simpler than for males because the age trend (Fig. 1) is less complex. There are three terms each for age and weight *Z*-score, and they are shown plotted against age in Fig. 3. Predicted BMR by age (upper curve) is for a subject of average weight and height, ethnically non-Caucasian and measured by open-circuit. It again shows the rise in childhood and slower fall in adulthood, as in Fig. 1.

The weight coefficient (Fig. 3, middle curve) changes with age in much the same way as predicted BMR, with its largest value at age 15, about 0.4 MJ day^{-1} per SD of weight. In infancy the weight coefficient is negative and smaller than the height (or rather length) coefficient of 0.064 MJ day^{-1} (Table 2 and Fig. 3, lower curve).

The difference in predicted BMR between ethnic Caucasians and non-Caucasians is 0.2 MJ day^{-1}, rather smaller than for males, while the effect of measurement technique is very small and marginally significant, 0.04 MJ day^{-1}.

To summarise so far, the regression models for the two sexes explain a large part of the variation in BMR, and the values of the coefficients appear reasonable with the

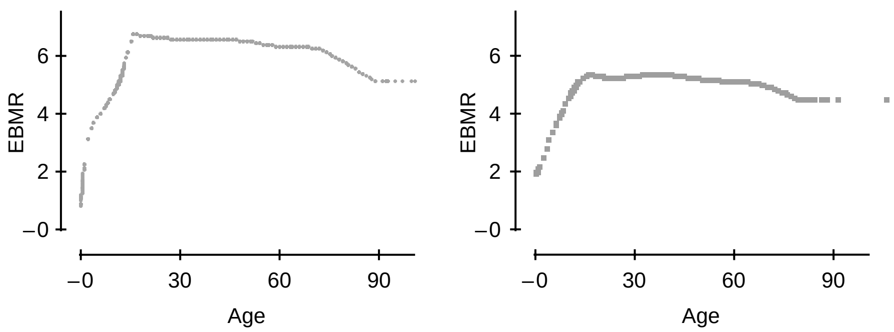

Fig. 1 Mean BMR (MJ day^{-1}) by age in males (left) and females (right). Cubic spline curves unadjusted for body size or other factors

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Table 1 Males: weighted regression analysis of BMR (dependent variable; MJ day^{-1}) on age, weight *Z*-score, height *Z*-score, ethnicity and measurement technique. The regression coefficient for weight *Z*-score depends on age – see text for details

Variable	Coefficient	SE of coefficient	*t* ratio	Prob
Constant	0.73	0.050	14.6	< 0.0001
Age	1.2	0.035	72.8	< 0.0001
Adult × Age	−1.4	0.033	−78.6	< 0.0001
1/Age	−0.17	0.040	−17.9	< 0.0001
Child × Age^8	0.051×10^{-8}	0.0013×10^{-8}	45.3	< 0.0001
Weight *Z*-score	0.040	0.016	2.6	0.3
Wtz × Age	0.032	0.0014	22.8	< 0.0001
Wtz × Adult × Age	−0.029	0.0013	−22.4	< 0.0001
Wtz × Adult/Age	6.1	0.64	9.2	< 0.0001
Height *Z*-score	0.043	0.0073	5.8	< 0.0001
Ethnic Caucasian	0.39	0.036	22.4	< 0.0001
Closed-circuit	0.12	0.014	8.2	< 0.0001

Abbrevations: RSD – residual standard deviation.
R^2 (adjusted) = 91.8%, RSD = 0.1018 with 8390 − 12 = 8378 degrees of freedom.

exception of weight *Z*-score, which changes with age in a complex way that appears to be related to mean BMR.

The reason why the weight *Z*-score coefficient is so age-dependent is this: it predicts the impact on BMR of a 1 SD change in weight at each age, and the SD of weight itself varies with age. At birth the SD is about 0.5 kg while in adults it is around 12 kg, some 24 times bigger. So on this basis the regression coefficient ought to be 24 times larger in adulthood than in infancy, and this is broadly what Figs 2 and 3 show.

