INTERMITTENT ENERGY RESTRICTION / INTERMITTENT FASTING

Sponsor

Nestlé Health Science Optifast® VLCD™

Overview

- What is intermittent energy restriction (IER)
- Rationale for IER
- Variations of IER
- Systematic Reviews and Meta-analyses of IER
- Severe Energy Restriction / Very Low Energy Diets (VLEDs)
- Discussion / Questions

What is intermittent fasting / intermittent energy restriction (IER)?

Cycle between:

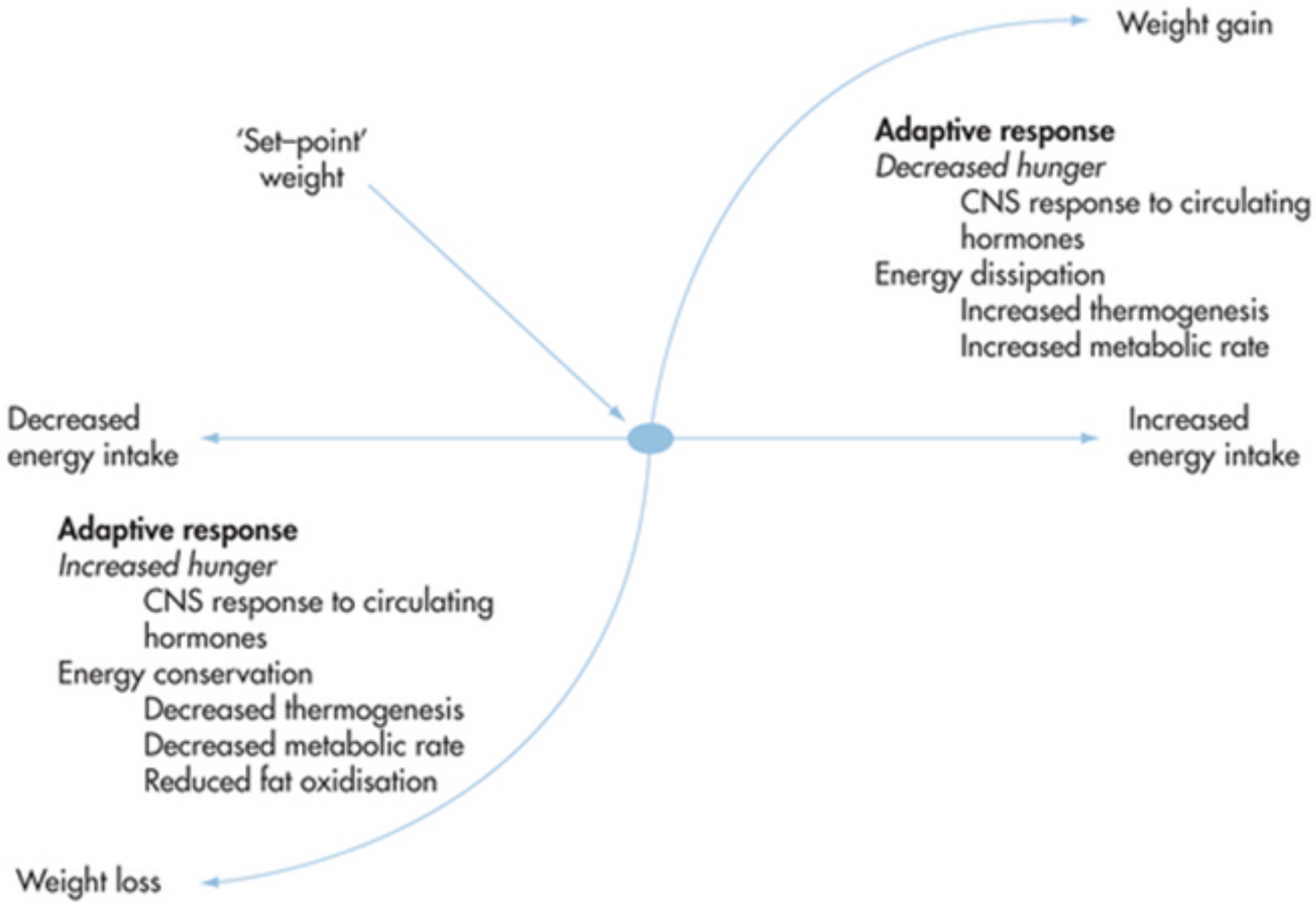
Periods of feeding / energy balance ('Feed day')

and

Periods of total fasting / severe energy restriction (~2000 - 2500 kJ/day) ('Fast day')

Daily energy restriction or continuous energy restriction (CER)

Adaptive Response to Energy Restriction



Rationale for intermittent energy restriction

- Can periods of energy balance during energy restriction attenuate / deactivate adaptive responses?
- More acceptable and easier to follow than daily restriction / continuous energy restriction (CER)?


