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NUTRITION

JULY 2023

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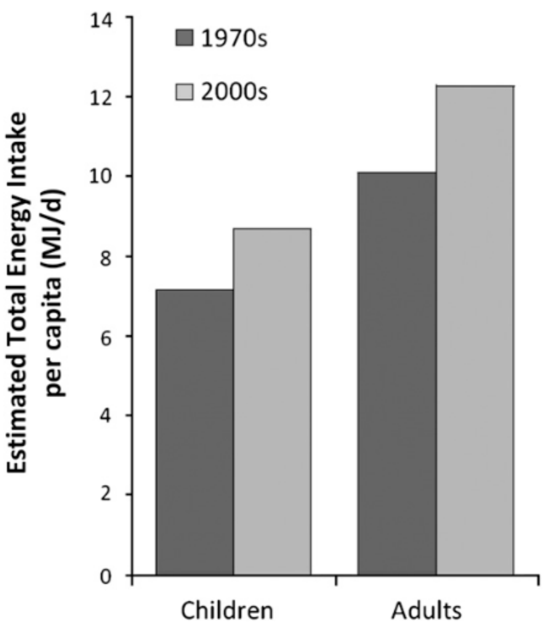
Robinson E, Khuttan M, McFarland-Lesser I, Patel Z, Jones A. Calorie reformulation: a systematic review and meta-analysis examining the effect of manipulating food energy density on daily energy intake. Int J Behav Nutr Phys Act. 2022 Apr 22;19(1):48.

What We Know, Think We Know, or Are Starting to Know

There is a scientific principle for thinking through any theory, known as parsimony: that the explanation that is simplest, or requires the least number of assumptions, is preferable. This is particularly helpful in nutrition where, depending on the grift of a grifter, explanations for the rise in obesity prevalence in the past 40-years range from dietary guidelines to seed oils to sugar.

In 2009, Boyd Swinburn *et al*. [1] modelled the changes in energy availability in the food supply, which demonstrated that greater food supply energy availability could explain the increased trajectory of population bodyweight levels. Estimated per capita energy intake, based on apportioning food supply energy availability, was ~500kcal/d higher by the 2000's in adults, and ~350kcal/d higher in children [see figure from the paper below to illustrate].



Certainly, the most parsimonious explanation for the rise of obesity prevalence is greater energy availability and intakes in the population. Yet behind those crude numbers lies a fundamental shift not only in energy availability, but in the contents and characteristics of population diets in industrialised countries [2,3].

To characterise this change in dietary composition and its potential influence on energy intake and bodyweight, the concept of energy density [i.e., the energy content divided by the weight of a food] has been a major focus of nutrition research [4,5]. For example, an individual consuming ~2,100kcal/d at an energy density of 1.8kcal per gram could decrease total energy intake without changing their total volume of food by lowering energy density [5].

This hypothetical is supported by experimental studies that manipulate energy density, which consistently demonstrate reductions in energy intake from lowering energy density [5–7]. However, there are few syntheses of the overall evidence on this question [8], and the present study was one of two meta-analyses published in the same year.

The Study

The study was a systematic review and meta-analysis of interventions that investigated the effects of different energy densities on energy intake. To be included, the primary studies were required to meet the following criteria:

- **Design**: Experimental studies using either within-person [where each participant completes all intervention and control conditions] or between-person [where participants in one group are compared to different participants in another group] designs.
- **Population**: Studies in either adults or children.
- **Intervention**: Manipulation of energy density in at least one meal in a day, up to all meals, with the lowest energy density level in a given study designated as the intervention.
- **Comparator**: The highest level of energy density was the comparator against the lowest level of energy density investigated in a given study.
- **Outcomes**: The primary outcome was total daily energy intake according to the energy density comparisons. Subgroup analyses included the number of meals in which energy density was manipulated, whether energy density differences were achieved from macronutrient manipulations or not, and number of experimental study days in the primary studies. Changes in bodyweight was also assessed.
- **Duration**: The minimum duration of a study was 1-day, with a minimum of three main meals in a day.

The outcomes were reported as standardised mean difference [SMD], a measure of effect size where 0.2, 0.5, and 0.8 were considered small, moderate, and large effect sizes, respectively. Certain outcomes were reported as differences expressed as energy [kcal]. 95% confidence intervals [CI] were also reported.

