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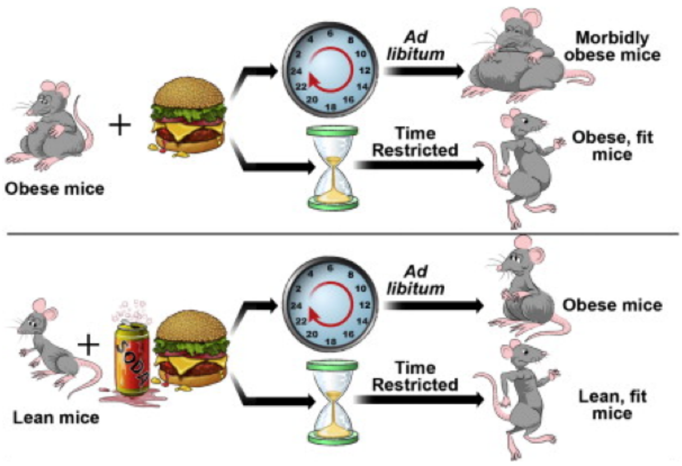
Young IE, Poobalan A, Steinbeck K, O'Connor HT, Parker HM. Distribution of energy intake across the day and weight loss: A systematic review and meta-analysis. Obes Rev. 2023 Mar;24(3):e13537.

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

The theory that timing of food intake could play a substantial role in bodyweight regulation and metabolic health has long existed in nutrition research [1–3]. However, with the distillation of science into infographics in more recent years, the hyperbole for this research area was blown up with a series of studies in mice suggesting that time-restricted eating could protect against fat gain independent of energy intake [4,5].



Compelling science in the Internet age. ***Figure*** *from* [4].

The hyperbole grew into a fever-pitch when human evidence could also be found to suggest that frontloading morning energy intake might result in significantly greater weight loss compared to the same energy intake consumed with dinner in the evening [6,7].

These lines of research with such a strong temporal aspect to their findings led to a rapid expansion of the field of 'chrono-nutrition', which broadly encompasses distribution of energy, meal frequency and regularity, duration of the eating period, and the relative importance of these factors for metabolic health and chronic disease risk [8–10].

However, disentangling the evidence in this area has presented challenges, often due to a lack of conceptual clarity, e.g., the overlap between distribution of energy and a restriction on the eating window [11,12]. There has also been a lack of clarity in the definition of outcomes, more common in the wider nutrition conversation, that if there is no difference in weight loss outcomes, there is "no difference", period.

Focusing specifically on distribution of energy intake as the exposure, there has been a relatively open question as to whether frontloading energy intake may influence weight loss as an outcome. This question was opened in 2013 when Jakubowicz et *al.* [6] compared a 700/500/200kcal breakfast/lunch/dinner to 200/500/700kcal breakfast/lunch/dinner (i.e., the inverse sequence of energy distribution), and found a 2.5-fold greater weight loss in the high-energy breakfast group after 12 weeks.

Until the present study, however, no meta-analysis of this evidence had been conducted.

The Study

The researchers conducted a systematic review and meta-analysis of studies that investigated the effects of early compared to later distribution of energy on weight loss. To be included in the analysis, studies were required to meet the following inclusion criteria:

- **Design**: Randomised or non-randomised clinical trials.
- **Population**: Adults aged over 18yrs of age with any baseline Body Mass Index [BMI].
- **Intervention**: A specified distribution of energy across the day with a proportion distributed earlier [i.e., breakfast or lunch] in the day.
- **Comparator**: A comparator group with a contrasting distribution of energy to the intervention.
- **Outcome**: Bodyweight loss was the primary outcome, with metabolic outcomes secondary.
- **Duration**: Not specified.

Subgroup analyses were also conducted to determine whether study duration [<12-weeks or ≥12-weeks] or sex of participants influenced the outcomes.

The outcomes were reported as mean difference [which is expressed in the unit of measurement, i.e., kg], together with 95% confidence intervals [CI].