The 8-Hour Diet
Lose the Weight and Change Your Life with a Plan so Easy, it's Like Clockwork
David Zinczenko Editor-in-Chief of Men'sHealth
THE 5:2 DIET
INTERMITTENT FASTING
THE 10 STEP BEGINNERS GUIDE TO THE 5:2 DIET EASILY LOSE WEIGHT AND LIVE A HEALTHY LIFE
INTERMITTENT FASTING
THIS BOOK INCLUDES:
5:2 BIKINI DIET
Eat Stop Eat
Expanded 5th Edition
INTERMITTENT FASTING
You Need To Know
JAMES BROWN
DR. MICHAEL VANDERSCHELDEN
THE SCIENTIFIC APPROACH TO INTERMITTENT FASTING
INTERMITTENT FASTING
2 books in 1 on Maximizing Weight Loss-Intermittent Fasting and Rapid Fat Loss Mastery
NICK JACKSON
Intermittent Fasting FOR WOMEN
THE NO-BULLSHIT GUIDE TO EFFORTLESS FAT LOSS
Joe Petrakovich
INTERMITTENT FASTING
5-STEP SYSTEM
KAYLA BATES
SMOOREN
LIZ ARMOND
The 5:2 FAST
For Begin
Ravi Kis
INTERMITTENT FASTING
Everything You Need to Know About Intermittent Fasting From Beginner to Expert
Build Lean Muscle and
JAMES SIN
COMPLETE
to
Heal Your Body Through Intermittent, Alternate-Day, and Extended Fasting
Jason Fung, MD
with Jimmy Moore
BY THE DOCTOR WHO INTRODUCED THE FASTING TREND TO THE WORLD
Dr Krista Varady and Bill Gottlieb
THE EVERY OTHER DAY DIET
4 WEEKS. 5 KG. 2 SIZES.
The only fasting diet proven by science
YOUR COMPLETE GUIDE TO THE FASTING REVOLUTION
THE 5:2 DIET BOOK
KATE HARRISON
The Every Other Day Diet
4 Weeks, 12 Pounds, 2 Sizes.
DR MICHAEL MOSLEY & MIMI SPENCER
the fast diet
FULL GUIDE
INTERMITTENT FASTING
SIIM LAND
THE ALTERNATE DIET
5:2 DIET
BREAKFAST RECIPES
OVER 50 EASY BREAKFASTS UNDER 200 CALORIES
LIZ ARMOND
INTERMITTENT FASTING
THE 5:2 DIET
Lose Weight
Live Longer
Feel Great
Plant-Based
INTERMITTENT FASTING
REA J. CLARK
Intermittent FASTING
ROBERT MCGOWAN
the 2 day diet
Diet two days a week. Eat normally for five.
Dr Michelle Harvie & Prof Tony Howell
JAMES B. JOHNSON, MD with Donald R. Laub, Sr, MD
The Alternate-Day Diet
Diet only HALF the time!
Turn on your 'skinny gene'
Shed the pounds
Live a longer and healthier life
Includes more than 30 low-calorie, nutrient-rich recipes
THE WARRIOR DIET
Switch on Your Biological Powerhouse–For High Energy, Explosive Strength, and a Leaner, Harder Body
ORI HOFMEKLER
Diet for Beginners
A Quick Start Guide to Intermittent Fasting, Rapid Weight Loss and a Long Healthy Life
Gina Crawford
DELAY, DON'T DENY
THE INTERMITTENT FASTING WEIGHT LOSS FORMULA
ROBERT DAVE JOHNSTON
Daily or 5
Life
5:2 Diet
pes for Men

Variations of intermittent energy restriction

- ***Time-Restricted Feeding (TRF):***
  8/6/4 hours feeding, 16/18/20 hours fasting

- ***Alternate Day "Fasting" (ADF):***
  75% energy restriction on 'fast' day alternated with a 'feed' day

- ***5:2 Diet:***
  'Fast' on 2 consecutive or non-consecutive days/week

- ***Warrior Diet:***
  Fast during the day and have one large meal at night

- ***Eat Stop Eat:***
  'Fast' for 24 hours 1-2 days/week

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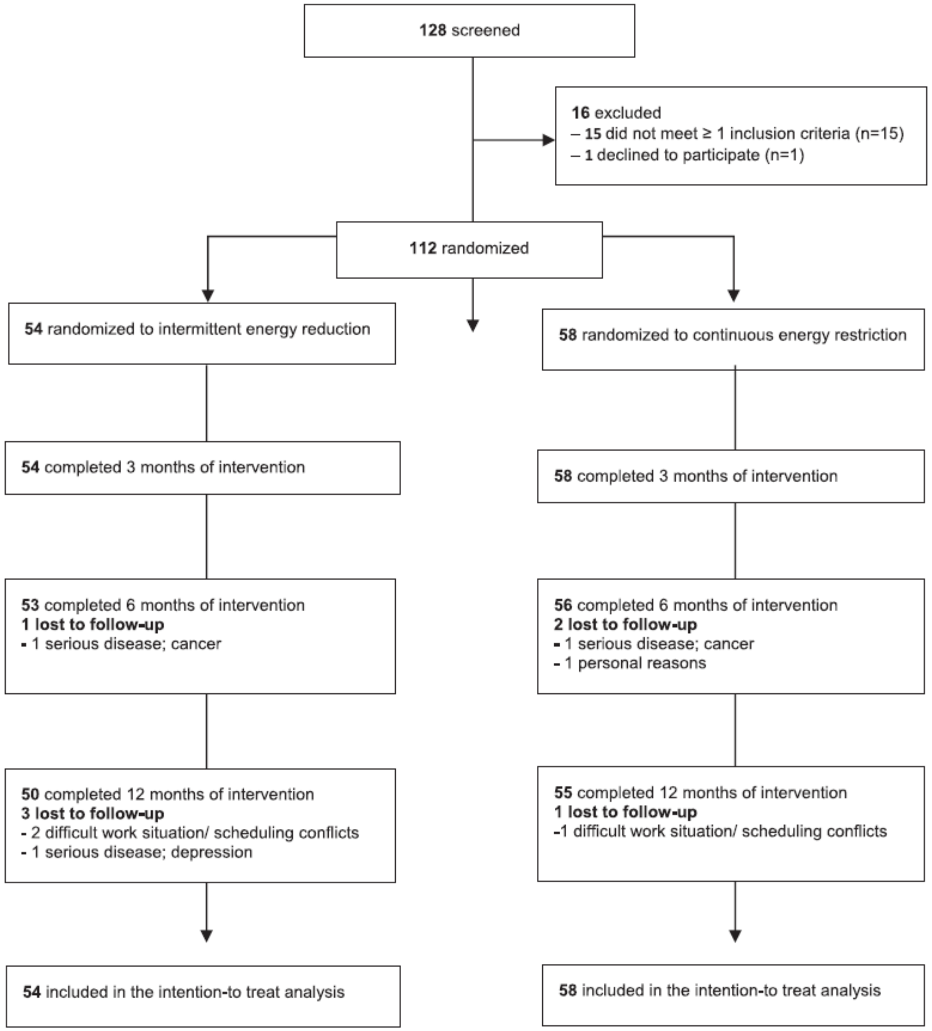
5:2 DIETS

