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Predicting Adult Weight Change in the Real World: A Systematic Review and Meta-analysis Accounting for Compensatory Changes in Energy Intake or Expenditure

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Abstract

Background—Public health and clinical interventions for obesity in free-living adults may be diminished by individual compensation for the intervention. Approaches to predict weight outcomes do not account for all mechanisms of compensation, so they are not well suited to predict outcomes in free-living adults. Our objective was to quantify the range of compensation in energy intake or expenditure observed in human randomized controlled trials (RCTs).

Methods—We searched multiple databases (PubMed, CINAHL, SCOPUS, Cochrane, ProQuest, PsycInfo) up to August 1, 2012 for RCTs evaluating the effect dietary and/or physical activity interventions on body weight/composition. Inclusion Criteria: subjects per treatment arm ≥ 5; ≥1 week intervention; a reported outcome of body weight /body composition; the intervention was either a prescribed amount of over- or underfeeding and/or supervised or monitored physical activity was prescribed; ≥ 80% compliance; an objective method was used to verify compliance with the intervention (e.g., observation, electronic monitoring). Data were independently extracted

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Authors' contributions: EJD, KAK and DBA conceived the study and developed the design and selection criteria. KAK performed the literature searches. KAK and EJD reviewed the literature, selected studies, extracted data, evaluated risk of bias and wrote significant portions of the manuscript. ASA assisted with literature selection, data extraction and summary calculations. JAD and KDK performed the statistical analysis and wrote some portions of the manuscript. DBA directed the statistical analysis and wrote some portions of the manuscript.

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and analyzed by multiple reviewers with consensus reached by discussion. We compared observed weight change to predicted weight change using two models that predict weight change accounting only for metabolic compensation.

Findings—Twenty-eight studies met inclusion criteria. Overfeeding studies indicate 96% less weight gain than expected if no compensation occurred. Dietary restriction and exercise studies may result in up to 12–44% and 55–64% less weight loss than expected, respectively, under an assumption of no behavioral compensation.

Interpretation—Compensation is substantial even in high-compliance conditions, resulting in far less weight change than would be expected. The simple algorithm we report allows for more realistic predictions of intervention effects in free-living populations by accounting for the significant compensation that occurs.

Keywords

obesity; weight loss; weight gain; meta-analysis; energy balance

Introduction

Obesity is a serious and prevalent public health concern (1). New public health and clinical interventions to reduce obesity are frequently advocated or implemented based on hypothetical estimates of an outcome that may have little empirical support (e.g., the 3500 kcal rule). For example, imagine an initiative from a large company that replaces its 250 kcal candy bars in its vending machines with 50 kcal protein bars in order to reduce energy intake (EI) from snacking among its employees. This initiative can be expected to produce (in those who consume at least 250 kcal per day from such snacks), on average, 5.7 kg of weight loss after one year (e.g., for a 35 year old man who is 183 cm tall and weighs 100 kg at baseline, body mass index = 30). This estimate is based on one of the mathematically validated prediction models (2) sometimes used to justify such interventions.(3) But is this estimate realistic?

Based on the evidence, this estimate is likely optimistic because current models for predicting weight change are not well-suited for use in free-living subjects. A common rule of thumb used for decades to predict weight change outcomes is that losing or gaining one pound of fat requires a deficit of 3,500 kcals of energy (4). This rule does not consider that human energy balance is a dynamic and adaptable system, or that lean and fat mass is lost during negative energy balance, and this leads to an underestimation of the change in EI or energy expenditure (EE) needed to produce weight change.(5–8) Recently, more sophisticated models have been developed to predict weight changes which consider the metabolic adaptations that occur during weight change.(9–12) To accurately predict weight change in free-living individuals, however, *both* 1) metabolic, and 2) behavioral compensatory mechanisms must be accounted for.

Specifically, we define the modes of possible compensation as follows:

- **Metabolic compensation:** Compensation for an energy balance intervention through physiological changes in metabolism. For example, current mathematical

models account for changes in resting metabolic rate, fluid balance, the thermic effect of food, and spontaneous physical activity resulting from an energy balance intervention.(11–13)

- **Behavioral compensation:** Compensation for an energy balance intervention through behavior changes. For example, when a dietary or physical activity intervention attempts to create negative energy balance, an individual may respond by reducing voluntary EE and/or increasing EI if these avenues are not strictly controlled. Similarly, during an energy balance intervention of added energy, voluntary EE may increase and/or EI may decrease from other sources.

