Supplementary data

Impact of meal frequency on anthropometric outcomes: a systematic review and network meta-analysis of randomized controlled trials

Schwingshackl L et al.

”Online Supplementary Material”

Supplemental Appendix 1:

Full search strategy (11th Match 2019): Ovid MEDLINE(R)

	Searches	Results
1	exp Meals/	4537
2	("meal frequency" or "feeding frequency" or "eat* frequen*" or (frequen* adj3 feed*) or "meal pattern" or "feeding pattern" or "eating pattern" or "eating habit" or (skip* adj3 meal) or (omit* adj3 meal) or (add* adj3 meal) or (often adj3 eat*) or (frequen* adj3 eat*) or (number adj3 meals)).mp.	7566
3	1 or 2	11760
4	Exp Body Weight Changes/ OR Body Mass Index/ OR Diet, Reducing/ OR Obesity/	287635
5	("Weight loss" or "losing weight" or "weight change" or obes* or "energy intake" or "fat intake" or "fat loss" or "calori* intake" or diabet* or glucose* or insulin or "hypercholester*" or "metaboli* change*" or "metaboli* effect*" or "reduc* energy" or lipid* or cholester* or "body composition" or LDL or HDL).mp.	1224251
6	4 or 5	1282863
7	3 and 6	5073
8	adult/ or (adult or grown* or individual*).mp.	6093326
9	7 and 8	2769
11	randomized controlled trial.pt.	476630
11	9 and 10	751

Supplemental Appendix 2: Full-text publications excluded with reason

Online Supplementary Reference	**Reason for exclusion**
(1)	Wrong study duration
(2, 3)	Wrong study design
(4-7)	Wrong intervention
(8-15)	Wrong comparator
(16-20)	Duplicate publication

Online Supplementary References

1. Westerterp-Plantenga MS, Kovacs EM, Melanson KJ. Habitual meal frequency and energy intake regulation in partially temporally isolated men. Int J Obes Relat Metab Disord 2002;26(1):102-10. doi: 10.1038/sj.ijo.0801855.

2. Bortz WM, Wroldsen A, Issekutz B, Jr., Rodahl K. Weight loss and frequency of feeding. N Engl J Med 1966;274(7):376-9. doi: 10.1056/nejm196602172740703.

3. Chapelot D, Marmonier C, Aubert R, Allegre C, Gausseres N, Fantino M, Louis-Sylvestre J. Consequence of omitting or adding a meal in man on body composition, food intake, and metabolism. Obesity (Silver Spring) 2006;14(2):215-27. doi: 10.1038/oby.2006.28.

4. Alhussain MH, Macdonald IA, Taylor MA. Irregular meal-pattern effects on energy expenditure, metabolism, and appetite regulation: a randomized controlled trial in healthy normal-weight women. Am J Clin Nutr 2016;104(1):21-32. doi: 10.3945/ajcn.115.125401.

5. Geliebter A, Astbury NM, Aviram-Friedman R, Yahav E, Hashim S. Skipping breakfast leads to weight loss but also elevated cholesterol compared with consuming daily breakfasts of oat porridge or frosted cornflakes in overweight individuals: a randomised controlled trial. J Nutr Sci 2014;3:e56. doi: 10.1017/jns.2014.51.

6. Poston WS, Haddock CK, Pinkston MM, Pace P, Karakoc ND, Reeves RS, Foreyt JP. Weight loss with meal replacement and meal replacement plus snacks: a randomized trial. Int J Obes (Lond) 2005;29(9):1107-14. doi: 10.1038/sj.ijo.0803007.

7. Vander Wal JS, Waller SM, Klurfeld DM, McBurney MI, Cho S, Kapila M, Dhurandhar NV. Effect of a post-dinner snack and partial meal replacement program on weight loss. Int J Food Sci Nutr 2006;57(1-2):97-106. doi: 10.1080/09637480600658369.

8. Betts JA, Richardson JD, Chowdhury EA, Holman GD, Tsintzas K, Thompson D. The causal role of breakfast in energy balance and health: a randomized controlled trial in lean adults. Am J Clin Nutr 2014;100(2):539-47. doi: 10.3945/ajcn.114.083402.

9. Chowdhury EA, Richardson JD, Holman GD, Tsintzas K, Thompson D, Betts JA. The causal role of breakfast in energy balance and health: a randomized controlled trial in obese adults. Am J Clin Nutr 2016;103(3):747-56. doi: 10.3945/ajcn.115.122044.

10. Dhurandhar EJ, Dawson J, Alcorn A, Larsen LH, Thomas EA, Cardel M, Bourland AC, Astrup A, St-Onge MP, Hill JO, et al. The effectiveness of breakfast recommendations on weight loss: a randomized controlled trial. Am J Clin Nutr 2014;100(2):507-13. doi: 10.3945/ajcn.114.089573.

11. LeCheminant GM, LeCheminant JD, Tucker LA, Bailey BW. A randomized controlled trial to study the effects of breakfast on energy intake, physical activity, and body fat in women who are nonhabitual breakfast eaters. Appetite 2017;112:44-51. doi: 10.1016/j.appet.2016.12.041.

12. Salehi M, Yousefinejad A, Pishdad G. The effect of a diet education with six iso-caloric meals on the body weight and blood glucose of diabetes type 2 patients. Food Science and Technology 2012;32:329-33.

13. Salehi M, Kazemi A, Hasan Zadeh J. The effects of 6 isocaloric meals pattern on blood lipid profile, glucose, hemoglobin a1c, insulin and malondialdehyde in type 2 diabetic patients: a randomized clinical trial. Iranian journal of medical sciences 2014;39(5):433-9.

14. Hatami Zargaran Z, Salehi M, Heydari ST, Babajafari S. The Effects of 6 Isocaloric Meals on Body Weight, Lipid Profiles, Leptin, and Adiponectin in Overweight Subjects (BMI > 25). International cardiovascular research journal 2014;8(2):52-6.

15. Thomsen C, Christiansen C, Rasmussen OW, Hermansen K. Comparison of the effects of two weeks' intervention with different meal frequencies on glucose metabolism, insulin sensitivity and lipid levels in non-insulin-dependent diabetic patients. Ann Nutr Metab 1997;41(3):173-80. doi: 10.1159/000177993.

16. Belinova L, Kahleova H, Malinska H, Topolcan O, Windrichova J, Oliyarnyk O, Kazdova L, Hill M, Pelikanova T. The effect of meal frequency in a reduced-energy regimen on the gastrointestinal and appetite hormones in patients with type 2 diabetes: A randomised crossover study. PLoS One 2017;12(4):e0174820. doi: 10.1371/journal.pone.0174820.

17. Carlson O, Martin B, Stote KS, Golden E, Maudsley S, Najjar SS, Ferrucci L, Ingram DK, Longo DL, Rumpler WV, et al. Impact of reduced meal frequency without caloric restriction on glucose regulation in healthy, normal-weight middle-aged men and women. Metabolism 2007;56(12):1729-34. doi: 10.1016/j.metabol.2007.07.018.

18. Jenkins DJ, Wolever TM, Vuksan V, Brighenti F, Cunnane SC, Rao AV, Jenkins AL, Buckley G, Patten R, Singer W, et al. Nibbling versus gorging: metabolic advantages of increased meal frequency. N Engl J Med 1989;321(14):929-34. doi: 10.1056/nejm198910053211403.

19. Kahleova H, Malinska H, Kazdova L, Belinova L, Tura A, Hill M, Pelikanova T. The Effect of Meal Frequency on the Fatty Acid Composition of Serum Phospholipids in Patients with Type 2 Diabetes. J Am Coll Nutr 2016;35(4):317-25. doi: 10.1080/07315724.2015.1046197.

