Lead article

A systematic review of the association between eating frequency, weight and health.

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Abstract

There is speculation amongst health professionals, the media and the public regarding eating frequency (EF) and its impact on weight and health. Nutritional weight loss and maintenance interventions longer than one week were reviewed for associations between EF and weight and health. Of the 176 studies identified, 25 relevant studies matched the criteria and only 10 of these were weight loss interventions. Generally, sample sizes were small, interventions were short term, and a wide array of definitions was used to define an eating occasion. Several key outcomes such as physical activity, adherence to assigned EF, and hunger were often not measured. The limited evidence available suggests that there is no association between EF and weight or health in either weight loss or maintenance interventions, with a possible inverse association between EF and lipids in weight maintenance interventions. Longer term, larger studies that include important weight and health outcomes are needed.

Key words: meal, snack, weight, obesity, grazing, gorging.

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Introduction

The media, the public, food industry, health professionals and practice guidelines for weight management alike speculate widely as to which eating frequency (EF) is best for weight management and health. However there is no consensus as to the optimum number of meals and/or snacks for weight management, and speculations regarding this are often contradictory.

A long held belief is that a higher EF can assist with weight management. Snack foods are often considered to be higher in carbohydrate, and therefore those who regularly snack may manage weight more successfully by the replacement of fat with carbohydrate. [1-5] Low EFs may also produce weight and health outcomes that mimic the metabolic syndrome in a variety of populations. [6] Another long held, but opposing, belief is that a higher EF may lead to weight gain as it provides more opportunities to eat during the day. Excess daily energy intake and weight gain could then follow. [7-9]

One of the key, and yet most controversial, arguments for regular eating for weight management is the supposed reduction in hunger that occurs with higher EFs. [5, 10, 11] However, advice to avoid snacking stems from the concern that hunger may remain unaffected [9] and daily energy intake, and subsequently weight, may increase with more opportunities to eat over the day. [7-9]

Physical activity (PA) could also be positively associated with EF as those with higher PA levels may eat more often due to greater appetite and increased energy demands. [5] Kirk [1] also expressed concern that population advice to decrease snacking for weight management may actually work against recommendations encouraging regular exercise as fewer larger meals may lead to gastric fullness and lethargy which may reduce motivation to exercise.

There is contention as to whether an inverse association indeed exists between EF and glucose and insulin. Several physiological reasons are proposed for an inverse association between EF and diabetes risk markers. These include: a lowered glycaemic load from spreading of the nutrients throughout the day; suppression of the release of free fatty acids from adipose tissue which promotes glucose disposal; [11] glucose-dependent insulinotropic polypeptide may be inversely associated with higher EF which leads to less insulin production with higher EFs; [9, 12] and the rate of stomach emptying may be slowed with smaller meals due to decreased stomach distension, thus a slower rate of nutrients is delivered to the intestine and less insulin is needed to control blood glucose levels. [9]

Plausible physiological mechanisms also exist for inverse associations between total and LDL cholesterol and higher EFs, [13] and epidemiological studies generally support this link. [9, 14] Insulin secretion appears to stimulate enzymes involved in cholesterol synthesis and promote lipogenesis in arterial tissue and growth of arterial smooth muscle cells. If insulin production, and hence circulating cholesterol levels, is reduced as a result of a grazing pattern, EF may help reduce the risk myocardial infarctions. [9, 11, 14, 15] Furthermore, “a reduction in cholesterol synthesis would result

in an increase in LDL receptors, further lowering serum cholesterol values." [14] Grazing may also provide more opportunity for reverse cholesterol transport to occur as cholesterol returns to the liver in the post-prandial state. [4, 9, 13, 15, 16]

Bellisle et al [17] and Mann [13] conducted reviews of the EF evidence in 1997 and focussed only on the effect of EF on weight loss and energy expenditure, and cardiovascular risk markers, respectively. Both found no clear association with EF. Bellisle et al [17] and Kirk et al [1] also reviewed the cross-sectional studies addressing EF and weight and highlighted that erroneous inverse associations were observed when dietary underreporting was not accounted for in the analyses.

This systematic review was conducted in response to the wide speculations from all sectors regarding the utility of manipulating EF for weight and health management, recent recommendations that EF research needs to be furthered, [9, 18] the fact that there have been no recent reviews of the accumulating published literature, and suggestions "..that such a fundamental aspect of our dietary habits, the number of meals we eat every day, has not yet been subject to rigorous scientific investigation is remarkable." [19]

Aim

The overall aim of this review was to address the following important questions in relation to longer-term weight loss and weight maintenance or 'usual diet' interventions in obese, overweight and normal weight adults. The following specific questions were posed.

- In healthy adults, does EF influence weight, body composition, blood pressure, quality of life, hunger, physical activity, glucose, insulin, insulin resistance, and blood lipid markers?
- Can EF be manipulated in the shorter term and is this sustainable over the longer term in the independent adult population?

Method

The following sources were included in the literature search process: MEDLINE, PROQUEST, CINAHL, PUBMED and COCHRANE DATABASE. Search terms were “snack”, “eating frequency”, “meal”, “grazing”, “gorging”, “nibbling”, “weight”, “weight loss”, “obese”, “overweight”, and all variations of these words. A “google” search was also conducted on the terms used in the literature database search to identify any general documents and/or reports that might prove useful. Reference lists of retrieved studies were also viewed.

Abstracts were scrutinised for relevance by two different authors and were included unless they met the following exclusion criteria:

a) included participants with known existing chronic disease, e.g. – diabetes;

b) used animals instead of humans;

c) analysed data on children and adolescents (< 20 years) or the elderly (> 70 years);

d) duration of intervention was less than 1 week;

e) was a nutrition intervention prior to 1980 or laboratory testing prior to 1990, except if referenced frequently by current literature;

f) did not compare different EFs (for example assessing same number of snacks with similar energy but different macronutrient content, or assessing morning consumption versus afternoon consumption with the same EF, or assessing regular EF (e.g. - EF=6) vs. irregular EF (e.g. – EF=3-9) but the average EF over the two treatments was the same (e.g. – EF=6); and

g) not written in English or the full text could not be obtained.