Effects of 5:2 (non-consecutive days) vs CER in adults during a 12-month period

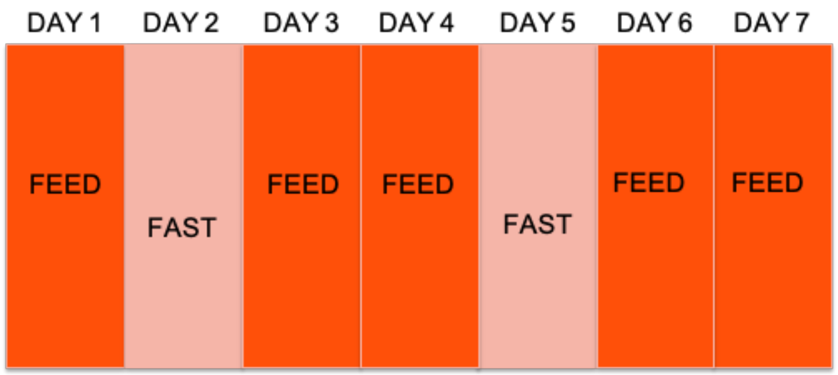
- N = 112, 30-45 kg/m^2
- Randomized to IER or CER (6-month weight-loss) then 6-month maintenance



Sundfør, Nutr Metab Cardiovasc, 2018

Effects of 5:2 (non-consecutive days) vs CER in adults during a 12-month period

- Randomized to IER or CER
  - CER: reduce energy intake evenly 7 days / week
  - 5:2: 400/600 kcal (female/male) on two non-consecutive, usual diet for 5 days



Example of 5:2 diet (non-consecutive days)

Sundfør, Nutr Metab Cardiovasc, 2018

Both IER and CER resulted in similar weight loss and improvements in cardiovascular risk factors after 1 year

- Weight loss similar in IER and CER groups (8 - 9 kg)

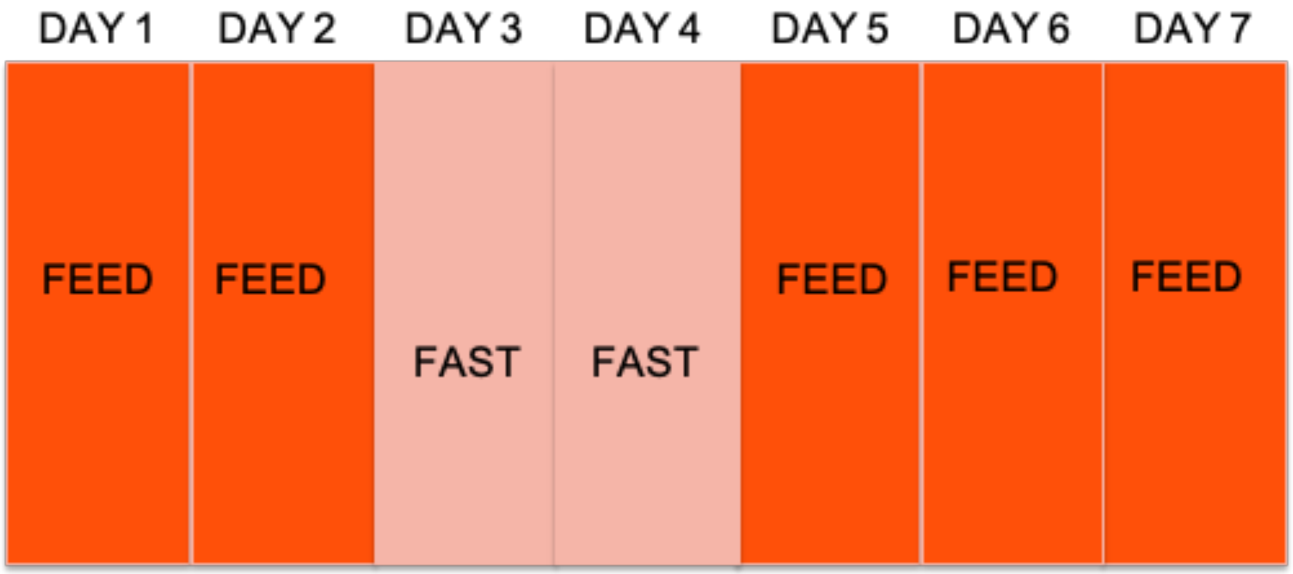
- Improvements in both groups with no difference between groups:
  - Waist circumference,
  - blood pressure,
  - triglycerides and HDL-cholesterol

