

Building and estimating a dynamic model of weight gain and loss for individuals and populations

Hazhir Rahmandad (Hazhir@vt.edu), Nasim S. Z. Sabounchi (Sabounchi@vt.edu)

Affiliation: Grado Department of Industrial and Systems Engineering, Virginia Tech, Northern Virginia Center, Falls Church, VA, 22043, USA

Abstract

The obesity trends in the U.S. and many other countries are alarming. Models that can assess the potential impact of alternative interventions are much needed in turning the obesity trend. The purpose of this research is to study the dynamics of obesity in the United States over time to build a generic system dynamics model that can be used for obesity policy analysis at multiple levels. The model is multi-level in the sense that it builds on individual level models for both childhood and adulthood to capture the energy balance and weight change throughout the life of individuals, and aggregates individual level models to population level trends. We discuss the application of simulated method of moments to the calibration of this model. This approach enables community, state, or national policy analysis building on a calibrated model and offers promising methodological advances in model calibration in the field of system dynamics.

1. Motivation and Introduction

The obesity trends in the U.S. and many other countries are alarming. The percentage of Americans who are obese has doubled to near 30% during the past four decades, and close to two third of the population is overweight (Bray and Bouchard 2004; Ogden, Carroll et al. 2006). The increase of obesity leads to significant costs and loss of quality life. The costs will double every 10 years if current trends continue (Wang, Beydoun et al. 2008). Multiple levels of factors are involved in creating the obesity problem. A few of these include biological, psychosocial, cultural, environmental, economic drivers, and also factors related to the food, physical and cultural environment which affect human behavior (Huang, Drewnoski et al. 2009). The multiplicity of actors involved and the mechanisms that influence obesity call for a systems approach to analyze the problem and assess interventions. Models that can assess the potential impact of alternative interventions are much needed in turning the obesity trend. Such models can facilitate policy analysis by expanding the boundaries of our mental models and enhancing

learning from evidence (Stermann 2006). An increasing set of public health problems are relying on such policy-oriented models to develop reliable policy options. For example simulation models are now playing a major role in outbreak response planning (Kaplan, Craft et al. 2002; Keeling, Woolhouse et al. 2003; Eubank, Guclu et al. 2004; Ferguson, Cummings et al. 2006). SD applications of public health problems include a wide range such as drug abuse (Caulkins, Crawford et al. 1993; Homer 1993; Behrens, Caulkins et al. 1999), bio-terror contingency planning (Kaplan, Craft et al. 2002), individual obesity (Abdel-Hamid 2002), diabetes (Jones, Homer et al. 2006), polio vaccination strategies (Thompson and Tebbens 2007), chronic disease (Homer, Hirsch et al. 2004; Homer, Hirsch et al. 2007), smoking (Levy, Hyland et al. 2007), cardio-vascular health (Homer, Milstein et al. 2008), and hepatitis (Behrens, Rauner et al. 2008), among others.

However building calibrated models of obesity using individual-level time series data has been hampered by practical and ethical considerations related to following and manipulating an individual's eating, physical activity, and weight change over extended periods of time including childhood years. Moreover, population level policy analysis requires models that are validated using representative population level data. Available dynamic models for obesity rely on short-term time series data and small sample sizes (Kozusko 2001; Flatt 2004; Christiansen, Garby et al. 2005; Butte, Christiansen et al. 2007; Hall 2010) which reduces their direct applicability for policy analysis at the population level.

1.1. Literature and Problem Definition

At its core, body weight gain and loss follow a simple logic: if the amount of energy intake (EI) from different food and drinks exceeds total energy expenditure (TEE) due to resting metabolic rate (RMR), digestion, and physical activity (PA), then body weight will increase, otherwise individual loses weight or remains at the current weight if $EI=TEE$. However policy-oriented modeling is complicated by multiple different factors. First, RMR is itself a function of body weight, composition (fraction of body weight in fat mass (FM) vs. fat free mass (FFM)), sex, ethnicity, and age (Harris and Benedict 1919; Cunningham 1980; Bernstein, Thornton et al. 1983; Schofield 1985; Astrup, Thorbek et al. 1990; Cunningham 1991; Maffeis, Schutz et al. 1993; Bitar, Fellmann et al. 1999; Frankenfield, Roth-Yousey et al. 2005). Changes in EI may influence RMR as well through a process known as adaptive thermogenesis (Rosenbaum, Leibel

et al. 1997; Jequier and Tappy 1999; Rosenbaum, Hirsch et al. 2008). Moreover, obesity is by definition about the tail of body mass index (BMI) distribution in a population. Models effective for obesity policy analysis should not only capture the dynamics of “average” individual, but should also be viable for predicting what happens to individuals in the tail of distribution.

Finally, policy interventions are often not directly changing EI or PA, but do so through different indirect methods that use taxes on sugar sweetened beverages, availability of physical activity opportunities, school cafeteria menus, and other interventions to change EI and PA. Quantifying the effect of an intervention on EI and PA for different population members is needed in order to assess the intervention’s impact on obesity. As a result of these challenges simulating population level weight gain and loss dynamics, and assessing alternative interventions in a new population group, requires dynamic models that 1) Capture the individual-level body weight dynamics realistically, building on biological processes that regulate energy balance in body. 2) Connect individual level and population level dynamics in a robust and generalizeable fashion. 3) Express the impact of interventions on energy intake and physical activity for different individuals.

Previous work provides a strong starting point to model body weight dynamics in a single individual. (Kozusko 2001; Abdel-Hamid 2002; Christiansen and Garby 2002; Kozusko 2002; Flatt 2004; Christiansen, Garby et al. 2005; Butte, Christiansen et al. 2007; Song and Thomas 2007; Thomas, Ciesla et al. 2009; Hall 2010). Modeling childhood weight gain and loss is more complex due to the presence of normal growth processes in children. Nevertheless a few researchers have tackled this topic by building childhood weight gain and loss models (Butte, Christiansen et al. 2007). While this literature provides a great starting point for modeling individual level body weight dynamics, three major shortcomings remain for using these models for population level policy analysis. First, none of the current models include both childhood and adulthood dynamics. Second, current models do not capture the dependence of RMR on age among adults, a factor that becomes relevant for modeling age-heterogeneous populations or dynamics over long time horizons. Finally, the current models focus on modeling a single “average” individual. Extending them to capture variations across individuals is critical for population health policy analysis.

In this study we plan to develop a dynamic model of individual weight change over time which overcomes the problems discussed above. Specifically, while the relationship between

RMR and age is not captured in current dynamic models of weight change; many statistical studies have included age as an independent variable in explaining RMR. (Harris and Benedict 1919; Cunningham 1980; Cunningham 1991; Vaughan, Zurlo et al. 1991; Poehlman 1992; Maffei, Schutz et al. 1993; Tershakovec, Kuppler et al. 2002; Speakman and Westerterp 2010). Some, (Poehlman 1992) find that “total daily energy expenditure and its components decline with advancing age” p.2057. However, Speakman and Westerterp (2010) find that in the second half of age (>57.8 for men and >39.8 for Women), RMR is negatively related to age, whereas in the first half it is positively related to age. Therefore we can use this literature to build models that capture the change in RMR over an adult’s life. Furthermore, we will combine childhood and adulthood equations from previous models to build a model that can be applied throughout the life of an individual.

To address the third challenge, we will focus on identifying population level variations in relevant parameters that are important in explaining the variations in body weight across individuals. For example one can expect that all variations in weight can be explained solely by variations in EI and PA across individuals. Alternatively, variations in these inputs may not be enough to explain population level variations, and estimates of inherent (e.g. genetic) differences across individuals in parameters that determine TEE may be required.

Estimating the aforementioned parameters requires strong empirical support. Ideally panel data on demographics, body weight and composition, EI, and PA for a large sample of individuals and over a long time would have provided the data to estimate relevant model parameters. However we could not identify any database with these characteristics. The most comprehensive study which has data on all the relevant variables and has reliably large sample sizes is the National Health and Nutrition Examination Survey (NHANES). While this survey is repeated bi-annually since 2000, and three waves of data have been collected for it in the decades before that, the survey does not follow the same individuals over time. Therefore we will leverage estimation methods that can use this cross-sectional data base to estimate dynamic models that span over multiple years.

2. Analysis and Results

The purpose of the research is to study the dynamics of obesity in the United States over time to build a generic system dynamics model that can be used for obesity policy analysis at multiple

levels. The model is multi-level in the sense that it builds on individual level Energy Models for both childhood and adulthood (Butte, Christiansen et al. 2007; Hall 2010) to capture the energy balance and weight change throughout the life of individuals, and aggregates individual level models to population level trends. This approach enables community, state, or national policy analysis building on a calibrated model. The model distinguishes individuals based on sex, age, ethnicity, and socio-economic characteristics and takes physical activity and energy intake as inputs and provides the dynamics of body weight and body composition as outputs.

We first introduce the individual level model of body weight dynamics used in this study. The population level model which consists of multiple replicas of individual model and their relationships will then be discussed. Finally we explain the calibration and parameter estimation processes and the results of the analysis.

