Supplemental Digital Content 1. Procedures for normalizing physiological data to body size

To perform unbiased comparisons of size-dependent physiological data in morphologically diverse populations such as children and adults, it is fundamentally important to normalize these data to body size. There exists multiple statistical approaches to remove this size bias, with ratiometric scaling, adjusted-regression analysis, analysis of covariance, and allometric scaling being among the most common. The most appropriate approach, however, will depend on whether the variables to be normalized satisfy the statistical assumptions associated with each procedure.

For data satisfying the statistical assumptions of least-squares, linear regression, one can rely on ratiometric scaling to remove body-size effects. However, the validity of this method is reliant on the linear regression relationship between the independent and dependent variables possessing a zero ordinate-intercept. If this is not the case, one can utilize adjusted regression analysis or analysis of covariance, to normalise physiological data to body size. In many instances, however, physiological data can display non-constant error variance (heteroscedasticity), and a non-linear relationship with body size, which violates the statistical assumptions that must be satisfied to perform ratiometric scaling, as well as adjusted regression analysis and analysis of covariance. For these scenarios, allometric scaling can be used as an alternative. This selection process is illustrated in Figure S1, while a brief description of these normalization procedures is provided below.

INSERT FIGURE S1 ABOUT HERE

Ratiometric scaling

Ratiometric scaling ($y \cdot x^{-1}$) uses least-squares linear regression to normalize physiological data to body size, and assumes that the linear regression line describing the relationship between the dependent physiological variable of interest (y) and the independent body-size variable (x) is linear, and passes through the origin (y-intercept equal to zero). When linear regression is used to normalise physiological data in this manner, it is also necessary to confirm that these data display constant error variance throughout the range of observations (homoscedasticity), which is achieved when all data points are evenly distributed about the regression line. Experimental data must also display a normal distribution (bell curve). If these assumptions are met, ratiometric scaling provides a suitable means of normalising physiological data to body size. Size-adjusted physiological data can be derived using ratiometric scaling by expressing the physiological variable (y) per unit of the morphological variable (x) using least-squares, linear regression (Equation 1).

$$y_i = a + b \cdot x_i + e_i \qquad \textbf{Equation 1}$$

where:

y_i = physiological variable	[physiological variable units]
x_i = morphological variable	[morphological variable units]
a = origin intercept (assumed to be zero)	[physiological variable units]
b = group regression slope	[morphological variable units]
e_i = constant error term	[physiological variable units]

Adjusted regression analysis

If the assumptions of ratiometric scaling have not been demonstrably verified, an adjusted form of linear regression analysis (based on analysis of covariance) for single groups, can be used

to normalise physiological data to body size. With this approach, the effects of body size are accounted for by first determining the group regression slope between the physiological outcome variable and the measure of body size. Normalised physiological data are then derived by subtracting each individual's physiological data from the product of this group regression slope and the difference between each individual's measure of body size and the group mean of this body size variable. Like least-squares regression, this method is valid only when a linear relationship exists between the numerator and denominator (linearity), data display a normal distribution (normality) and that all data points display similar variations from the regression line across the range of observations (homoscedasticity). When these assumptions are met, adjusted regression analysis can be used to normalize the physiological variable of interest within each subject group using Equation 2:

$$y_{adj} = y_i - b\,(x_i - \bar{x}) + e_i \qquad \textbf{Equation 2}$$

where:

y_{adj} = size-adjusted physiological variable	[physiological variable units]
y_i = physiological variable	[physiological variable units]
x_i = morphological variable	[morphological variable units]
b = group regression slope	[morphological variable units]
$\bar{x}$ = group mean of morphological variable	[morphological variable units]
e_i = constant error term	[physiological variable units]

Analysis of covariance

To normalize physiological data to body size in two or more groups, analysis of covariance can be used. This method adjusts for variations in the covariate (body size) by first deriving linear regression relationships between the physiological and body size variable for each of the groups

under investigation. Size-adjusted group means are then created by subtracting the average slope of these group regression lines and the difference between the group mean and grand mean (mean of all groups) of the body size variable from the group mean of the physiological variable. In addition to the least-squares linear regression assumptions required for adjusted regression analysis (linearity, normality and homoscedasticity), it is necessary to verify the assumptions of regression slope homogeneity and homogeneity of variance for analysis of covariance. The former of these additional assumptions is satisfied when the slopes of the group regression relationship between the physiological and body size variable do not differ significantly between each group, while the latter assumption is confirmed when the variance associated with each variable is equal (homogeneous) between groups. In instances where these assumptions can be verified, analysis of covariance is suitable for normalising physiological data to body size among two or more groups.