Outcome variables that were included in the analysis were: weight; body composition measures; blood pressure; quality of life; hunger, physical activity; glucose; insulin; insulin resistance; standard blood lipids and adherence to assigned EF.

The quality of each study was assessed by examining the degree to which the variables were described, the presence of power calculations, the assignment of participants to the various treatments and the appropriateness of the statistical analyses.

Major limitations of EF research

Lack of standardised definition of key terms

A major limitation of EF research is the lack of standardised definitions of key terms such as eating occasion, meal, and snack. [5, 20, 21] Definitions differed markedly and this limited the comparability of results between studies, [5] and the ability to conduct meta-analyses with confidence that consistent results regarding EF and weight and health would be obtained. [22] Comparisons between these studies are even more difficult as definitions of key EF terms were not always reported in the literature. [16, 21] Standardised definitions of key terms are needed to consistently investigate the role of EF on health. [20, 23]

Small sample sizes

Most of the studies selected in this review had small sample sizes and did not provide power calculations. The majority of studies that were not randomised controlled trials (RCT) had sample sizes ranging from 5 to 38, with 1 having a sample size of 80. [15] Nine of the RCTs had sample sizes ranging from 7 to 19, with six having sample sizes of 52, 62, 72, 80, 100, and 140. [24-29] Small sample sizes could mean that relationships between EF and weight and health outcomes could be masked by a lack of power.

Results and Discussion

One hundred and seventy-six (176) abstracts related to EF were reviewed and twenty-five (25) studies were selected for inclusion in the review. Only 10 of these studies were weight loss interventions.

No systematic reviews on this topic were located. Of the studies identified, 15 (60%) RCTs comparing different EFs were found; 7 of these studies were weight loss interventions. The remaining studies had less strong study design and included: 1 pre-test post-test trial; 1 case-control trial; 3 non-randomised cross-over trials (1 pre-set order); 1 partly randomised cross-over trial, 2 alternate allocation cross-over trials; 1 incomplete cross-over trial; and 1 case-series trial.

Table 1 and Table 2 below summarise the weight loss and weight maintenance interventions, respectively, that met the review criteria. An array of EFs were tested in the weight loss and maintenance studies, ranging from 1 meal per day through to 9

meals per day or 17 snacks per day, respectively, with the majority of studies testing 3 meals per day.

Weight

While theories link EF to weight loss and weight gain, there is strong evidence to suggest that there is no association between EF and weight status. While three weight maintenance studies [15, 30, 31] reported significant, but small fluctuations in weight by EF over 4, 8 and 2 weeks respectively, the remainder of the weight loss and weight maintenance literature that measured weight (n=21) found that EF has no relationship with weight. Bellisle's 1997 review of the EF weight loss literature [17] had similar conclusions.

Jahns [20] proposed that standardised energy intakes across a range of EFs may not result in an association between EF and weight, but ad libitum intakes may produce a positive association. Only one weight loss study used individualised energy intakes and found no association [24] and the majority of weight maintenance articles examined usual or individualised energy intakes and also found no association between weight and EF. Antoine et al [32] proposed that EF might provide additional benefit in weight loss studies employing higher energy intakes (5.7 – 7.6 MJ) whereas no additional benefit may be seen with low energy intakes (2.5 – 3.4 MJ) ".. either because weight loss is at its maximum rate.., or because the amount of food ingested is too low to induce sufficient variations in the mechanism of weight loss." Three of the weight loss studies selected for this review had higher energy intakes between 5.9 and 7.5 MJ [24, 33, 34] but found no association between EF and weight. Similarly, weight maintenance studies used a range of energy intakes and generally found no association. De Graaf [35] argues that our grazing patterns have not changed throughout

196 human evolution but that the energy density of snacks is greater now than during
197 Palaeolithic times. Thus it may not be that EF is contributing to weight gain as much
198 as our choice of energy-dense foods.
199
200 A meta-analysis of the relationship between weight and EF could not be reliably
201 conducted as the array of meal and snack definitions employed in the various articles
202 limits comparability between studies.

203 *Body composition*

204 The limited evidence available suggests no association between body composition and
205 EF for both weight loss and maintenance interventions (Table 1 and Table 2). Body
206 composition was measured in 8 of the 10 weight loss intervention studies and in only
207 3 weight maintenance studies, [29, 30, 36] with only one of these three measuring fat free
208 mass. Two older weight loss studies, [32, 37]one that was not a RCT, found an inverse
209 association between nitrogen output and EF. One weight maintenance study found a
210 significant body fat loss of only 0.37kg over 4 weeks when changing from 4 to 3
211 meals only, [36] and another found a significantly lower body fat (~2.1kg) over 8 weeks
212 on a lower EF. [30] However, there is strong evidence to suggest that there is no
213 relationship between body composition and EF. [25, 27, 29, 32, 33, 38, 39] A range of
214 techniques were used to measure body composition and this may explain why results
215 are mixed.
216
217 Only two of the selected articles reported waist circumferences (8%). Both were
218 randomised controlled weight loss trials finding no associations between waist and

EF, [24, 25] with durations of 2 months and 1 year, respectively. Waist has not been measured in weight maintenance trials.

Blood pressure

The association between EF and blood pressure (BP) has not been extensively investigated. Only 6 (24%) of the interventions that were located measured BP, all were RCTs, and half of these were weight loss interventions. A weight maintenance trial by Stote et al [30] found that BP (systolic and diastolic) was ~6% higher on 1 meal compared with 3 meals per day after 8 weeks. However, the remaining interventions observed no association between BP and EF, [24, 26, 27, 40, 41] covered a range of EFs (1 – 9) and two of these were of significant duration (6 – 12 months). [24, 26]

Quality of life

Quality of life is an important and measurable outcome in weight management trials; and weight loss has the potential to improve wellbeing. [42] Research addressing the impact of EF on quality of life has not been conducted to date.