Results: The systematic review identified 31 studies, of which 27 were conducted in adults and the remainder in children. 19 studies were conducted in the U.S., 9 in Europe, and 3 in Singapore. All included studies used within-person designs. Most studies [*n* = 18] were 1-day studies, and the majority of studies [*n* = 23] manipulated a single meal or limited number of meals or foods.

14 studies manipulated energy density by altering macronutrient composition, commonly by reducing energy from dietary fat. The lowest energy density in any study was 0.11–0.13kcal/g, while the highest was 5.47kcal/g. 14 studies used participant self-reported energy intakes.

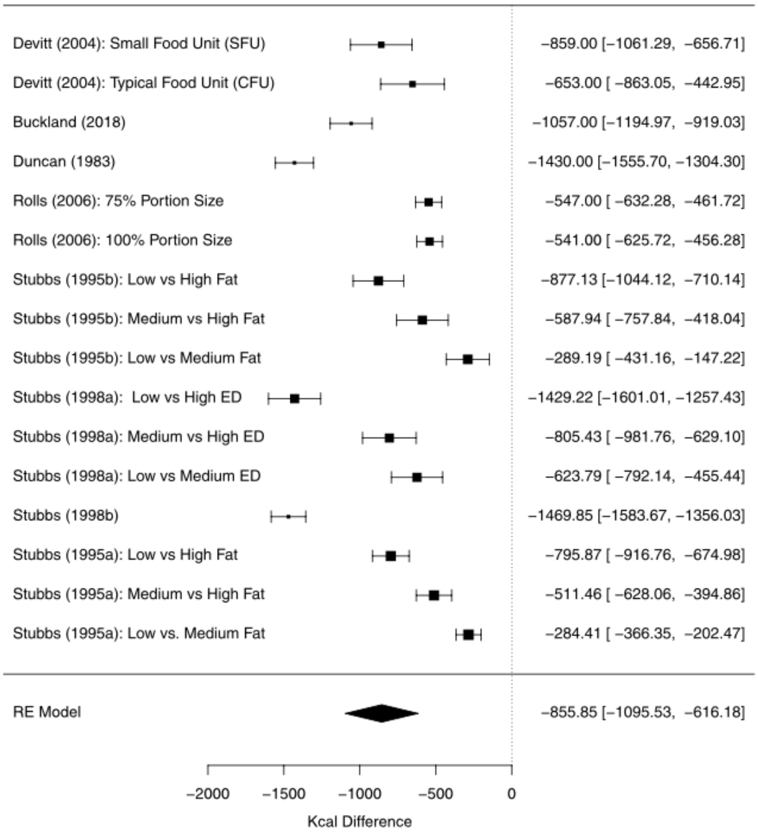
Primary Outcome – Effects of Energy Density on Energy Intake: Based on 90 different energy density comparisons from all 31 included studies, the lowest energy density was associated with significant reductions in energy intake with a large effect size [SMD 1.0, 95% CI 0.74 to 1.26]. On identification and removal of outlier data points, the overall strength of effect was attenuated but remained a large effect size [SMD 0.87, 95% CI 0.72 to 1.00].

Subgroup Analyses

Method of Manipulating Energy Density: There was no significant differences in effect sizes between studies that manipulated energy density by altering macronutrient composition [a large effect size; SMD 0.95, 95% CI 0.69 to 1.20], or studies that manipulated energy density but kept macronutrients constant [also a large effect size; SMD 0.85, 95% CI 0.64 to 1.06].

Levels of Energy Density: The highest level of energy density in any comparison was not a significant predictor of the effects of energy density on energy intake. Thus, whether the highest energy density level in a study was either ≥1.75kcal/g or ≤1.75kcal/g resulted in similar effects on energy intake compared to a lower level of energy density.

Number of Meals/Foods with Energy Density Manipulated: In studies that manipulated energy density in all meals/foods there was an average difference of 855kcal [95% CI 616 to 1095kcal] less energy intake in the lower energy density conditions. On identification and removal of outlier data points, the overall magnitude of difference was reduced but remained significantly different, with 709kcal [95% CI 602 to 815kcal] less energy intake in the lower energy density condition. The **forest plot** from the paper below illustrates this analysis, with large magnitudes of effects of lower energy density conditions on reducing total energy intake.