- Weight regain was minimal and similar between IER and CER

- IER reported higher hunger scores than CER

Sundfør Nutr Metab Cardiovasc 2018,
Conley Nutr Diet 2018

Effects of 5:2 (consecutive days) vs CER in adults



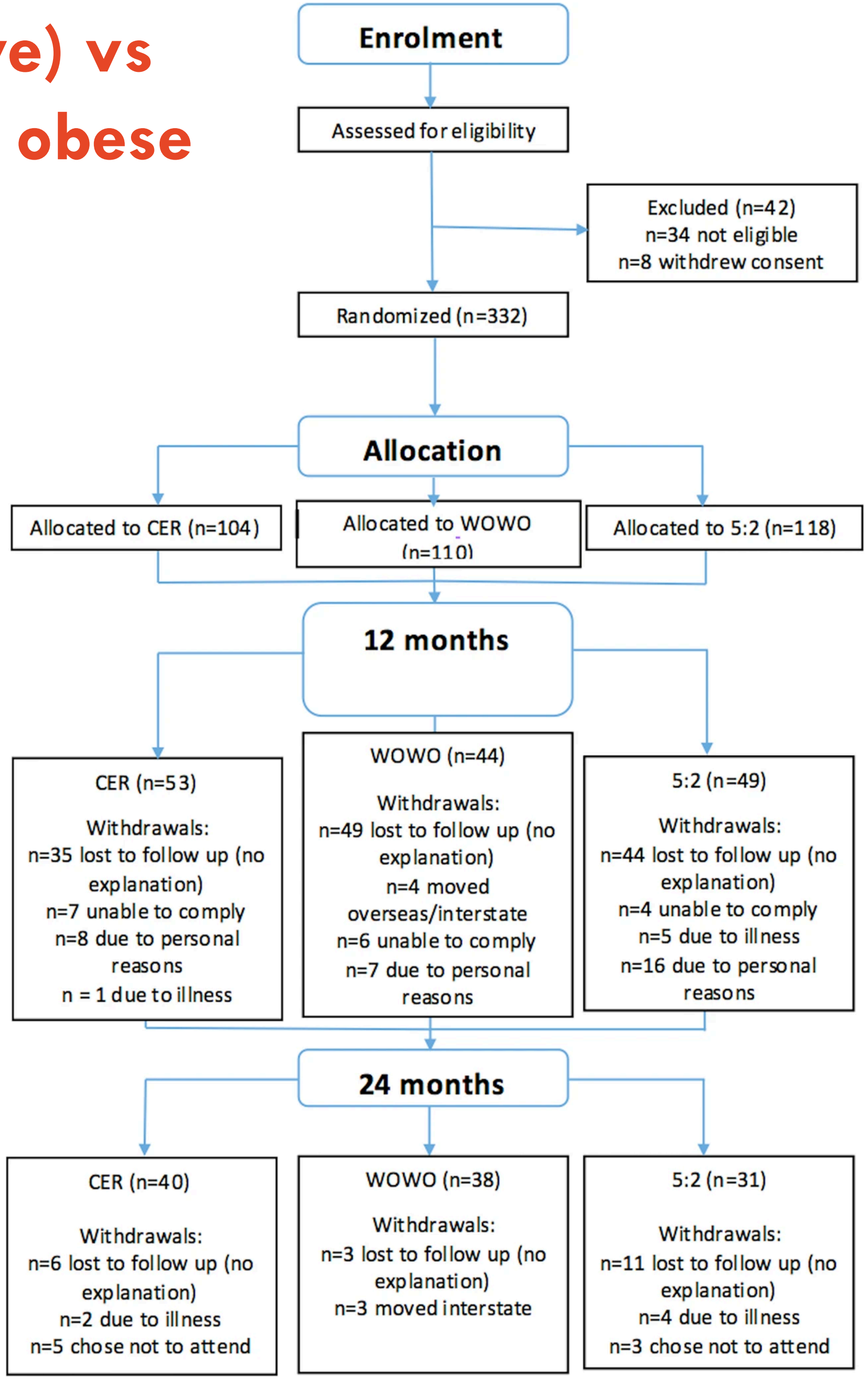
5:2 (consecutive days) as effective as CER in weight loss, insulin sensitivity and health biomarkers

- IER and CER equally effective for weight loss
- Both groups experienced comparable reductions in:
  - Leptin
  - Free androgen index
  - High sensitivity C-reactive protein
  - Total and LDL cholesterol, triglycerides
  - Blood pressure
- ↑ Sex hormone binding globulin, IGF binding proteins 1and 2
- ↓ Fasting insulin, insulin resistance, greater with IER than CER
- ↔ time to attain 5 % weight loss between groups

Harvie IJO 2011, Antoni British J nutr 2018

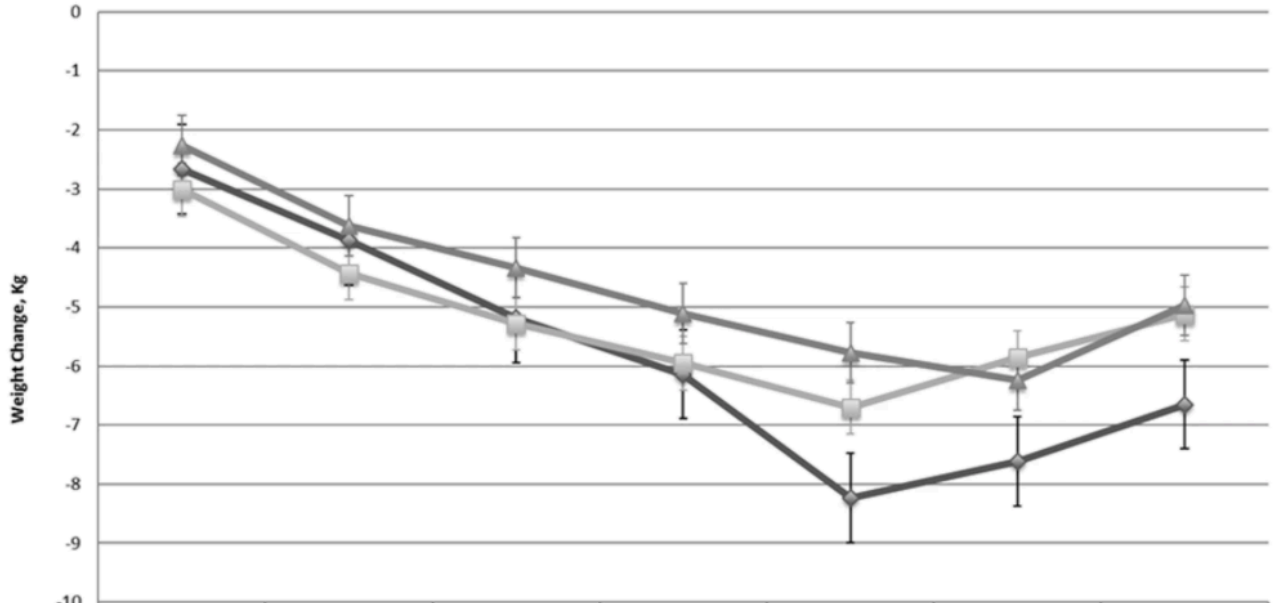
IER (consecutive/non-consecutive) vs CER in adults with overweight / obese during 12- and 24- months