2.1 Individual Level Model of Body Weight Dynamics

Several models of body weight dynamics have been discussed in the literature (Kozusko 2001; Abdel-Hamid 2002; Christiansen and Garby 2002; Kozusko 2002; Flatt 2004; Christiansen, Garby et al. 2005; Butte, Christiansen et al. 2007; Song and Thomas 2007; Thomas, Ciesla et al. 2009; Hall 2010). These models vary in their level of complexity and the feedback mechanisms they capture. Common across most these models are the state variables fat mass (FM) and fat free mass (FFM) which constitute the majority of body weight in a normal person. More detailed models may consider the stock of glycogen, protein, and extracellular fluid mass and adaptive thermogenesis among other stock variables (Flatt 2004; Hall 2006; Hall 2010). While additional complexity could be important in evaluating dynamics that unfold in hours or days, results of comparative studies by Hall (Chow and Hall 2008; Hall 2010) suggest that for longer term dynamics FM and FFM provide much explanatory power with very little complexity. We therefore rely on these two variables as the main stocks in our individual model.

In considering weight dynamics, total energy intake is the most important factor about food and beverage consumed by an individual. While individuals could get their calories from carbohydrates, fats, or proteins, the impact on weight dynamics is not significantly different as long as the same number of calories is taken in. Therefore we focus on total EI and do not distinguish between different nutrients.

Factors influencing energy expenditure are a bit more diverse. At its core, these include the resting metabolic rate (RMR: the energy required to perform vital body functions while body

is at rest) which contributes to 50-75% of energy expenditure, the physical activity energy needs, and the energy for digestion of food and nutrients consumed and generation of new tissue. RMR itself depends on the body composition (energy needs for maintaining FM and FFM are different) as well as individual differences on individual, age, and gender specific variations not captured by FM and FFM. Energy expenditure attributed to physical activity (PA) is largely proportional to the total weight (BW=FM+FFM) and the intensity of PA. As we discussed before, there is no unified model for childhood and adulthood body weight dynamics in the literature, we therefore use slight modification of the models by Hall (2010) and Butte Christiansen et al.(2007) to represent the total energy expenditure (TEE) in adults and children respectively by equations (1) and (2):

$$TEE_{Adult} = K + \gamma_L \cdot FFM + \gamma_F \cdot FM + PA_{Total} \cdot BW + \eta_L \cdot \frac{dFFM}{dt} + \eta_F \cdot \frac{dFM}{dt} + \lambda \cdot EI \quad (1)$$

$$TEE_{Child} = (\beta_L \cdot FFM + \beta_F \cdot FM) \cdot PAL + \theta \cdot \frac{dBW}{dt} + \lambda \cdot EI \quad (2)$$

The parameters of the childhood model are somewhat imprecisely specified because 1) The Butte Christiansen et al. (2007) study does not include children under 4 years of age, and is heavily under sampled for those above 15. 2) Many of the relationships expressed in their model are based on tanner stage, rather than age. As a result, we have to estimate the dependence of β_L on age to complete the childhood model. The estimation procedure is discussed in calibration section below.

Changes in the FM and FFM are dependent on the difference between energy intake and energy expenditure (EI-TEE). Specifically, the net energy surplus (shortage) is partitioned to be added (lost) between FM and FFM. The partitioning function is different for adult and children, where the adult model uses the empirical equation $1/(1+0.502 \cdot FM)$ (Forbes 2000; Chow and Hall 2008) as the fraction of energy surplus/shortage contributing to changes in FFM and the childhood model uses an age and sex specific table function.

Individual variations in the childhood and adulthood models are captured in variables PAL and K respectively, keeping all other parameters constant across individuals. Our individual model switches from childhood to adulthood equations when an individual reaches the age 20. The relationship between K and PAL are discussed in section 2.3.

Figure 1, provides an overview of the causal pathways in the individual level model. The equations behind the solid lines are taken from previous models in the literature (Butte,

Christiansen et al. 2007; Hall 2010) while the equations represented by dashed lines are estimated statistically using NHANES data (See Figure 1 below). Full model is available in the appendix.

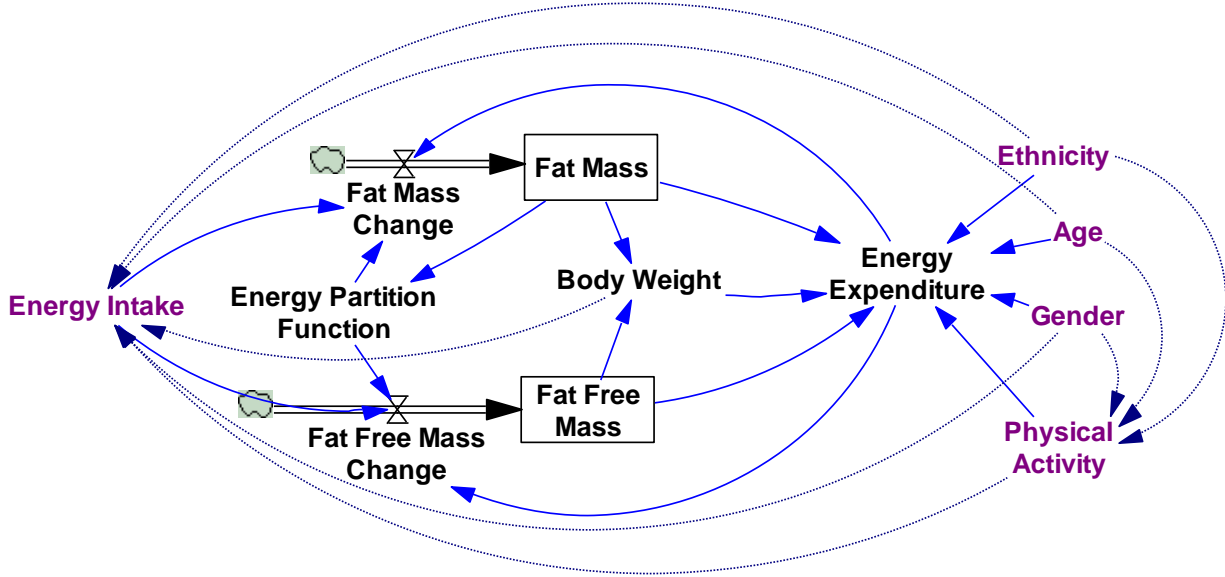


Figure 1- Overview of individual level model and its major feedback loops and estimated relationships.

2.2 Estimating Energy Intake and Physical Activity

NHANES data is not time series. Therefore EI and PA levels reported in the survey cannot be directly used to recreate an individual’s EI and PA over the course of simulation. On the other hand EI and PA values are required as inputs to simulate the individual level model. To overcome this challenge we need equations that generate realistic time series values for EI and PA for each individual in a population, while being consistent with overall distributional characteristics of the data in NHANES. The process of estimating these equations, is complex and beyond the scope of the current paper which focuses on body weight dynamics. However the resulting equations which are used in the simulation model are reported here with a brief explanation.

Energy intake for individual i at time t depends on the expected energy intake for an individual with the same profile as individual i (EEI), adjusted based on a normalization factor (e) and an individual variation factor (ϵ) as shown in equation (3):

$$EI_i = EEI_i + e_i \cdot \epsilon_i \quad (3)$$

Expected energy intake (EEI) is calculated from a regression equation that is estimated based on NHANES data. Normalized values for 34 different independent variables ranging from age, sex, ethnicity, to body weight, year, and socio-economic status are used in this regression and the resulting coefficients of regression (β_j ; available in Appendix A) are used in equation (4) to calculate EEI:

$$EEI_i = \sum \beta_j \hat{X}_{ij} \quad (4)$$

Normalization is conducted to correct for heteroskedasticity in the regression (e.g. typically, error terms are much larger for people who are heavier and eat more). The expected error term is used for the normalization of independent variable j for individual ‘ i ’ as in the following equation:

$$\hat{X}_{ij} = X_{ij}/e_i \quad (5)$$

These expected error terms are calculated by doing another regression (i.e. equation (6)) that estimates non-normalized error terms based on different individual characteristics.

(Regression coefficients α_j can be found in Appendix A):

$$e_i = \sqrt{e^{\sum \alpha_j X_{ij}}} \quad (6)$$

Finally, the individual variation term is assumed to be a random normal variable which is gradually changing for each individual within the overall distribution of $v \sim N(0, \sigma)$. The variance parameter σ represents the variations in individual energy intake attributable to persistent within-individual differences (rather than temporary differences from one day to the next) and from multiple measurements of EI for the same individual available in NHANES is estimated to be 1.53. The parameter τ is estimated in the calibration procedure (see below) and dt is the time step for numerical integration:

$$\varepsilon_i(t + dt) = \frac{\varphi \cdot v(t) + (1 - \varphi) \cdot \varepsilon_i}{\sqrt{\varphi^2 + (1 - \varphi)^2}}; \quad \varphi = dt/\tau \quad (7)$$

This formulation partitions differences between individuals’ measured EI into 1) predictable factors (those estimated in the regression) 2) Unobservable heterogeneity among individuals (captured in ε term) and 3) Measurement error, which is estimated (using the fact that NHANES offers two EI estimates based on two different measurements for many individuals) and removed from the rest of analysis. We also allow the unobservable heterogeneity factor, ε , among individuals to change over time. For example an individual who initially was in the 95th

percentile of EI among his peers (those with the same independent variables), could gradually change his EI habits and move to a different percentile, without changing the overall distribution of EI for the population. By estimating the parameter τ we are able to estimate how fast individual energy intake percentile changes, if at all.