In studies that manipulated one meal/foods or less than all meals/foods in a day, the magnitude of effect was 237kcal [95% CI 148 to 327kcal] less energy intake in the lower energy density condition. This magnitude of effect was also reduced after identification and removal of outliers from the analysis but remained significant with 207kcal [95% CI 160 to 256kcal] less energy intake in the lower energy density condition.

Effects on Subsequent Energy Intake: In studies that used a "pre-load" type of design, where energy density was manipulated at a single meal and energy intake measured at subsequent non-manipulated meals, lower energy density meals were associated with 330kcal [95% CI 224 to 437kcal] less energy intake compared to higher energy density meals.

Effects on Bodyweight: Only five studies provided data on bodyweight as an outcome. Lower energy density conditions were associated with a 0.69kg weight loss [95% CI, -1.43 to 0.04]. As the confidence intervals crossed 0 [which is the 'null' in a continuous outcome measure like weight in kg], this was not significant, although the overall direction of effect was toward weight loss.

The Critical Breakdown

Pros: The study was preregistered with the PROSPERO register of systematic reviews, and the statistical analysis protocol was also preregistered. The literature search was expansive, including relevant databases, reference lists of identified studies, and unpublished research. The primary outcomes and secondary outcomes were clearly stated, and the analysis included several insightful subgroup analyses. The risk of bias assessment was adapted to experimental nutrition feeding studies. All included studies used within-person designs, where each participant served as their own control and thus minimises biases due to differences in appetite and energy intake between participants. The main analyses included a large number of effect size comparisons derived from the primary included studies.

Cons: This is a messy meta-analysis. The inclusion criteria were not confined to laboratory-controlled feeding studies, and ten studies did not use randomisation to allocate participants to different energy density conditions. Data on the method of manipulation is sparse, and there is no information on food volume [i.e., weight], which is a crucial aspect of energy density manipulations. Almost half of included studies used self-reported energy intake, which reduces the reliability of the effect estimates. A majority of studies were single-day experiments, thus there is limited generalisability to more habitual dietary intake. There was very high heterogeneity in almost all analyses, which indicates that the primary included studies were not combinable and not suitable for meta-analysis [discussed further under ***Key Characteristic***, below]. There was evidence of publication bias in the included studies.

Key Characteristic

As noted above as a main limitation of this study, this was a messy meta-analysis. Let's expand on this point so you grasp some additional important concepts of interpreting meta-analysis outputs. The top-line focus of the results from a meta-analysis is the summary estimate of effect, whether expressed as a relative measure or risk, the mean difference of a specific measure, or SMD as an effect size [together with the accompanying 95% CI].

However, there is more data presented in the results that require understanding, particularly statistical heterogeneity. This reflects heterogeneity, i.e., variation, in the design and methodology of the included studies. There are different statistical tests to determine the extent of heterogeneity, and the present study used the I-Squared index, which is symbolically represented as I^2. As a general rule, an I^2 test of 0–25%, 25–50%, and >75% is often considered low, moderate, and high heterogeneity, respectively.

Think of high heterogeneity as indicating that the participant samples in the included studies were so different that the observed effects have a high chance of varying from the true population effect of the intervention. This is not ideal for generalisability, and it indicates that the included studies are not suitable for meta-analysis; they are not comparing "apples with apples", so we can't assume the results mean "apples for all".

In the primary analysis, the I^2 test was 92.1%; removing outliers reduced the effect size while lowering the I^2 test to 60.6%. In the analysis limited to energy density manipulated across all meals/foods, the I^2 test was 97.4%; removing outliers also reduced the effect size while lowering the I^2 test to 85.4%.

The fact that the effect sizes were all attenuated on removal of outliers, without substantially reducing the extent of heterogeneity, means we must tread carefully in considering these findings a reliable estimate of the effects of energy density manipulations in the population.

Interesting Finding

Building on from the previous section, is there a way we could try to stress test the findings? One way we could think about the potential impact of energy density manipulations was provided by the insightful subgroup analyses where the studies were separated according to whether energy density in all meals in an experimental day were manipulated or not.

The main analysis suggested that lower energy density conditions were associated with 855kcal less energy intake; this remained a large estimate on removal of outliers, of 709kcal less energy intake. Both findings had very high heterogeneity, so we're cautious.