Results: 9 trials were included in the meta-analysis, all of which were randomised controlled trials in design. The total number of participants across all trials was 485; *n* = 244 for early energy distribution and *n* = 241 for later energy distribution. Individual study sample sizes ranged from *n* = 9 to *n* = 193 participants. One trial was conducted in a laboratory setting, while the remainder were all free-living interventions. All studies used energy-restricted diets. The duration of the studies ranged from 5-weeks to 12-weeks.

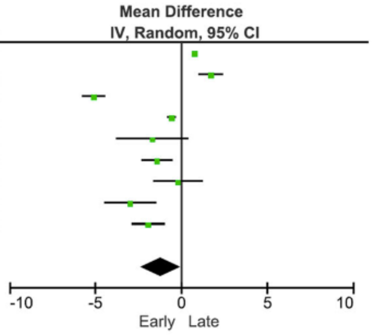
Distribution of Energy in Included Trials: For the early distribution patterns, the average distribution of total daily energy intake was 34% at breakfast, 38% at lunch, and 20% at dinner. For the later distribution patterns, the average distribution of total daily energy intake was 19% at breakfast, 30% at lunch, and 40% at dinner.

Primary Outcome – Bodyweight: Comparing early to later distribution of energy, the meta-analysis of all included studies showed that early energy distribution resulted in 1.23kg [95% CI 0.06 to 2.40kg] greater weight loss compared to later energy distribution [see **forest plot**, below].

On removal of a study [Madjd et al., 2016] that compared two different timings of dinner, rather than a true early vs. later energy comparison, the overall summary effect was no longer significant, with an average weight loss of 1.14kg and [95% CI range from 2.38kg weight loss to 0.11kg weight gain].

	Early			Late				Mean Difference	
Study or Subgroup	Mean [kg]	SD [kg]	Total	Mean [kg]	SD [kg]	Total	Weight	IV, Random, 95% CI	Year
Keim 1997	-2.91	0.08	4	-3.69	0.15	6	12.2%	0.78 [0.64, 0.92]	1997
Jakubowicz 2012	-13.6	2.3	74	-15.3	1.9	70	11.7%	1.70 [1.01, 2.39]	2012
Jakubowicz 2013	-8.7	1.4	38	-3.6	1.5	36	11.8%	-5.10 [-5.76, -4.44]	2013
Rabinovitz 2014	-2.43	0.46	23	-1.86	0.4	23	12.2%	-0.57 [-0.82, -0.32]	2014
Lombardo 2014	-8.2	3	18	-6.5	3.4	18	8.8%	-1.70 [-3.79, 0.39]	2014
Madjd 2016	-5.73	1.91	35	-4.31	1.93	34	11.4%	-1.42 [-2.33, -0.51]	2016
Versteeg 2017	-7	1.4	12	-6.8	2	11	10.4%	-0.20 [-1.62, 1.22]	2017
Raynor 2018	-7.55	1.008	4	-4.58	1.144	4	10.2%	-2.97 [-4.46, -1.48]	2018
Madjd 2020	-6.74	1.92	36	-4.81	2.22	39	11.3%	-1.93 [-2.87, -0.99]	2020
Total (95% CI)			**244**			**241**	**100.0%**	**-1.23 [-2.40, -0.06]**	

Heterogeneity: Tau² = 2.93; Chi² = 416.94, df = 8 (P < 0.00001); I² = 98%
Test for overall effect: Z = 2.05 (P = 0.04)



Secondary Outcomes:

- ***Fasting Glucose***: Based on three studies with a total of 157 participants, fasting glucose decreased by 0.15mmol/L [95% CI 0.06 to 0.23mmol/L] with early energy distribution compared to later.
- ***Insulin Resistance***: Based on three studies with a total of 180 participants, HOMA-IR [a measure of hepatic insulin resistance based on an equation incorporating fasting glucose and fasting insulin], decreased by 0.38 points [95% CI 0.11 to 0.64] with early energy distribution compared to later. References values for HOMA-IR are age, sex, and ethnicity dependent, but a rough heuristic is that >2.0 indicates insulin resistance.
- ***LDL-C***: Based on four studies with a total of 226 participants, LDL-C decreased by 0.16mmol/L [95% CI 0.04 to 0.28mmol/L] with early energy distribution compared to later.