- N = 332
- Randomised to 3 groups:
  - CER: Women: 4200 kJ/d; Men: 5040 kJ/d
  - Week-on-week-off: alternating between same energy restriction as CER and habitual diet
  - 5:2: Women: 2100 kJ/d; Men: 2520 kJ/d on 2 days of energy restriction, consecutive or non-consecutive



Headland ML R IJO 2018,
Headland ML R IJO 2020

IER not different for weight loss, cardiometabolic risk factors vs CER after 12 months in adults with overweight / obesity



	2 Weeks/4 Weeks	4 Weeks/8 Weeks	6 Weeks/12 Weeks	8 Weeks/16 Weeks	28 Weeks	40 Weeks	52 Weeks
CER	-2.66	-3.87	-5.19	-6.14	-8.24	-7.61	-6.65
WOWO	-3.01	-4.43	-5.28	-5.95	-6.7	-5.85	-5.12
5:2	-2.27	-3.63	-4.33	-5.11	-5.78	-6.24	-4.97

- Similar dropout rate
- No difference between groups in body fat, HDL-cholesterol and triglycerides at 12 months
- No changes in fasting glucose or LDL-cholesterol

Headland ML R IJO 2018

24-months follow-up

		Time (weeks)				*P* value (time)	*P* value[a]	*P* value[b]
	n	0	8/16	52	104			
Weight (kg)	109	90.3 ± 15.3	84.5 ± 14.8	84.4 ± 15.5	86.7 ± 15.8	<0.001	0.06	0.71
BMI (kg/m^2)	109	33.0 ± 4.5	30.9 ± 4.4	30.9 ± 4.7	31.7 ± 4.9	<0.001	0.12	0.78
Fat mass (kg)	91	40.3 ± 10.5	36.3 ± 11.1	35.3 ± 11.1	37.2 ± 11.5	<0.001	0.09	0.69
Lean mass (kg)	91	47.9 ± 9.7	46.3 ± 9.6	47.0 ± 9.6	47.2 ± 9.2	<0.001	0.40	0.78
Glucose	109	5.6 ± 0.5	5.5 ± 0.6	5.5 ± 0.6	5.5 ± 1.2	0.51	0.41	0.37
Total cholesterol	109	6.0 ± 1.1	5.7 ± 1.1	6.0 ± 1.1	5.9 ± 0.9	0.02	0.65	0.75
HDL	109	1.5 ± 0.5	1.5 ± 0.4	1.6 ± 0.4	1.3 ± 0.4	0.50	0.86	0.58
LDL	109	4.1 ± 1.1	4.0 ± 1.1	4.2 ± 1.1	4.0 ± 1.0	0.26	0.55	0.65
Triglycerides	109	1.4 ± 0.7	1.1 ± 0.5	1.2 ± 0.6	1.4 ± 0.7	0.90	0.50	0.20

[a]P value between WOWO and CER at 104 weeks

[b]P value between 5:2 and CER at 104 weeks time by diet effect

Headland ML R IJO 2020

Spontaneous reduction in energy intake on unrestricted days

TABLE 2 Energy intake at baseline and on the different unrestricted days of intermittent energy restriction in Study 1 (n = 44) and Study 2 (n = 67) in (kJ/day)

	Baseline reported intake	Recommended intake on unrestricted day, 93% of estimated energy requirements	Day immediately before restricted day	Other un-restricted day	Mean (95% CI) difference between days immediately before and other unrestricted day	p value Day immediately before and other unrestricted day	Day immediately after restricted day	Other un-restricted day	Mean (95% CI) difference between days immediately after and other unrestricted day	p value Day immediately after and other unrestricted day
Study 1 energy intake (kJ/day) n = 44	7,928 (7,397, 8,458)	7,728 (7,536–7,921)	6,226 (5,799, 6,648) (59 days)[a]	6,230 (5,866, 6,594) (177 days)[a]	−4 (−381, 368)	.98	6,427 (5,966, 6,883) (59 days)[a]	6,226 (5,841, 6,607) (177 days)[a]	201 (−335, 736)	.46
Study 2 energy intake (kJ/day) n = 67	8,484 (8,049, 8,923)	7,546 (7,399–7,691)	5,925 (5,535, 6,318) (73 days)[a]	6,117 (5,807, 6,427) (632 days)[a]	−192 (−506, 121)	.23	6,042 (5,665, 6,418) (166 days)[a]	6,134 (5,820, 6,443) (632 days)[a]	−92 (−393, 209)	.55

› **Study 1:** IER (2 consecutive days ~70% ER, 5 unrestricted days /week) for 6 months
Study 2: 2 forms of IER (2 consecutive days ER, 5 unrestricted days /week) for 4 months

› Reduction in EI below baseline EI (by 21% and 29%) and prescribed EI (by 19%) during unrestricted days including the days immediately before and after restricted days may contribute to the weight loss success

Harvey J, Food Science and Nutrition, 2017

Summary 5:2

- Clear benefits to 5:2 diet
- IER is as effective as CER with regard to weight (fat) loss, insulin sensitivity and other health biomarkers and cardiovascular benefits
- Consecutive or non-consecutive days?