Others have shown that behavioral compensation occurs for physical activity interventions (14). Behavioral compensation may also occur for interventions that reduce caloric intake or add calorie-containing foods to the diet. (15, 16) Current prediction models are intended for use where interventions are implemented with high fidelity (i.e., intended intervention exposure was achieved) in isolation, and when metabolic compensation is the only route of compensation for the intervention possible. During interventions in free-living subjects, however, compensation can occur through metabolic compensation *and* through behavioral compensation. Behavioral compensation may diminish the effects of an intervention, making it important to quantify and account for it when predicting outcomes in free-living populations. It is imperative that more realistic models be used for predicting outcomes, for the reasons stated recently:

> "*…to establish a less controversial legacy for this important field, we should avoid past traps and be explicit about reasonable expectations. Implausible results that are "too good to be true" still threaten nutritional research on many fronts, including survey measurements, observational associations, treatment effects in randomized trials, and estimates of the impact on populations*."(17)

We therefore set out to build an empirically-based model to predict weight change outcomes in free-living subjects, and to quantify the extent to which observed weight change in free-living subjects differs from that predicted under the assumption of no behavioral compensation. The approach we took was to use systematic review techniques to collect study data and conduct meta-regression on studies meeting *a priori* inclusion criteria. These criteria guided identification of high fidelity interventions implemented in free-living adults. The subjects had some ability to behaviorally compensate for the intervention, yet the reported information about the intervention and compliance verification allowed for a high degree of confidence in treatment fidelity. For our main analysis, we compared the predictions from models which assume no active compensation (2, 18) to observed outcomes as an estimate of the effects of behavioral compensation.

Methods

Systematic Review of the Literature and Study Selection

Articles, abstracts and doctoral dissertations were retrieved using searches performed on the following electronic databases: PubMed, Cochrane Library, SCOPUS, PsycInfo, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Dissertation Abstracts. We

searched PubMed without MeSH headings to identify publications for inclusion, using the following limits: date August 1, 2012 back to earliest records of human studies. Detailed search methods are provided on the PROSPERO registry website (Registry #CRD42013002912). No ethics committee approval was required since the data used are published summary statistics.

All studies were evaluated according to the following inclusion criteria: 1) the data were from adult human RCTs in free-living subjects, 2) the intervention was either a prescribed amount of over- or underfeeding given and reported (or could be converted) in kcal and/or supervised or monitored physical activity was prescribed and verified, 3) an objective verification method was used to verify the intervention at ≥ 80% (e.g., observation, electronic monitoring, provision of food with returned unused portions), 4) the study had a total sample size of at least 5 participants at enrollment, 5) the study protocol included an intervention period of at least 7 days, 6) the publication was available in the English language, and 7) the study was published and listed in the above databases on or before August 1, 2012.

Our exclusion criteria are detailed in the online supplementary material. Briefly, we excluded studies on samples that were completely or predominantly made up of individuals younger than 18 years old or older than 60 years, or having any health conditions that may affect weight. The filtering process of the initial search results is detailed in Figure 1 and also described in more detail in the online supplement.

Statistical Analysis

Quantifying the effect of behavioral compensation– comparison to metabolic compensation models—We entered sample demographic and intervention data into each of the metabolic compensation model calculators to most closely represent each intervention as described in the published papers to estimate weight changes that would occur if only metabolic compensation occurred. Since we included data that had samples of both men and women where separate baseline data and results were not reported (only combined summaries), we entered the data for both genders and mathematically adjusted the outputs for the relative proportions of men and women. For the NIDDK simulator (2), we assumed a baseline value (when not otherwise reported) of sedentary activity level (1.4 METs). The difference between the observed weight change for each study and the weight change predicted by these models is indicative of the degree of *behavioral* compensation that is observed for the interventions in free-living adults included in our review and meta-analysis.

All model data were analyzed with R routines (19) and descriptive summaries were generated with Microsoft® Excel version 2010. Further details of statistical approaches used for the predictive model building are on the online supplement. Risk of bias was assessed by two authors (EJD and KAK) independently and discrepancies were discussed until consensus was reached.

Role of Funding Source

The funding agency (International Life Science Institute – North America) had no role in the design, conduct, analysis, manuscript preparation or decision to publish the results of this study.

Results

Results of Publication Search

We retrieved citations dated back to 1935, but more than two thirds of the initial publications retrieved were published after 2001. The final dataset for building the predictive model consisted of 28 studies published between 1987 and 2012 including 15 exercise studies, 9 studies with added energy, 3 dietary restriction studies, and 2 studies that included both dietary restriction and exercise in the intervention (see Table 1 for a complete listing of included studies with select summary data and intervention descriptions). The primary reasons for exclusion after full text review were studies not being truly randomized or not having a control group, followed by reliance only on self-report for EI or physical activity without any objective verification of compliance. Studies were all published journal articles except for two dissertations.(20, 21) Eleven studies had samples that were either 100% men or 100% women. Three other studies reported results by gender separately if both males and females were included in the sample. Only six studies (21%) reported the racial makeup of the samples; therefore, this factor was excluded from further analysis. Mean ages of the samples ranged from 20.6 years to 60 years. Mean baseline body mass index (BMI) of the samples ranged from 22.6 to 35.1 kg/m^2.