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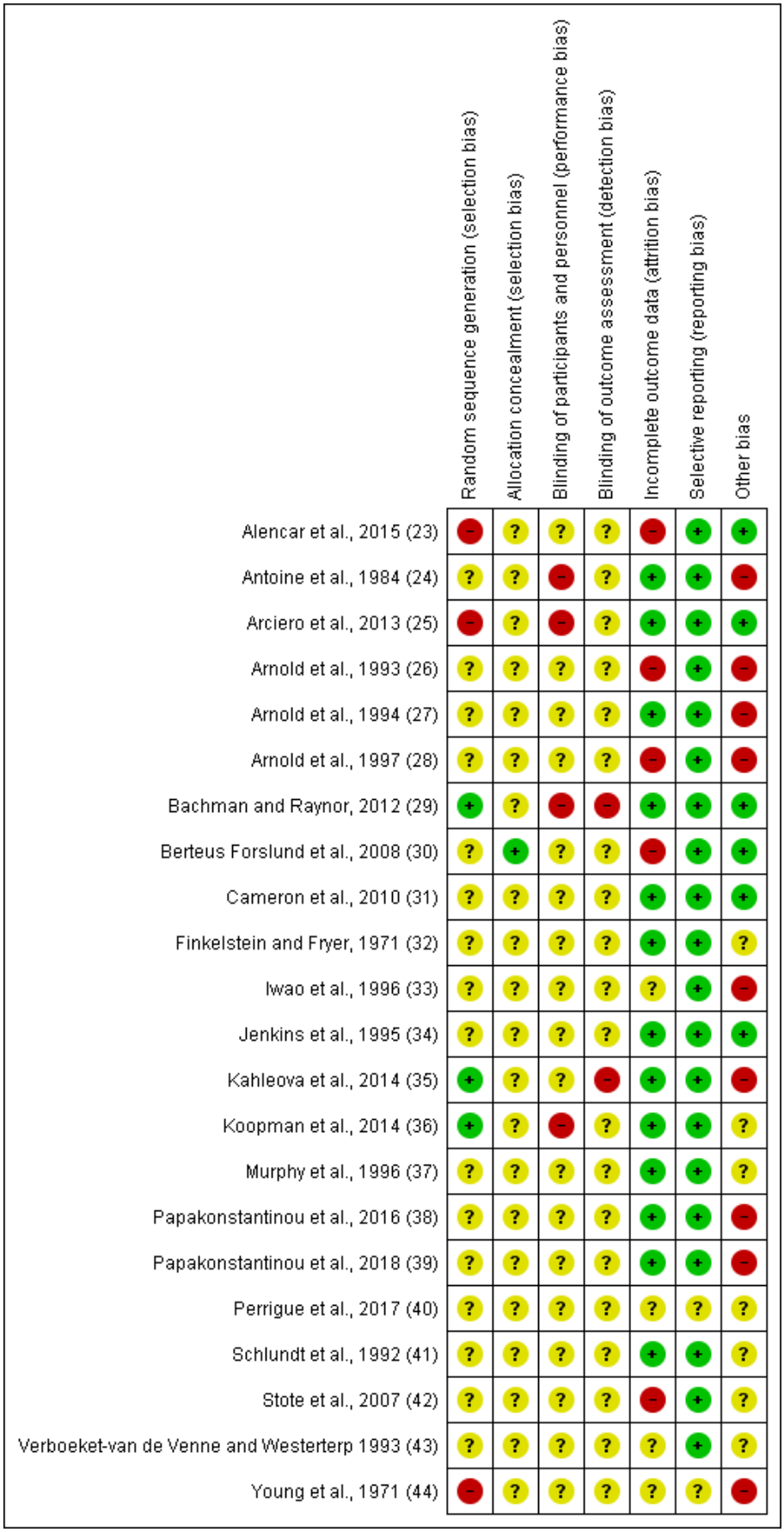
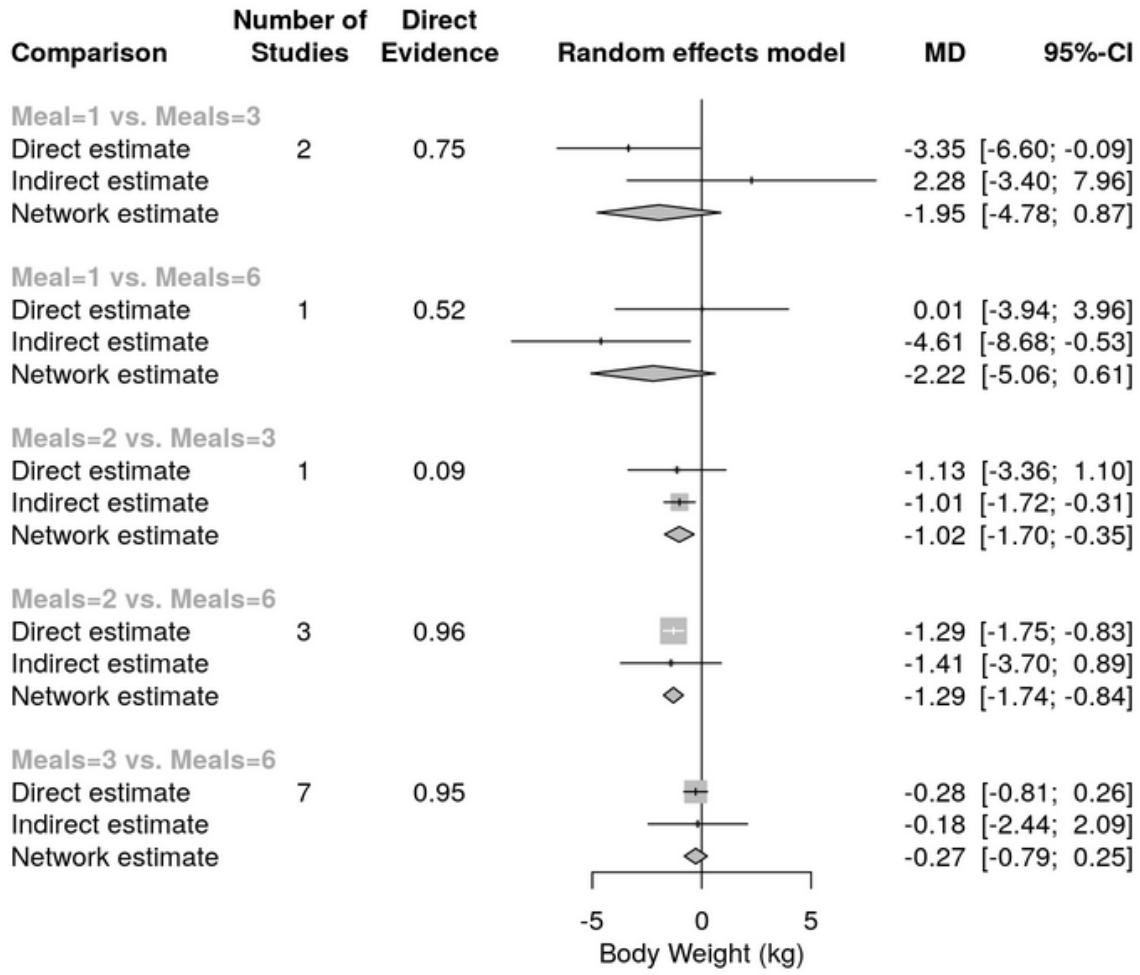
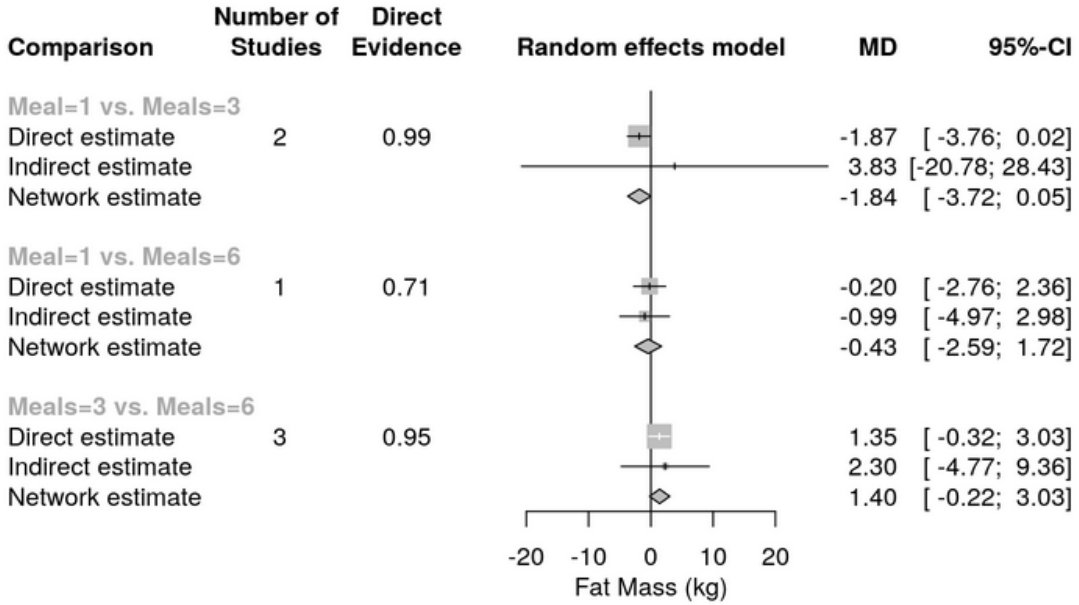

Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Alencar et al., 2015 (23)
Antoine et al., 1984 (24)
Arciero et al., 2013 (25)
Arnold et al., 1993 (26)
Arnold et al., 1994 (27)
Arnold et al., 1997 (28)
Bachman and Raynor, 2012 (29)
Berteus Forslund et al., 2008 (30)
Cameron et al., 2010 (31)
Finkelstein and Fryer, 1971 (32)
Iwao et al., 1996 (33)
Jenkins et al., 1995 (34)
Kahleova et al., 2014 (35)
Koopman et al., 2014 (36)
Murphy et al., 1996 (37)
Papakonstantinou et al., 2016 (38)
Papakonstantinou et al., 2018 (39)
Perrigue et al., 2017 (40)
Schlundt et al., 1992 (41)
Stote et al., 2007 (42)
Verboeket-van de Venne and Westerterp 1993 (43)
Young et al., 1971 (44)

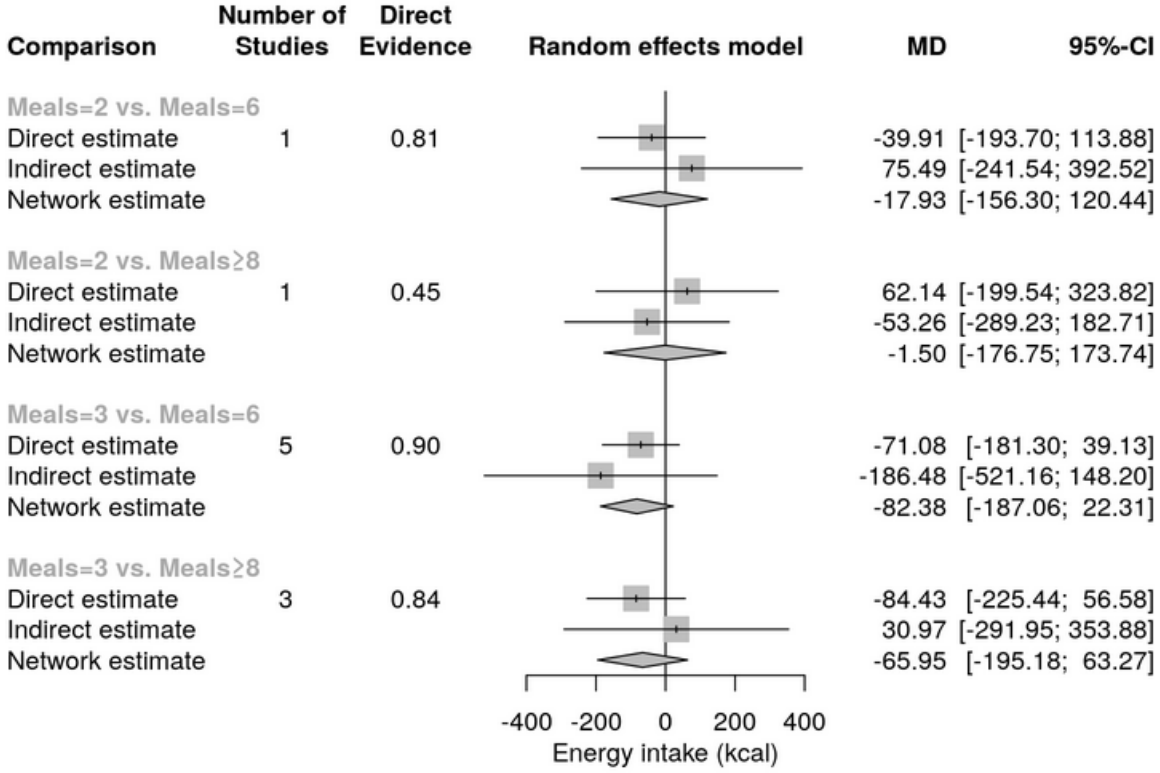
Supplemental Figure 1: Risk of bias evaluation of the included RCTs.