5:2 DIETS AND TYPE 2 DIABETES

Effects of 5:2 vs CER on glycemic control and weight loss in patients with T2D during a 12-month period

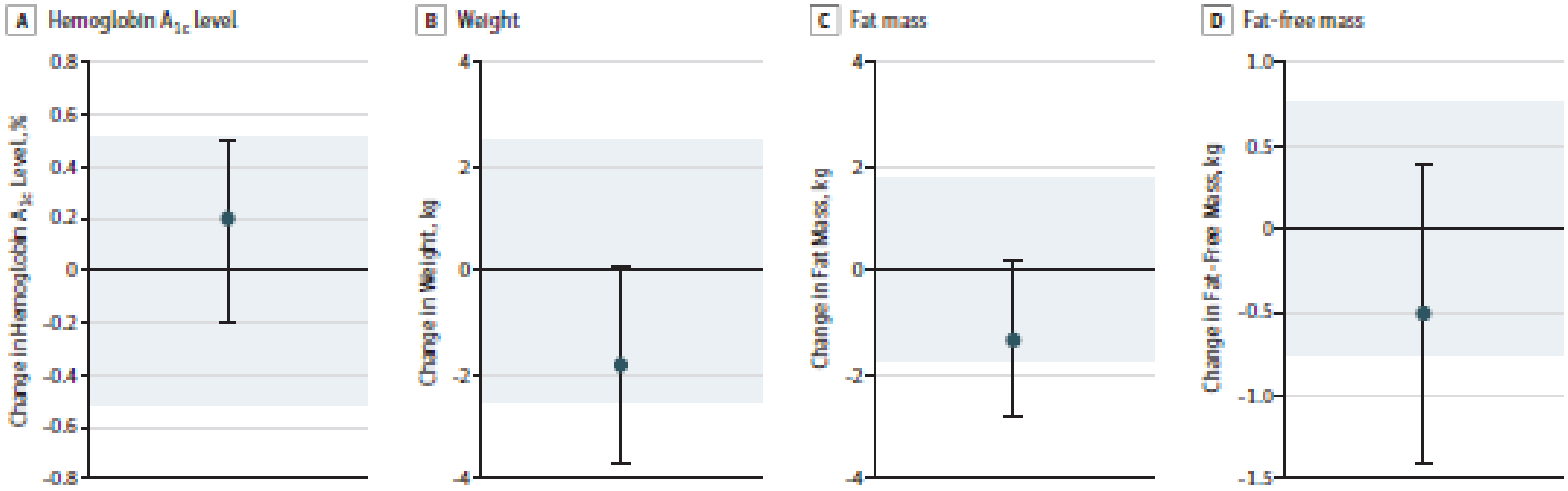
- Adults with type 2 diabetes with overweight/obese: N = 137
- Randomised to 2 groups:
  - CER: 1200-1500 kcal/d for 7 days/week for 12 months
  - 5:2: 500-600 kcal/d on 2 nonconsecutive days/week and usual diet for the other 5 days

- Medication management protocol - medications likely to cause hypoglycemia were reduced at baseline.

Carter S JAMA 2018

IER is an effective alternative diet strategy for the reduction of HbA1c and is comparable with CER in adults with T2D

Figure 2. Mean Between-Group Difference in Change in Hemoglobin A_{1c} Level, Weight, and Body Composition for the Intermittent vs Continuous Groups (Intention-to-Treat Analysis)



To convert hemoglobin A_{1c} to proportion of total hemoglobin, multiply by 0.01. Error bars indicate 2-sided 90% confidence intervals. Tinted area indicates zone of equivalence.

Carter S JAMA 2018

Glucose monitoring for safe use of a 2-day IER in patients with type 2 diabetes

- Is adjusted medication protocol superior to fixed protocol at reducing hypoglycaemic events during a 2 week 5:2 diet?
- 60% participants on adjusted protocol had no hypoglycaemic events.

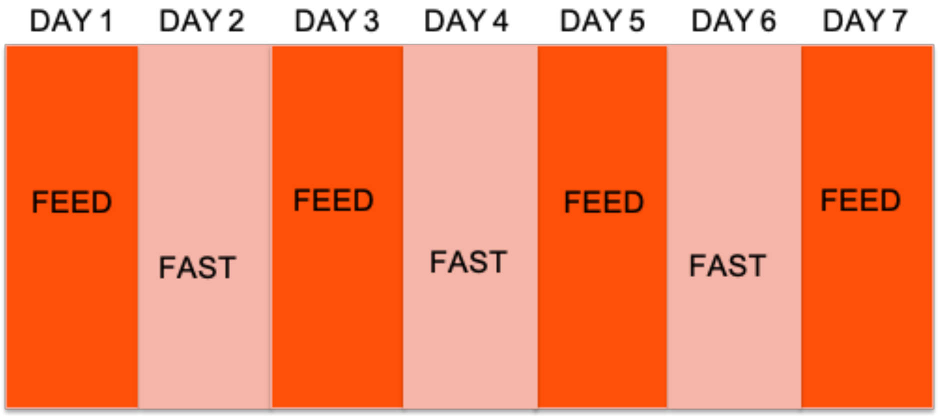
Table 1 – Fixed and adjusted medication protocol.

HbA1c	Fixed medication protocol		Adjusted medication protocol
	Sulphonylureas	Insulin	Hypoglycaemia
<7% (<53 mmol/mol)	Discontinue at baseline	Discontinue at baseline	One or more events (<3.9 mmol/L for ≥15 min) over 2 weeks then follow protocol 1 level greater than appropriate. *E.g: If HbA1c is >7–8% then the participant should follow the <7% protocol.*
>7–8% (>53–64 mmol/mol)	Discontinue on IER days only	Long and intermediate-acting insulin discontinued the night before the IER. All insulin discontinued on the day of the IER. Insulin will not be resumed until a full day's caloric intake is planned (if taken in the morning) or achieved (if taken in the evening).	
>8–10% (>64–86 mmol/mol)	Discontinue on IER days only	All insulin discontinued on the day of the IER. Insulin will not be resumed until a full day's caloric intake is planned (if taken in the morning) or achieved (if taken in the evening).	
>10–12% (>86–108 mmol/mol)	Continues	Short-acting insulin is discontinued, intermediate-acting is halved and long-acting insulin is reduced by 10 units or 10% whichever is greater, on IER days only.	
>12% (>108 mmol/mol)	Continues	Short-acting insulin is discontinued and long-acting insulin continued.	