Interestingly, however, Kevin Hall and his group found that a low-fat diet with an energy density of 0.9kcal/g resulted in ~690kcal lower energy intake over 2-weeks compared to a low-carb diet with an energy density of 1.9kcal/g [we have covered this study in a previous Deepdive]. Hall's study was conducted in a metabolic ward with all diets controlled and participants served three meals a day, where they could eat *ad libitum*.

The other meta-analysis on this topic published the same year as the present study also found in studies where energy density was manipulated in more than one meal, the lower energy density condition was associated with a 535kcal lower energy intake [(8)]. However, the I^2 test for that analysis was 92%, drawing the same issues in interpretation as the present study.

Thus, if the "true effect" of lower energy density conditions may be as large as some of these effect estimates suggest, the variation between studies precludes us from such a conclusion.

Relevance

Where might the true effect of energy density manipulations lie? The present study may have provided a clue; the analysis indicated that longer duration studies produced smaller effects on daily energy intake. This is consistent with previous analyses suggesting energy density primarily predicts short-term, not long-term, energy intake [4,6,7].

Hall's 14-day metabolic study provides one of the longer studies that maintained strict control of study conditions, and in that study the average energy intake on the low energy density diet was relatively constant. However, that diet was also a low-fat diet, and other researchers have speculated that over the longer-term variation in energy density is merely reflective of changes in fat and carbohydrate intakes [4,6,7].

In the PREMIER trial [which used a DASH dietary intervention], weight loss at 6-months was correlated with the reduction in energy density of foods consumed, however, the strength of correlation was relatively weak [r = 0.28]. In another study that we covered in a previous Deepdive, consuming a low energy density diet [0.8kcal/g] facilitated appetite control in women with low satiety responsiveness.

Overall, the data on energy density suggests that any influence of energy density on energy intake over longer periods would require that lower energy density be sustained over time [4]. This may be a challenge, as there is evidence that short-term effects of lowering energy density on energy intake may be compensated for by larger portion sizes [4].

Application to Practice

In seeking to tie this area together, it is important to note that much of the inconsistencies in the research relate to the magnitude of effect, and to the duration of effect. The magnitude of effect of energy density *per se* on energy intake, independent of other factors, appears to be greatest in the short-term.

Over the longer-term, total energy intake is the most important factor in mediating bodyweight, however, the influence of energy density in this context appears to relate to macronutrient variations and food-based differences. For example, higher fruits and vegetable intakes are a characteristic of lower energy density diets, while higher dietary fat intakes are characteristic of higher energy density.

Lower energy density foods also may provide a higher volume of total daily food intake, which appears to be a factor in enhancing satiety on lower energy density diets. Thus, it may be that at the individual level, energy density is inherently accounted for in healthy dietary patterns that emphasise certain food-based characteristic, such as the DASH diet.

Given that high energy density foods do predict greater energy intake [as we covered in this Research Lecture], this evidence is also relevant for public health interventions that may seek to target the total energy availability of the energy dense food environment in which we find ourselves trying to navigate.

References

1. Swinburn B, Sacks G, Ravussin E. Increased food energy supply is more than sufficient to explain the US epidemic of obesity. Am J Clin Nutr. 2009 Dec;90(6):1453–6.

2. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in Diet and Lifestyle and Long-Term Weight Gain in Women and Men. New England Journal of Medicine. 2011 Jun 23;364(25):2392–404.

3. Mozaffarian D. Dietary and Policy Priorities for Cardiovascular Disease, Diabetes, and Obesity – A Comprehensive Review. Circulation. 2016;133(2):187–225.

4. de Castro JM. Dietary Energy Density Is Associated with Increased Intake in Free-Living Humans. J Nutr. 2004 Feb;134(2):335–41.

5. Rolls B. The relationship between dietary energy density and. Physiol Behav. 2014;97(5):609–15.

6. Westerterp-Plantenga M. Effects of energy density of daily food intake on long-term energy intake. Physiol Behav. 2004 Jul;81(5):765–71.

7. Westerterp-Plantenga MS. Analysis of energy density of food in relation to energy intake regulation in human subjects. British Journal of Nutrition. 2001 Mar 9;85(3):351–61.

8. Klos B, Cook J, Crepaz L, Weiland A, Zipfel S, Mack I. Impact of energy density on energy intake in children and adults: a systematic review and meta-analysis of randomized controlled trials. Eur J Nutr. 2023 Apr 2;62(3):1059–76.