A similar (but slightly simpler) set of regression equations are developed to generate physical activity values beyond the base level (PA_{Active}) for each individual in a population. The variations across individuals are captured using a log-normal distribution with standard deviation σ_{PA} which is estimated in calibration. Put together, these equations can provide the synthetic, but empirically grounded, input data on EI and PA for any arbitrary population group. For example, one can generate realistic time series EI and PA inputs for a group of K-12 school children with a given ethnicity and socioeconomic characteristic mix. These relationships are highlighted in Figure 1 with dashed lines.

2.3 Population Model

Multiple replications of the individual level model (Section 2.1) can be simulated together to generate population level characteristics of interest such as percentage of the population that is overweight or obese. However creation of the population model requires more than just replicating the individual level model. Specifically, where a parameter is assumed to be different across individuals, the distributional characteristics of that parameter should be specified for the population. For example, individuals vary in their RMR constant term, K , within the adulthood model. However, previous research does not specify the distributional characteristics of K , such as its mean and standard deviation. Previous models also do not specify the dependence of K on age and gender, among others. Even after fixing all individual-independent model parameters based on the literature, such distributional parameters need to be empirically estimated for the population model.

Besides individual factors influencing EI and PA_{Active} (See section 2.2), in our model we define a single individual variance factor which captures differences in RMR across different individuals. The basic idea is that even if two individuals have the same exact FM, FFM, EI and PA, they may still have different weight trajectories over time due to small differences in how their bodies process nutrients. Such differences should be expected and could be traced back to individual level genetic or environmental factors not represented in our relatively simple model.

We formulate this individual factor (ϵ) to depend on gender (G) and ethnicity (\mathbf{T} : a vector (thus bold) of dummy variables for different ethnicities in NHANES), according to the following equation:

$$\epsilon_i = \text{Max}(0, \alpha_G \cdot G + \boldsymbol{\alpha}_T \cdot \mathbf{T} + N(0, \sigma_\epsilon)) \quad (8)$$

Here parameters α_G , $\boldsymbol{\alpha}_T$, and σ_ϵ should be estimated in the calibration process. These parameters will determine if there are ethnic and gender specific variations on how individuals' bodies react to different EI and PA profiles, and how much different individuals vary on this front once controlling for gender and ethnicity. Individual factor parameter then influences the childhood and adulthood models according to the following equations:

$$PAL = \rho_{ch} + \epsilon_i + PA_{Active} * BW / (\beta_L \cdot FFM + \beta_F \cdot FM) \quad (9)$$

$$PA_{Total} = PA_{Active} + PA_{Base} \quad (10)$$

$$K = \text{Max}(0, s_K * \epsilon_i - \frac{(s_K * \epsilon_i - k_{min})e^{l(Age_i - t_D)}}{1 + e^{l(Age_i - t_D)}}) \quad (11)$$

The value of PA_{Base} is taken from the Hall's model to be around 5 Kcal/Kg/Day. These equations ensure that the range of PAL remains consistent with empirical evidence (between 1.5 and 2); that physical activity is accounted for in a comparable fashion in both childhood and adulthood models, and that the dependence of RMR constant term (K) on age can be included in our estimation process. The parameters ρ_{ch} , s_K , l , and t_D should be estimated from the data to specify the magnitude of RMR constant term over an individual's life.

2.4 Model Calibration and Parameter Estimation

An innovative feature of this study is its methodological contribution towards estimating dynamic models based on cross-sectional individual level data from a population. As discussed before, no current database offers the large scale time series data typically used for estimating dynamic models similar to the one we are working with here. However, we note that the data in NHANES provides a lot of information in terms of the distribution of weights (and body composition) for different subgroups in the population. A good population level model should be able to match those distributions closely, and the quality of that match can inform parameter estimation and hypothesis testing. For example we can look at the sample mean and variance of body weights for 5-7 year old African American Male in NHANES data in 2005-2006 and compare that to synthetic results for a similar population (with similar demographics) simulated

using our model. If the two statistics (sample mean and variance) for the real population match those in the simulated population, we can have some confidence about the ability of the model to recreate the historical results. In fact we can also change model parameters to reduce the discrepancy between different statistics, i.e. to calibrate the model and estimate the unknown parameters. Given that our model can be applied to simulate weight change for individuals across different age, ethnicity, and gender groups, we could scale up the comparison above for many different sub-population statistics to increase the precision of the comparisons, and to find better parameter estimates. This is the core idea we follow in this study.

This method can be identified as an instance of the Simulated Method of Moments (SMM) which is one of the most versatile econometric estimation methods available (McFadden 1989; Lee and Ingram 1991; Duffie and Singleton 1993). In this perspective, the mean and variance of body weight for each group is a distributional “moment” from the population, for which simulation and real data could be obtained and compared. More generally, denote the \mathbf{x} be the vector of observed variables (e.g. the individual weight and body compositions for all the population members), $\mathbf{x}^s(\boldsymbol{\theta})$ the simulated vector for the same variables in simulation s generated using parameter vector $\boldsymbol{\theta}$ in the model, and $\boldsymbol{\mu}(\mathbf{x})$ a vector of functions of the observed data. The SMM uses the following optimization problem to estimate the parameter vector $\boldsymbol{\theta}$:

$$\hat{\boldsymbol{\theta}}(\mathbf{W}) = \arg \min_{\boldsymbol{\theta}} [\boldsymbol{\mu}(\mathbf{x}) - \frac{1}{S} \sum_{s=1}^S \boldsymbol{\mu}(\mathbf{x}^s(\boldsymbol{\theta}))]' \cdot \mathbf{W}^{-1} \cdot [\boldsymbol{\mu}(\mathbf{x}) - \frac{1}{S} \sum_{s=1}^S \boldsymbol{\mu}(\mathbf{x}^s(\boldsymbol{\theta}))] \quad (12)$$

The matrix \mathbf{W} denotes the weighting function used. When multiple moments are to be compared, and the difference between pairs minimized through changing model parameters, one needs to assign weights to the error term resulting from each pair of simulated and empirical moments. If the model has no specification error, a large set of weighting functions provide consistent estimate. However, to increase the efficiency of the estimates and to increase robustness against model mis-specification, these weights should depend on the variability inherent in each moment, and its correlation with other moments. For example if the mean body weight for a population group is very uncertain, e.g. due to the limited number of data points available for that group, we should put a limited weight on the error term arising from the difference between empirical and simulated moments for that sub-group. In contrast, more established moments should be given higher weights. These weights are typically proportional to the observed covariance matrix for $\boldsymbol{\mu}(\mathbf{x}^s(\boldsymbol{\theta}))$. Note that as a result this procedure requires

multiple simulations to generate estimates for the $\mu(\mathbf{x}^s(\boldsymbol{\theta}))$ and its covariance matrix and conduct a single comparison with data.

In our application we define the moments (μ function) to be the mean and variance of population weights for 110 subpopulation groups (11 age groups, 5 ethnicities, and 2 genders), resulting in 220 moments to be matched against observed moments in a population of 5971 individuals from 2005-2006 NHANES for whom all the relevant data points are available. The number of individuals in each sub population varies between 1 (a few of the groups in the 80< age group) and 280 for African American male teenagers. In practice the computational costs of the SMM method could be prohibitive: simulating a large population (over 5000) of individuals is costly, multiple (S) replications may be required to calculate the objective function, and many (several to hundreds of thousands) simulations are required for any numerical optimization algorithm to find the unknown parameter vector. In order to overcome computational barriers, we modify the method to use $S=1$, and use sample mean, variance, and kurtosis to calculate estimates for the variance of sample mean and variance of sample variance. These estimates are used for the weights (W; a diagonal matrix is used) in the optimization problem above.

Figure 2, provides an overview of the statistical analysis and calibration procedure used. To capture the changes in EI and PA overtime, the statistical analysis used data from three rounds of continuous NHANES, conducted in 2001-2002, 2003-2004, and 2005-2006. This allows us to simulate body weight change in each individual over the 2001-2006 period, which is ample time to reach long term trajectories of body weight for each individual, starting from initial weights specified by expected values in 2001. The EI and PA values also depend on body weight, therefore the regression equations are embedded as part of the simulation model and create the synthetic EI and PA trajectories endogenously. The results of the body weight mean and variance for different sub-population groups is compared against the same metrics from the 2005-2006 NHANES data, and the weighted difference is minimized by calibrating the free parameters of the model.