Hunger

Given the speculation with hunger and eating frequency, it was surprising that only 2 (8%) of the articles in this review measured hunger levels, and none of these were weight loss interventions. Inverse associations between EF and hunger were observed at a single meal, [30, 43] but no differences in hunger observed when hunger was measured over the entire day. [43] These studies were also short term (1 – 8 weeks) and feelings of hunger may subside as subjects become accustomed to the altered EF. [44] Longer term EF studies measuring hunger, particularly during weight loss, are needed.

Physical activity

Only five articles selected in this review specifically measured PA and two of these were weight loss interventions. [24, 27] Given that most of these articles were investigating a relationship between weight change and EF, it was disappointing that PA was not measured for confounding. A weight maintenance study measuring energy expenditure using heart rate found those having a 1.5-3MJ snack had 0.4-0.5MJ significantly higher expenditure than when consuming a 0MJ snack [29]; a 0MJ snack can be considered 'not snacking' if the definition of a snack is the consumption of at least 50 Cal [45]. The remaining four studies showed no association. [24, 27, 30, 31] These studies used an array of PA measures. Two other studies measured sleeping or resting metabolic rate and found no relationship with EF also. [37, 38]

Diabetes risk markers

Twelve (48%) of the studies measured risk markers for diabetes and only 4 of these were during weight loss interventions. Results were mixed. Young et al [46] found that oral glucose tolerance (OGT) was reduced on 1 meal during 5-week weight loss treatments, suggesting an adverse effect for lower EFs. Alternatively, all 3 weight loss studies that did not find an association between glucose or insulin and EF [24, 26, 33] were randomised controlled trials, 2 of which had an intervention period of at least 24 weeks and these studies measured 3 or 4 EFs compared with 6. Jenkins' et al [14, 47] weight maintenance trial found that mean insulin levels over 12 hours were 27.9% lower after the 17 snacks intervention compared with 3 meals after 2 weeks, however, this study was limited by the small number of men involved (n=7). Two other weight maintenance studies found that insulin/glucose curves were flatter on the higher EF diets, [40, 48] but the area under the curve (AUC) was statistically similar [40] or statistical

analysis was not performed to confirm differences. [48] Five other weight maintenance studies did not find a significant association between EF and diabetes risk markers, with EFs ranging from 1 to 9 meals. [30, 36, 41, 49, 50] Those studies finding associations with EF had 5 weeks or less duration, whereas studies at 24 and 52 weeks found no associations. [24, 26] "It is not yet clear whether long-term adherence to a high-frequency meal pattern will ultimately result in better glucose tolerance." [3]

There are several reasons why an association between EF and markers for diabetes risk may not be observed. Subjects may need a longer period of time on an altered EF to effect insulin and glucose profiles. [51, 52] Also, metabolic advantages of higher EFs may be blunted during standard weight loss interventions as they already provide a reduced glycaemic load. [11, 14] Higher EFs also may not metabolically benefit those with normal baseline glucose tolerance, [46] particularly compared to people with diabetes. [53] Further, much higher EFs may be needed to achieve metabolic benefit (e.g. EF of 16), and lack of adherence to the altered EF may also explain why benefits are not observed. [54]

Insulin resistance was not measured in any of the selected articles. The effect of EF on insulin resistance during weight loss or weight maintenance is largely unknown; however, there may be no effect given that there is little evidence to suggest an effect with either glucose or insulin.

Heart disease risk markers

Eight of the 10 weight loss studies measured blood lipids. Two weight loss studies found inverse associations between EF: and HDL cholesterol [24] (RCT); and total cholesterol (TC) [46]. All other weight loss studies that measured lipids found no

associations, [25-27, 32, 33, 39] indicating that there is strong evidence that EF will not positively impact on lipid levels during weight loss. Conversely, 73% of weight maintenance studies that measured blood lipids found an inverse association with EF. [14, 16, 30, 40, 47, 49, 50, 55, 56] Even though TC and LDL levels may improve with higher EFs, HDL levels may not; although one of these studies found a positive association with HDL. [56] Three weight maintenance studies that measured blood lipids (27%) found no clear associations with EF. [15, 36, 41] EF and blood lipids may be inversely related in weight maintenance studies that: employ higher fat intakes (>36%); use an array of EFs (1 – 17 EF) and ages (18 – 68); use both genders; and investigate normal and overweight subjects with normal baseline TC levels.

Jenkins et al [14] proposed that large differences in EFs of 8 or more may be required to observe an association. The weight loss and maintenance studies showed no clear trends. Juhel et al [57] reported that those with high fat and cholesterol intakes may benefit more from higher EFs. Trends from the weight maintenance studies support this theory, with no clear trends in the weight loss studies, although the weight loss study with the highest fat intake (51%) found an association. [46] An inverse association between EF and lipids in normolipidaemic individuals, and not with hyperlipidaemic individuals, has also been proposed. [9, 13, 23] Weight loss studies did not show a clear trend. Weight maintenance studies generally supported this theory with 88% of studies in normolipidaemic populations finding inverse associations between EF and lipids. The only two hyperlipidaemic studies conducted found no association [41] or did not conduct statistical analysis but reported a positive inverse trend with TC. [46] Mann [13] proposed that there may not be additional benefits from higher EFs in the longer term as the body may adapt to the new pattern. Further,

316 cardiovascular benefits brought about by higher EFs may be negated by any weight
317 gain brought about by adopting a higher EF. [11]
318
319 It is not certain what effect EF will have on lipids in the long-term as most EF studies
320 were short term with small numbers of people. [3] The short term weight maintenance
321 studies suggest a moderate to strong link between EF and cardiovascular risk markers,
322 and that there is little evidence to suggest that manipulating EF during weight loss
323 results in an adverse health outcome. [9, 13]