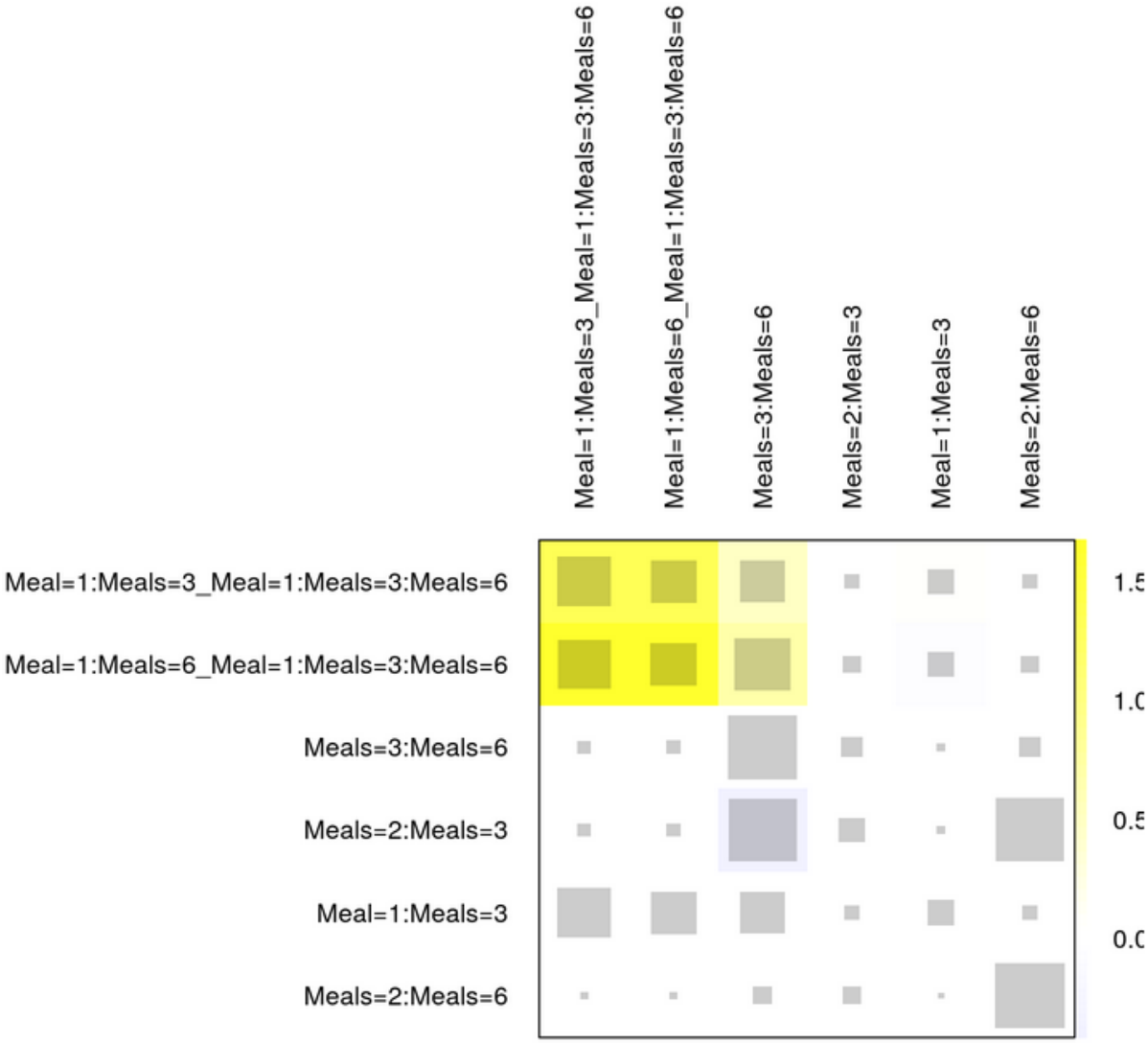
Supplemental Figure 2: Summary effect estimates of different meal frequencies on body weight (kg).



Supplemental Figure 3: Summary effect estimates of different meal frequencies on fat mass (kg).

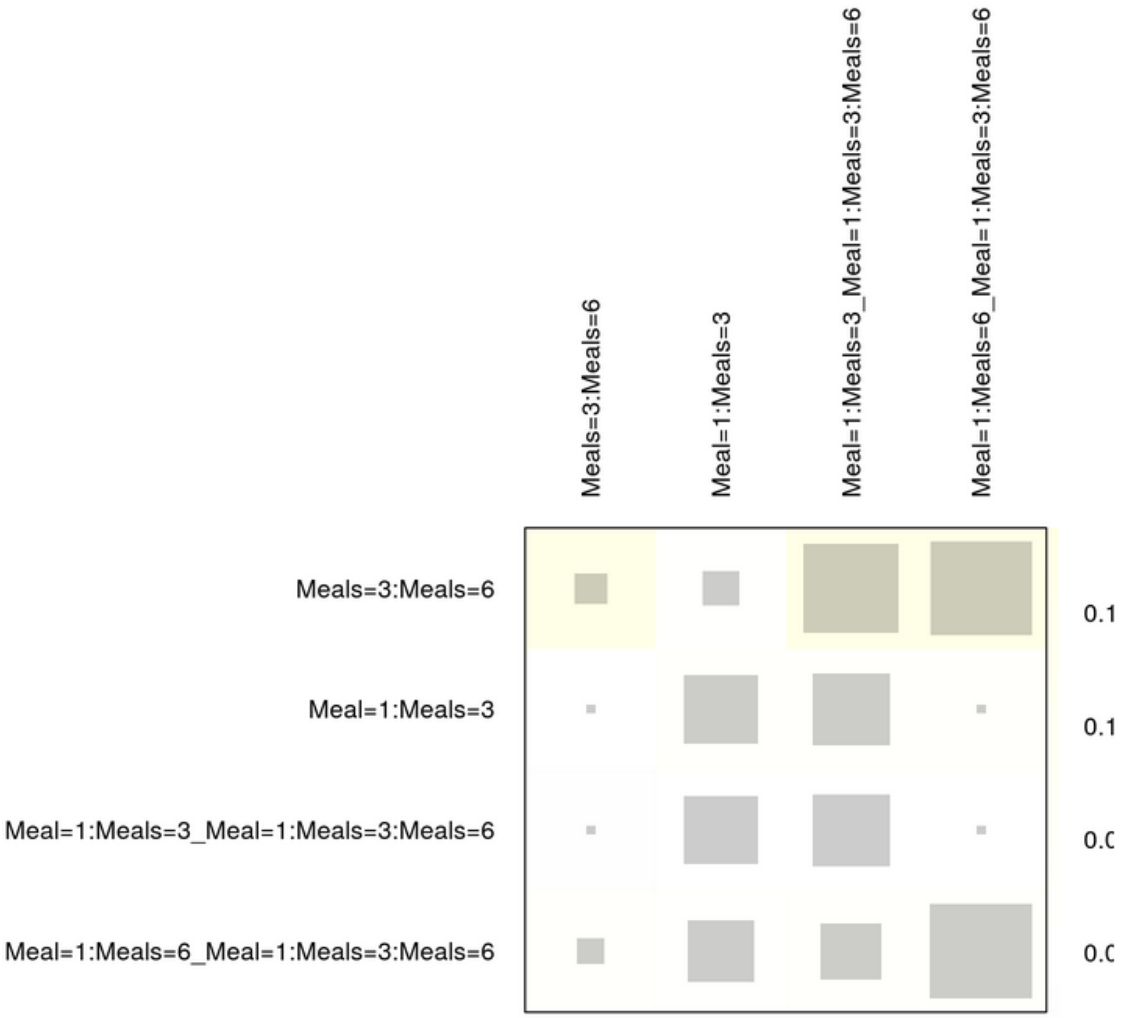


Supplemental Figure 4: Summary effect estimates of different meal frequencies on energy intake (kcal/d).

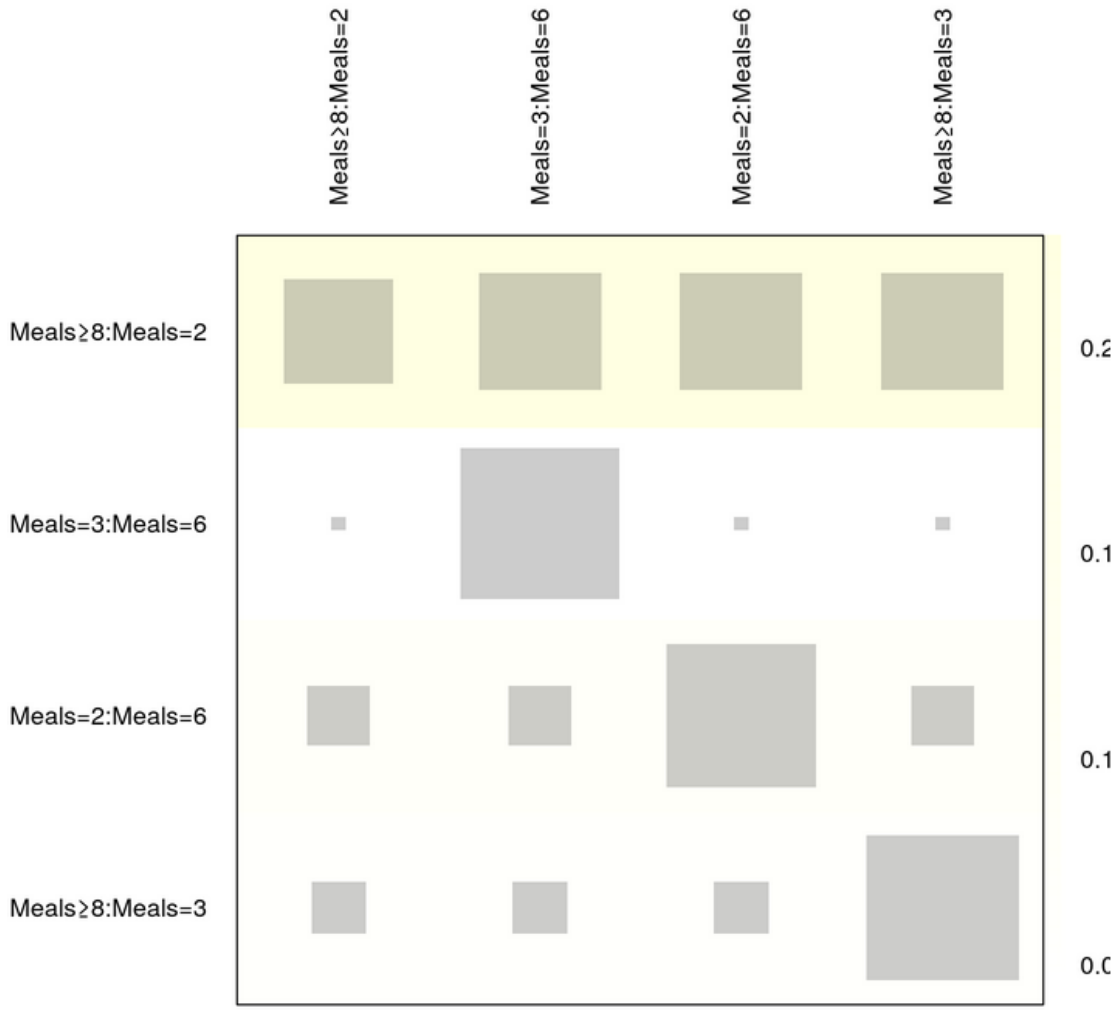


Supplemental Figure 5: Net heat plot for body weight.

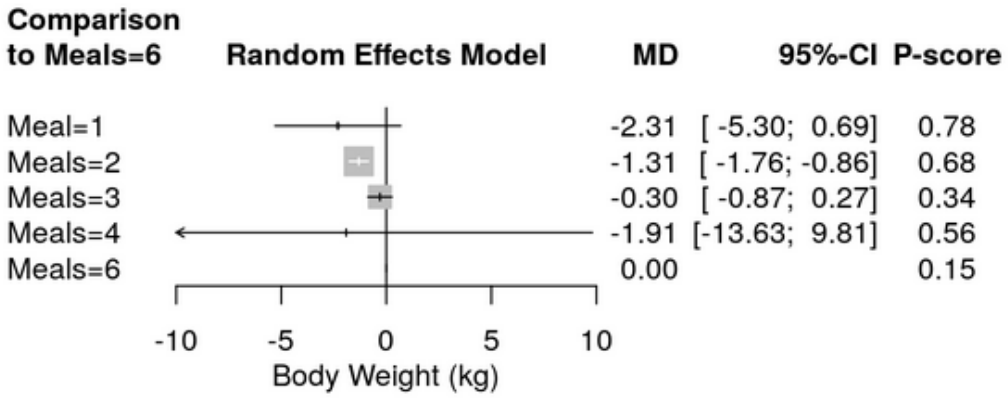
This plot is a heat map where the colors on the diagonal represent the inconsistency contribution of the corresponding design and the colors on the off-diagonal are associated with the change in inconsistency between direct and indirect evidence in a network estimate in the row after relaxing the consistency assumption for the effect of a design in the column. A blue colored element indicates that the evidence of the design in the column supports the evidence in the row; a red colored element indicates that the evidence of the design in the column contrasts to the evidence in the row.



