A novel estimation of energy balance through the calibration of consumer devices in free-living, US adults and children

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Study Site(s): Children's Mercy Hospital (Don Chisholm Center) and University of Kansas Medical Center.

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1. STUDY OBJECTIVES/HYPOTHESIS

Our research group has successfully developed a system of assessment methodologies and statistical techniques that can accurately assess energy balance and estimate energy intake [EI] using research-grade but non-gold standard techniques.[16-18] The purpose of this study is to apply these techniques using consumer devices to assess rate of energy storage [ES] and energy expenditure [EE], then estimate EI using the intake-balance technique.

We believe calibration models developed in the proposed study will be able to be translated to other consumer devices with only minor modifications given common hardware (e.g. triaxial accelerometery), resulting in overall improved ability to assess energy balance and EI at a population level and positive health outcomes.

Aim 1. Validate and calibrate consumer devices to estimate energy balance using gold-standard methods and a Bayesian semi-parametric approach. *Hypothesis 1*: We will be able to jointly model measurement error for both EE and ES to create a calibration model that reduces bias and improves accuracy of consumer devices of EE and ES.

Aim 2. Estimate energy intake using the intake-balance technique using consumer monitors. *Hypothesis 2*: We will use calibrated EE and ES from consumer monitors to estimate EI using the intake-balance technique, with values being superior to self-reported EI.

2. RATIONALE

The challenges of accurate estimation of energy intake are well-documented.[5-7] Recently, mathematical models have been formulated based on the principles of the first law of thermodynamics (rate of energy storage [ES] = rate of energy intake [EI] – rate of energy expenditure [EE]).[8] that allow researchers to estimate energy balance. For example, if one is able to accurately measure two of the variables of the energy balance equation (e.g., changed ES and rate of EE), it is mathematically possible to solve for the third (e.g., EI). Based on a variety of existing data sets containing EE, EI, and changes in ES (e.g., body composition using a two-compartment model of fat mass and fat-free mass), researchers have developed and refined a technique termed the intake-balance method to estimate EI.[9-11] The result is a simple, easy-to-use equation that offers great promise in the quest for estimating EI using objectively measured methods.

A current limitation in using the intake-balance method to estimate EI is the feasibility in measuring EE and ES. While both can be accomplished with a high degree of accuracy, the gold-standard methods of assessment of each (doubly-labeled water [DLW] for EE, dual-energy absorptiometry [DXA] for ES) is too costly and resource-intensive for most applications. Alternatively, consumer devices designed to measure physical activity and body composition are generally affordable, easy to use, and popular (an estimated 45 million will be sold in 2017),[12] but have varying levels of validity and reliability.[13-15]

3. STUDY DESIGN

There are four stages in the proposed project:

1. We will validate EE and ES (hereafter, Fitbit_EE and Fitbit_ES) from a consumer physical activity monitor (Fitbit Alta HR™) and body composition analyzer (Fitbit Aria™) with gold-standard measures of DLW for EE and DXA for ES during an initial 14- day baseline period;
2. We will estimate EI using the intake-balance method during the 14-day baseline period;
3. We will calibrate daily Fitbit_EE and Fitbit_ES from consumer devices using a Bayesian semi-parametric measurement error modeling approach to estimate energy balance during a second 14-day period immediately following the baseline period.
4. We will reassess our validation and calibration models of consumer devices during a third 14-day assessment period to evaluate changes associated with growth and development with gold-standard measures of DLW for EE and DXA for ES.

4. TARGET STUDY POPLUATION SPECIFICS

Participants will include 24 children or adults, ages 8-90. Participants will be recruited from the community. We intend to enroll participants within the same family (child, parents, and siblings) as long as they meet the age criteria.

Inclusion Criteria

- Healthy children and adults, aged 8-90.
- Able to be physically active.

Exclusion Criteria

- History of restrained eating, eating disorders, bariatric surgery, or other significant medical diagnosis that could impact metabolism.
- Participants taking thyroid medications, beta blockers, or other stimulants (medications are known to affect metabolism).

5. DATA COLLECTION

Data Collection Procedures

The study will include 4 visits to CMH and assessments to be conducted at home.