But it is a complicated concept and would be better avoided. The problem lies in the way the regression model is formulated, predicting BMR in absolute units. It does not work well for weight, and it is also less than ideal for ethnicity or measurement technique. Both these variables ought to have a smaller effect in childhood than in adulthood, yet the model constrains the two effects to be the same. It would be better if instead the model predicted proportional change in BMR, on which basis childhood and adulthood are more likely to be comparable.

Table 2 Females: weighted regression analysis of BMR (dependent variable; MJ day^{-1}) on age, weight *Z*-score, height *Z*-score, ethnicity and measurement technique. The regression coefficient for weight *Z*-score depends on age – see text for details

Variable	Coefficient	SE of coefficient	*t* ratio	Prob
Constant	0.66	0.038	17.1	< 0.0001
Age	1.3	0.010	121	< 0.0001
Adult × Age	−1.4	0.014	−97.5	< 0.0001
1/Age	−0.12	0.0070	−16.6	< 0.0001
Weight *Z*-score	−0.043	0.012	−3.6	0.0004
Wtz × Age	0.11	0.0038	27.8	< 0.0001
Wtz × Adult × Age	−0.14	0.0061	−22.2	< 0.0001
Height *Z*-score	0.064	0.0068	9.4	< 0.0001
Ethnic Caucasian	0.20	0.017	11.8	< 0.0001
Closed-circuit	0.035	0.015	2.4	0.02

Abbrevations: RSD – residual SD.
R^2 (adjusted) = 94.6%, RSD = 0.1016 with 5191 − 10 = 5181 degrees of freedom.

This leads to the proportional analysis, where the effect of weight *Z*-score is measured in percentage terms, which is effectively independent of size and hence age.

Proportional regression model

Males

Table 3 gives the regression model for 100 log BMR in males. It explains 83% of the variance and the residual CV is 10.0%, i.e. slightly better than the absolute model. All the regression coefficients can be viewed as the percentage effect on BMR, for example the weight *Z*-score coefficient of 6.4 means that the effect of a 1 SD change in weight is a 6.4% change in BMR. This is over seven times larger than the corresponding coefficient for height *Z*-score (0.9%). There is no evidence that either of the coefficients varies with age.

The age trend in predicted BMR is shown in Fig. 4, adjusted to mean weight and height, ethnic non-Caucasian and open-circuit. This is obtained by anti-logging the predicted log BMR. The trend is similar to that seen in Figs 1 and 2. Figure 4 also emphasises that the weight and

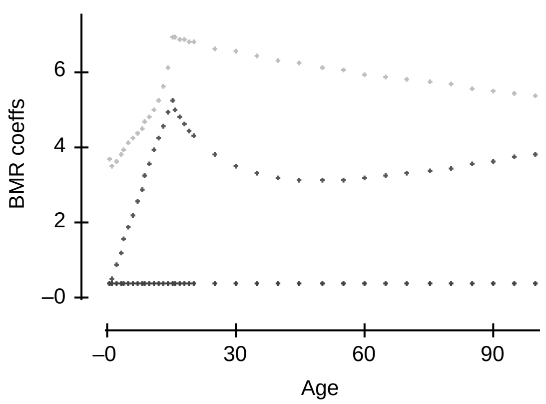

Fig. 2 Males, absolute model: predicted BMR by age (top curve, MJ day^{-1}), coefficient of weight *Z*-score as function of age (×10, middle curve), and coefficient of height *Z*-score (×10, bottom line)

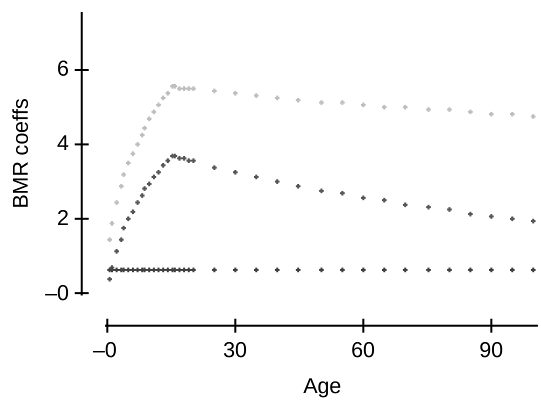

Fig. 3 Females, absolute model: predicted BMR by age (top curve, MJ day^{-1}), coefficient of weight *Z*-score as function of age (×10, middle curve), and coefficient of height *Z*-score (×10, bottom line)