324 *Dietary adherence*

325 A standardised measure of adherence for use in health intervention trials is not
326 available. [58] Adherence, while being a powerful confounder, may also assist in
327 explaining whether interventions were easy to follow, which would provide valuable
328 insights into successful strategies for weight management.
329
330 Fifteen studies (60%) did not report whether subjects successfully achieved and
331 maintained their allocated EF. Those studies that measured EF adherence had
332 contradictory results. [15, 16, 24-26, 28, 29, 38, 40, 41] The majority of these studies were short
333 term and adherence may be easier to achieve over shorter periods. The longer-term
334 studies found that maintaining snacking and non-snacking during weight loss over 6
335 or 12 months was challenging. [24, 26] A 1 year weight loss study in adolescents also
336 found that altered EF behaviours were not sustained at 2 years. [59] While an EF may
337 be achievable over the shorter term, it is questionable whether alterations to EF are
338 sustainable over the long-term.
339
340

Lack of long-term interventions and post-intervention follow up

Weight management requires strategies with demonstrated longer term effectiveness. Only two weight loss studies had duration of 6 months or greater, [24, 26] the remainder of weight management studies were 1 week to 12 weeks. Most of these are too short to use as a basis for recommendations for longer-term weight management.

Only one article conducted post-intervention follow up and, between the end of the intervention and 3 months post-intervention, found no differences in weight (3m: 74.8±6.0 to 80.9±3.6; 2m: 78.8±2.5 to 81.8±2.7), body fat (3m: 38.1±1.6 to 38.4±1.4; 2m: 39.5±1.1 to 40.6±1.0) or resting metabolic rate (kJ/hr: 3m: 248±7.1 to 271±12.1; 2m: 264±8.8 to 280±10.0) between those who did and did not eat breakfast. [27] A 1 year weight loss intervention in adolescents that encouraged breakfast consumption and discouraged snacking found that weight regain had occurred at the 2 year follow up. [59] Concerns have also been raised that altering EFs may further promote pathological eating behaviours in susceptible people. [9] Very little research has investigated the long-term effects of altering EF. [2]

Conclusion

Despite at least 40 years of research in this field, there is a paucity of recent, longer-term studies with sufficiently large sample sizes that investigate the effects of EF during weight loss or weight maintenance on weight and health outcomes. Figure 1 shows the weight and health outcomes that may be associated with EF but, based on the evidence to date, these associations are largely untested in the longer term.

Very little is known of the effects of altering EF in the longer term. [23] Obesity is a chronic, long-term condition and if EF is considered a strategy for weight loss it would be prudent to know the longer-term effects of altering dietary patterns.

Surprisingly, many important explanatory and confounding variables such as physical activity, EF adherence, quality of life and hunger were not measured extensively, if at all, in the EF literature and future EF research should measure these.

Weight, body composition and biochemical markers of heart disease and diabetes were investigated more extensively. While research generally shows no association between EF and weight and health during weight loss [17] and weight maintenance, the majority of weight maintenance studies argue that an inverse relationship between heart disease markers and EF exists, with plausible physiological mechanisms to support this.

The limited evidence to date suggests that the manipulation of EF has limited utility as a weight and health management strategy. Longer term, randomised controlled trials investigating the impact of EF on weight and health outcomes during weight loss and weight maintenance phases are required [60] in order to guide population recommendations for weight management. [3, 13]

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Table 1 Summary of weight loss studies meeting criteria for eating frequency literature review

Study Details	**EF**	Weight (kg)	Body comp	Blood Pressure (mmHg)	Physical Activity	Glucose (mmol/L)	Insulin (mIU/L)	TC (mmol/L)	LDL (mmol/L)	HDL (mmol/L)	Trigs (mmol/L)	EF adherence	**Overall findings**
Randomised Controlled Trials													
Berteus Forslund et al (2007) [24] Sweden, 52 wk block RCT; 140 adults (36 M), mean age 39 – 40 yrs, mean BMI 38	3m	Change (%): 3.6±4.9	Waist at Baseline only: 117.0± 11.7	Sys Change: -3.3 ± 11.3 Dias Change: -2.4± 10.3	% not active: Work: 32.7 to 30.6 Leisure: 30.6 to 14.3	Change: -0.16± 0.46	Change: -4.0± 11.0	Change: -0.11± 0.59	Change: -0.10± 0.50	Change: 0.1±0.21	Change: -0.17± 0.88	No. of snacks: 1.8±0.9 to 0.7±0.7	√ **HDL** Inverse association Number of snacks eaten was different between groups.
	3m3s	4.7±6.7, p = 0.3	115.7± 12.8, §	-4.0± 12.7, NS -2.3± 9.9, NS	40.9 to 38.6, p =0.63 38.6 to 22.7, p = 0.75	-0.33± 0.78, NS	-3.4± 10.3, NS	-0.16± 0.64, NS	-0.08± 0.60, NS	0.02±0.15, **p = 0.033**	-0.23± 0.58, NS	1.9±1.6 to 2.3±0.9, **p<0.0001**	
Vander Wal et al (2006) [25] USA, 8 wk RCT; 80 adults (19M), mean age 45 – 48 yrs; mean BMI 38	~3m2s Post-dinner snack	Change: -3.71± 3.29	Waist Change: -5.56±6.01 % body fat change: -1.45±1.70					Change: -0.05 ±0.53	Change: -0.11±0.56	Change: -0.05±0.18	Change: 0.32± 1.00	> 75% of meal replacement & dinner snacks eaten; > 75% of participants were adherent.	**X** No significant findings.
	~3m1s No post-dinner snack	-4.71± 3.84, NS	-7.30± 5.89, NS -1.27± 2.64, NS					-0.46± 0.84, NS	-0.29± 0.78, NS	-0.13± 0.25, NS	-0.04± 1.00, NS		
Poston et al (2005) [26] USA, 24 wk block RCT, 100 adults, 4 - 16% M, mean age 40 – 42 yrs, mean BMI 31 – 33	~3m Snacker - now meals only	Change: 2.85± 3.2		Sys BP: 119.9±12.2 to 118.9±12.1 Dias BP: 73.8± 9.9 to 72.1±9.4		5.4±0.6 to 5.0±0.5	3.4±3.8 to 2.1±1.3	5.3±0.6 to 5.3±0.7	3.2±0.6 to 3.3±0.8	1.48± 0.32 to 1.55± 0.3	1.4±1.0 to 0.9±0.5	Both baseline snackers and baseline non-snackers who had meals and snacks reported > snacking frequency than baseline non-snackers who had meals only (p = 0.007, p = 0.041). No other differences noted.	**X** No significant findings.
	~3m3s Non-snacker -- meals + 3s	3.48± 5.5		118.8±11.4 to 118.4±15.9 73.5±11.4 to 73.9±9.4		5.4±0.5 to 5.0±0.4	3.1±2.4 to 2.0±1.4	5.0±0.8 to 5.0±0.7	3.0±0.7 to 3.0±0.6	1.39±0.28 to 1.47±0.33	1.4±1.1 to 1.1±0.6		
	~3m3s Snacker - meals + 3s	2.42± 3.2		119.3±15.7 to 114.6±18.2 74.1±11.7 to 70.3±7.2		5.1±0.5 to 5.1±0.5	2.4±1.3 to 2.5±1.8	5.7±0.8 to 5.2±0.9	3.6±0.7 to 3.3±0.6	1.60±0.35 to 1.55±0.41	1.0±0.5 to 0.9±0.4		
	~3m Non-snacker – meals	2.08± 3.4. p=0.629		115.8±17.2 to 111.8±11.5,NS 69.7±9.3 to 68.2±9.3, NS		5.3±0.6 to 5.0±.0.3, NS	2.8±1.9 to 1.8± 1.0, NS	5.2±1.1 to 6.2±1.5, NS	3.3±0.9 to 4.1±1.1, NS	1.44±0.22 to 1.53± 0.19, NS	1.2±0.9 to 1.3±1.0, NS		