Participants will receive a Fitbit Alta HR™, a wristworn tri-axial activity monitor with optical heart rate monitoring (**Figure 1**, top), and a Fitbit Aria™ smart scale which measures fat mass and fat-free mass using bioimpedance (**Figure 1**, bottom). Participants will be instructed to wear the monitor at all times (except for swimming or showering) and measure their body composition on the scale daily for 6 weeks. Fitbit_EE and Fitbit_ES will be uploaded using Bluetooth and Wi-Fi, respectively, to the Fitbit Dashboard™ and accessed by study staff using Fitabase™, a research platform that collects data in collaboration with Fitbit, Inc. Fitbit_EE and Fitbit_ES will be calibrated during two 14-day assessment periods (study start and study end) using DLW and DXA. 'True' EE will be measured using a standard 14-day DLW protocol[19] with samples collected on Day 0, 7, and 14. 'True' ES will be calculated using DXA measurements on Day 0 and Day 14. Fitbit_EE and Fitbit_ES during the assessment period will then be calibrated to 'true' EE and ES using a Bayesian semi-parametric approach, using free knot splines and Reversible Jump MCMC algorithms previously developed through work in our lab.[18] This calibration model will then be applied to daily Fitbit_EE and Fitbit_ES collected during the middle 14-day assessment period to assess daily energy balance. Finally, we will estimate EI from Fitbit measurements using the equation[16, 17]:

Figure 1. Fitbit Alta HR (top) and Aria (bottom).

$$calculated\ energy\ intake = 1{,}020\frac{\Delta FFM}{\Delta t} + 9{,}500\frac{\Delta FM}{\Delta t} + EE$$

Where ΔFFM and ΔFM represent change in each variable; Δt represents days between start and end of an assessment period; 1,020 represents the energy density in kcals of FFM per kg; and 9,500 represents the energy density of FM per kg, both based on established values; [20] EE represents daily energy expenditure during the assessment period.

Doubly-labeled Water Procedures

- Energy expenditure will be assessed using the doubly labelled water (DLW) technique over a two week period. The DLW technique uses enhanced levels of naturally occurring stable (i.e., non-radioactive) isotopes of hydrogen (deuterium; 2H) and oxygen (18O) to accurately measure energy expenditure via indirect calorimetry in free-living organisms. DLW was first introduced for human use in 1982. The method is safe and has been validated extensively in both humans and other animals (including children and infants). Participants will be administered a dose of DLW with 1.5 ml/kg body weight of a mixture of 10% enriched H218O, and 99% enriched 2H2O (Cambridge Isotopes, Cambridge, MA). Participants will provide a urine sample (>15 mL) on day 0, 7, and 14, which will be analyzed by Pennington Biomedical Research Center to calculate elimination rates of the isotopes from the body.

DXA Procedures

- Assessment of body composition, including fat mass, fat free mass, and visceral adipose tissue, will be completed using dual energy X-ray absorptiometry (DXA). DXA is a non-invasive procedure which participants will lie on a table and a detector will be passed over the body. The procedures involves approximately 1/3 the radiation in a normal chest X-ray and should take approximately 10 – 20 minutes. All anthropometric measurements will be performed with the participant dressed in surgical scrubs and in bare feet. BMI (weight [kg]/height [m]2) will be calculated from the average of three height and weight measurements using a wall-mounted stadiometer and electronic scale and recorded to the nearest 0.1 cm and 0.1 kg, respectively.

Diet Recalls

- Energy intake will be assessed subjectively via interviewer-administered dietary recalls. Three dietary recalls will occur on randomly selected non-consecutive days over each one-week treatment condition (including at least one weekend day) to minimize preparation that could bias recall by the participants. All interviews will be conducted over the telephone, will ask about all foods consumed over the previous 24 hours using a multi-pass approach, and energy intake will be calculated using the Nutrient Data System for Research software (NDSR Version 2014).

Records to be kept

Data collected will be deidentified with a subject ID number. A linking list will used, which will contain the subject ID, subject's name, gender, and date of birth. This log will only be accessible be the PI and the study team.

Secure Storage of Data

Consent statements and participant data will be kept in separate locked file cabinets so that individuals are not easily connected to the study results. All digital data will be stored on a firewall and password-protected project server at Children's Mercy Hospital. Data collected at the CMH Don Chisholm Center CMH will be analyzed and stored in secure shared drive at the Don Chisholm Center.