Building a Predictive Model

We expected to find enough studies to build a robust regression model, incorporating mean participant characteristics and evaluating any significant interactions. However, the relatively low number and sparsely distributed data prevented reliable estimates from our final model. Details of the model and its estimations can be found in the online supplement, Figure S1 and Table S2.

Comparison to Metabolic Compensation Models – Estimating Behavioral Compensation

To address our main research question (What is the effect of behavioral compensation that occurs in free-living subjects who receive an energy balance intervention on weight outcomes?),we generated output for each study using the NIDDK and Pennington weight change prediction calculators (2, 18) to estimate weight changes that would occur if only metabolic compensation occurred. The difference between the observed weight loss for each study and the weight change predicted by these models is indicative of behavioral compensation occurring during the intervention. The NIDDK and Pennington models are highly correlated (Pearson's $r = 0.98$, $p < .0001$) in predicted weight change (Figure S2). In general, the Pennington calculator is slightly more conservative than the predictions made by the NIDDK calculator.

The overall degree of behavioral compensation estimated by the gap between the observed and metabolic compensation-only predicted values is illustrated in Figure S3, panels A & B.

Both slopes being less than 1 (i.e., 0.344 and 0.399 for the NIDDK and Pennington Models, respectively) indicates that the observed weight change is less than predicted after accounting for metabolic compensation. This quantifies the degree of behavioral compensation that is occurring (i.e., the compensation that is in addition to the metabolic compensation, resulting in less weight change than expected).

The degree of behavioral compensation appears to differ depending on intervention type. As shown in Figure S3, Panels A & B, all types of interventions demonstrated less weight change than either the Pennington or NIDDK calculators predicted. The plot of overfeeding trials has a slope (95% confidence interval) of 0.06 (−0.04, 0.16) and 0.07 (−0.05, 0.18), plotted against the NIDDK and Pennington calculators, respectively (Figure 2, Panels A & B). A slope of 1 would indicate that, on average, the interventions produced exactly as much weight change as expected from the mathematical models, which assume no behavioral compensation. As such, this suggests that behavioral compensation may result in as much as 96% less weight gain than predicted by metabolic calculators when adding energy to the diet. The slopes of the plots for dietary restriction and exercise studies are more similar to each other. Specifically, slopes (95% confidence interval) of 0.56 (0.17, 0.96) and 0.88 (0.36, 1.40) were plotted against the NIDDK and Pennington calculators, respectively, for dietary restriction studies (Figure 2). For exercise intervention studies, slopes (confidence interval) of 0.38 (0.16, 0.60) and 0.46 (0.19, 0.72) were plotted against the NIDDK and Pennington calculators, respectively (Figure 3). Thus, behavioral compensation may result in up to 12–44% less weight loss than predicted for dietary restriction studies and 55–64% less weight loss than predicted for exercise intervention studies.

Risk of Bias Assessment for Included Studies

See online supplement for risk of bias summary and detailed ratings figure (Figure S4) for each included study. The greatest proportions of study aspects with high risk of bias were judged to be lack of analysis for incomplete data (attrition bias – e.g., use of intention to treat analysis, ITT) and lack of attention placebo for control groups. Four studies reported results using ITT.

Discussion

We generated simple adjustment factors to predict weight change resulting from energy balance interventions in free-living adult populations, with the ability to compensate both behaviorally and metabolically, using 73 treatment versus control arm comparisons from 28 studies. One of the notable findings was the small number of studies meeting our inclusion criteria (i.e., where compliance was objectively measured) making it difficult to study the role of behavioral compensation in a free-living context beyond a very basic level. Although our estimates are the only ones for this purpose to-date based on the currently available literature, this highlights a gap in the literature of studies designed to determine the impact of energy balance perturbations in humans in the context of a full range of compensation that prevents a more precise estimate. Since these studies are crucial to understanding the effect of public health interventions, their limited quantity underscores a need for future research in this area.