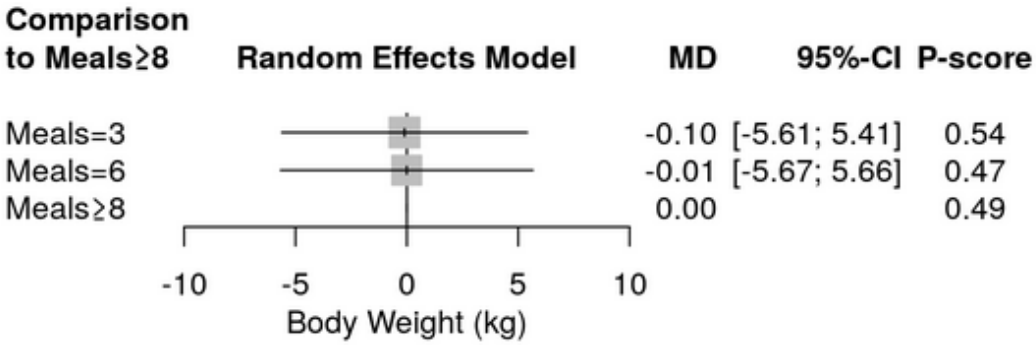
Supplemental Figure 6: Net heat plot for fat mass.



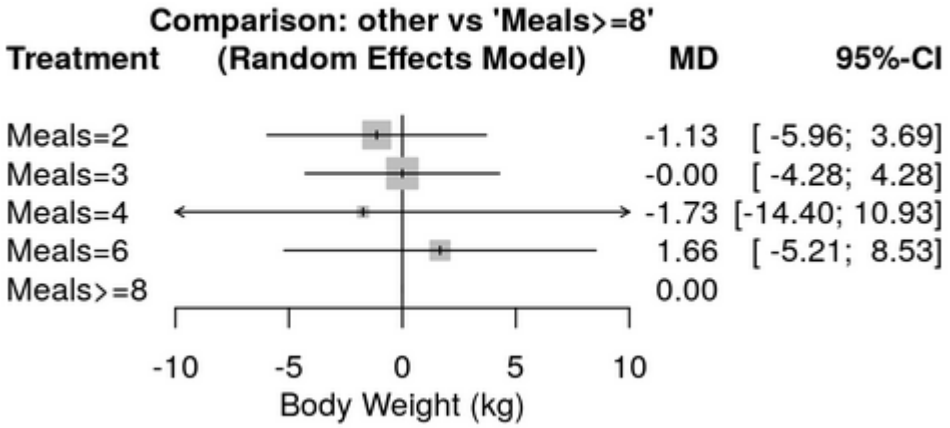
Supplemental Figure 7: Net heat plot for energy intake.



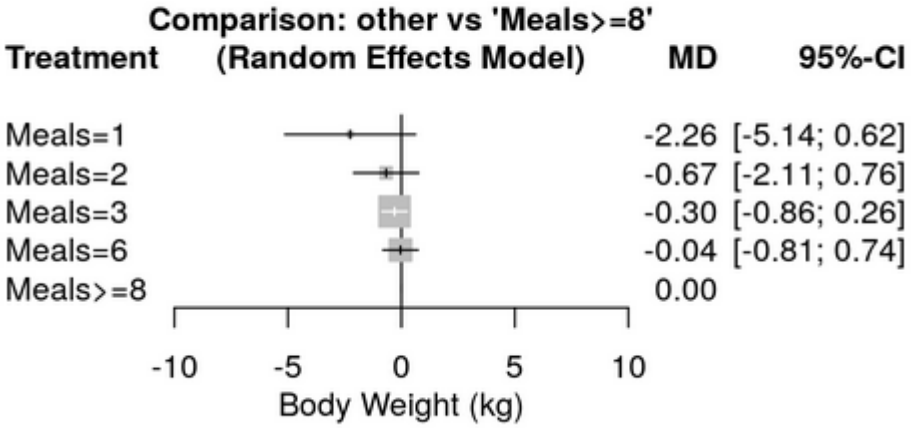
Supplemental Figure 8: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in patients with obesity.



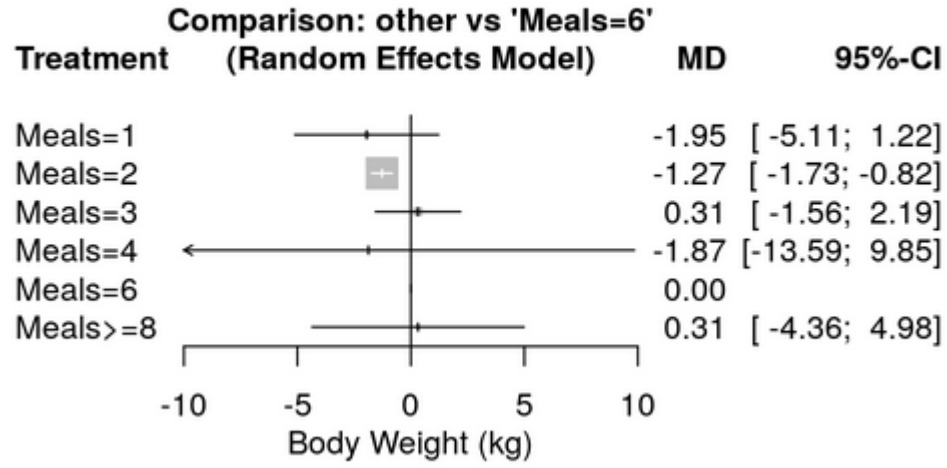
Supplemental Figure 9: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in overweight participants.



Supplemental Figure 10: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in studies without provision of foods.

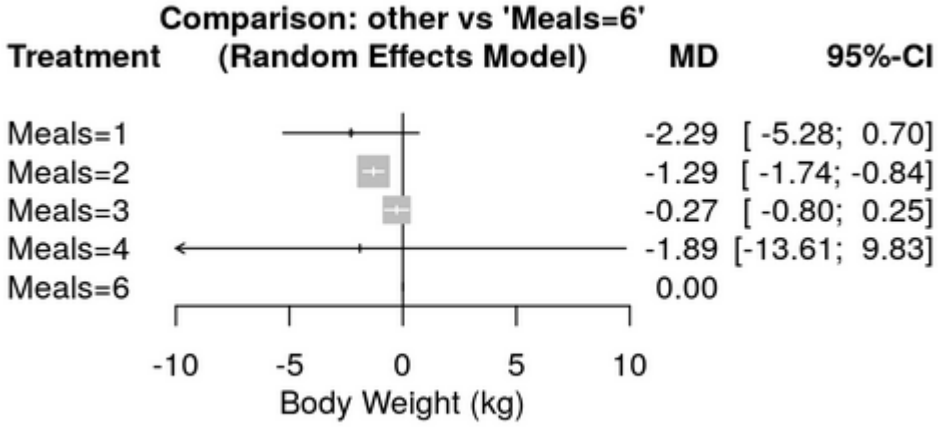


Supplemental Figure 11: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in studies with provision of foods.

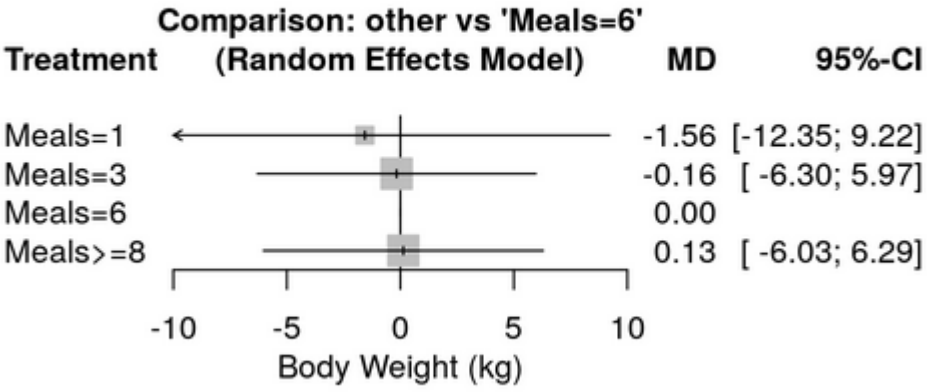


Supplemental Figure 12: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in studies were participants did not consume meals in the research center.

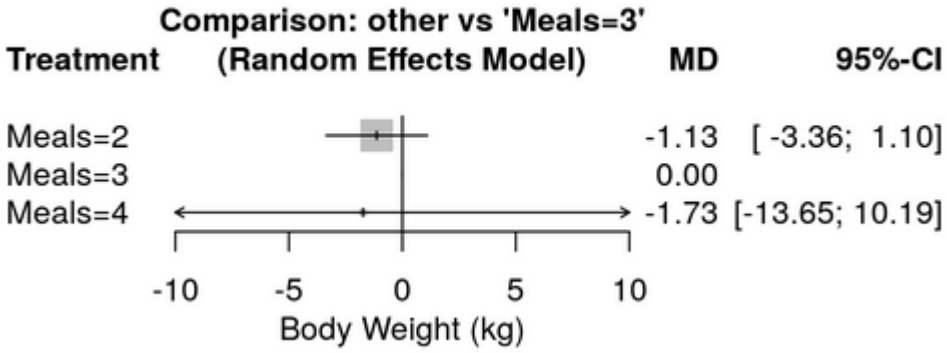
Supplemental Figure 13: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in studies were participants consumed meals in the research center.



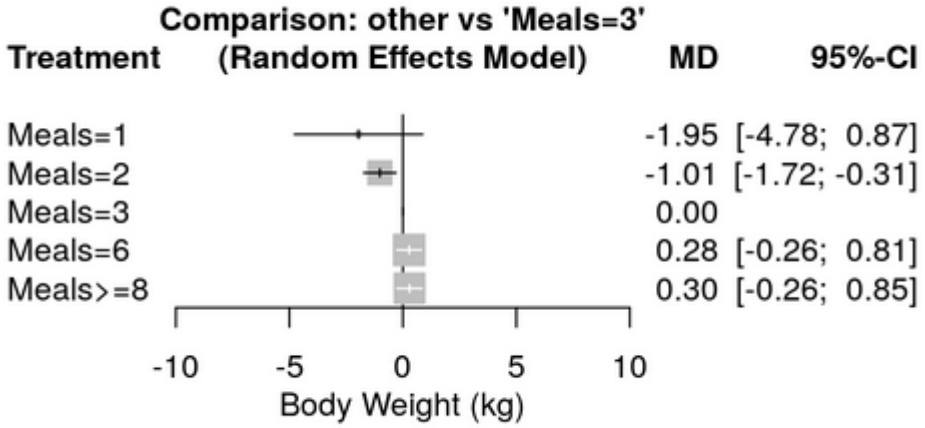
Supplemental Figure 14: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in studies with hypocaloric energy intake.