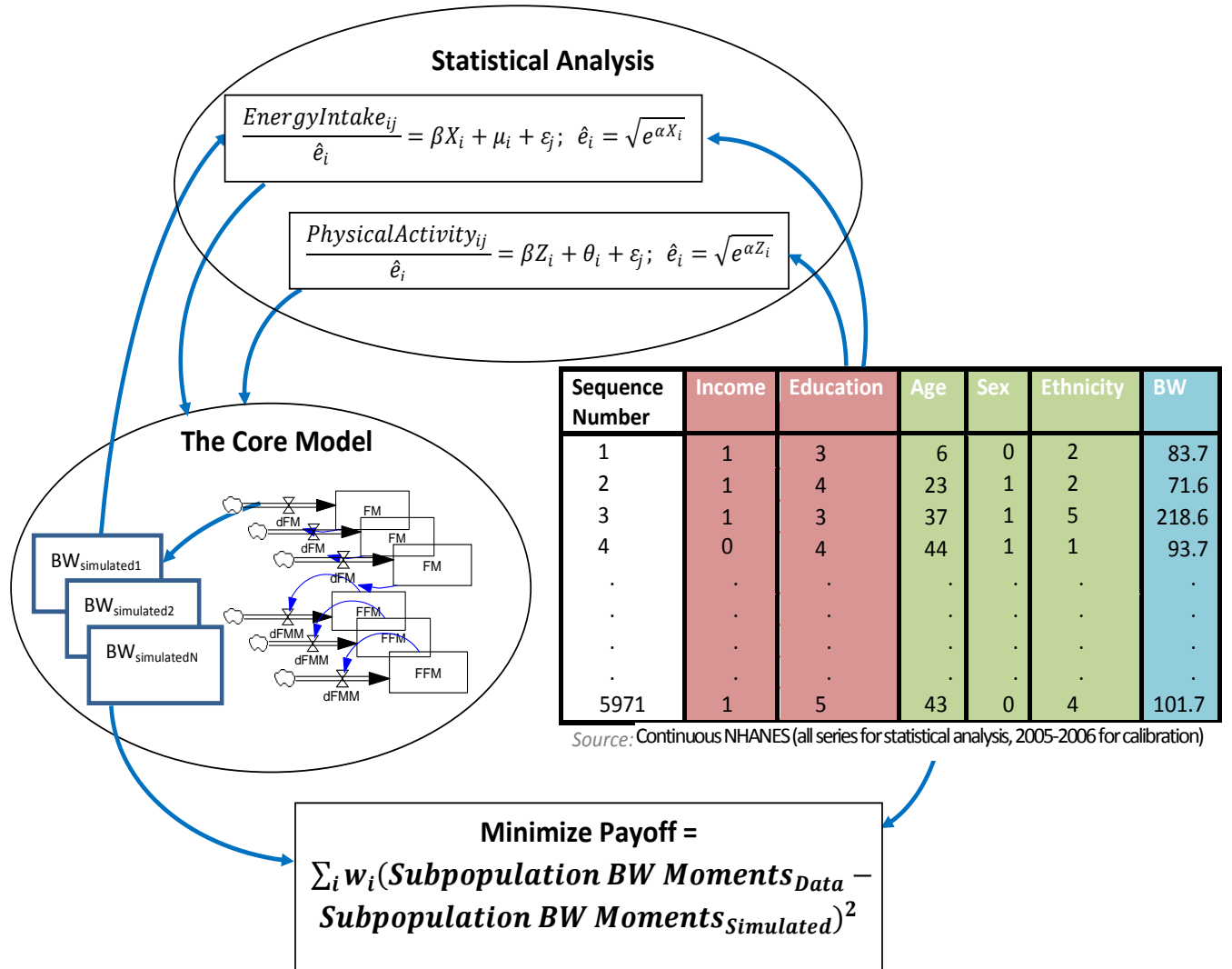


Figure 2- Overview of statistical estimation and calibration procedures.

The parameters estimated in the calibration procedure include those explaining EI and individual factor distributions at the population level (τ , σ_{PA} , α_G , α_T , σ_c , ρ_{ch} , s_k , l , and t_D) as well as parameters specifying the dependence of β_L on age during childhood. This relationship captures the biological observation that children's energy expenditure per unit of weight declines over time as they grow older. Consistent with Butte et al. (2007), an inverse S-shape functional form for this relationship is assumed (input to the function is individual i 's Age, A_i). Here β_L comes out as the average of β_{L0} and β_{LF} at age a_β and symmetrically decreasing between these two extremes with a logistic curve with a slope related to s_β . Parameters β_{L0} , β_{LF} , a_β , and s_β are estimated in the calibration procedure.

$$\beta_L = \beta_{L0} - \frac{(\beta_{L0} - \beta_{LF})e^{-s_\beta(A_i - a_\beta)}}{1 + e^{-s_\beta(A_i - a_\beta)}} \quad (13)$$

2.5 Calibration Results

Following the procedure discussed in section 2.4, we conducted the calibration procedure. The algorithms are implemented in Vensim™, and using model compilation and other time-saving techniques we could calibrate the model through overnight simulations on an Intel Core 2 Quad CPU @ 2.66GHz with 4GB memory. The obtained payoff (see equation 12) was 6568. Table 1 reports the parameter estimates for the calibrated model. Parameters specifying β_L the relationship with age show reasonable ranges and values consistent with previous literature (Butte, Christiansen et al. 2007). Other parameters are harder to evaluate based on external metrics because many of them are introduced for the first time in the literature and prior values are not available.

Table 1- Estimated parameter values from calibration. Values identified by * point to estimates that fall on the boundaries of searched parameter space.

	Description	Value	Units
τ	EI Change time constant (Eq*** please add equation numbers for all parameters below)	1.14	Year
σ_{PA}	Standard deviation of log-normal random term multiplied by average individual physical activity to provide values for a single individual	0.001*	dmnl
α_G	Male individual factor (0 is for female)	-1*	dmnl
α_{TW}	Ethnicity individual factor for white (Mexican American assumed 0)	-0.88	dmnl
α_{TB}	Ethnicity individual factor for African Americans (Mexican American assumed 0)	-0.39	dmnl
α_{TH}	Ethnicity individual factor for other Hispanic (Mexican American assumed 0)	-1*	dmnl
α_{TO}	Ethnicity individual factor for other ethnicities (Mexican American assumed 0)	-1*	dmnl
σ_ϵ	Standard deviation of individual factor term distinguishing between individuals.	1*	dmnl
ρ_{ch}	Constant term for PAL used in childhood	4*	dmnl
k_{min}	Minimum value for the relationship between constant term of RMR and age.	- 100,000*	Kcal/Year
s_k	Individual scale factor for adults	333874	Kcal/Year
l	Slope at inflection point for the relationship between constant term of RMR and age.	0.019	1/Year
t_D	Age at inflection point for the relationship between constant term of	20*	Year

	RMR and age.		
β_{LO}	Starting value for the relationship between β_L and age.	36.13	Kcal/Kg/ Day
β_{LF}	Final value for the relationship between β_L and age.	5.47	Kcal/Kg/ Day
a_β	Age at inflection point for the relationship between β_L and age.	7.13	Year
s_β	Slope at the inflection point for the relationship between β_L and age.	0.55	1/Year

Figure 3, reports a few sample histograms for weight distributions of different subpopulations compared across simulated (blue, left bars) and empirical (red right bars) data. While the overlaps between the distributions are relatively good, a few systematic biases could be observed. First, the simulation results tend to include too many under-weight individuals. Moreover there are often a few very obese individuals in the empirical data who are not replicated in the simulations. The overall fit between the model and empirical data on mean weight is mixed. For most population groups the average weight is within 10% of the empirical results. But for a few of the groups, the variations observed are as high as 50% which lead to relatively high penalty function in the calibration. Mean weight for boys is slightly overestimated, is fairly precise for girls, and is underestimated for adults, especially at older ages.

The model developed here is promising as a first step to develop a generic, multi-purpose platform for testing the impact of different interventions designed to fight obesity. As such, the model can be easily configured to include different variations in EI and/or PA resulting from an intervention, and predict the changes in population weight as a result. For example, what would be the impact of changing the food offered in school cafeterias? Fox, Gordon et al. (2009), estimate that children in schools obtain 160-200 Kcal/Day from competitive foods provided in school cafeteria. Therefore the impact of any intervention focused on altering competitive food offerings will likely be limited to this level of change in EI. Figure 4 reports one such simulation experiment in which EI for a cohort of K-12 children is reduced by 180 Kcal/Day at the beginning of 2011 and the average weight and its distribution is followed over the next decade.