There were no significant effects of energy distribution on HbA1c, triglycerides, or HDL-C. Two studies that reported subjective appetite measures found significant improvements in satiety and hunger with early energy distribution, however, these studies were reported in the results and not meta-analysed [due to lack of data from only the pair of studies].

The Critical Breakdown

Pros: The study had a clearly stated aim and clear inclusion criteria. The study was preregistered with the register for systematic reviews [PROSPERO] and there are no apparent deviations from the preregistration. Relevant databases were used to search for primary studies, which also extended to the reference lists of identified papers. The exposure of energy distribution was explicitly stated, which excluded studies on intermittent fasting, time-restricted eating [TRE], or Ramadan [discussed further under ***Key Characteristic***, below]. Risk of bias was assessed and clearly presented. The results were clearly presented.

Cons: The overall power of the meta-analysis is low, based on a limited number of small individual studies and total number of participants in each respective early vs. late energy distribution condition [~240 in each]. 7/9 studies were assessed as moderate risk of bias, while 2/9 were assessed as high risk of bias. There was no assessment of publication bias. Randomisation method was satisfactory in only 5/9 included studies. 8/9 studies were conducted in free-living conditions and diet was not fully controlled in these studies. Given the influence of early vs. late energy intake on appetite regulation [13,14], these factors likely influence any effect of energy distribution on weight loss [discussed further under ***Interesting Finding***, below].

Key Characteristic

Arguably the key characteristic of the present meta-analysis, reflecting the point made in the introduction about the importance of conceptual clarity, is focusing specifically on temporal distribution of energy between early vs. late, which precluded inclusion of TRE studies. This is needed given that TRE studies inherently have a temporal component, i.e., in an early-TRE protocol all meals may be consumed between 7am and 2pm (11,12,15).

The reason this distinction is important is because one question raised in the chrono-nutrition research has been whether effects are driven by energy restriction alone, or whether factors like the distribution of energy or the extended fasting period that accompanies a TRE protocol may explain some of the observed effects.

All of the included studies in the present meta-analysis used energy restricted diets, so there are two component parts: the distribution of energy and the energy deficit. And the findings imply that, comparing two energy-restricted diets with early vs. later energy distribution, the earlier distribution may have a modest additional benefit for weight loss. However, we cannot confidently make that conclusion because the included studies are primarily free-living interventions, and the early energy distribution may have resulted in lower energy intakes compared to the later distribution comparison groups.

Interesting Finding

Why could the earlier distribution of energy intake potentially lead to greater reductions in energy intake in a free-living context? The weight of evidence suggests that it may be related to satiety and appetite regulation. The satiety ratio, which assesses how long an individual waits to eat again relative to the energy content of the prior eating occasion, has been shown to be highest in the morning and decline steadily over the course of the day (1).

A tightly controlled metabolic ward study by Ravussin et *al*. (15) that used an early-TRE protocol showed significant reductions in appetite compared to a control condition consuming the same diet [total energy and macronutrients] equally distributed over 12 h. While of course, based on what we've discussed above under ***Key Characteristic***, this was a TRE study and not entirely comparable to differences in energy distribution without a restriction on the eating window, it is consistent with wider research.

For example, the most tightly controlled study to date that compared early vs. later energy distribution but with controlled diets found no difference in weight loss, but significant reductions in appetite in the early energy distribution condition (13). And recall that while there were not sufficient studies to meta-analyse, the present study did report that the two studies which reported on appetite also found significant improvements in satiety and hunger with early energy distribution.

We have covered some of this evidence in a previous Research Lecture, *Is Appetite Control Dependent on Time of Day?*, which you may find helpful if you haven't already watched it. Overall, it is unlikely that morning energy intake enhanced weight loss in any magic way, but probably resulted in greater appetite regulation and, consequently, less energy intake.

Relevance

This is the first quantitative synthesis of the evidence related to temporal distribution of energy and weight loss, and that in itself a useful addition to the evidence. And overall, the findings are relatively paltry in terms of magnitude of effect of early compared to later energy distribution on weight loss.