Analysis of covariance can be used to correct each group mean of the physiological variable for variations in the covariate (body size), by first deriving linear relationships between the morphological variable and physiological variable for each subgroup. The average slope from these regression equations can then be used to adjust the physiological variable to the mean of the morphological variable across both groups (grand mean) and derive a size-adjusted group mean using Equation 3.

$$y'_{adj} = y_i - b\,(x_i - x_g) + e_i \qquad \textbf{Equation 3}$$

where:

y'_{adj} = size-adjusted group mean [physiological variable units]

y_i = group mean of the physiological variable [physiological variable units]

b = average between-groups regression slope [morphological variable units]

x_i = group mean of the morphological variable [morphological variable units]

x_g = grand mean of the morphological variable [morphological variable units]

e_i = constant error term [physiological variable units]

Allometry

For situations in which neither the assumptions of ratiometric scaling nor those of adjusted regression or analysis of covariance have been satisfied, allometric scaling can be used to normalize physiological data to body size. Unlike the methods previously described, which rely on a linear relationship between the physiological data and body size data, allometric scaling assumes the relationship between the physiological and body size variable shares a disproportionate, or non-isometric relationship, with increases in body size corresponding to disproportionate changes in the physiological variable. Allometry normalises physiological data (y) by scaling the body size variable (x) to an exponent (b), using a power function model ($y.x^{-b}$). This scaling exponent is derived from the slope of the log-linear regression relationship between the logarithmically transformed physiological and body size variable. When this scaling exponent is equal to one, these data satisfy the assumption associated with the ratiometric scaling (isometry). In this instance, ratiometric normalization is valid. A slope between zero and one (negative allometric relationship) occurs when increases in body size exceed increases in the physiological variable, while an exponent greater than one represents a positive allometric relationship, where the physiological variable increases at a greater rate than increases in body size.

Since log-linear regression is used to derive the scaling exponent required for allometric scaling, this procedure also assumes these logarithmically transformed data are normally distributed, and that linearity exists between the log-transformed physiological and morphological variables. Moreover, the allometric model contains a multiplicative error term, which assumes that the distance of each data point away from the regression line (residual error) increases in proportion to the regression relationship between the dependent and independent variables

(heteroscedasticity). Therefore, under circumstances where physiological data display evidence of non-linearity or residual errors that are size-dependent, allometric scaling provides a suitable alternative to ratiometric scaling and adjusted regression for normalising physiological data to body size in single groups.

The physiological variable (y) of interest can be allometrically scaled to the morphological variable (x) using an exponent (b), according to a power function model using Equation 4:

$$y_i = a \cdot x_i^b + e_i \qquad \textbf{Equation 4}$$

where:

y_i = physiological variable [physiological variable units]

x_i = morphological variable [morphological variable units]

a = origin intercept [physiological variable units]

b = scaling exponent (slope) [morphological variable units]

e_i = multiplicative error term [physiological variable units]

The origin intercept and the exponent (slope) can then be derived by expressing the power function model as natural logarithms and fitting a straight line to these data using log-linear regression (Equation 5), and back-transforming the resulting equation to form the power function model:

$$\log(y) = \log(a) + b \cdot \log(x) + \log(e_i) \qquad \textbf{Equation 5}$$

where:

$\log(y)$ = log of the physiological variable [physiological variable units]

$\log(a)$ = log of the origin intercept [physiological variable units]

b = slope (exponent) of the regression line [morphological variable units]

$\log(x)$ = log of the morphological variable [morphological variable units]

142 $\log(e_i)$ = log of the multiplicative error term [physiological variable units]