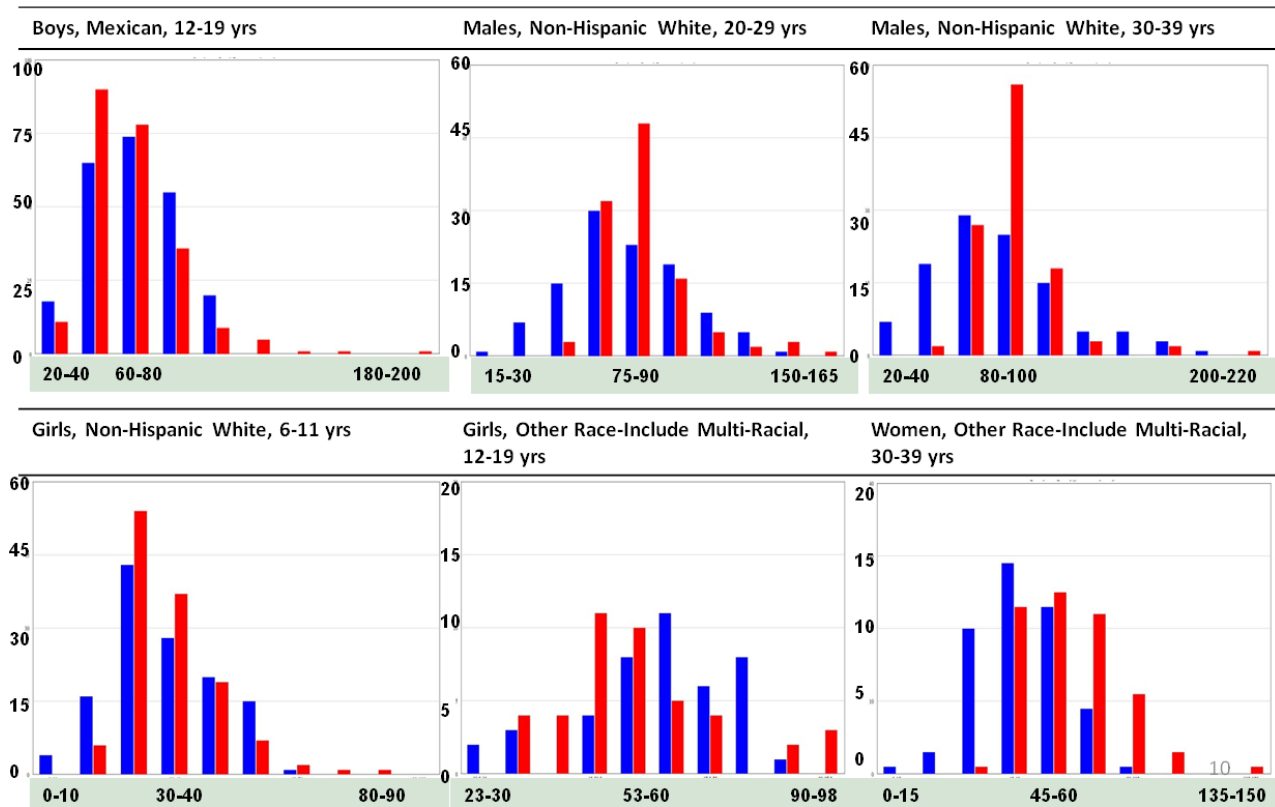


Figure 3-Sample results comparing body weight distributions for simulation (blue/left) and empirical(red/right) data across a few population subgroups.

The model developed here is promising as a first step to develop a generic, multi-purpose platform for testing the impact of different interventions designed to fight obesity. As such, the model can be easily configured to include different variations in EI and/or PA resulting from an intervention, and predict the changes in population weight as a result. For example, what would be the impact of changing the food offered in school cafeterias? Fox, Gordon et al. (2009), estimate that children in schools obtain 160-200 Kcal/Day from competitive foods provided in school cafeteria. Therefore the impact of any intervention focused on altering competitive food offerings will likely be limited to this level of change in EI. Figure 4 reports one such simulation experiment in which EI for a cohort of K-12 children is reduced by 180 Kcal/Day at the beginning of 2011 and the average weight and its distribution is followed over the next decade.

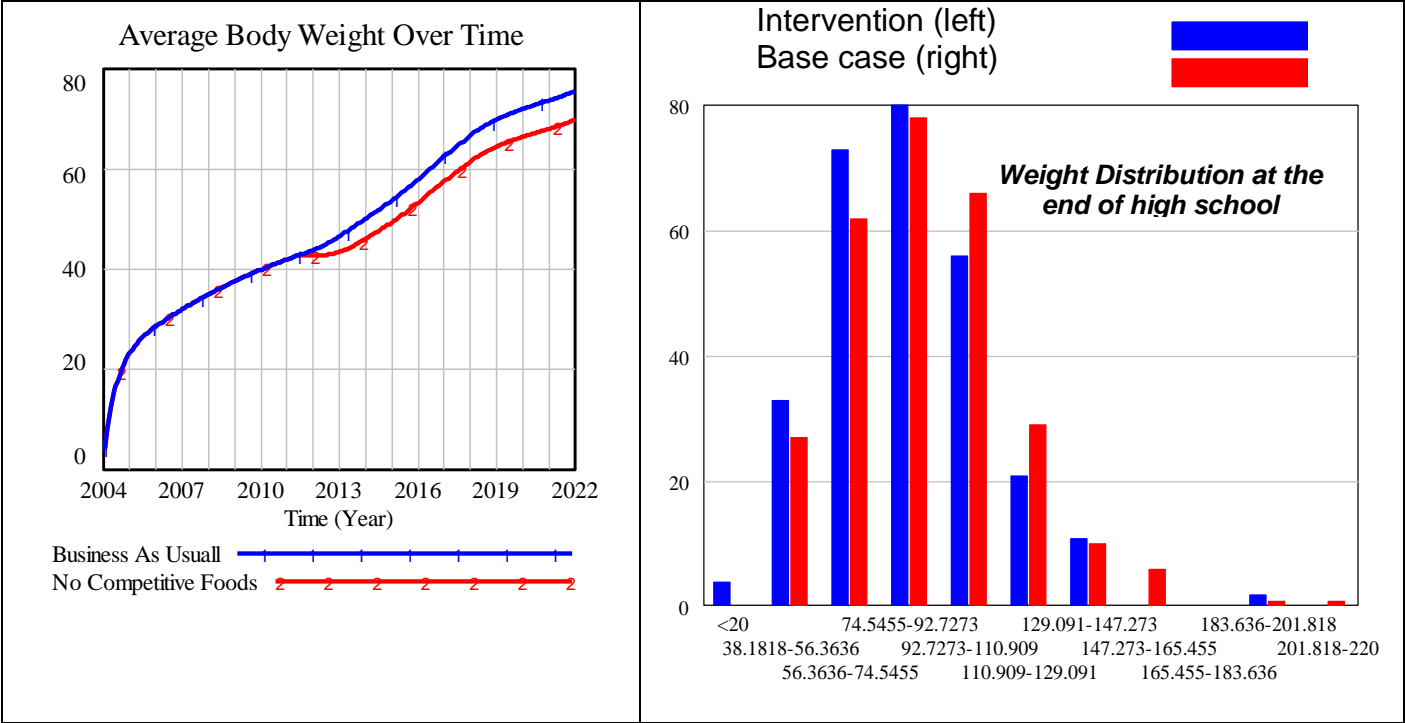


Figure 4-Results from a hypothetical intervention reducing K-12 student energy intake by 180Kcal/Day starting 2011.

It is important to note that a major part of capturing the impact of interventions relates to assessing the impact of each intervention on EI and PA. Our model does not provide any direct way to measure or simulate that causal link and relies on empirical estimates provided from other studies. Nevertheless, to the extent that such estimates exist, this model provides a flexible environment for testing their impact on body weight distribution in general, and obesity patterns in particular.

3. Discussion and Limitations:

The contributions of this work are twofold. First, for the first time in the public health literature we provide an integrated model of weight gain and loss that covers both childhood and adulthood and connect it to population level weight dynamics. The resulting model provides a flexible, validated, module to be integrated in any policy analysis project. The model is robust to extreme conditions, does not require parameter estimation, and can be plugged with any hypothetical interventions.

Second, we adopt the SMM for application to arbitrary system dynamics models. SMM is very flexible and enables SD models to be estimated using not only panel or time series data but

also cross sectional population statistics. This can open the door to much wider use of nonlinear feedback-rich models in data intensive domains traditionally dominated by simpler regression models. Computational challenges involved in the estimation process should be considered judiciously to maximize the impact of this methodological innovation in future research.

The results presented here provide a first cut at a complex modeling and estimation project, and future work should focus on improving the results in light of less-than-perfect fit between the model and the data in many settings. In fact we experimented with a few different specifications and calibrated the model under several different assumptions, but the underestimation of weight for older adults remains a robust result in the model. Two alternative hypotheses could explain this issue. First, the individual level models used as the starting point for this study may be deficient and require structural or parametric changes. We are currently exploring this possibility by conducting a meta-analysis of different studies connecting RMR and different individual level variables. Furthermore, energy intake data in NHANES may be inaccurate due to personal reports not being verified independently (Pryer, Vrijheid et al. 1997; Pomerleau, Ostbye et al. 1999; Asbeck, Mast et al. 2002; Pikhholz, Swinburn et al. 2004; Poslusna, Ruprich et al. 2009). This is especially problematic if the reporting bias varies across age, gender, and ethnicity due to memory recall problems and value of different body images in the respondent's mind. Should we conclude that this is the main culprit in the resulting variations between the model and the data, we will need to consider other data sources which have avoided this bias through more objective energy intake assessments. Finally, concerns for computational costs and plausibility of resulting parameters lead us to restrict the searched parameter space. However, several parameters were estimated to be on the imposed boundaries of the parameter space, which suggests a larger parameter space may need to be explored in the optimization problem.