Perhaps the most robust finding from our study most relevant to public health is that currently available predictions consistently overestimate weight change, which is evidence of significantly diminished weight change resulting from behavioral compensation. This is in spite of some instances where explicit instructions were given to make no other changes in routine habits, a form of compliance that is less commonly tracked or verified. In particular, the treatment effect of added calories was only, on average, ~5% of the weight gain predicted from models assuming no behavioral compensation. Several included studies reported a mean weight loss effect from added energy. This indicates that even if a new food is introduced to the diet, for example adding a daily snack or beverage, EI and/or EE can be adjusted reasonably well, resulting in very little weight gain relative to how much would be expected if this behavioral compensation did not occur. Behavioral compensation for negative energy balance interventions such as exercise or dietary restriction is also evident from our analysis, and results in 37–45%, and 56–88% of the weight loss predicted from metabolic-only compensation models, respectively. In our initial example of reducing EI via snacks by 200 kcals per day for the hypothetical man, the adjusted estimate of weight change after one year would be closer to 3.2 kg. This is lower than the 5.7 kg estimate given by the body weight simulator that predicts metabolic compensation only.

Therefore, our results suggest that current public health interventions or clinical interventions that alter one aspect of energy balance, without holding other aspects constant, may result in more modest weight changes than predicted or desired. A similar approach has been reported in pediatric studies (3), but it did not attempt to account for both behavioral and metabolic compensation components. It is important to take all modes of compensation into consideration when planning an intervention with targeted amounts of weight change, and when anticipating its outcomes. It is likely that increased doses of energy perturbations are required. Increased control over compliance and compensation are necessary to achieve target outcomes. Estimates of what is required to achieve a specific weight change may be made more accurate for the purposes of public health recommendations if the present estimations are considered.

Our results suggest that there might be a differential effect of treatment type on the degree of behavioral compensation. However, an aspect of our dataset needs to be considered in interpreting this result. Dietary restriction interventions are associated with greater treatment effects, and less behavioral compensation, than either exercise or overfeeding interventions. However, this finding may be because the dietary restriction interventions included in our analysis only allowed for behavioral compensation through EE changes, whereas all exercise and overfeeding interventions allowed for behavioral compensation through both dietary intake and EE changes.

Our approach has strengths and limitations. First, our inclusion criteria were rigorous. All included studies have at least 80% compliance with the prescribed intervention, with compliance verified objectively (no reliance solely on self-report). In addition, the dose was corrected in our calculations for the level of compliance reported in the study. Further, included studies were RCTs, and our outcome for generating the predictive model and for comparing to metabolic compensation models was the control group adjusted weight change. Therefore, our models are built to assess true treatment effect, and are corrected for

any weight change due to factors such as regression to the mean, maturation, historical factors, behaviors that result from simply participating in a study, rather than from the treatment itself.

Several limitations should also be considered when interpreting our analysis. Weight was not always the primary outcome in studies that met our inclusion criteria. This is particularly true for those with added EI in the form of nuts. Differences in stated outcomes of interest, time with researchers and other factors may affect weight outcomes for individual studies. In addition, body composition may be an important outcome that we were not able to adequately analyze because of the limited number of studies including body composition measurements such as changes in fat mass and fat-free mass. Because of our rigorous inclusion criteria, our dataset is small (28 studies). The types of studies we selected are necessary for making definitive conclusions about the impact of perturbations in one aspect of energy balance on body weight. Studies also tended to be shorter in duration, thus it is difficult to make conclusions about long-term effects. This is a large gap in the literature, and a more systematic approach to large, well-controlled studies to answer these questions is warranted. Additionally, 16 of the 28 studies reported data only for those participants who completed the intervention period, and across all studies there was a 17.8% dropout rate (Table 1), which may have biased our estimates of weight change towards overestimation. We used the intention to treat data when reported (four studies). Eight studies reported no dropouts.

Future research is needed to understand potential differences in compensation between dietary interventions (added or reduced energy), different food forms, macronutrient compositions. Also, certain factors should be considered as potential confounders when quantifying the compensatory response to a specific intervention. For example, bioavailability of energy in food, efficiencies in physical activity and food utilization, seasonal effects, and durations of interventions may all influence both the metabolic and behavioral compensatory response to an intervention. It is also unclear if compensation would remain constant over time. Moreover, evaluating the influence of participant characteristics related to eating behavior (cognitive restraint, dis-inhibition and hunger) and compensation during interventions is needed as this may hold promise for optimizing treatment effectiveness.