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Table 3 Males: regression analysis of dependent variable; 100 log BMR (%) on age, weight *Z*-score, height *Z*-score, ethnicity and measurement technique. See text for details

Variable	Coefficient	SE of coefficient	*t* ratio	Prob
Constant	84.5	1.2	70.9	<0.0001
Age	-15.8	0.79	-19.9	<0.0001
Log age	50.4	0.83	61.0	<0.0001
Child × Age^6	2.29×10^{-6}	0.044×10^{-6}	52.1	<0.0001
Adult × Log Age	-11.7	1.7	-7.0	<0.0001
Weight *Z*-score	6.4	0.12	53.7	<0.0001
Height *Z*-score	0.86	0.13	6.8	<0.0001
Ethnic Caucasian	7.3	0.29	25.3	<0.0001
Closed-circuit	2.9	0.26	11.3	<0.0001

Abbrevations: RSD – residual SD.
R^2 (adjusted) = 82.9%, RSD = 9.99 with 8390 − 9 = 8381 degrees of freedom.

height coefficients (in % units) do not change with age, in contrast to those for the absolute model in Fig. 2.

The ethnic effect in Table 3 is similar to that in Table 1, with BMR in Caucasians 7% greater than in non-Caucasians, while closed-circuit is 3% greater than open-circuit. Both terms are more significant than for the absolute model in Table 1 as judged by their *t* ratios.

But the interpretation of the ethnicity effect is problematic, as it is very sensitive to the inclusion or exclusion of certain studies. The Caucasian ethnicity coefficient of +7.3% reduces to +6.5% if the two most influential outlying publications 203 ($n = 589$) and 205 ($n = 571$) are adjusted for, where the mean BMRs are, respectively, 4.2% and 5.1% greater than predicted. Two other clear outliers, publications 155 ($n = 130$) and 38 ($n = 125$), are 15% and 13% *less* than predicted, and their further adjustment reduces the Caucasian effect to +5.9%. Adjusting for these four publications also halves the closed-circuit effect, from 2.9% to 1.5%.

Figure 5 (left) shows the mean standardised residuals for each publication, plotted against their sample size. The narrow central region denotes 3 standard errors above and below zero, i.e. the 99.8% confidence interval. The

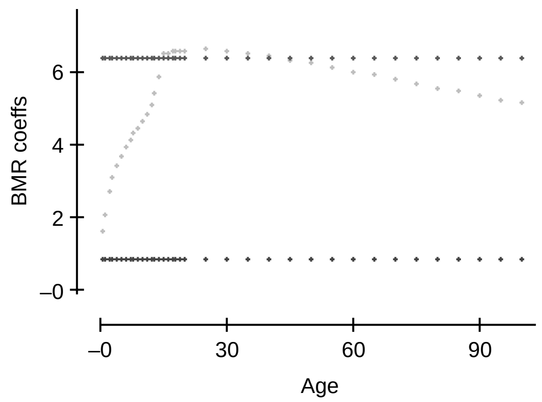

Fig. 4 Males, proportional model: predicted BMR by age (curve, MJ day^{-1}), coefficient of weight *Z*-score (upper line, %) and coefficient of height *Z*-score (lower line, %)

Table 4 Males: comparison of regression coefficients of 100 log BMR (%) without (left) and with (right) adjustment for publications