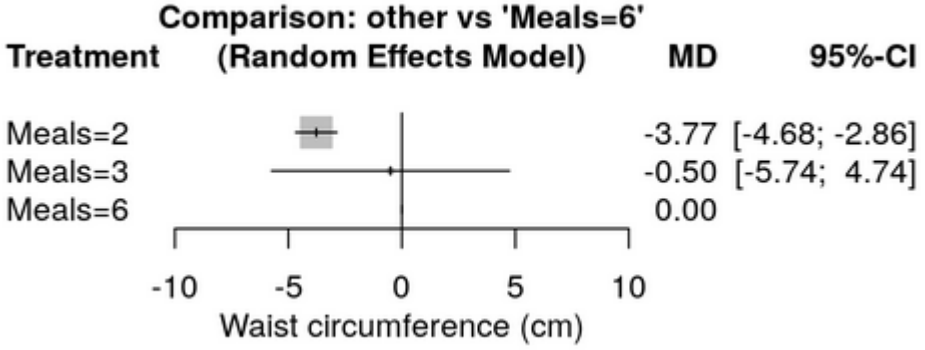
Supplemental Figure 15: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in studies with eucaloric energy intake.



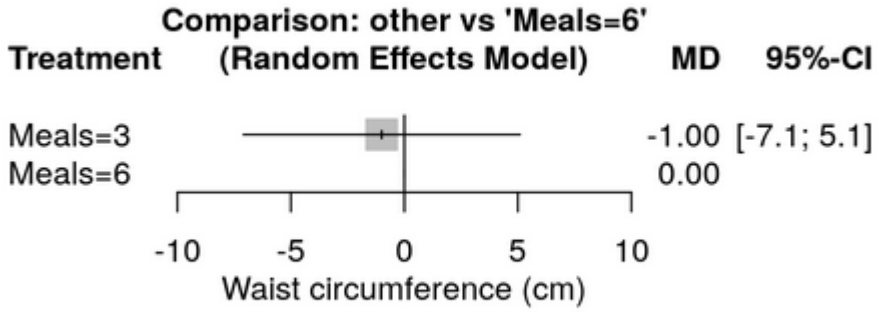
Supplemental Figure 16: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in studies with breakfast skipping.



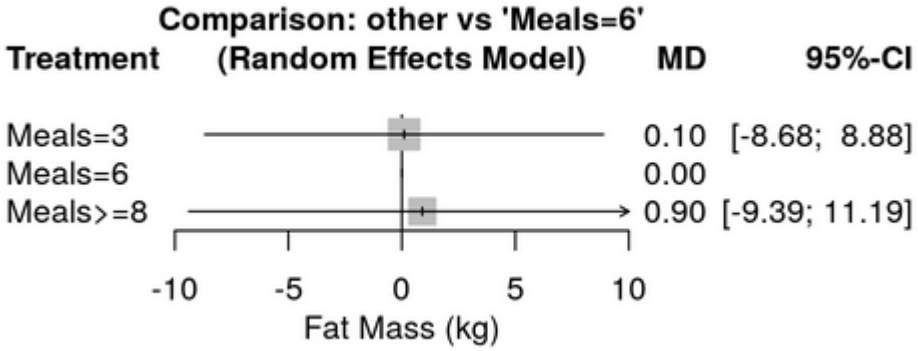
Supplemental Figure 17: Sensitivity analysis showing the summary effect estimates of different meal frequencies on body weight (kg) in studies without breakfast skipping.



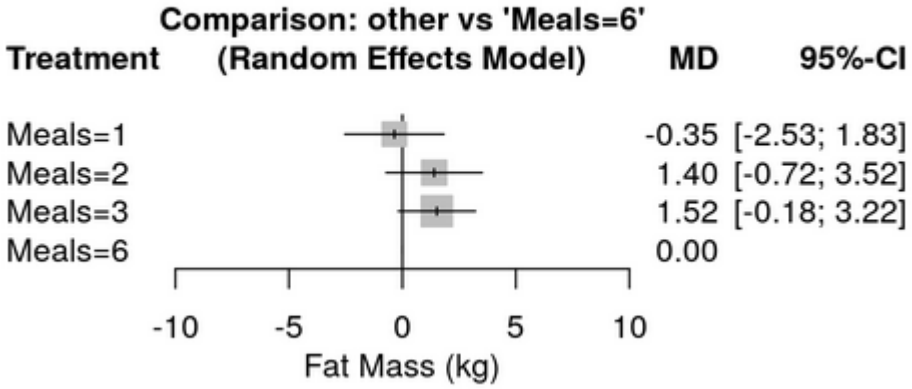
Supplemental Figure 18: Sensitivity analysis showing the summary effect estimates of different meal frequencies on waist circumference (cm) in studies with hypcaloric energy intake.



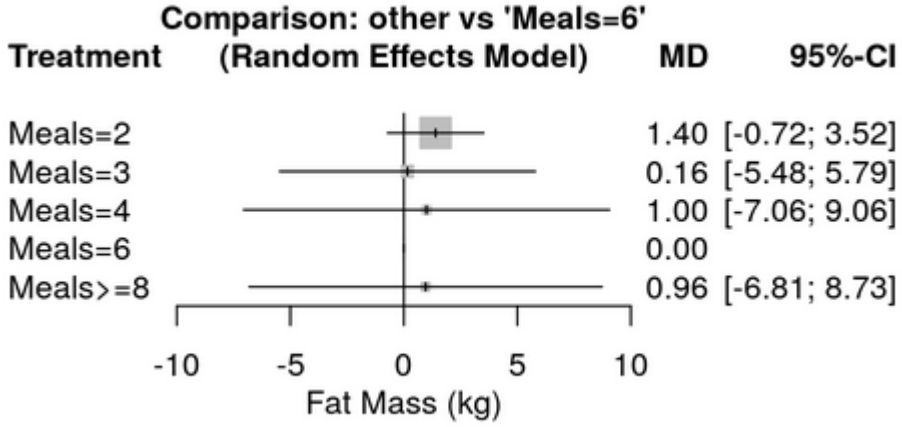
Supplemental Figure 19: Sensitivity analysis showing the summary effect estimates of different meal frequencies on waist circumference (cm) in studies with eucaloric energy intake.



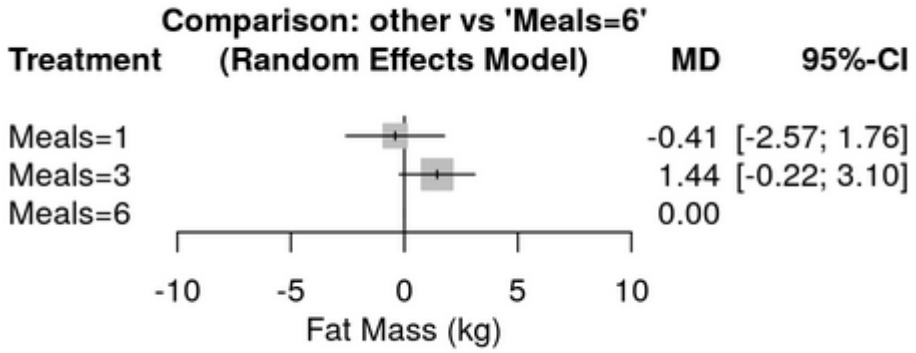
Supplemental Figure 20: Sensitivity analysis showing the summary effect estimates of different meal frequencies on fat mass (kg) in studies without provision of foods.



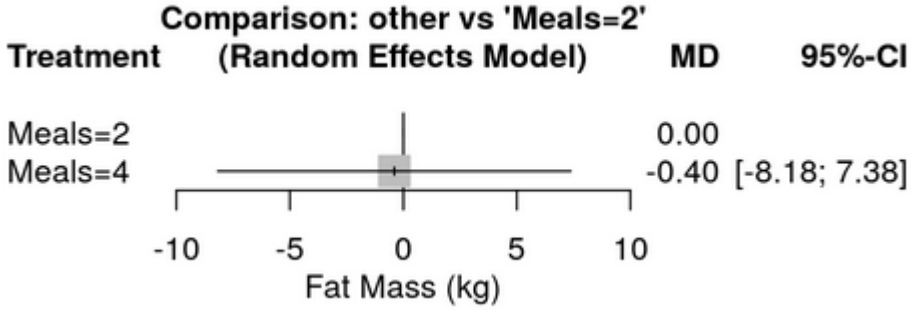
Supplemental Figure 21: Sensitivity analysis showing the summary effect estimates of different meal frequencies on fat mass (kg) in studies with provision of foods.



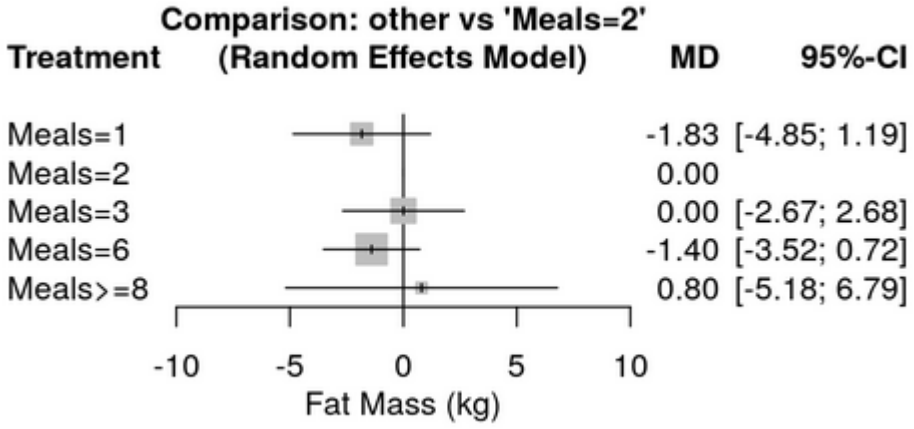
Supplemental Figure 22: Sensitivity analysis showing the summary effect estimates of different meal frequencies on fat mass (kg) in studies with hypocaloric energy intake.



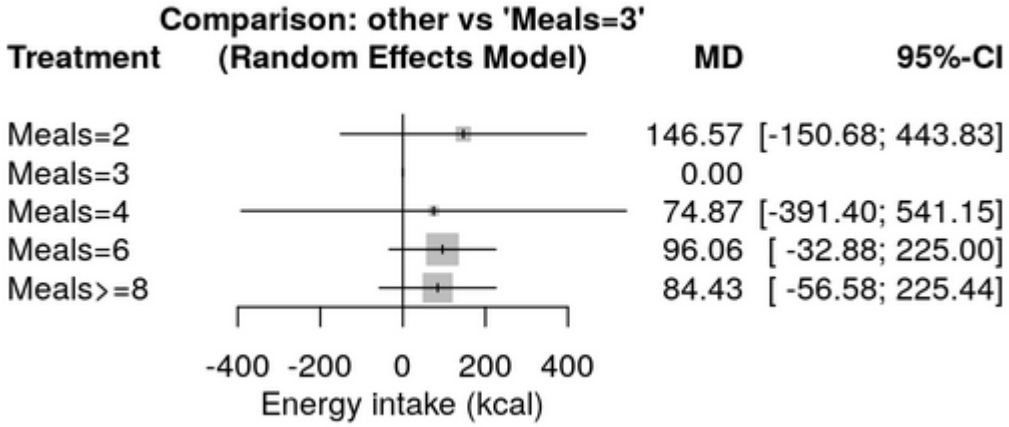
Supplemental Figure 23: Sensitivity analysis showing the summary effect estimates of different meal frequencies on fat mass (kg) in studies with eucaloric energy intake.