Study Details	**EF**	Weight (kg)	Body comp	Blood Pressure (mmHg)	Physical Activity	Glucose (mmol/L)	Insulin (mIU/L)	TC (mmol/L)	LDL (mmol/L)	HDL (mmol/L)	Trigs (mmol/L)	EF adherence	**Overall findings**
Verboeket-van de Venne et al (1993) [38] Netherlands, 4 wk RCT, 14 F, mean age 46yrs, mean BMI 30.2	2m	Change: 4.1±0.5;	FM change: 2.3±0.6 FFM change: 1.8±0.5		*At 4 wks (kJ/d)*: 7838± 416							Mean EF: 6.4±0.3 to 2.1±0.1	**X** No significant findings. Adherence to EF achieved.
	3–5m	4.7±0.4, NS	FM: 2.7±0.5, NS FFM: 2.0±0.4, NS		3-5m: 7867±202, NS							6.7±0.7 to 4.3±0.3	
Schlundt et al (1992) [27] USA, 12 wk block RCT, 52 obese F, aged 18-55yrs, mean BMI 30.6	~2m B/fast eater but now no b/fast	Change: 8.9±4.2	FM (%): ~2m: 43.1±1.1 to 39.5±1.1FFM: 25% of wt lost as FFM	115/76 to 109/71, NS§.	RMR, kJ/hr: ~2m: 280± 11.7 to 264± 8.8			5.59± 0.23 to 5.02± 0.20, NS treatment-by-strata-by-time: **p < 0.05**			1.42± 0.15 to 1.20± 0.15; NS§.		√ **TC** – largest reduction with those that did not change their baseline breakfast pattern, but no differences between groups.
	~2m B/fast skipper and now no b/fast	6.0±3.9											
	~3m B/fast eater and now eat b/fast	6.2±3.3	FM ~3m: 41.5±1.3 to 38.1±1.6 NS*. FFM: 25% of wt lost as FFM, NS§.		~3m: 266± 9.2 to 248± 7.1, NS								
	~3m B/fast skipper and now eats b/fast	7.7±3.3, NS											
Antoine et al (1984) [32] France, 2 wk RCT cross-over, 10 obese F, mean 41 yrs; mean BMI 31.8	3m	Change (kg/d): -0.15± 0.05	Change (N g/d): -1.89± 1.6					6m to 3m: 6.1 to 4			6m to 3m: Change: between 0.8 and 1.2,		√ Daily **nitrogen** loss inverse association
	6m	-0.18± 0.05, p<0.08.	-0.71± 1.5, **p < 0.05**.					3m to 6m: 7.8 to 5.7, NS			3m to 6m: between 1 and 1.2; NS		
Finkelstein et al (1971) [33] USA, 60d RCT, 8F, 20 - 22 yrs, BMI 27 – 33	3m (+ night snack)	Change: 6.1±2.7,	Body fat (SFT mm): 24 to 22 N (g over 12 days): 6.7 – 7.1			Over 60day treatment: 3.6 – 5.7, NS		4.5±1.1 to 4.3±0.7					**X** No significant findings.
	6m	5.5±1.5, NS	Body fat: 30 to 26, NS FFM: 6.7 – 7.1, NS					4.4±0.8 to 5.0±0.9, NS					