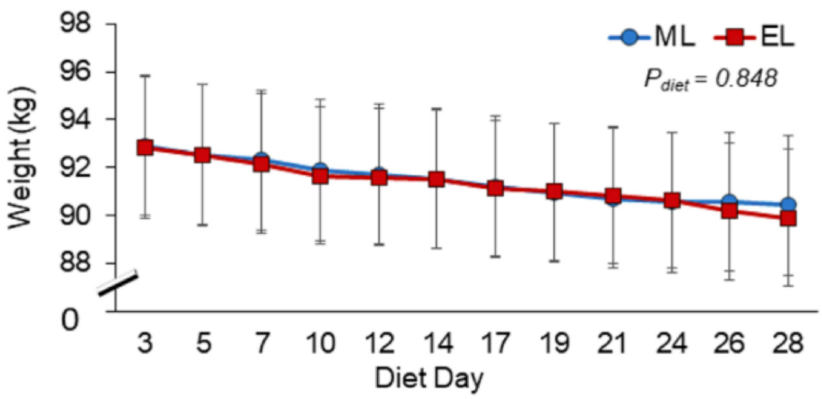
Nevertheless, the authors offer up some sacred cows in this area in their Discussion, suggesting that higher thermogenesis and circadian synchronisation may explain the greater morning weight loss [rather than, as discussed above under ***Interesting Finding***, effects on appetite regulation].

While it is possible to refer to research suggesting higher thermic effect of feeding [TEF] in response to a morning breakfast meal compared to an evening dinner meal (16,17), we recently challenged this by showing that the underlying variation in resting metabolic rate [RMR] across the day explains the apparent difference in TEF (18). In sum, this apparent difference reflects the method of calculating TEF and failure to include variation in RMR in the calculations of TEF (18).

Other aspects of time-of-day effects have been suggested to influence energy balance, specifically overall energy expenditure. However, the 'Bath Breakfast Project' demonstrated no alterations in energy expenditure or metabolic hormones from six weeks of breakfast consumption compared to fasting until midday (19,20).

Underlying circadian synchronisation may certainly be influencing metabolic outcomes, and the present meta-analysis did find reductions in fasting glucose and insulin resistance with early energy distribution. This is consistent with tightly controlled human studies that have shown glucose tolerance is highest in the morning and diminished in the evening, which results in prolonged postprandial elevations in blood glucose compared to the early part of the day (2).

However, we can at least slay the sacred cows of enhanced weight loss and its hypothesised relationship with energy expenditure. The recently published 'Big Breakfast Study' from Professor Alex Johnstone's group at the University of Aberdeen comprehensively measured all components of energy expenditure, both RMR and total energy expenditure, in addition to controlling diets of the participants (13). The study compared an early vs. later distribution of energy and found no difference in weight loss over 4-weeks; both patterns of energy distribution led to equal weight loss of ~3.3kg [see **figure**, below].



The present meta-analysis was registered and conducted prior to the publication of the 'Big Breakfast Study', and thus it was not included in the meta-analysis. Nevertheless, the 'Big Breakfast Study' supersedes all prior free-living interventions for its methodological quality, and its findings should be taken as a truer reflection of whether early vs. later energy distribution influences weight loss.

Application to Practice

A couple of key considerations arise for how we might think about applying the findings in this area in a practical context. The first is to be clear about the question being asked, which we can think about in terms of internal vs. external validity, i.e., the difference between *efficacy* ["does this work?"] and *effectiveness* ["does this work in real life?"].

The internal validity question would ask whether there is any effect of early energy distribution on weight loss that is *independent* of total energy intake, which was the angle often suggested by some earlier studies [indeed, the very studies included in this meta-analysis]. And the answer to that, from tightly controlled research, is 'no'. Early energy intake does not, for example, enhance TEF or lead to increases in other components of energy expenditure.

However, the external validity question would ask whether early energy distribution is effective for promoting weight loss in a 'real-world' context. And the answer to that, from free-living studies, is 'possibly'; there may be some individuals who benefit from the appetite regulatory effects of eating more earlier in the day. To what extent that influences weight loss appears, on balance of evidence, to be modest.

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