Carter S, Diabetes Res Clin Pract, 2019

ALTERNATE DAY FASTING

Alternate day fasting (ADF)

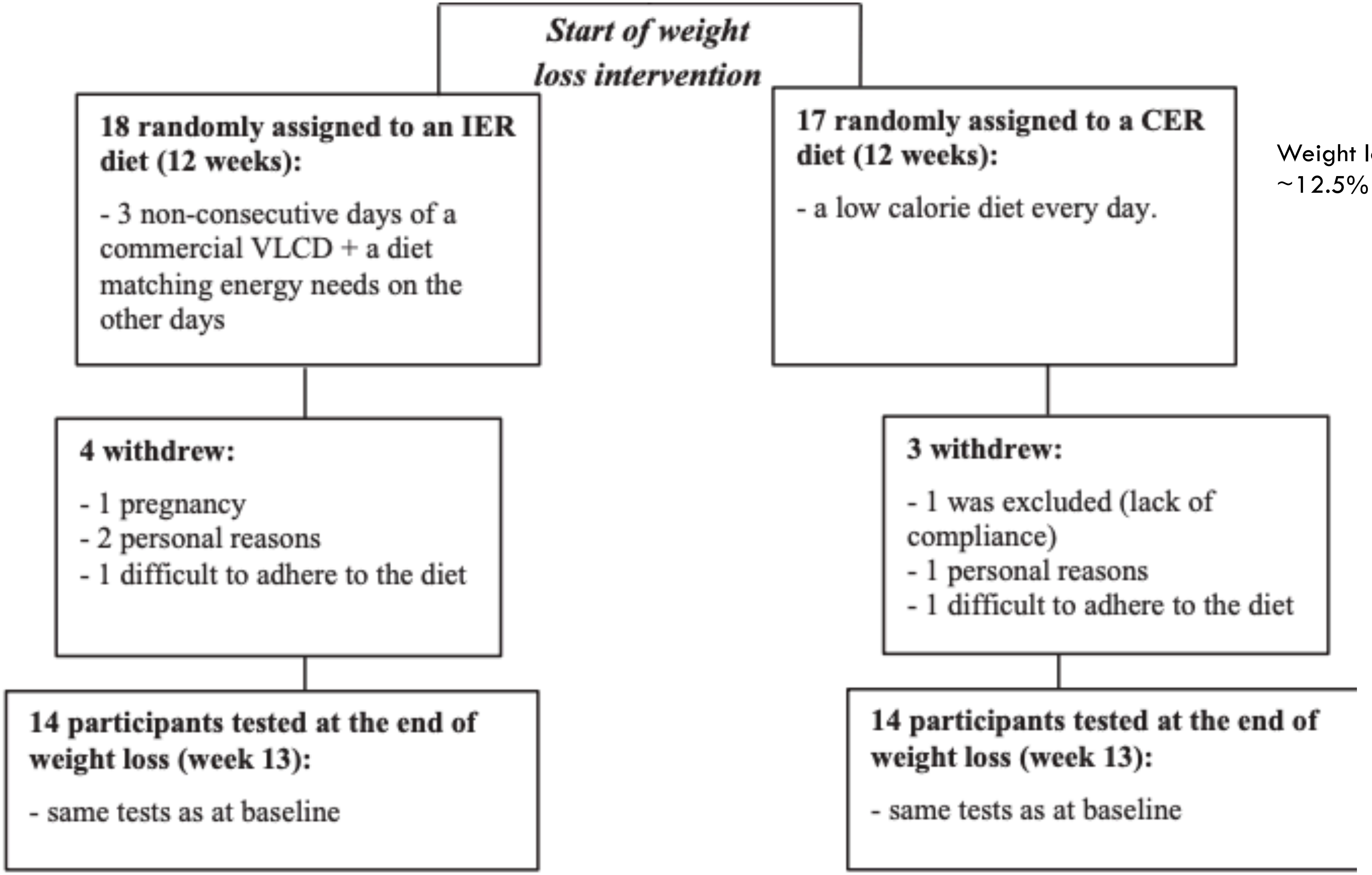


- Alternating ‘feed’ and ‘fast’ days
- Feed days: usually no restrictions on types / quantities of foods over 24 hrs
- Fast days: ~500 kcal over 24 hrs. ADF for weight loss, recommended to consume at least 50 g of protein to decrease hunger.
- Calories can be consumed all at once, or spread through day, without affecting rate of weight loss.

Hoddy Obesity, 2014

- Another ADF strategy involves 0 kcal on the fast day, also known as zero-calorie ADF.

Compensatory responses induced by weight loss following IER (3 non-consecutive days) and CER



Weight loss: ~12.5%

Coutinho S, Clin Nutr, 2018

IER or CER does not appear to modulate the compensatory mechanisms activated by weight loss

Changes in anthropometric measurements, RMR, fasting RQ, and exercise efficiency in the IER and CER groups.