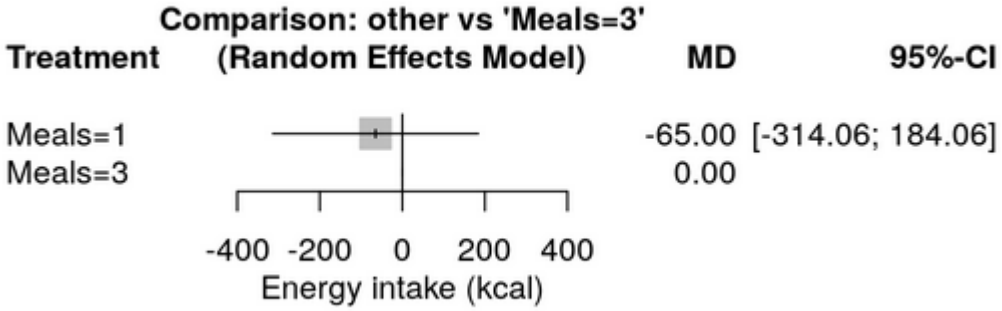
Supplemental Figure 24: Sensitivity analysis showing the summary effect estimates of different meal frequencies on fat mass (kg) in studies with breakfast skipping.



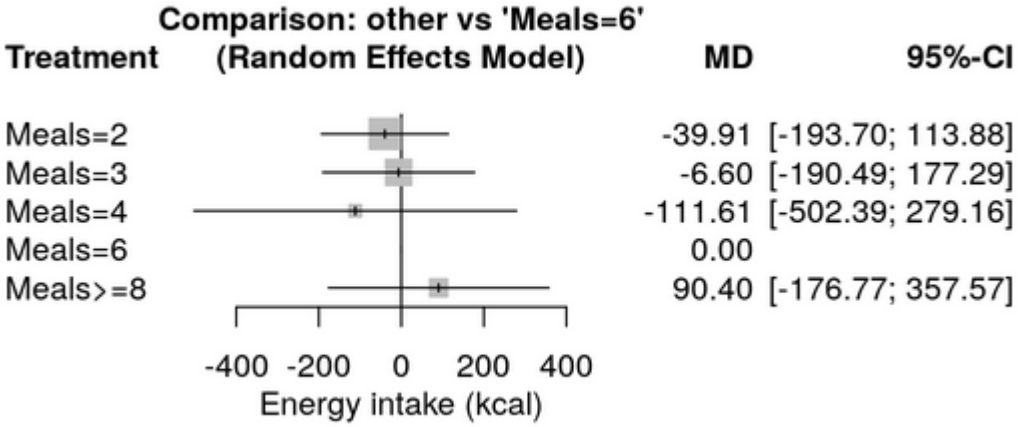
Supplemental Figure 25: Sensitivity analysis showing the summary effect estimates of different meal frequencies on fat mass (kg) in studies without breakfast skipping.



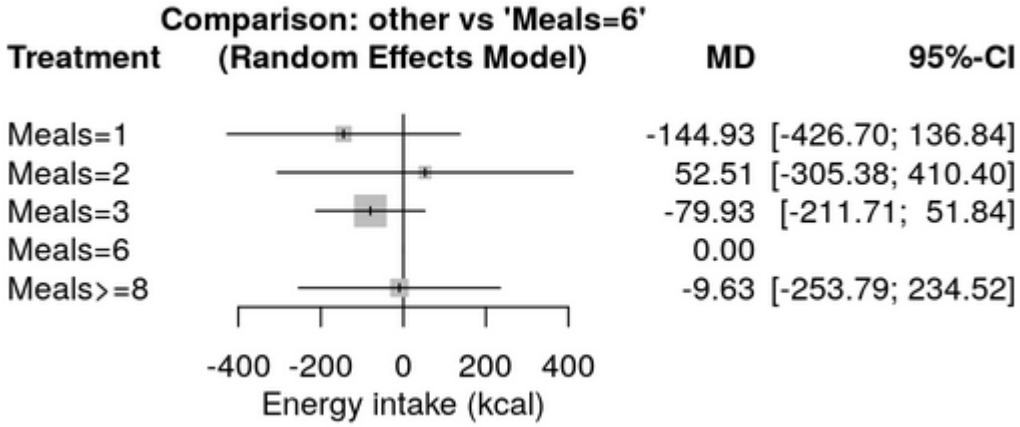
Supplemental Figure 26: Sensitivity analysis showing the summary effect estimates of different meal frequencies on energy intake (kcal/d) in studies without provision of foods.



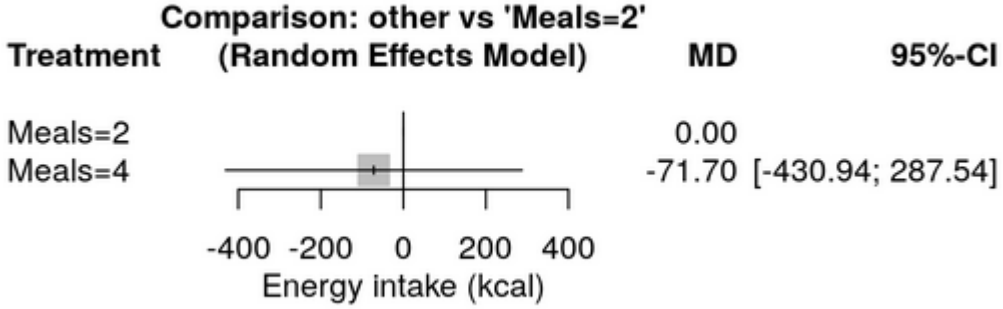
Supplemental Figure 27: Sensitivity analysis showing the summary effect estimates of different meal frequencies on energy intake (kcal/d) in studies with provision of foods.



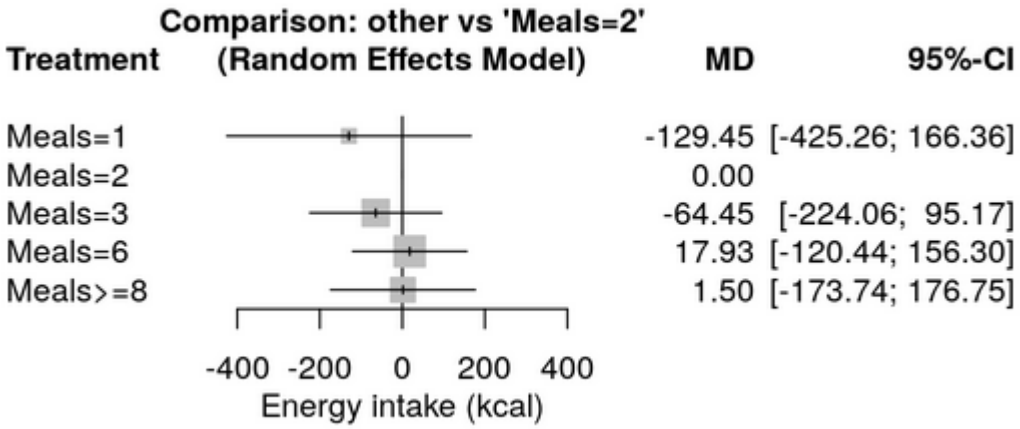
Supplemental Figure 28: Sensitivity analysis showing the summary effect estimates of different meal frequencies on energy intake (kcal/d) in studies with hypocaloric energy intake.



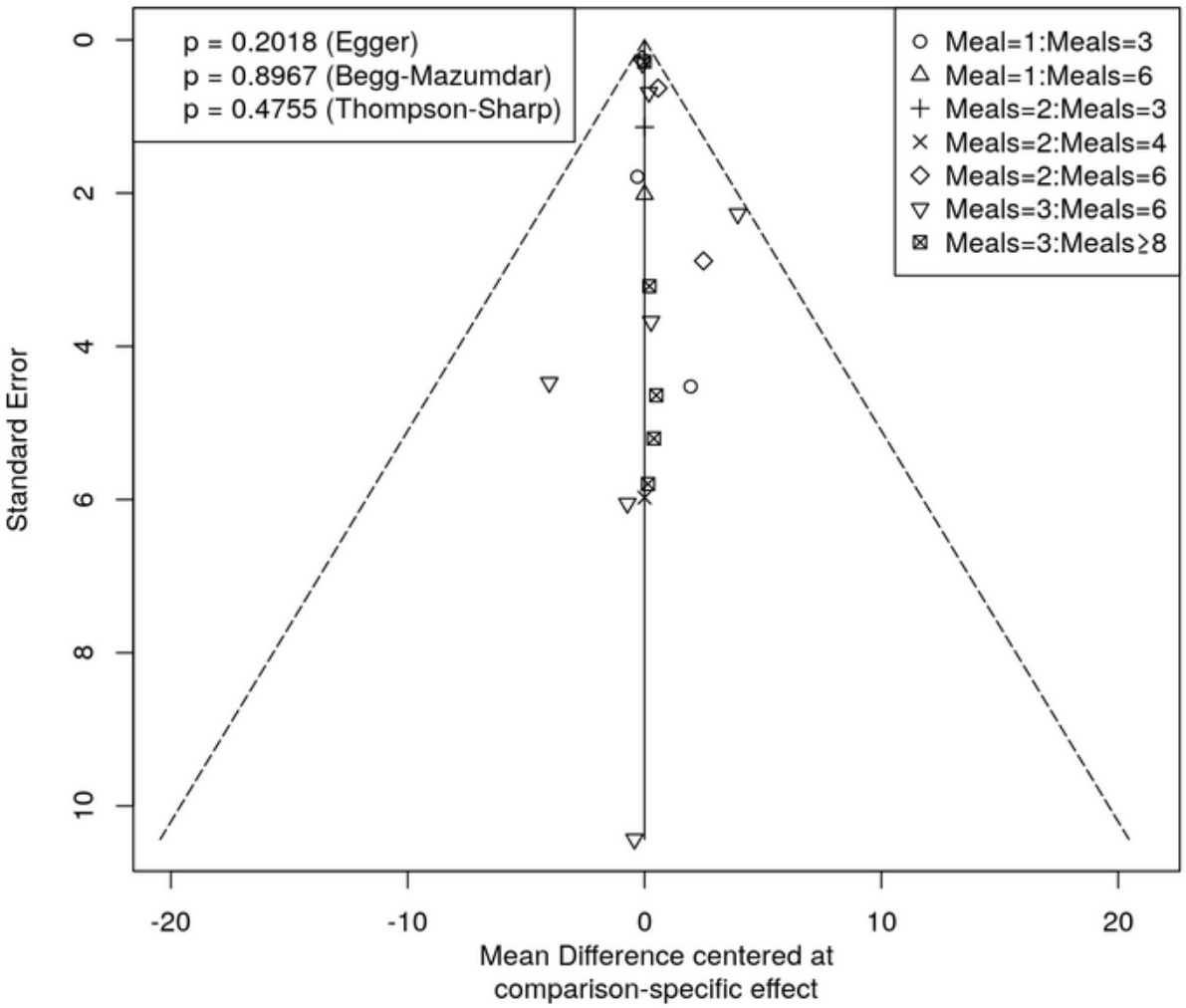
Supplemental Figure 29: Sensitivity analysis showing the summary effect estimates of different meal frequencies on energy intake (kcal/d) in studies with eucaloric energy intake.