Appendix A

Given Parameters based on original models/literature

basal energy need of FM kf = 2354
Units: kcal/(kg*Year)

beta = 0.24 * 0 + 0.1
Units: Dmnl

C = 10.4
Units: kg

deltaBase = 5 * 365
Units: kcal/(kg*Year)

efficiency in conversion of energy to FFM eff = 0.42
Units: Dmnl

efficiency in conversion of energy to FM ef = 0.85
Units: Dmnl

EtaF = 180
Units: kcal/kg

EtaL = 230
Units: kcal/kg

Fat Energy Content cf = 9250
Units: kcal/kg

GammaF = 3.2 * 365
Units: kcal/(kg*Year)

GammaL = 22 * 365
Units: kcal/(kg*Year)

Lean Energy Content cff = 1070
Units: kcal/kg

MaxEI = 4e+006
Units: kcal/Year

MinDieTime = 0.25
Units: Year

MinIndivFactor = 0.2
Units: **undefined**

RhoF = 9400
Units: kcal/kg

RhoL = 1800
Units: kcal/kg

SwitchAge = 20
Units: Year

Thermic Effect of Food = 0.1
Units: Dmnl

Variables/Parameters estimated directly from the regression results.

BetaWeight[RegDim] = 0, 0, -0.99024, -1.38012, -0.26398, -1.23871, 5.04669,
-0.08268, -0.00079, 2.96e-005, -1.89e-007, 4.11142, 0.057612, -0.00568
, 9.61e-005, -5.02e-007, 1.1844, -0.28625, 2.5016, 5.50454, 0, 0, 0,
0, 1.47752, 1.94486, 1.92287, -1.19836, 0.290778, -0.00499, -0.74844,
-0.63011, 0.334631, 1.38368
Units: Dmnl

EIRegAlpha[RegDim] = 0.000470207, -8.347e-009, 0.130388, 0.0946955, 0.0418888
, -0.21005, 0.153314, -0.00653885, 0.000118584, -1.01442e-006, 3.27e-009
, 0.141181, -0.00305543, -1.0581e-006, 4.94118e-007, -3.323e-009, 0.0636715
, 0.147778, 0.197214, 0.234985, 0.00187009, 1.14759e-006, -2.60287e-006
, -0.000200152, 0.0297876, 0.0686771, 0.047488, -0.159513, -0.0878334
, 0.0167312, -0.0969955, -0.0959532, 0.039817, 10.777
Units: Dmnl

EIRegBeta[RegDim] = -0.265904, 0, -49.4757, 22.971, 48.6868, 75.8632, 111.42
, -8.57332, 0.256955, -0.00327348, 1.48904e-005, 141.584, -9.98975, 0.292064
, -0.00370248, 1.68698e-005, 58.8631, 47.0249, 27.7222, -54.9654, -2.68104
, 0, 0.000471804, 0.262445, 145.455, 157.439, 224.007, 291.642, 127.043
, -85.1863, -27.2202, -89.4859, -91.3247, 3.4304
Units: Dmnl

EIVarFactor = INITIAL(1.533)
Units: Dmnl

ePredict[Person] = sqrt (exp (sum (EIRegAlpha[RegDim!] * IndivX[Person,RegDim!
]))))
Units: Dmnl

ExpectedEI[Person] = sum (EIRegBeta[RegDim!] * IndivXdiv[Person,RegDim!])
Units: kcal/year

IndivX[Person,PA] = PAFac[Person]
IndivX[Person,T] = TimeFactor[T]
IndivX[Person,AF] = (Age[Person] * IndSex[Person]) ^ (AF - 6)
IndivX[Person,AM] = (Age[Person] * (1 - IndSex[Person])) ^ (AM - 11)
IndivX[Person,Et] = If then else (Ethnicity Code[Person] = Et - 16, 1, 0)
IndivX[Person,BW1] = Min (BW[Person] , 200)
IndivX[Person,BW2] = Min (BW[Person] , 200) ^ 2
IndivX[Person,BWPA] = Min (BW[Person] , 200) * PAFac[Person]
IndivX[Person,Et3PA] = If then else (Ethnicity Code[Person] = 3, 1, 0) * PAFac[Person]
IndivX[Person,Edu] = If then else (Education[Person] = Edu - 23, 1, 0)
IndivX[Person,Inc] = Income[Person]
IndivX[Person,Edu4Inc] = IndivX[Person,Ed4] * Income[Person]
IndivX[Person,Cons] = 1

$\text{IndivX}[\text{Person}, \text{PA2}] = \text{PAFac}[\text{Person}]^2$
 $\text{IndivX}[\text{Person}, \text{Edu2Inc}] = \text{IndivX}[\text{Person}, \text{Ed2}] * \text{Income}[\text{Person}]$
 $\text{IndivX}[\text{Person}, \text{Edu3Inc}] = \text{IndivX}[\text{Person}, \text{Ed3}] * \text{Income}[\text{Person}]$
 $\text{IndivX}[\text{Person}, \text{Edu5Inc}] = \text{IndivX}[\text{Person}, \text{Ed5}] * \text{Income}[\text{Person}]$
 $\text{IndivX}[\text{Person}, \text{Female}] = \text{IndSex}[\text{Person}]$
 Units: **undefined**

$\text{IndivXBegin}[\text{Person}, \text{PA}] = \text{INITIAL}(0)$
 $\text{IndivXBegin}[\text{Person}, \text{T}] = \text{INITIAL}(\text{TimeFactor}[\text{T}])$
 $\text{IndivXBegin}[\text{Person}, \text{AF}] = \text{INITIAL}((\text{Age}[\text{Person}] * \text{IndSex}[\text{Person}])^{(\text{AF} - 6)})$
 $\text{IndivXBegin}[\text{Person}, \text{AM}] = \text{INITIAL}((\text{Age}[\text{Person}] * (1 - \text{IndSex}[\text{Person}]))^{(\text{AM} - 11)})$
 $\text{IndivXBegin}[\text{Person}, \text{Et}] = \text{INITIAL}(\text{If then else}(\text{Ethnicity Code}[\text{Person}] = \text{Et} - 16, 1, 0))$
 $\text{IndivXBegin}[\text{Person}, \text{BW1}] = 0$
 $\text{IndivXBegin}[\text{Person}, \text{BW2}] = 0$
 $\text{IndivXBegin}[\text{Person}, \text{BWPA}] = 0$
 $\text{IndivXBegin}[\text{Person}, \text{Et3PA}] = 0$
 $\text{IndivXBegin}[\text{Person}, \text{Edu}] = \text{INITIAL}(\text{If then else}(\text{Education}[\text{Person}] = \text{Edu} - 23, 1, 0))$
 $\text{IndivXBegin}[\text{Person}, \text{Inc}] = \text{INITIAL}(\text{Income}[\text{Person}])$
 $\text{IndivXBegin}[\text{Person}, \text{Edu4Inc}] = \text{INITIAL}(\text{IndivXBegin}[\text{Person}, \text{Ed4}] * \text{Income}[\text{Person}])$
 $\text{IndivXBegin}[\text{Person}, \text{Cons}] = 1$
 $\text{IndivXBegin}[\text{Person}, \text{PA2}] = 0$
 $\text{IndivXBegin}[\text{Person}, \text{Edu2Inc}] = \text{INITIAL}(\text{IndivXBegin}[\text{Person}, \text{Ed2}] * \text{Income}[\text{Person}])$
 $\text{IndivXBegin}[\text{Person}, \text{Edu3Inc}] = \text{INITIAL}(\text{IndivXBegin}[\text{Person}, \text{Ed3}] * \text{Income}[\text{Person}])$
 $\text{IndivXBegin}[\text{Person}, \text{Edu5Inc}] = \text{INITIAL}(\text{IndivXBegin}[\text{Person}, \text{Ed5}] * \text{Income}[\text{Person}])$
 $\text{IndivXBegin}[\text{Person}, \text{Female}] = \text{INITIAL}(\text{IndSex}[\text{Person}])$
 Units: **undefined**

$\text{IndivXdiv}[\text{Person}, \text{RegDim}] = \text{If then else}(\text{RegDim} = 34, 1, \text{IndivX}[\text{Person}, \text{RegDim}] / \text{ePredict}[\text{Person}])$
 Units: **undefined**

$\text{MeanBWFac} = (1 - \text{LN}(0.5 / \exp(1) + 1)) / 2$
 Units: Dmnl

$\text{StdBWFac} = \text{INITIAL}(\text{sqrt}(\text{LN}(\text{StdBWInit} / \exp(1) + 1)))$
 Units: Dmnl

The rest of the model, including Adult and Child Body Weight modules

$\text{Age}[\text{Person}] = \text{Max}(0, \text{Time} - \text{BirthTime}[\text{Person}])$
 Units: Year

$\text{basal energy need of FFM kff}[\text{Person}] = (\text{Initkff} - (\text{Initkff} - \text{Finalkff}) * \exp(\text{ESlope} * (\text{Age}[\text{Person}] - \text{SlpStr}))) / (1 + \exp(\text{ESlope} * (\text{Age}[\text{Person}] - \text{SlpStr}))) * 365$
 Units: kcal/(kg*Year)

$\text{Basal Methabolic Rate BMR}[\text{Person}] = (\text{FM}[\text{Person}] * \text{basal energy need of FM kf} + \text{FFM}[\text{Person}] * \text{basal energy need of FFM kff}[\text{Person}])$
 Units: kcal/Year

$\text{BirthTime}[\text{Person}] = \text{INITIAL}(\text{BirthTimeData}[\text{Person}] - \text{RANDOM UNIFORM}(0, 1, \text{NoiseSeed}))$
 Units: Year