To conclude, we have presented the first empirically-based, quantitative estimation for the range of behavioral compensation that may be observed for energy balance interventions. This information may assist in the estimation of weight outcomes of clinical health interventions. It may also inform public health projections for obesity interventions or public health initiatives.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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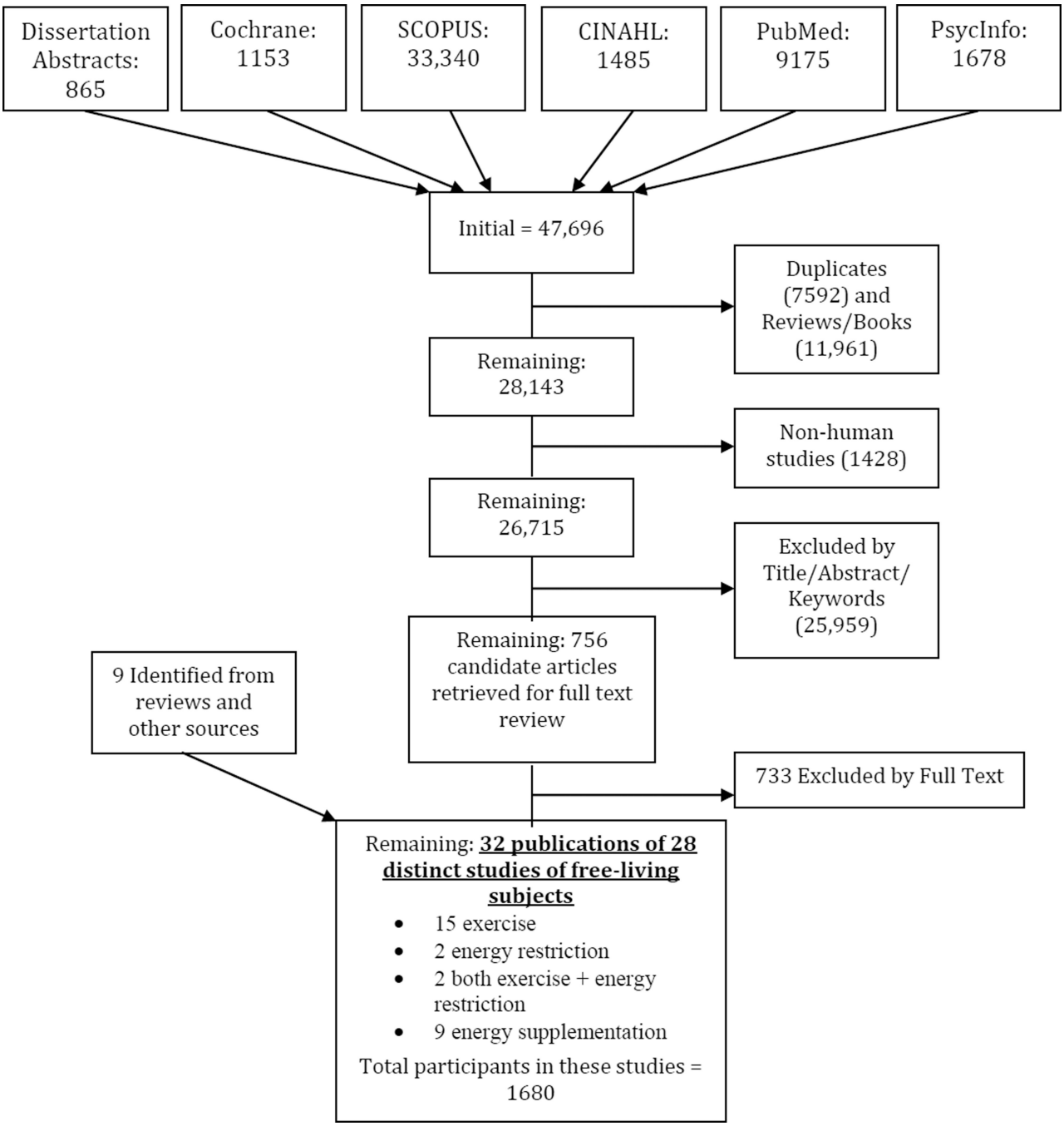