Study Details	**EF**	Weight (kg)	Body comp	Blood Pressure (mmHg)	Physical Activity	Glucose (mmol/L)	Insulin (mIU/L)	TC (mmol/L)	LDL (mmol/L)	HDL (mmol/L)	Trigs (mmol/L)	EF adherence	**Overall findings**
Other trials													
Garrow et al (1981) [37] UK, 1 wk cross-over to 3m, then either 1m or 5m. 14 F, mean 41yrs, mean BMI 37.7	1m	Change (kg/d): 0.26,	FFM loss (N, g/d): 2.1										√ **Nitrogen** loss – lower EF had greater loss.
	5m	0.22, NS	1.3, **p < 0.001**										
Young et al (1971) (1971) [34, 46] USA, 5 wk cross-over design, stratified by level of wt loss on 3m for > 2 wks, 11 M, 20-25 yrs, mean wt 108kg, on average 42.5% overweight, TC 7 – 8 mmol/L[13]	1m	Change kg/4wk: 6.08± 1.03	Greater vs. lesser EF: SFT (mm) 8.00 ±11.25, NS. Body circumferences (cm): 3.23±3.94, NS. FM loss (underwater weighing - kg) -0.12 ±0.84, NS. FFM (N retention, g/4 wk): -0.99 ±15.29, NS			Difference (sq cm) (6m or 3m vs. 1m): -29.3± 11.0, **p < 0.03**		Difference (Greater vs. lesser EF): -0.6± 0.2, **p < 0.01**			Difference (Greater vs. lesser EF): -0.2± 0.1, NS		√ **Oral glucose tolerance & TC** - greater EF (6m & 3m) had greater change
	3m	4.88± 1.31											
	6m	6.10± 1.75; NS											
Bortz et al (1966) [39] USA, 18 d cross-over trial, 6F, 19-56 yrs, obese	3m	Change: (kg/d) §	FFM (N): conservation trend during low energy intake. §					4.6			1.3		**X** Stat analysis not done.
	1m	0.23;						4.5			1.3		
	9m	0.24.						4.3			1.3		

All values above show the levels at baseline and at the end of the study unless otherwise stated. Hunger was not measured in weight loss studies. ~ = approximation of EF, § = no data provided, B/fast = breakfast, Baseline only = only baseline values reported., BMI = body mass index, Change = change from baseline to end of study, d= day, Dias = diastolic, EF = eating frequency, FFM = fat free mass, FM = fat mass, M = male, m = meal, N = nitrogen, NS= not significant but p-value not provided, RCT = randomised controlled trial, RMR = resting metabolic rate, s = snack, Sys = systolic, wk = week, wt = weight, yrs = years

Table 2 Summary of 'weight maintenance' or 'usual diet' studies meeting criteria for eating frequency literature review

Study Details	EF	Weight (kg)	Body comp	Blood Pressure (mmHg)	Physical Activity	Glucose (mmol/L)	Insulin (mIU/L)	TC (mmol/L)	LDL (mmol/L)	HDL (mmol/L)	Trigs (mmol/L)	EF adherence/ Hunger	**Overall findings**
Randomised Controlled Trials													
Stote et al (2007) [30] USA, 8 wk randomised, crossover, 5 M & 10 F, aged 40 – 50 years, BMI 18 – 25	1m	At 8 wks: 65.9 ± 3.2	At 8 wks: FM: 14.2±1.0; FFM: 50.9 ± 0.4	At 8 wks: Sys: 116.1 ± 1.9 Dias: 69.8± 1.3	At 8 wks: PA: NS §	At 8 wks: 4.8 ± 0.1		At 8 wks: 5.6 ± 0.1	At 8 wks: 3.5 ± 0.1	At 8 wks: 1.60 ± 0.05	At 8 wks: 1.1 ± 0.1	At 8 wks: Hunger (mm): ~ 75	√ **Weight** & **FM** positive**; BP, TC, LDL, HDL & Hunger** inverse association**.**
	3m	67.3 ± 3.2, **p=0.01**	FM: 16.3 ± 1.0, **p= 0.001**. FFM: 49.4± 0.4, p = 0.06	Sys: 109.5 ± 1.9, **p = 0.02** Dias: 66.0 ± 1.3, **p= 0.04**		5.0 ± 0.1, p = 0.14		4.9 ± 0.1, **p=0.001**	2.9 ± 0.1, **p=0.001**	1.47 ± 0.05, **p=0.01**	1.2 ± 0.1, p=0.08	~55, **p= 0.003**	
Jenkins et al (1995) (1989) [14, 47] Canada, 2 wk randomised crossover trial, 7 M, mean age 40 yrs, 110% mean IBW (98 – 121)	3m	75.3± 2.9 to 74.4± 3.0				Glucose tolerance (% per minute): 1.32± 0.13	**Over 12 hrs:** 27.9± 6.3% lower on 17s **p= 0.004**	8.5±2.5% lower on 17s, **p<0.02**	13.5±3.4% lower on 17s, **p<0.01**	1.27± 0.10 to 1.22± 0.12	1.90±0.47 to 1.15±0.18		√ **Insulin tolerance test, TC** & **LDL** inverse association**.**
	17 snacks	74.9± 3.0 to 74.4± 2.9, NS				17s: 1.21± 0.09, NS **Over 12 hrs:** 17s 3.8±2.4% p=0.088				1.23± 0.09 to 1.20± 0.11, NS	1.67±0.39 to 1.23±0.19, NS		
Arnold et al (1994) [41] NZ, 4 wk randomised cross-over trial, 11 M, 5 F, mean age 50, mean BMI 26.5, mean TC 6.78mmol/L	3m	During trial: 78.38± 16.53		Sys & Dias BP: NS§		4.55± 0.35	16.12±9.83	Baseline: 6.78± 0.62; 4 wks: 6.73± 0.74	Baseline: 4.60±0.65; 4 wks: 4.77± 0.66	Baseline: 1.10± 0.22; 4 wks: 1.13± 0.29	Baseline: 2.48±1.24; 4 wks: 1.91±0.67	Average EF: 3.1±0.3	**X** No significant findings.
	9m	78.53± 16.26, NS				4.44± 0.46, NS	4 wks: 13.97±5.06, NS	4 wks: 6.81± 0.88, NS	4 wks: 4.87± 0.78, NS	4 wks: 1.09± 0.27, NS	4 wks: 1.96±0.69, NS	7.9±0.8.	
Arnold et al (1993) [40] NZ, 2 wk randomised cross-over trial, 9M, 10F, healthy, mean age 32yrs, BMI 23.1	3m	Day 13&15 68.2 ± 14.4		NS §		Day 15: 0–2 hours: 4.3±0.53 to 4.00±1.05	Day 15: 0-2 hours: 8.6±2.6 to 33.1± 22.5	Baseline 4.49±0.87 Day 13&15 3m: 4.33±0.8	Baseline 2.89±0.71 Day 13&15 3m: 2.70±0.71	Baseline 1.22±0.17 Day 13&15: 1.23±0.22	Baseline 0.87±0.42; Day 13&15: 0.90±0.48	Average EF: 3.2±0.2	√ **TC, LDL, HDL** inverse association.
	9m	68.0 ± 14.2; NS				4.45±0.55 to 4.26±0.79, NS	11.8± 7.9 to 38.9± 24.2, NS	Baseline 4.49±0.87 Day 15: 4.05±0.75, **p < 0.005**	Baseline 2.89±0.71 Day 15: 2.48±0.6, **p < 0.005**	Baseline 1.22±0.17 Day 15: 1.18±0.19, **p < 0.05**	Baseline 0.87±0.42 Day 15: 0.88±0.46, NS	8.3±0.6	