$\text{BW}[\text{Person}] = \text{FFM}[\text{Person}] + \text{FM}[\text{Person}]$
 Units: kg

$$\text{BWfactor[Person]} = \text{BW[Person]} * \text{Delta[Person]}$$

Units: kcal/Year

$$\text{Conversion Energy CE[Person]} = \text{Indicated Weight Change dBM[Person]} * (\text{Total Energy Coefficient for Tissue Deposition c[Person]} - \text{Energy Deposition Coefficient in Tissue[Person]})$$

Units: kcal/Year

$$\text{Delta[Person]} = \text{deltaBase} + \text{deltaPA[Person]}$$

Units: kcal/(kg*Year)

$$\text{deltaPA[Person]} = \text{IndivAvePA[Person]} * 365 * \text{IndividualPAFactor[Person]}$$

Units: kcal/(kg*Year)

$$\text{DEnergyIntake[Person]} = \text{EnergyIntake EI[Person]} - \text{Base Energy Intake}$$

Units: kcal/Year

$$\text{dFFM B[Person]} = \text{Indicated Weight Change dBM[Person]} * (1 - \text{Fat Deposit Fraction fr[Person]}) * \text{IsBorn[Person]}$$

Units: kg/Year

$$\text{dFFM H[Person]} = (\text{EnergyPFunction[Person]} * (\text{EnergyIntake EI[Person]} - \text{EnergyExpenditure[Person]})) / \text{RhoL}$$

Units: kg/Year

$$\text{dFM[Person]} = \text{Max} ((1 - \text{SWModel[Person]}) * \text{dFM B[Person]} + \text{SWModel[Person]} * \text{dFM H[Person]} , - \text{FM[Person]} / \text{MinDieTime})$$

Units: kg/Year

$$\text{dFM B[Person]} = \text{Fat Deposit Fraction fr[Person]} * \text{Indicated Weight Change dBM[Person]} * \text{IsBorn[Person]}$$

Units: kg/Year

$$\text{dFM H[Person]} = ((1 - \text{EnergyPFunction[Person]}) * (\text{EnergyIntake EI[Person]} - \text{EnergyExpenditure[Person]})) / \text{RhoF}$$

Units: kg/Year

$$\text{dFMM[Person]} = \text{Max} ((1 - \text{SWModel[Person]}) * \text{dFFM B[Person]} + \text{SWModel[Person]} * \text{dFFM H[Person]} , - \text{FFM[Person]} / \text{MinDieTime})$$

Units: kg/Year

$$\text{Diet Induced EE DIEE[Person]} = \text{EnergyIntake EI[Person]} * \text{Thermic Effect of Food}$$

Units: kcal/Year

$$\text{dIfactor[Person]} = \text{beta} * \text{DEnergyIntake[Person]}$$

Units: kcal/Year

$$\text{EIRandomFactorGenerator[People]} = \text{RANDOM NORMAL} (-10, 10, 0, \text{EIVarFactor} , \text{NoiseSeed}) + 1$$

Units: Dmnl

$$\text{Energy Deposition Coefficient in Tissue[Person]} = (\text{Fat Deposit Fraction fr[Person]} * \text{Fat Energy Content cf} + (1 - \text{Fat Deposit Fraction fr[Person]}) * \text{Lean Energy Content cff})$$

Units: kcal/kg

$$\text{Energy Expenditure Minus CE[Person]} = \text{Basal Methabolic Rate BMR[Person]} * \text{Physical Activity PAL[Person]} + \text{Diet Induced EE DIEE[Person]}$$

Units: kcal/Year

EnergyExpenditure[Person] = KConstant[Person] / (1 + IFactor[Person]) + EnergyExpenditure without K[Person]
Units: kcal/Year

EnergyExpenditure without K[Person] = (FFMfactor[Person] + FMfactor[Person] + BWfactor[Person] +
dIfactor[Person] + Iterm[Person]) / (1 + IFactor[Person])
Units: kcal/Year

EnergyIntake EI[Person] = Min (MaxEI , (Max (ExpectedEI[Person] / 5, ExpectedEI[Person] +
PersonalEnergyIntakeFactor[Person]) * ePredict[Person]) * 365)
Units: kcal/Year

EnergyPFunction[Person] = CConstant[Person] / (CConstant[Person] + FM[Person])
Units: Dmnl

Fat Deposit Fraction fr[Person] = fr Table boy (Age[Person]) * (1 - IndSex[Person]) + IndSex[Person] * fr Table
girl (Age[Person])
Units: Dmnl

FFM[Person] = INTEG(dFMM[Person] , Initial FFM[Person])
Units: kg

FFMfactor[Person] = FFM[Person] * GammaL
Units: kcal/Year

FM[Person] = INTEG(dFM[Person] , Initial FM[Person])
Units: kg

FMfactor[Person] = FM[Person] * GammaF
Units: kcal/Year

fr Table boy ([(0,0)-(20,1)],(8,0.45),(11,0.26),(12.5,0.06),(14,0.35),(17,0.47),(20,0.67))
Units: Dmnl

fr Table girl ([(0,0)-(20,1)],(8,0.42),(11,0.41),(12.5,0.5),(14,0.58),(17,0.67),(20,0.76))
Units: Dmnl

FracFM[Person] = FM[Person] / BW[Person]
Units: Dmnl

IFactor[Person] = EtaF * (1 - EnergyPFunction[Person]) / RhoF + EtaL * EnergyPFunction[Person] / RhoL
Units: Dmnl

IndEthn[Ethnicity,Person] = INITIAL(If then else (Ethnicity Code[Person] = Ethnicity, 1, 0))
Units: **undefined**

Indicated Weight Change dBM[Person] = (EnergyIntake EI[Person] - Energy Expenditure Minus CE[Person]) / (2
* Total Energy Coefficient for Tissue Deposition c[Person] - Energy Deposition Coefficient in Tissue[Person])
Units: kg/Year

indiv factor[Person] = INITIAL(sum (Indiv Sex[Person,Sex!] * Female Indiv Factor[Sex!]) + sum (
EthIndivFac[Ethnicity!] * IndEthn[Ethnicity!,Person]) * RANDOM NORMAL (0, 2, 1, IndivSTDev, NoiseSeed))
Units: Dmnl

Indiv Sex[Person,Sex] = INITIAL(If then else (IndSex[Person] = Sex - 1, 1, 0))
Units: **undefined**

PAFac[Person] = deltaPA[Person] / 365
Units: kcal/day

PersonalEnergyIntakeFactor[People] = INTEG((((wNew * EIRandomFactorGenerator[People] + (1 - wNew) *
PersonalEnergyIntakeFactor[People]) / sqrt (wNew ^ 2 + (1 - wNew) ^ 2)) - PersonalEnergyIntakeFactor[People]
)/ TIME STEP , EIRandomFactorGenerator[People])
Units: Dmnl

Physical Activity PAL[Person] = ChildhoodFactor + IndivFactor[Person] + deltaPA[Person] * BW[Person] / Basal
Methabolic Rate BMR[Person]
Units: Dmnl

StdBWInit = 0.1
Units: Dmnl

SWModel[Person] = If then else (Age[Person] < SwitchAge , 0, 1)
Units: Dmnl

SWTablefr = 0
Units: Dmnl

SWTablekff = 0
Units: Dmnl

TIME STEP = 0.125
Units: Year

Total Energy Coefficient for Tissue Deposition c[Person] = (Fat Deposit Fraction fr[Person] * Fat Energy Content
cf / efficiency in conversion of energy to FM ef+ (1 - Fat Deposit Fraction fr[Person]) * Lean Energy Content cff/
efficiency in conversion of energy to FFM eff)
Units: kcal/kg

Total Energy Expenditure TEE[Person] = Energy Expenditure Minus CE[Person] + Conversion Energy CE[Person]
Units: kcal/Year