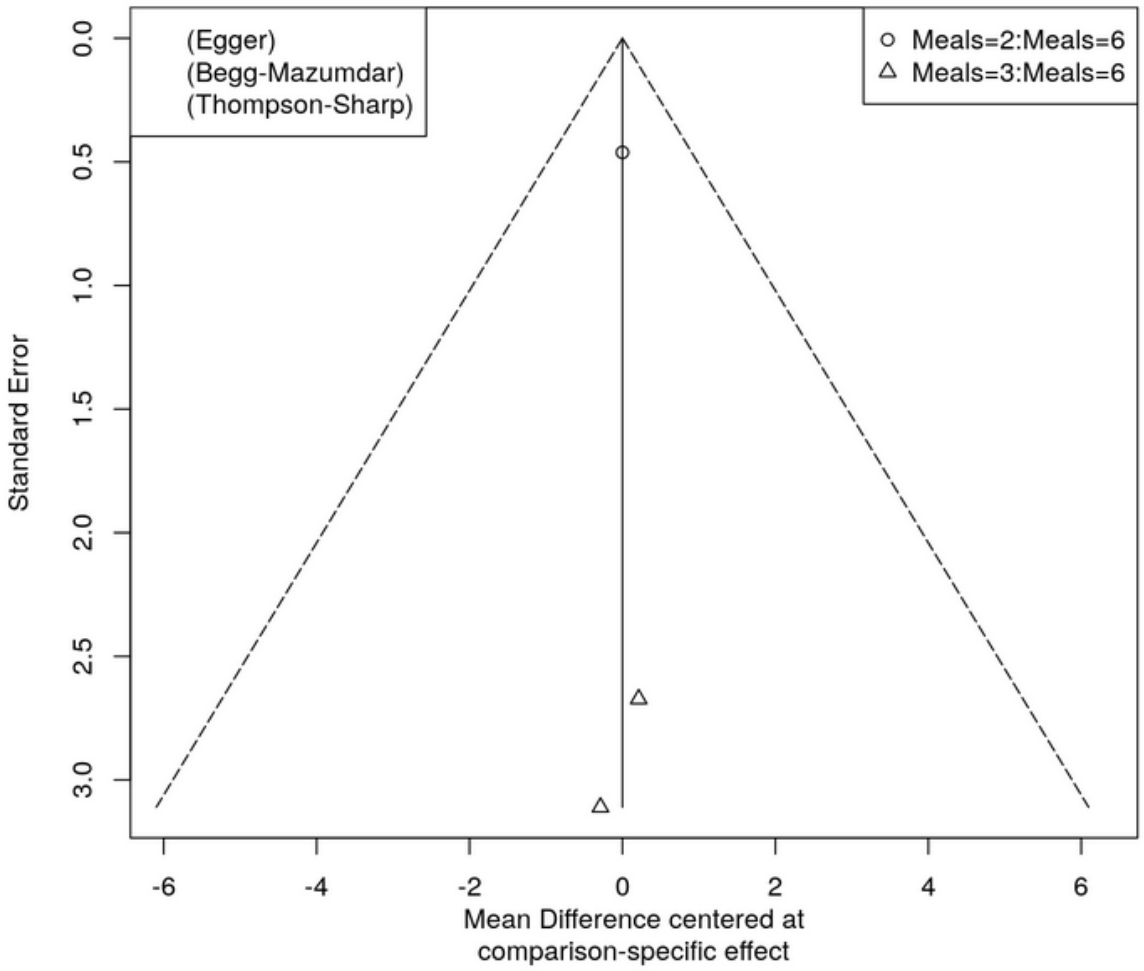
Supplemental Figure 30: Sensitivity analysis showing the summary effect estimates of different meal frequencies on energy intake (kcal/d) in studies with breakfast skipping.



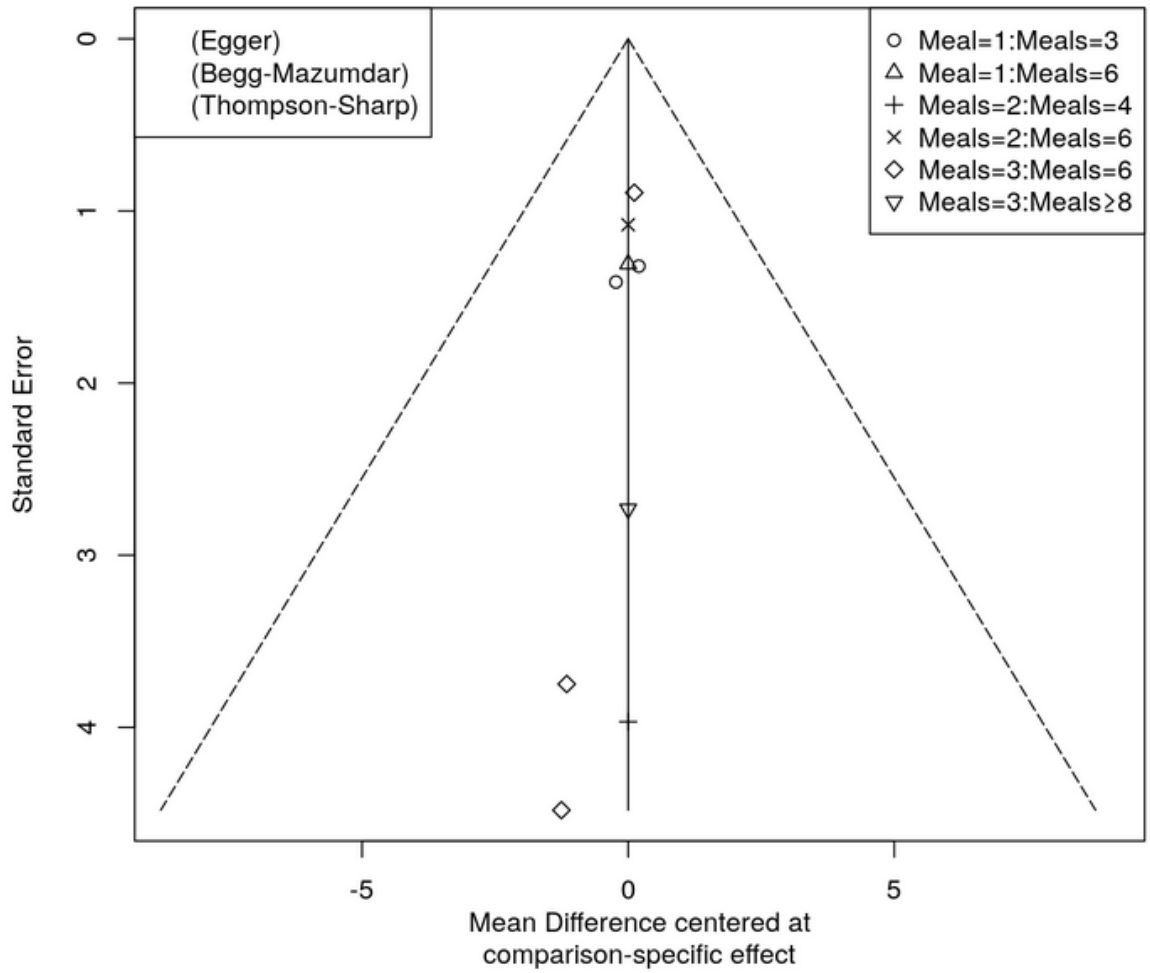
Supplemental Figure 31: Sensitivity analysis showing the summary effect estimates of different meal frequencies on energy intake (kcal/d) in studies without breakfast skipping.



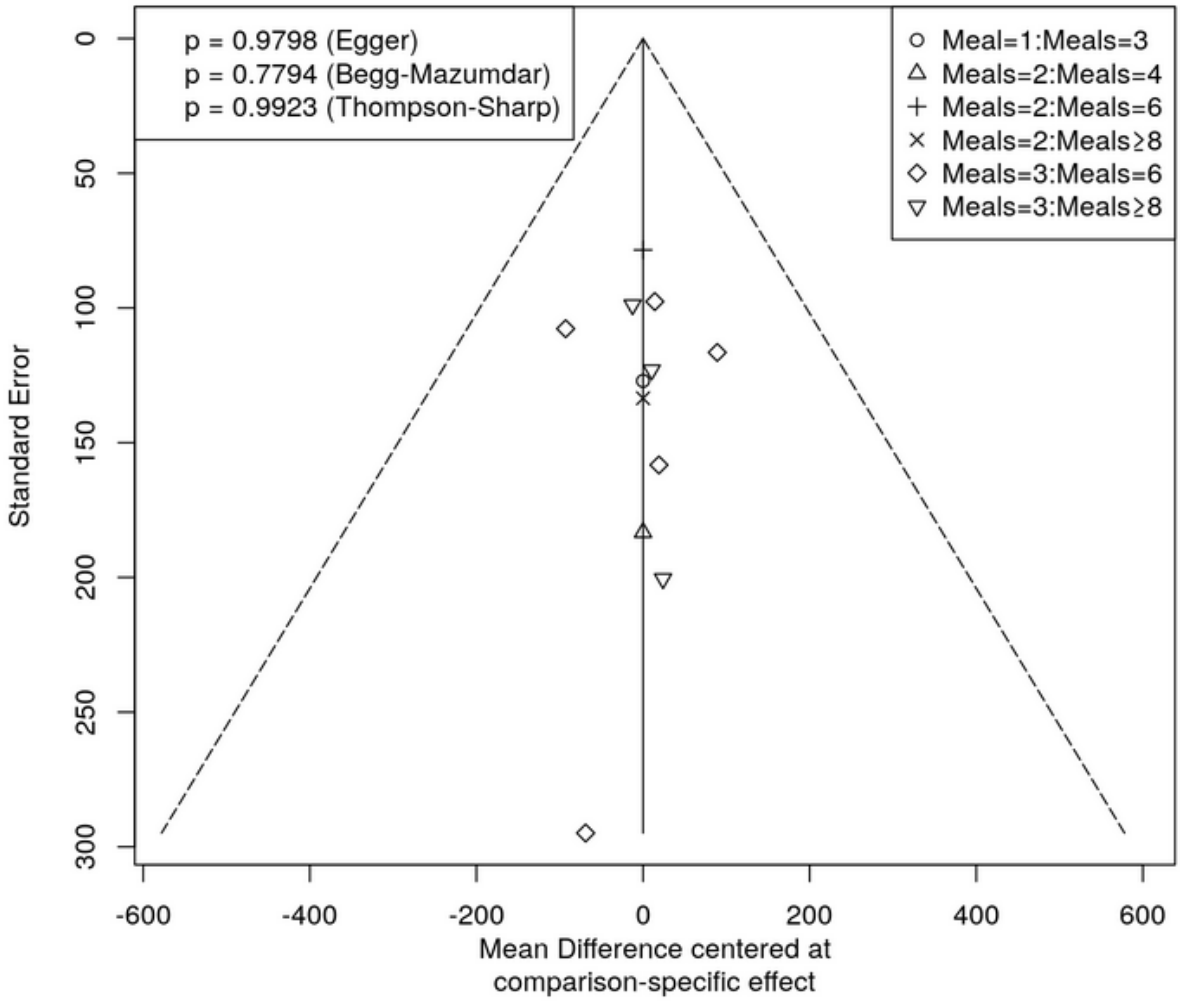
Supplemental Figure 32: Funnel plot for body weight.