Study Details	EF	Weight (kg)	Body comp	Blood Pressure (mmHg)	Physical Activity	Glucose (mmol/L)	Insulin (mIU/L)	TC (mmol/L)	LDL (mmol/L)	HDL (mmol/L)	Trigs (mmol/L)	EF adherence/ Hunger	**Overall findings**
Jordan et al (1989) [56] USA, 6wk random cross-over trial, 17M, mean age 55 yrs	3m to 6m	Change: (%): 0.3± 2.65, NS						6.1±0.4 to 6.0±0.3	4.3±0.3 to 4.2±0.2	0.91±0.05 to 1.06±0.05	2.0±0.3 to 1.6±0.2		√ **HDL** changed in both groups**, Trigs** changed from 3m to 6m only.
	6m to 3m							6.0±0.4 to 5.6±0.3, NS	4.3±0.3 to 3.8±0.2, NS	0.93± 0.08 to 1.14± 0.05, **p≤0.05**	1.7±0.2 to 1.4±0.2, **p≤0.05**		
Whybrow et al (2007) [29] Scotland, 2 wk (1 wk run-in) randomised, cross-over trial, 36 M & 36F, healthy, mean age 32 – 35 yrs, BMI 19 – 35	~3m (0MJ snack)	Change: -0.26	Body fat (SFT): NS §		Heart rate: 11.0± 0.05							93.8% of 3MJ snacks vs. 97.7% of 0MJ snacks consumed, **p = 0.023.** ≥89% of mandatory snacks consumed.	√ **Heart rate** lower in 0MJ snack group.
	~3m2s (1.5MJ snack (2s/d))	-0.24			11.4± 0.05								
	~3m4s (3MJ snack (4s/d))	-0.14, p= 0.293			11.5± 0.05, **p=0.018**								
Waller et al (2004) [28] USA, 4 wk RCT, 14 M & 48 F, mean age 48 & 52 yrs, BMI 36 & 34.	~3m1s Cereal 90 mins after dinner	Change (in those deemed adherent) 0.84± 1.62										14 of 32 in 3m1s group consumed night cereal on ≥5/7 days; Cereal adherence & wt loss: r =-0.36, p = 0.057.	**X** No significant findings.
	~3m No night cereal snack	0.18± 1.42, p = 0.06.											
Johnstone et al (2000) [43] UK, 9d randomised, crossover trial, 8M, mean age 27 yrs, mean BMI 23.6	~3m No snack	Change (Day 3 to 9): -0.16 ± 0.06										Hunger (24 hr (mm)): 37; (SED 2.7), Hunger (at 12:00 (mm)): 37 (SED 5)	√ **Hunger** inverse association at midday.
	~3m3s 70% C snacks	0.33± 0.05										30 (SED 2.7) 23 (SED 5)	
	~3m3s 70% P snacks	0.48± 0.06										32 (SED 2.7) 26 (SED 5)	
	~3m3s 70% fat snacks	-0.03 ±0.04, NS										34 (SED 2.7) p=0.102. 19 (SED 5), **p = 0.017**	