	Publications unadjusted		Publications adjusted	
Variable	Coefficient	*t* ratio	Coefficient	*t* ratio
Constant	84.5	70.9	89.2	53.8
Age	-15.8	-19.9	-10.7	-10.6
Log age	50.4	61.0	42.9	38.1
Child × Age^6	2.29×10^{-6}	52.1	2.27×10^{-6}	26.6
Adult × Log Age	-11.7	-7.0	-20.4	-9.3
Weight *Z*-score	6.4	53.7	6.0	52.5
Height *Z*-score	0.86	6.8	1.3	10.5
Ethnic Caucasian	7.3	25.3	4.5	6.4
Closed-circuit	2.9	11.3	0	–

most influential publications are those with the largest samples. Publication 205 is the top point to the right, and 203 is just below it to its right, both with sample sizes exceeding 500. Publications 155 and 38 are below the central region with sample sizes around 125.

Figure 5 also shows the effect of adjusting for these four publications (right). Their standardised residuals become zero by definition, so that they shift up or down accordingly. The other publications are slightly affected by the refitted model, so their points shift marginally as well.

Because their mean standardised residuals are forced to zero, and because all their subjects are uniform in ethnicity and measurement technique, the adjusted publications no longer have any influence on the Caucasian or closed-circuit coefficients.

A further analysis adjusts for all the publications using fixed effects, see Table 4. The publications term (not shown) is highly significant ($F = 22.1$ on 131 and 8251 degrees of freedom), and its inclusion reduces the residual CV to 8.7%.

The coefficients are rather different with and without the publication adjustment, particularly, Caucasian ethnicity which falls from 7.3% to 4.5%. The latter figure represents the effect comparing groups within each publication, and as such it should be robust to methodological differences between studies, but its

Table 5 Females: regression analysis of dependent variable; 100 log BMR (%) on age, weight *Z*-score, height *Z*-score, ethnicity and measurement technique

Variable	Coefficient	SE of coefficient	*t* ratio	Prob
Constant	60.7	0.93	65.0	<0.0001
Log age	39.7	0.34	115.0	<0.0001
Adult × Age	-77.1	0.96	-80.4	<0.0001
Weight *Z*-score	6.2	0.14	44.5	<0.0001
Height *Z*-score	1.6	0.15	10.8	<0.0001
Ethnic Caucasian	4.3	0.35	12.1	<0.0001
Closed-circuit	1.2	0.31	3.9	0.0001

Abbrevations: RSD – residual SD.
R^2 (adjusted) = 79.2%, RSD = 10.32 with 5191 − 7 = 5184 degrees of freedom.

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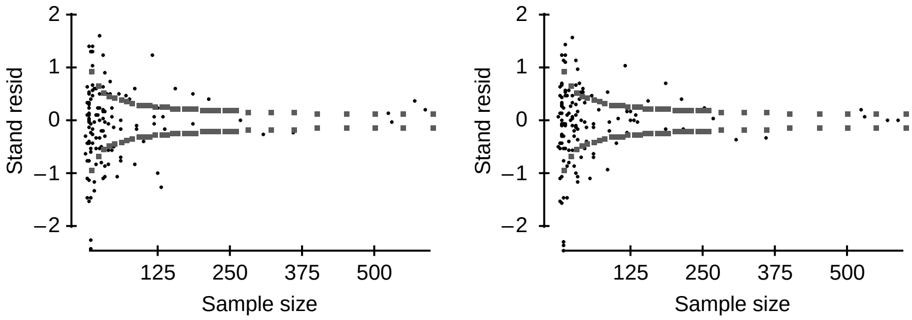

Fig. 5 Males, proportional model: mean standardised residuals for each publication plotted against their sample size. The heavy curves indicate ±3 standard errors, so points outside the central funnel region are highly significantly biased. In the left graph all publications are unadjusted, while in the right graph four outlying publications have been adjusted to zero

much reduced *t* ratio reflects the loss of between-publication information.

Females

Table 5 gives the proportional regression model for 100 log BMR in females. It explains 79% of the variance and the residual CV is 10.3%, slightly larger than the absolute model (10.2%). The age effect is relatively simple with just two terms, while the weight and height effects are constant over age.