wNew = INITIAL(TIME STEP / EIRankHalfLife)
Units: Dmnl

References

- Abdel-Hamid, T. K. (2002). "Modeling the dynamics of human energy regulation and its implications for obesity treatment." System Dynamics Review **18**(4): 431-471.
- Asbeck, I., M. Mast, et al. (2002). "Severe underreporting of energy intake in normal weight subjects: use of an appropriate standard and relation to restrained eating." Public Health Nutr **5**(5): 683-690.
- Astrup, A., G. Thorbek, et al. (1990). "Prediction of 24-h energy expenditure and its components from physical characteristics and body composition in normal-weight humans." The American Journal Of Clinical Nutrition **52**(5): 777-783.
- Behrens, D. A., J. P. Caulkins, et al. (1999). "A dynamic model of drug initiation: implications for treatment and drug control." Mathematical Biosciences **159**(1): 1-20.
- Behrens, D. A., M. S. Rauner, et al. (2008). "Modelling the spread of hepatitis C via commercial tattoo parlours: implications for public health interventions." Or Spectrum **30**(2): 269-288.
- Bernstein, R., J. Thornton, et al. (1983). "Prediction of the resting metabolic rate in obese patients." The American Journal Of Clinical Nutrition **37**(4): 595-602.
- Bitar, A., N. Fellmann, et al. (1999). "Variations and determinants of energy expenditure as measured by whole-body indirect calorimetry during puberty and adolescence." The American Journal Of Clinical Nutrition **69**(6): 1209-1216.
- Bray, G. A. and C. Bouchard (2004). Handbook of obesity : etiology and pathophysiology. New York, Marcel Dekker.
- Butte, N. F., E. Christiansen, et al. (2007). "Energy Imbalance Underlying the Development of Childhood Obesity." Obesity **15**(12): 3056-3066.
- Caulkins, J. P., G. Crawford, et al. (1993). "Simulation of Adaptive Response - a Model of Drug Interdiction." Mathematical and Computer Modelling **17**(2): 37-52.
- Chow, C. C. and K. D. Hall (2008). "The Dynamics of Human Body Weight Change." PLoS Computational Biology **4**(3): e1000045.
- Christiansen, E. and L. Garby (2002). "Prediction of body weight changes caused by changes in energy balance." European Journal of Clinical Investigation **32**(11): 826-830.
- Christiansen, E., L. Garby, et al. (2005). "Quantitative analysis of the energy requirements for development of obesity." Journal of Theoretical Biology **234**(1): 99-106.
- Cunningham, J. (1991). "Body composition as a determinant of energy expenditure: a synthetic review and a proposed general prediction equation." The American Journal Of Clinical Nutrition **54**(6): 963-969.
- Cunningham, J. J. (1980). "A reanalysis of the factors influencing basal metabolic rate in normal adults." The American Journal Of Clinical Nutrition **33**(11): 2372-2374.
- Duffie, D. and K. J. Singleton (1993). "Simulated Moments Estimation of Markov Models of Asset Prices." Econometrica **61**(4): 929-952.
- Eubank, S., H. Guclu, et al. (2004). "Modelling disease outbreaks in realistic urban social networks." Nature **429**(6988): 180-184.
- Ferguson, N. M., D. A. T. Cummings, et al. (2006). "Strategies for mitigating an influenza pandemic." Nature **442**(7101): 448-452.
- Flatt, J.-P. (2004). "Carbohydrate-Fat Interactions and Obesity Examined by a Two-Compartment Computer Model." Obesity **12**(12): 2013-2022.

- Forbes, G. B. (2000). "Body fat content influences the body composition response to nutrition and exercise." Ann N Y Acad Sci **904**: 359-365.
- Fox, M. K., A. Gordon, et al. (2009). "Availability and Consumption of Competitive Foods in US Public Schools." Journal of the American Dietetic Association **109**(2, Supplement 1): S57-S66.
- Frankenfield, D., L. Roth-Yousey, et al. (2005). "Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: a systematic review." Journal of the American Dietetic Association **105**(5): 775-789.
- Hall, K. D. (2006). "Computational model of in vivo human energy metabolism during semistarvation and refeeding." American Journal Of Physiology. Endocrinology And Metabolism **291**(1): E23-E37.
- Hall, K. D. (2010). "Mechanisms of metabolic fuel selection: modeling human metabolism and body-weight change." IEEE Engineering In Medicine And Biology Magazine **29**(1): 36-41.
- Hall, K. D. (2010). "Predicting metabolic adaptation, body weight change, and energy intake in humans." American Journal Of Physiology. Endocrinology And Metabolism **298**(3): E449-E466.
- Harris, J. and F. Benedict (1919). A biometric Study of basal metabolism in man. Washington, DC., Carnegie Institution.
- Homer, J., G. Hirsch, et al. (2007). "Chronic illness in a complex health economy: the perils and promises of downstream and upstream reforms." System Dynamics Review **23**(2-3): 313-343.
- Homer, J., G. Hirsch, et al. (2004). "Models for collaboration: how system dynamics helped a community organize cost-effective care for chronic illness." System Dynamics Review **20**(3): 199-222.
- Homer, J., B. Milstein, et al. (2008). "Modeling the Local Dynamics of Cardiovascular Health: Risk Factors, Context, and Capacity." Preventing Chronic Disease **5**(2).
- Homer, J. B. (1993). "A System Dynamics Model for Cocaine Prevalence Estimation and Trend Projection." Journal of Drug Issues **23**(2): 251-279.
- Huang, T. T., A. Drewnosksi, et al. (2009). "A systems-oriented multilevel framework for addressing obesity in the 21st century." Preventing Chronic Disease **6**(3): 1-10.
- Jequier, E. and L. Tappy (1999). "Regulation of body weight in humans." Physiol Rev **79**(2): 451-480.
- Jones, A. P., J. B. Homer, et al. (2006). "Understanding diabetes population dynamics through simulation modeling and experimentation." American Journal of Public Health **96**(3): 488-494.
- Kaplan, E. H., D. L. Craft, et al. (2002). "Emergency response to a smallpox attack: The case for mass vaccination." Proceedings of the National Academy of Sciences **99**(16): 10935-10940.
- Kaplan, E. H., D. L. Craft, et al. (2002). "Emergency response to a smallpox attack: The case for mass vaccination." Proceedings of the National Academy of Sciences of the United States of America **99**(16): 10935-10940.
- Keeling, M. J., M. E. J. Woolhouse, et al. (2003). "Modelling vaccination strategies against foot-and-mouth disease." Nature **421**(6919): 136-142.
- Kozusko, F. (2001). "Body weight setpoint, metabolic adaption and human starvation." Bulletin of Mathematical Biology **63**(2): 393-403.

- Kozusko, F. P. (2002). "The effects of body composition on setpoint based weight loss." Mathematical and Computer Modelling **35**(9-10): 973-982.
- Lee, B. S. and B. Ingram (1991). "Simulation Estimation of Time-Series Models." Journal of econometrics **47**(2-3): 197-205.
- Levy, D. T., A. Hyland, et al. (2007). "The role of public policies in reducing smoking prevalence in California: Results from the California Tobacco Policy Simulation Model." Health Policy **82**(2): 167-185.
- Maffeis, C., Y. Schutz, et al. (1993). "Resting metabolic rate in six- to ten-year-old obese and nonobese children." The Journal Of Pediatrics **122**(4): 556-562.
- McFadden, D. (1989). "A Method of Simulated Moments for Estimation of Discrete Response Models without Numerical-Integration." Econometrica **57**(5): 995-1026.
- Ogden, C. L., M. D. Carroll, et al. (2006). "Prevalence of overweight and obesity in the United States, 1999-2004." JAMA: The Journal Of The American Medical Association **295**(13): 1549-1555.
- Pikholz, C., B. Swinburn, et al. (2004). "Under-reporting of energy intake in the 1997 National Nutrition Survey." N Z Med J **117**(1202): U1079.
- Poehlman, E. T. (1992). "Energy expenditure and requirements in aging humans." The Journal of nutrition **122**(11): 2057-2065.
- Pomerleau, J., T. Ostbye, et al. (1999). "Potential underreporting of energy intake in the Ontario Health Survey and its relationship with nutrient and food intakes." European Journal of Epidemiology **15**(6): 553-557.
- Poslusna, K., J. Ruprich, et al. (2009). "Misreporting of energy and micronutrient intake estimated by food records and 24 hour recalls, control and adjustment methods in practice." British Journal of Nutrition **101**: S73-S85.
- Pryer, J. A., M. Vrijheid, et al. (1997). "Who are the 'low energy reporters' in the dietary and nutritional survey of British adults?" Int J Epidemiol **26**(1): 146-154.
- Rosenbaum, M., J. Hirsch, et al. (2008). "Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight." Am J Clin Nutr **88**(4): 906-912.
- Rosenbaum, M., R. L. Leibel, et al. (1997). N Engl J Med **337**(6): 396-407.
- Schofield, W. N. (1985). "Predicting basal metabolic rate, new standards and review of previous work." Human nutrition. Clinical nutrition **39 Suppl 1**: 5-41.
- Song, B. and D. M. Thomas (2007). "Dynamics of starvation in humans." Journal Of Mathematical Biology **54**(1): 27-43.
- Speakman, J. R. and K. R. Westerterp (2010). "Associations between energy demands, physical activity, and body composition in adult humans between 18 and 96 y of age." The American Journal Of Clinical Nutrition **92**(4): 826-834.
- Sterman, J. D. (2006). "Learning from evidence in a complex world." Am J Public Health **96**(3): 505-514.
- Tershakovec, A. M., K. M. Kuppler, et al. (2002). "Age, sex, ethnicity, body composition, and resting energy expenditure of obese African American and white children and adolescents." The American Journal Of Clinical Nutrition **75**(5): 867-871.
- Thomas, D. M., A. Ciesla, et al. (2009). "A mathematical model of weight change with adaptation." Mathematical biosciences and engineering : MBE **6**(4): 873-887.
- Thompson, K. M. and R. J. D. Tebbens (2007). "Eradication versus control for poliomyelitis: an economic analysis." Lancet **369**(9570): 1363-1371.

- Vaughan, L., F. Zurlo, et al. (1991). "Aging and energy expenditure." The American Journal Of Clinical Nutrition **53**(4): 821-825.
- Wang, Y., M. A. Beydoun, et al. (2008). "Will all Americans become overweight or obese? estimating the progression and cost of the US obesity epidemic." Obesity (Silver Spring, Md.) **16**(10): 2323-2330.