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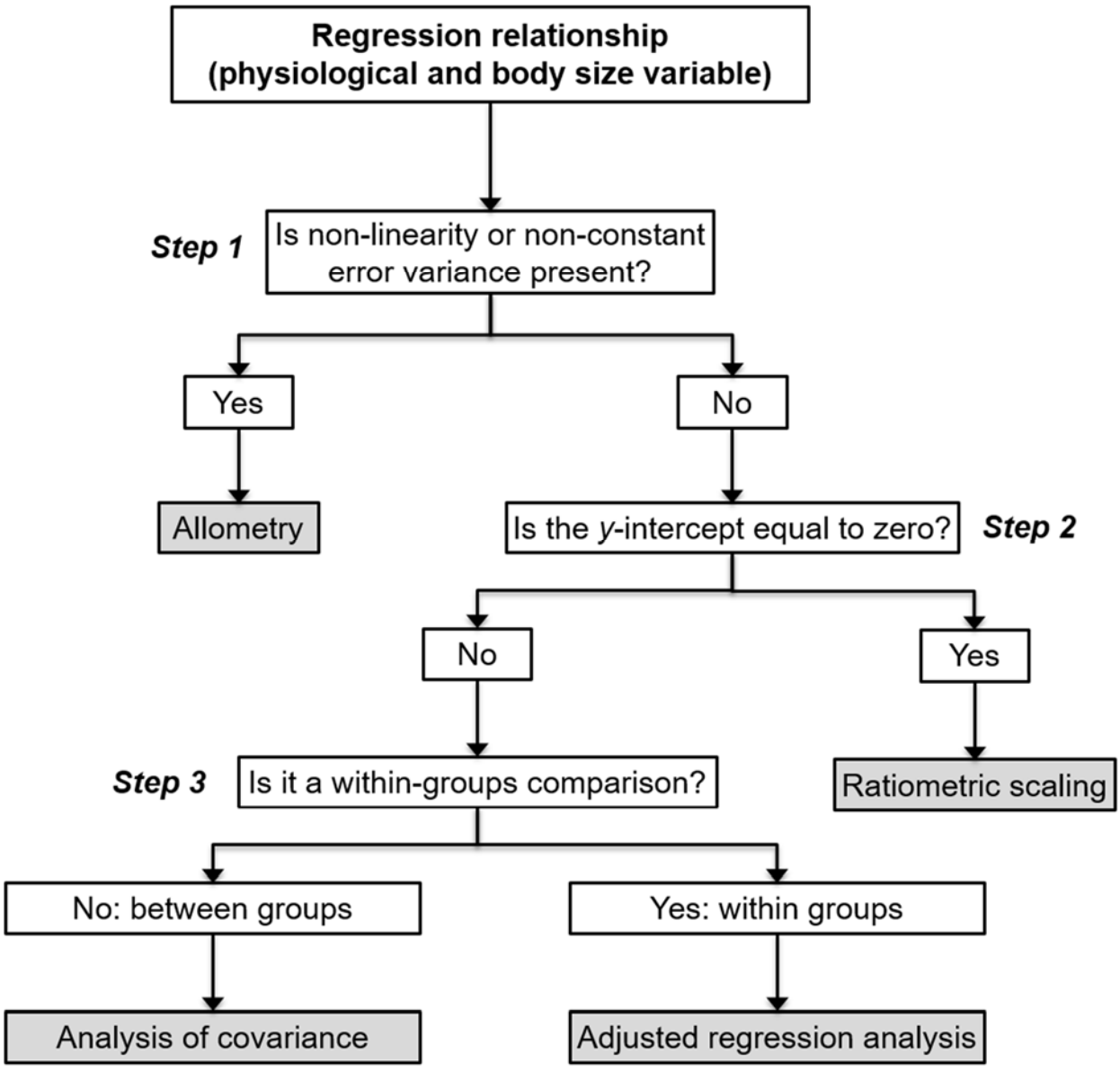
144 It is important to note that while there exists appropriate allometric scaling exponents for
145 normalizing cardiorespiratory data to body size (e.g., $\dot{V}O_2$peak, cardiac output), there exists a
146 paucity of similar research on normalizing thermoregulatory processes (e.g., whole-body sweat
147 rate). To achieve this, it is first necessary to assess the possibility of non-linearity of these
148 responses within a dataset that is sufficiently large and heterogeneous in body size to make valid
149 inferences. In addition, since various secondary factors can independently influence such
150 responses (e.g., sex, chronic disease), it is important to consider these covariates either statistically,
151 or by examining these relationships in individuals that are homogeneous except for body size. This
152 represents an important area of future research for improving our ability to perform unbiased child-
153 adult comparisons of thermoregulatory responses.

FIGURES

Figure S1: Decision tree representing the three steps for selecting the most appropriate scaling procedure for normalizing physiological data to body size. Step one involves preparing scatter, residual and quantile comparison plots of the physiological variable of interest (y) and the body size variable (x) to check the assumptions of linear regression between the physiological and morphological variable are demonstrably verified. If non-linearity or non-constant error variance is present, allometric scaling should be used. Step two involves determining whether the linear regression relationship between the physiological and morphological variable displays a zero ordinate-intercept. In these instances, ratiometric scaling is appropriate. For Step three, if the regression exhibits a non-zero ordinate-intercept, use adjusted regression analysis for within-groups comparisons or analysis of covariance for between-groups comparisons.

165 **FIGURE S1**



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