The age trend in predicted BMR is shown in Fig. 6, adjusted to mean weight and height, ethnic non-Caucasian and open-circuit. The trend is similar to that seen in Figs 1 and 3. The weight coefficient of 6.2% is similar to those for males in Table 4 and Fig. 4, while the height coefficient of 1.7% is rather larger.

The effect of ethnicity, with Caucasians 4.3% greater than non-Caucasians, is similar to that for males in Table 4 with the publication adjustment (4.5%). By contrast the closed-circuit effect is much smaller than for males, 1.2% versus 2.9%. Table 6 shows the effect of adjusting for publication differences. The effect is highly significant ($F = 16.7$ on 131 and 5072 degrees of freedom), and it reduces the residual CV to 8.9%. The age, weight and height trends are virtually unaffected and the ethnic effect is slightly reduced. The similarity of the unadjusted and adjusted results suggests that biases due to individual publications are smaller and less important for females than males.

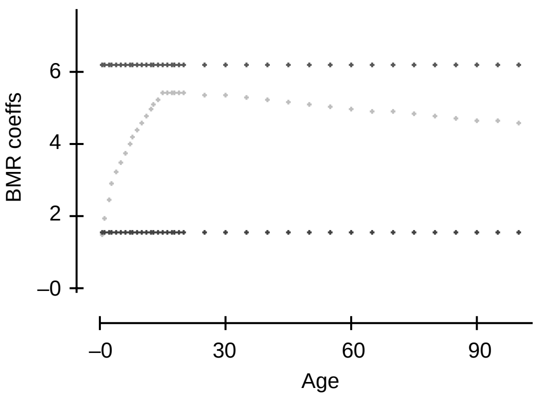

Fig. 6 Females, proportional model: predicted BMR by age (curve, MJ day^{-1}), coefficient of weight Z-score (upper line, %) and coefficient of height Z-score (lower line, %)

Discussion

The analysis described here is intended to use the data as efficiently as possible. It defines the age trend in BMR from infancy to old age as a single regression function, with parsimonious adjustments for weight and height. Adjustments for ethnicity and measurement technique are also included, but they are less convincing due to their confounding with the publications providing the data.

Of the two models considered, with absolute and proportional effects, the proportional model describes the age trends by sex using fewer terms than the absolute model, the weight and height Z-score coefficients are constant across age, and the ethnic and technique effects are more realistic operating on a percentage than an absolute basis. For all these reasons the percentage model is recommended as the model of choice.

The major factors in the analysis are age and weight for age. Height for age is also consistently positive at all ages, which together with weight for age provides an

Table 6 Females: comparison of regression of 100 log BMR (%) on covariates without (left) and with (right) adjustment for publications

	Publications unadjusted		Publications adjusted	
Variable	Coefficient	*t* ratio	Coefficient	*t* ratio
Constant	60.7	65.0	62.4	41.8
Log Age	39.7	115.0	39.5	73.7
Adult × Age	−77.1	−80.4	−76.8	−58.4
Weight Z-score	6.2	44.5	6.0	45.1
Height Z-score	1.6	10.8	1.5	10.2
Ethnic Caucasian	4.3	12.1	3.7	5.0
Closed-circuit	1.2	3.9	0	–

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adjustment for weight for height analogous to the body mass index (BMI). This is needed in the analysis because greater weight for height implies greater adiposity, relatively less lean (active) mass and hence a lower BMR. So weight has a strong and direct effect on BMR, representing body size, while weight for height has a smaller inverse effect reflecting adiposity. Weight for height is effectively weight less height, and combining the two adjustments gives a positive weight effect and a positive (i.e. inverse negative) height effect. The positive height coefficient confirms that BMR is reduced in high weight for height subjects after adjusting for weight. It also means incidentally that further BMI adjustment is unnecessary.