Supplemental Figure 33: Funnel plot for waist circumference.



Supplemental Figure 34: Funnel plot for fat mass.



Supplemental Figure 35: Funnel plot for energy intake.

Supplemental Table 1: GRADE evaluation for waist circumference (cm) and all comparisons.*

	Direct evidence			Indirect evidence		Network meta-analysis	
Comparison (meals/d)	**N studies**	**MD (95% CI)**	**Certainty of evidence**	**MD (95% CI)**	**Certainty of evidence**	**MD (95% CI)**	**Certainty of evidence**
2 vs. 3	0	-	-	-3.06 (-7.13, 1.02)	⊕⊕⊕◯	-3.06 (-7.13, 1.02)	⊕⊕◯◯ [1]
2 vs. 6	1	-3.77 (-4.68, -2.86)	⊕⊕⊕◯ [2]	-	-	-3.77 (-4.68, -2.86)	⊕⊕⊕◯
3 vs. 6	2	-0.71 (-4.68, 3.26)	⊕⊕⊕◯ [2]	-	-	-0.71 (-4.68, 3.26)	⊕⊕◯◯ [1]

MD: mean difference; CI: confidence interval;

Certainty of evidence grading: ⊕⊕⊕⊕ High; ⊕⊕⊕◯ Moderate; ⊕⊕◯◯ Low; ⊕◯◯◯ Very low.

[1] downgraded due to imprecision (95% CI overlaps important benefit: -2 cm; or important harm: +2 cm), [2] downgraded due to risk of bias (at least 1 RCT with high risk of bias).

*Direct estimates were evaluated with the following GRADE criteria: risk of bias, indirectness, inconsistency and publication bias. As suggested recently by the GRADE working group, consideration of imprecision is not necessary when rating the direct and indirect estimates to inform the rating of NMA estimates.

Supplemental Table 2: GRADE evaluation for fat mass (kg) and all comparisons.*

	Direct evidence			Indirect evidence		Network meta-analysis	
Comparison (meals/d)	**N studies**	**MD (95% CI)**	**Certainty of evidence**	**MD (95% CI)**	**Certainty of evidence**	**MD (95% CI)**	**Certainty of evidence**
1 vs. 2	0	-	-	-1.83 (-4.85, 1.19)	⊕◯◯◯ [6]	-1.83 (-4.85, 1.19)	⊕◯◯◯ [2]
1 vs. 3	2	-1.87 (-3.76, 0.02)	⊕⊕◯◯ [1, 3]	3.83 (-20.78, 28.43)	⊕◯◯◯ [6]	-1.84 (-3.72, 0.05)	⊕◯◯◯ [2, 4, 5]
1 vs. 4	0	-	-	-1.43 (-9.78, 6.91)	⊕◯◯◯ [6]	-1.43 (-9.78, 6.91)	⊕◯◯◯ [2 (↓↓)]
1 vs. 6	1	-0.20 (-2.76, 2.36)	⊕⊕⊕◯ [3]	-0.99 (-4.97, 2.98)	⊕◯◯◯ [6]	-0.43(-2.59, 1.72)	⊕⊕◯◯ [2, 4, 5]
1 vs. ≥8	0	-	-	2.64 (-3.04, 8.31)	⊕◯◯◯ [6]	2.64 (-3.04, 8.31)	⊕◯◯◯ [2 (↓↓)]
2 vs. 3	0	-	-	-0.00 (-2.68, 2.67)	⊕⊕◯◯ [6]	-0.00 (-2.68, 2.67)	⊕◯◯◯ [2]
2 vs. 4	1	0.40 (-7.38, 8.18)	⊕⊕⊕⊕	-	-	0.40 (-7.38, 8.18)	⊕⊕◯◯ [2 (↓↓)]
2 vs. 6	1	1.40 (-0.71, 3.52)	⊕⊕⊕◯ [3]	-	-	1.40 (-0.71, 3.52)	⊕⊕◯◯ [2]
2 vs. ≥8	0	-	-	0.80 (-5.18, 6.79)	⊕◯◯◯ [6]	0.80 (-5.18, 6.79)	⊕◯◯◯ [2 (↓↓)]
3 vs. 4	0	-	-	0.40 (-7.82, 8.63)	⊕◯◯◯ [6]	0.40 (-7.82, 8.63)	⊕◯◯◯ [2]
3 vs. 6	3	1.35 (-0.32, 3.03)	⊕⊕⊕◯ [3]	2.30 (-4.77, 9.36)	⊕◯◯◯ [6]	1.40 (-0.22, 3.03)	⊕⊕◯◯ [2, 4]
3 vs. ≥8	1	0.80 (-4.55, 6.15)	⊕⊕⊕⊕	-	-	0.80 (-4.55, 6.15)	⊕⊕◯◯ [2 (↓↓)]
4 vs. 6	0	-	-	1.00 (-7.06, 9.06)	⊕◯◯◯ [6]	1.00 (-7.06, 9.06)	⊕◯◯◯ [2 (↓↓)]
4 vs. ≥8	0	-	-	1.20 (-8.61, 11.02)	⊕◯◯◯ [6]	1.20 (-8.61, 11.02)	⊕◯◯◯ [2 (↓↓)]
6 vs. ≥8	0	-	-	2.20 (-3.39, 7.80)	⊕◯◯◯ [6]	2.20 (-3.39, 7.80)	⊕◯◯◯ [2 (↓↓)]

MD: mean difference; CI: confidence interval;

Certainty of evidence grading: ⊕⊕⊕⊕ High; ⊕⊕⊕◯ Moderate; ⊕⊕◯◯ Low; ⊕◯◯◯ Very low.

[1] downgraded due to inconsistency (I^2 ≥50%), [2] downgraded due to imprecision (95% CI overlaps important benefit: -1 kg; or important harm: +1 kg), [3] downgraded due to risk of bias (at least 1 RCTs with high risk of bias), [4] direct evidence contributing more to the NMA estimate (>50%), [5] not downgraded due to incoherence (dominant estimate similar to network estimate), [6] downgraded due to intransitivity (i.e. patients with obesity and healthy participants included).

*Direct estimates were evaluated with the following GRADE criteria: risk of bias, indirectness, inconsistency and publication bias. As suggested recently by the GRADE working group, consideration of imprecision is not necessary when rating the direct and indirect estimates to inform the rating of NMA estimates.

Supplemental Table 3: GRADE evaluation for energy intake (kcal/d) and all comparisons.*

	Direct evidence			Indirect evidence		Network meta-analysis	
Comparison	**N studies**	**MD (95% CI)**	**Certainty of evidence**	**MD (95% CI)**	**Certainty of evidence**	**MD (95% CI)**	**Certainty of evidence**
1 vs. 2	0	-	-	-129 (-425, 166)	⊕⊕◯◯ [5]	-129 (-425, 166)	⊕◯◯◯ [4]
1 vs. 3	1	-65 (-314, 184)	⊕⊕⊕◯ [2]	-	-	-65 (-314, 184)	⊕⊕◯◯ [4]
1 vs. 4	0	-	-	-58 (-523, 408)	⊕⊕◯◯ [5]	-58 (-523, 408)	⊕◯◯◯ [4 (↓↓)]
1 vs. 6	0	-	-	-147 (-418, 123)	⊕⊕◯◯ [5]	-147 (-418, 123)	⊕◯◯◯ [4]
1 vs. ≥8	0	-	-	-131 (-412, 150)	⊕⊕◯◯ [5]	-131 (-412, 150)	⊕◯◯◯ [4]
2 vs. 3	0	-	-	64 (-95, 224)	⊕⊕◯◯ [5]	64 (-95, 224)	⊕◯◯◯ [4]
2 vs. 4	1	72 (-288, 431)	⊕⊕⊕⊕	-	-	72 (-288, 431)	⊕⊕◯◯ [4 (↓↓)]
2 vs. 6	1	-40 (-194, 114)	⊕⊕⊕◯ [2]	75 (-242, 393)	⊕⊕◯◯ [5]	-18 (-156, 120)	⊕⊕◯◯ [1, 3, 4]
2 vs. ≥8	1	62 (-200, 324)	⊕⊕⊕⊕	-53 (-289, 183)	⊕⊕⊕◯ [5]	-2 (-177, 174)	⊕⊕◯◯ [1, 4]
3 vs. 4	0	-	-	7 (-386, 400)	⊕⊕◯◯ [5]	7 (-386, 400)	⊕◯◯◯ [4 (↓↓)]
3 vs. 6	5	-71 (-181, 39)	⊕⊕⊕◯ [2]	-186 (-521, 148)	⊕⊕◯◯ [5]	-82 (-187, 22)	⊕⊕◯◯ [3, 4]
3 vs. ≥8	3	-84 (-225, 57)	⊕⊕⊕◯ [2]	31 (-292, 354)	⊕⊕◯◯ [5]	-66 (-195,63)	⊕⊕◯◯ [1, 3, 4]
4 vs. 6	0	-	-	-89 (-475, 295)	⊕⊕◯◯ [5]	-89 (-475, 295)	⊕◯◯◯ [4 (↓↓)]
4 vs. ≥8	0	-	-	-73 (-473, 326)	⊕⊕◯◯ [5]	-73 (-473, 326)	⊕◯◯◯ [4 (↓↓)]
6 vs. ≥8	0	-	-	-16 (-138, 171)	⊕⊕◯◯ [5]	-16 (-138, 171)	⊕◯◯◯ [4]

MD: mean difference; CI: confidence interval; ⊕⊕⊕⊕ High; ⊕⊕⊕◯ Moderate; ⊕⊕◯◯ Low; ⊕◯◯◯ Very low.

[1] not downgraded due to incoherence (dominant estimate similar to network estimate), [2] downgraded due to risk of bias (at least 1 RCTs with high risk of bias), [3] direct evidence contributing more to the NMA estimate (>50%), [4] downgraded due to imprecision (95% CI overlaps important benefit: -100 kcal/d; or important harm: 100 kcal/d), [5] downgraded due to intransitivity (i.e. obese and healthy included).

*Direct estimates were evaluated with the following GRADE criteria: risk of bias, indirectness, inconsistency and publication bias. As suggested recently by the GRADE working group, consideration of imprecision (important benefit: -100 kcal/d; or important harm: +100 kcal/d) is not necessary when rating the direct and indirect estimates to inform the rating of NMA estimates.