Figure 1.
PRISMA Diagram - Literature search and study selection process

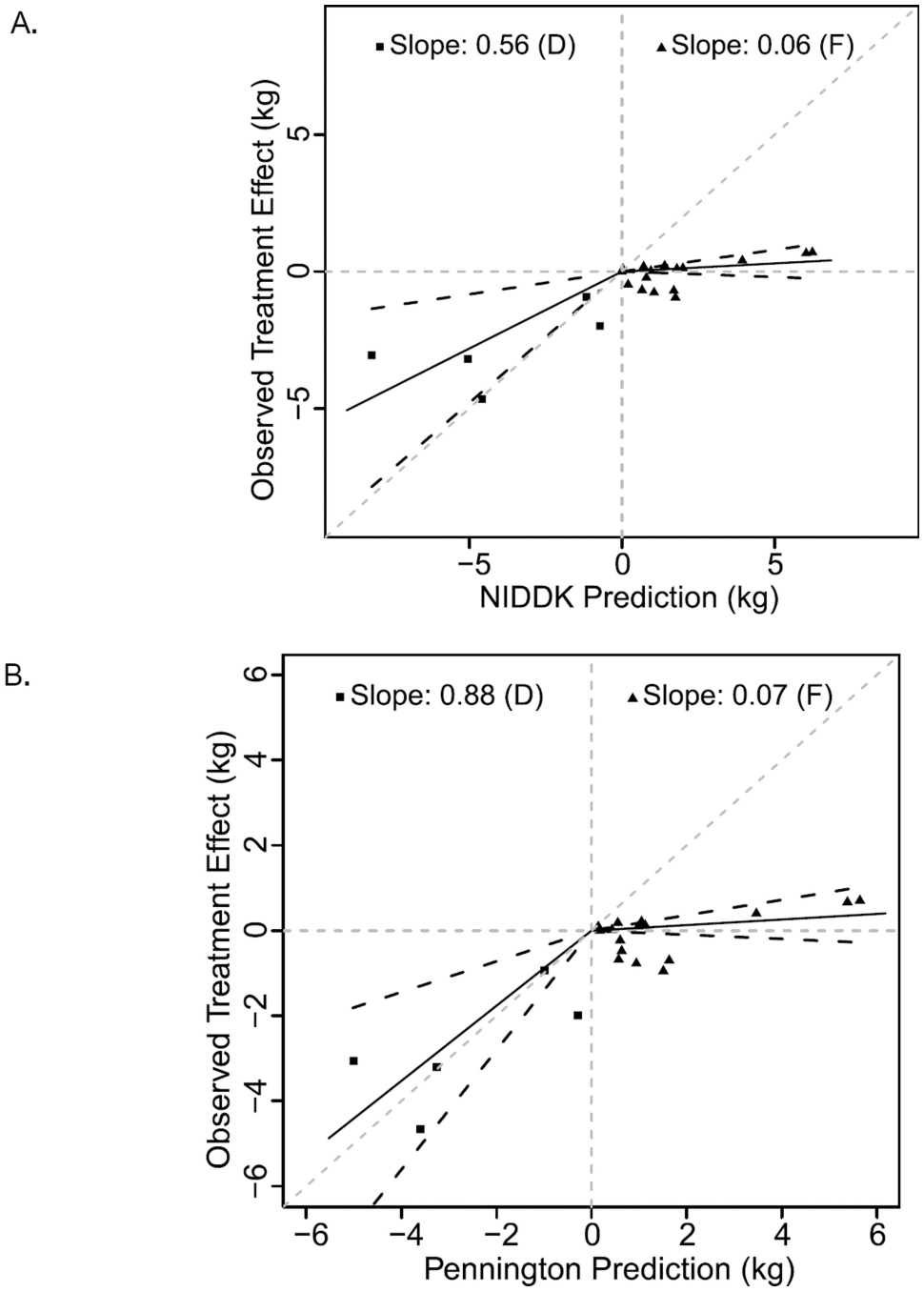

Figure 2.

NIDDK and Pennington calculator predictions for caloric restriction (D, squares) and overfeeding (F, triangles) interventions. NIDDK (A) and Pennington (B) model predictions (x-axis) versus actual observed weight changes for all studies (y-axis) Each individual point represents a control vs. treatment comparison; the solid lines are lines of best fit for slope and black dashed lines are 95% confidence intervals. Gray dashed lines are axes and lines of identity. Overall, predictions are an overestimate of observed weight change.