Note though that weight for height is only an imperfect proxy for adiposity – individuals of a given weight and height can vary considerably in terms of body fat. This may explain some of the substantial heterogeneity seen between studies despite adjusting for age, sex, weight, height, ethnicity and measurement technique. Of course there may be other unmeasured inter-study technical differences, but it is possible that the heterogeneity also reflects residual differences in body composition. Mean percent body fat is likely to differ between studies, and a higher body fat for a given sex, age, weight and height implies a lower BMR. In the absence of information on body fat, potentially large biases could exist between studies.

How large might this bias be – what is the relationship between Δ (delta) body fat and ΔBMR? BMR increases by 1.4% per SD of height (from Tables 4 and 6), and the SD of height in adults is 4%[1]. Height is in the model as a form of BMI, and a 1% change in height corresponds to a −2% change in BMI (as height is squared). So 1.4% ΔBMR corresponds to 4% Δ height or −8% ΔBMI, or conversely 1% ΔBMI equates to −0.18% ΔBMR.

From Deurenberg *et al.*[4] a 1% change in body fat corresponds to 1.2 times ΔBMI in adults. Taking mean BMI as 25, a unit change in BMI corresponds to a 1 in 25 or 4% change in BMI. Relating body fat and BMR through BMI gives:

$$1\%\,\Delta\text{body fat} \Rightarrow 1.2\times 4\% = 4.8\%\,\Delta\text{BMI} \Rightarrow 4.8\times -0.18\% = -0.9\%\,\Delta\text{BMR}.$$

So in broad terms a 1% rise in body fat corresponds to a 1% fall in BMR. This puts into perspective the publication biases described earlier, +4% for the two largest studies and −14% for two smaller studies. It is unlikely that the studies could be that biased in terms of % body fat, i.e. 4–14% adjusted for age, weight and height. So on balance body composition differences are unlikely to explain the outliers, and technical factors are a more likely explanation.

The coefficients for ethnicity and measurement technique are very sensitive to the inclusion or exclusion of the influential datasets. There have been proposals to exclude some of the data to avoid biases of this sort, but excluding data is an inefficient way to address the problem. The approach used here is to identify publications which are particularly influential and then to remove their between-publication influence, by shifting their data up or down to match the mean, while retaining their within-publication information. This is particularly important for the males, where adjusting for four publications reduces the Caucasian ethnicity effect from 7.3% to 5.9%. Adjusting for all publications reduces it further to 4.5% (Table 4). For comparison the effect in females is between 3.7% and 4.3% (Table 6). Taken together, the results suggest that BMR in Caucasians is some 4% greater than in non-Caucasians of the same sex, age and body build.

Closed-circuit estimates of BMR in males appear to be 2.9% higher than open-circuit estimates (Table 3). But this, like ethnicity, is greatly affected by the few influential publications, and adjusting for the four main ones reduces the difference to 1.4%. Unfortunately it is not possible to adjust for all publications as was done with ethnicity, since each publication consistently used either one method or the other, so there is no within-publication information. The closed-circuit effect in females is smaller at 1.2%, and the evidence from Table 6 that the female publications are relatively unbiased suggests that the true effect is close to 1%. Whether or not an effect of this size is worth including in the model is open to doubt.

All things considered, the best prediction equations to use are probably the publications-adjusted proportional models in Table 4 (males) and Table 6 (females). The coefficients for weight, height and Caucasian are very similar in the two sexes (6%, 1.4% and 4%, respectively), while the closed-circuit effect is constrained to zero. The equations would be straightforward to implement in a spreadsheet, e.g. Microsoft Excel, for which software already exists to convert weight and height to *Z*-scores with the British 1990 reference[5].

In conclusion, parsimonious regression equations to predict BMR in terms of weight and height are provided for both sexes from birth through childhood and adulthood. A proportional model structure fits the data better than an absolute model structure. The equations include adjustments for Caucasian versus non-Caucasian ethnicity and for closed versus open-circuit calorimetry, but the coefficients, particularly for males, are sensitive to the presence or absence of certain influential studies in the analysis.

Contributors

CJKH assembled the Oxford Brookes BMR database and contributed to the analysis plan. TJC carried out the analysis and wrote the paper.

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