Study Details	EF	Weight (kg)	Body comp	Blood Pressure (mmHg)	Physical Activity	Glucose (mmol/L)	Insulin (mIU/L)	TC (mmol/L)	LDL (mmol/L)	HDL (mmol/L)	Trigs (mmol/L)	EF adherence/ Hunger	**Overall findings**
Other trials													
Chapelot et al (2006) [36] France, 28d pre-test post-test trial, 24 M, 19 – 25 yrs, BMI 19–24	4m to 3m	68.3±1.4 to 68.8±1.5	FM: 10.1±0.9 to 10.5±1.0			5.43±0.24 to 5.50±0.11	26.5±2.9 to 26.1±3.4				1.16±0.16 to 0.99±0.08;		√ **Fat mass** only significantly changed when usual EF changed from 4 to 3 meals per day.
	3m to 4m	69.8±1.6 to 69.9±1.5, NS	9.2±0.8 to 9.3±0.8, **p < 0.05 for 4to3m change only.**			5.65±0.14 to 5.87±0.15, NS	23.1±2.6 to 21.3±3.6, NS				0.84 ± 0.08 to 1.11±0.11, NS		
King et al (1999) [15] Ireland, 4 wk block partly randomised trial, 80 M, mean 44 - 53 yrs, BMI < 30 (mean BMI 25.8 - 28)	~EF =3 30% fat reduction & EF ≥ 5 ↓ to 3	87.9±6.2 to 86.4±6.8						6.86±0.68 to 6.35±0.83	4.89±0.7 to 4.42±0.89	1.11±0.25 to 1.11±0.28	1.96±0.95 to 1.88±0.82	Average EF: 5.1±0.6 to 3.6±1.6	√ **Weight –** groups with EF = 3 significantly reduced from baseline to 4 wks, otherwise no differences.
	~EF≥5 30% fat reduction	82.9± 20.6 to 82.3±9.5						6.75±1.96 to 6.32±0.81	4.72±0.94 to 3.94±1.31	1.11±0.22 to 1.25±0.56	2.14±0.82 to 2.11±0.68	5.0±1.0 to 4.7±1.0	
	~EF=3 EF ≥ 5 ↓ to 3	86.1± 11.3 to 83.4± 10.4						6.57± 0.7 to 5.99±0.92	4.51± 0.76 to 4.26±0.88	0.99±0.21 to 1.00±0.24	2.40±1.82 to 1.68±0.74	5.6± 1.4 to 3.8±0.9	
	~EF=6 ↑ EF from < 4 to 6	81.2± 10.2 to 80.8±9.9, **p = 0.05**						6.63±1.42 to 6.52±1.05, NS	4.56±0.79 to 4.39±1.02, NS	1.14±3.0 to 1.14±0.26, NS	2.33±1.55 to 2.06±0.66, NS	3.8±0.4 to 5.2±1.2	
Maislos et al (1998) [49] Israel, 8 wk case-control trial, 38 healthy M&F, mean age 24 & 30 yrs	1m during Ramadan	Baseline, after Ram & 4 wks post-Ram: 68±4 to 67±5 to 68±6, NS			NS §	Baseline, after Ram & 4 wks post-Ram:1m: 4.27±0.66 to 4.44±0.33 to 4.00±0.61		Baseline, after Ram & 4 wks post-Ram: 4.4±1.2 to 4.7±1.4 to 4.3±1.0	Baseline, after Ram & 4 wks post-Ram: 2.7±1.2 to 2.9±1.3 to 2.8±1.3	Baseline, after Ram & 4 wks post-Ram: 0.91±0.28 to 1.13±0.27 to 0.97±0.26 **p<0.001**			√ **HDL** within 1m increased by 23%, during Ramadan; but no differences between groups.
	3-4m (control)					§ NS		4.7±0.8 to 5.1±0.7 to 4.9±0.6, NS	3.2±0.9 to 3.4±0.7 to 3.1±0.6, NS	1.32±0.25 to 1.42±0.34 to 1.24±0.26, NS			

Study Details	EF	Weight (kg)	Body comp	Blood Pressure (mmHg)	Physical Activity	Glucose (mmol/L)	Insulin (mIU/L)	TC (mmol/L)	LDL (mmol/L)	HDL (mmol/L)	Trigs (mmol/L)	EF adherence/ Hunger	**Overall findings**
McGrath et al (1994) [16] Ireland, 3 wk crossover trial, 23 M, mean 29 & 30), mean BMI ~24	6m to 3m							4.76±0.87 to 4.82±0.92	3.10±0.76 to 3.20±0.83	1.20±0.24 to 1.20±0.21	1.06±0.62 to 0.86±0.38;	Average EF: 6.0±0.8 to 3.3±0.3	√ **TC & LDL** – significant cross-over effect; otherwise no differences.
	3m to 6m							5.00±0.98 to 4.62±0.93, **p=0.038**	3.37±1.06 to 2.96±0.95, **p=0.038**	1.33±0.29 to 1.34±0.28, p=0.935	0.88±0.37 to 0.75±0.25, p=0.662	3.1±0.1 to 5.9±0.9	
Maislos et al (1993) [50] Israel, 4 wk case series trial, 16M, 8F, mean age 27 (18-45yrs), mean BMI 24.6	1m during Ramadan & usual EF post-Ram	End & 1 mth after Ram: 68.0 ± 17.0 to 68.2 ± 16.0, NS				End & 1 mth after Ram: 4.61 ± 0.28 to 4.39 ± 0.22, NS		End & 1 mth after Ram: 4.02 ± 1.00 to 3.88 ± 0.93, p=0.1	End & 1 mth after Ram: 2.52 ± 0.64 to 2.57 ± 0.75, NS	End & 1 mth after Ram: 0.95 ± 0.26 to 0.72 ± 0.20, **p < 0.005**	End & 1 mth after Ram: 1.10 ± 0.61 to 1.29 ± 0.55, NS		√ **HDL** decreased as EF increased.
Dallosso et al (1982) [31] England, 2 wk (1 wk run-in) alternate allocation cross-over trial, 8M students, aged 21 – 27, BMI 21.8	2m	72.9± 11.7 to 73.7± 11.3			24h EE (kJ/d): ~2% mean diff between 6m & 2m, NS								√ **Weight** for difference between day 1 & 14 of 2m group only.
	6m	73.2± 11.6 to 73.1± 11.7; **p<0.005**											
Gwinup et al (1963) (1963) [48, 55] USA, 2 wk non-random, pre-set order trial, 5 subjects, TC 3.6 to 10.4 mmol/L	3m	Changed ~2 – 5 kg in each person				Oral Glucose tolerance - AUC trend highest to lowest: 1m; 3m; then 10m		Trend for inverse association					**X** statistical analysis not done
	10m												
	1m												

All values above show the levels at baseline and at the end of the study unless otherwise stated. ~ = approximation of EF, § = no data provided, AUC = area under the curve, BMI = body mass index, C = carbohydrate, Change = change from baseline to end of study, d = day, Dias = diastolic, Diff = difference, EE = energy expenditure, EF = eating frequency, F = female, FFM = fat free mass, FM = fat mass. hrs = hours, M = male, m = meal, mth = month, NS= not significant but p-value not provided, P = protein, Ram = Ramadan, RCT = randomised controlled trial, s = snack, SED = standard error of the difference, Sys = systolic, wk(s) = week(s), wt = weight, yrs = years..

Figure 1 Simplified theoretical construct of the parameters that should be investigated in a longer term eating frequency nutrition intervention. [a]

[a] This depiction includes items that are measurable and arguably influenced by a longer-term EF nutrition intervention.

Dotted arrows represent unproven theories regarding the role of eating frequency (EF) (i.e. – EF may influence: physical activity levels; appetite; and quality of life).