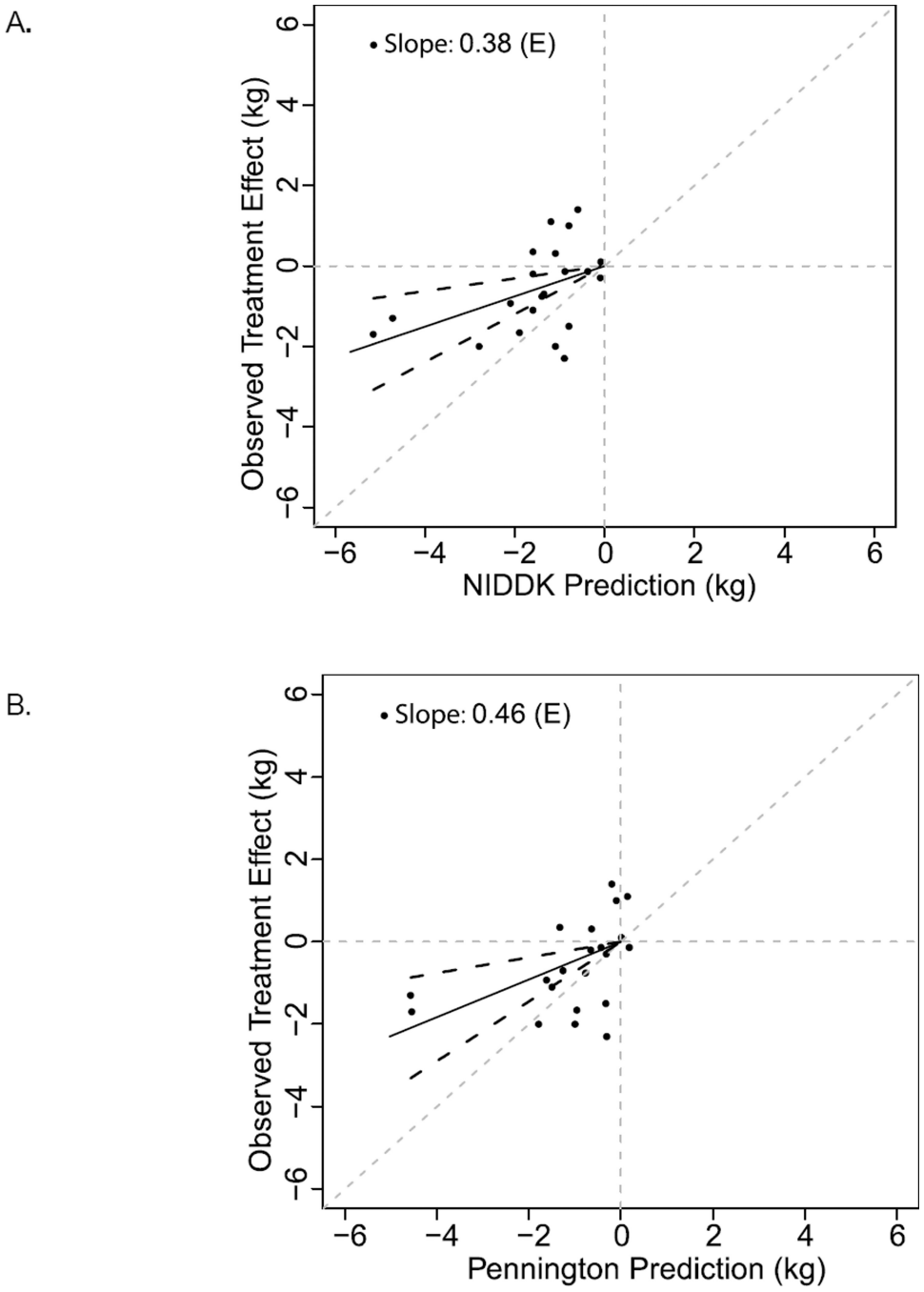

Figure 3.

NIDDK and Pennington calculator predictions for exercise interventions (E). NIDDK (A) and Pennington (B) model predictions (x-axis) versus actual observed weight changes for all studies (y-axis). Each individual point represents a treatment vs. control comparison; the solid lines are lines of best fit for slope and black dashed lines are 95% confidence intervals. Gray dashed lines are axes and lines of identity. Overall, predictions are an overestimate of observed weight change.

Table 1

Master list and summary of included studies grouped by treatment type and sorted in ascending year of publication