Fitabase Data Security:

Data from the Fitbits will be monitored and reported to our research team in real-time using the Fitabase software (Small Steps Labs, LLC, San Diego, CA). Fitabase is an independent software company that provides real-time data from the Fitbit to researchers via an application program interface. Thus, we may be provided with real-time information regarding wear time and also minute-by-minute information regarding activity intensity (e.g. sedentary, moderate, etc.). Only participant ID# will be associated with this data. We will create fitbit accounts for everyone using a generic email account with many associated logins. We will not use participant names or actual birthdates (only birthyear) so no identifying information is associated with the account.

6. STUDY DURATION/STUDY TIMELINE

Target start date is July 2017
Stage 2, recruitment and data collection, January 2018 – June 2018
Stage 3, data analysis and manuscript development, June 2018- August 2018
Total study duration will be 1 year.

We will recruit potential participants from the community, which could include CMH patients, employees, or students. We plan to post a recruitment flyer within CMH in clinic areas and employee breakrooms, as patients, employees, or students would be eligible to participate. Potential participants from the community will then contact us from the information on the flyer if they are interested in the study.

Once potential participants are identified and express interest, we will schedule an orientation (visit 1) at CMH Don Chisholm during which informed consent will be obtained. Participants will be given the Actigraph activity monitor, the FitBit tracker, the FitBit scale, and be trained on how to use them. Participants will complete the DXA and the DLW procedures. The day zero urine sample will be obtained at visit 1.

After visit 1, participants will be asked to complete the urine samples at home (day 8). Participants will also be contacted to complete the diet recall procedures. Participants will be asked to wear the FitBit tracker and use the FitBit Scale daily starting at visit 1 until the end of the study. The Actigraph monitor will be worn between visit 1 and 2, and visit 3 and 4.

Visit 2 will occur 2 weeks after visit 1. Urine samples will be returned. A DXA will be obtained.

Visit 3 will occur 4 weeks after visit 1. Procedures at visit 3 are identical to visit 1.

Visit 4 will occur 2 weeks after visit 3. Procedures at visit 4 are identical to visit 2.

7. STATISTICAL CONSIDERATIONS

Measures

- Primary measures: Energy intake, energy expenditure and body composition
- Secondary measure(s): Demographics

General Design Issues

The proposed pilot study is a calibration study, which will generate data needed for a larger study.

Sample size determination

As a pilot study, we will have resources to collect data from N=24 participants. We will use this data to determine power requirements for a larger study.

Data Analyses
Statistical significance for comparison between the different data collection methodologies will be tested using analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. Statistical significance will be set at $P<.05$ (two-sided) for all analyses.

8. HUMAN SUBJECTS
Institutional Review Board (IRB) Review and Informed Consent
The IRB of record is Children's Mercy Hospital.

This protocol, and any subsequent modifications, will be reviewed and approved by the Pediatric IRB at The Children's Mercy Hospital & Clinics.

Potential participants will be recruited from the community.. Once the participants are contacted by CMH study staff, they will be given more details about the study and sent the consent form to review.

The study team will do a 10 minute phone screening with the parent to determine eligibility, and will schedule a time for the parent and child to come in for an orientation. The parent and child will them come to the Don Chisholm center at CMH for visit 1. The consent form will be reviewed and ample time will be given for the parent and child to consider participation. Prior to performing any procedures related to this study, the permission/assent form or consent form will be reviewed carefully with the participant and parent in person.

Subject Confidentiality
All records will be kept in a locked file cabinet. Human subject's names will be kept on a password protected database and will be linked only with a study identification number for this research. There are no patient identifiers recorded in the research record. All computer entry and networking programs will be done using study identification only. All data will be entered into a computer that is password protected. Data will be stored in a locked office of the investigators and maintained for a minimum of three years after the completion of the study.

Subject Payment
Subjects will be paid via ClinCard $50 total for participation. Payment will be given in $25 increments at visit 2 and visit 4 once the Actigraph activity monitor is returned. SSN is required for payment, and will be entered directly into the Greenphire secure website. SSN will not be retained in the subject's study file. Participants may also be compensated for mileage or a hotel stay based on their distance traveled (they will be given a choice of one or the other).

Participants will be able to keep the Fitbit Alta HR™ activity tracker ($150 value) and the Fitbit Aria™ smart scale ($130 value). If participants are within the same family, they will be given one Fitbit Aria™ smart scale per household.

9. PUBLICATION OF RESEARCH FINDINGS

- Results are intended to be presented at pediatrics or physical activity-related conferences by the study team within the next year.
- Results are intended to be published in a physical activity or public health journals.

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