Reference(s)	Intervention	Sample Studied (mean age - yrs, pct female, baseline BMI kg/m^2)	Adjusted Daily Dose(s) (kcal: treatment - control)	Study Duration (weeks)	Intervention Notes	N Randomized, Completed, Analyzed	Method of Missing Data Handling	Overall Mean Compliance
Johnstone, AM, et al. 2008 (22)	Diet	38, 0%, 35.1	−167.2	4	High protein, ketogenic diet	20, 17, 17	completers	100
Das SK, et al., 2009 (23)	Diet	35, 76.3%, 27.6	−285.6	26	Caloric restriction	46, 39, 39	completers	100
Zachwieja JJ, et al., 2001 (24)	Diet and exercise	24, 45.8%, 24.1	−675	2	Caloric restriction and daily treadmill exercise	24, 24, 24	no drops	90
Moreira EA, et al., 2011 (25)	Diet and exercise (separate treatments)	49, 68, 30	−556.0, −753.3	11	25% caloric restriction (controlled feeding) vs. aerobic exercise (individualized and supervised sessions 3×/week)	36, 35, 36	ITT	99
Leon AS, et al., 1996 (26)	Exercise	32.6, 0%, 26	−245.6	12	Walking and stair climbing	22, 16, 16	completers	86
Van Etten LMLA, et al., 1997 (27)	Exercise	33.7, 0%, 23.7	−31.6	18	Weight training	26, 26, 26	completers	95
Murphy MH, et al., 1998 (28)	Exercise	44.4, 100%, 25.76	−81.6, −84.5	10	Long versus short bouts of walking	47, 34, 34	completers	86.5
Crandall KJ, 1999 (21)	Exercise	51.75, 44, 30.8	−76.7	12	Recumbent cycle ergometer	13, 13, 13	no drops	100
Shaw I & Shaw BS, 2006 (29)	Exercise	41, 92%, 32.6	−13.7	8	Resistance training	28, 28, 28	completers	91.1
Kirk EP, et al., 2007 (30)	Exercise	20.6, 0%, 28.2	−104.7	24	High-intensity resistance training	25, 19, 19	completers	96
Whybrow S, et al., 2008 (31)	Exercise	27.2, 50%, 23.6	−455.6, −513.6, −907.1	2	Progressive exercise on cycle ergometer or treadmill	12, 12, 12	no drops	100
Guadalupe-Grau A, et al., 2009 (32)	Exercise	23.7, 65.2%, 23.03	−51.7	9	Strength training and plyometric jumps	88, 72, 66	completers	85
Alves JG, et al., 2009 (33)	Exercise	38.2, 100%, 30	−106.1	26	Group exercises	156, 146, 156	ITT, BOCF	96
Turner JE, et al., 2010 (34)	Exercise	54,0%, 28	−187.3	24	Structured exercise	54, 41, 29	completers	94

Reference(s)	Intervention	Sample Studied (mean age - yrs, pct female, baseline BMI kg/m^2)	Adjusted Daily Dose(s) (kcal: treatment - control)	Study Duration (weeks)	Intervention Notes	N Randomized, Completed, Analyzed	Method of Missing Data Handling	Overall Mean Compliance
Bell GJ, et al., 2010 (35)	Exercise	49, 100%, 34.7	−399.0, −395.1	24	Pedometer based walking program	211, 128, 128	completers	84.77
Vispute SS, et al., 2011 (36)	Exercise	23.66, 41.7%, 24.6	−41.9	6	Abdominal exercises	24, 24, 24	no drops	95.71
Hornbuckle LM, et al., 2012 (37)	Exercise	28.5, 0%, 25.42	−57.7	12	Resistance training	44, 32, 44	ITT	96
Heydari M, et al., 2012 (38)	Exercise	37.7, 56.3%, 27.8	−186.4	12	High-intensity intermittent exercise	46, 38, 38	completers	100
Thompson AM, et al., 2008 (39) Church, T. S., et al., 2010 (40)	Exercise	49.7, 72.8%, 31.8	−174.8	16	Supervised aerobic exercise	162, 137, 162	ITT	91
Addington EA, 1998 (20)	Feeding	38.74, 63.8%, 32.09	2.9 (aspartame group), 142.9 (SSB group)	4	Artificially sweetened beverage (aspartame) versus Sugar Sweetened Beverage (SSB)	150, 111, 111	completers	100
Lammert, O., et al., 2000 (41)	Feeding	22.4,0%, 22.61	191	3	Overfeeding carbohydrate or fat	20, 20, 20	no drops	100
Martin A, et al., 2000 (42)	Feeding	37.7, 56.3%, 27.8	597.1	2	Low versus high calorie breakfast	10, 10, 10	no drops	100
SabateJ, et al., 2005 (43)	Feeding	42.6, 45.2%, 23.7	219	26	Walnuts	90, 90, 90	no drops	95
Whybrow S, et al., 2006 (44)	Feeding	60, 26.7%, 27.7	122.8, 227.5	8	Added fruits and vegetables	90, 62, 62	completers	92.6
Whybrow S, et al., 2007 (45)	Feeding	35.05, 50%, 25.35	343.9, 687.9	2	Added snacks	100, 87, 72	completers	96
Sheridan MJ, et al., 2007 (46)	Feeding	24.9, 0%, 28.7	314.8	4	Pistachio nuts	15, 15, 15	no drops	99
Casas-Agustench P, et al., 2011 (47)	Feeding	54.4, 56.3%, 26.5	176.9	12	Mixed nuts	52, 50, 50	completers	94
Maersk M, et al., 2012 (48)	Feeding	28, 0%, 22.2	3.1, 365.2, 385.5	26	1 liter per day of diet soda, SSB or milk versus water	60, 47, 47	completers	85

ITT = Intention to Treat analysis reported
BOCF = Baseline Observation Carried Forward