	IER group			CER group			P-value**
	Baseline	End of WL	P-value*	Baseline	End of WL	P-value*	
Weight (kg)	107.2 ± 3.4	93.3 ± 3.4	<0.001	97.5 ± 3.4	85.7 ± 3.4	<0.001	0.089
FM (kg)	47.0 ± 2.0	35.7 ± 2.0	<0.001	43.0 ± 2.0	33.4 ± 2.0	<0.001	0.141
FM (%)	43.9 ± 1.6	38.5 ± 1.6	<0.001	44.1 ± 1.6	38.9 ± 1.6	<0.001	0.706
FFM (kg)	60.4 ± 2.7	57.6 ± 2.7	<0.001	54.5 ± 2.7	52.6 ± 2.7	<0.001	0.262
FFM (%)	56.1 ± 1.6	61.5 ± 1.6	<0.001	55.9 ± 1.6	61.1 ± 1.6	<0.001	0.741
RMR (kcal/day)	1488 ± 55	1368 ± 55	<0.001	1342 ± 55	1302 ± 55	0.193	0.151

No difference between groups in:
Subjective appetite ratings (hunger, fullness, desire to eat), or
Appetite-regulating hormones (CCK, PYY, GLP-1)

Coutinho S, Clin Nutr, 2018

JAMA Internal Medicine | Original Investigation

Effect of Alternate-Day Fasting on Weight Loss, Weight Maintenance, and Cardioprotection Among Metabolically Healthy Obese Adults
A Randomized Clinical Trial

John F. Trepanowski, PhD; Cynthia M. Kroeger, PhD; Adrienne Barnosky, MD; Monica C. Klempel, PhD; Surabhi Bhutani, PhD; Kristin K. Hoddy, PhD, RD; Kelsey Gabel, MS, RD; Sally Freels, PhD; Joseph Rigdon, PhD; Jennifer Rood, PhD; Eric Ravussin, PhD; Krista A. Varady, PhD

Supplemental content

IMPORTANCE Alternate-day fasting has become increasingly popular, yet, to date, no long-term randomized clinical trials have evaluated its efficacy.

OBJECTIVE To compare the effects of alternate-day fasting vs daily calorie restriction on weight loss, weight maintenance, and risk indicators for cardiovascular disease.

DESIGN, SETTING, AND PARTICIPANTS A single-center randomized clinical trial of obese adults (18 to 64 years of age; mean body mass index, 34) was conducted between October 1, 2011, and January 15, 2015, at an academic institution in Chicago, Illinois.

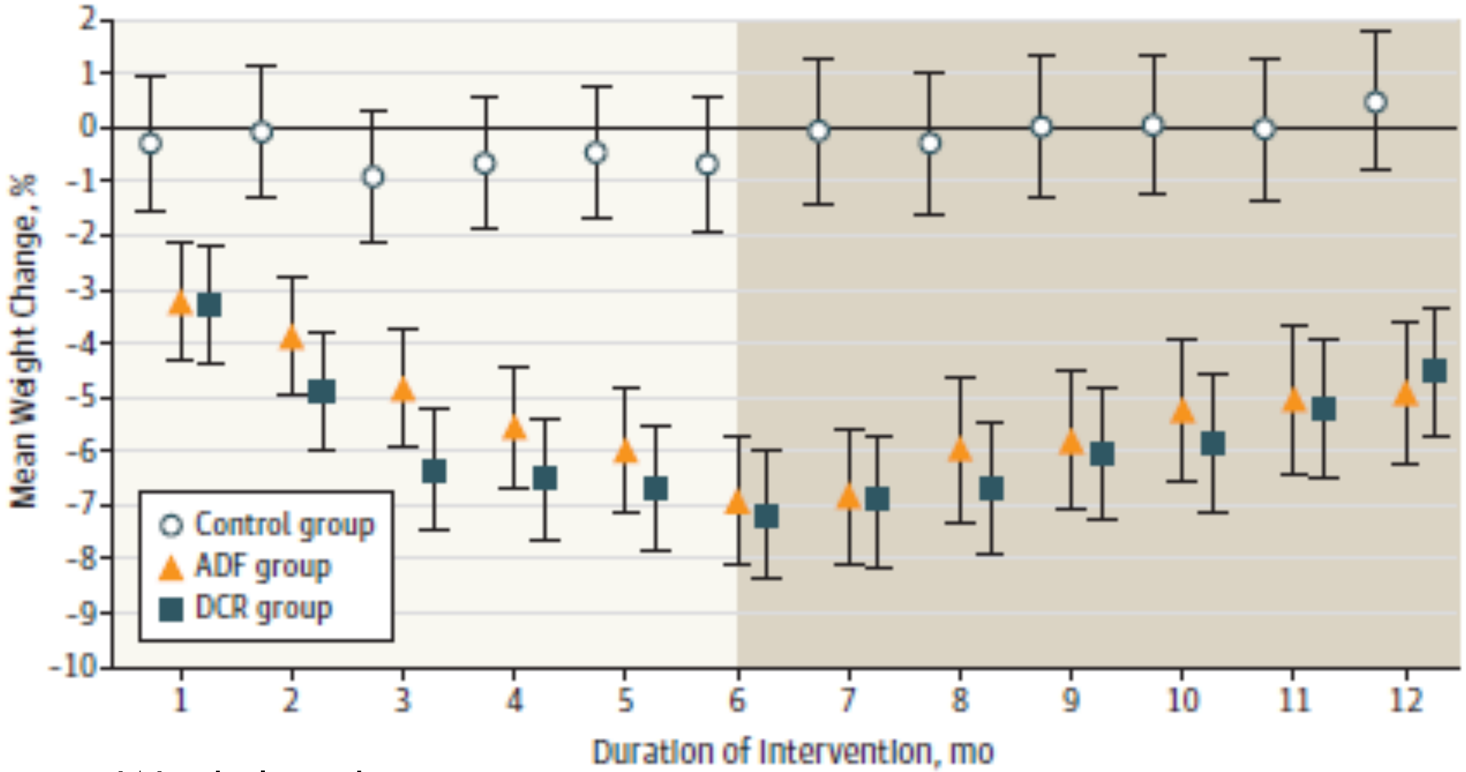
INTERVENTIONS Participants were randomized to 1 of 3 groups for 1 year: alternate-day fasting (25% of energy needs on fast days; 125% of energy needs on alternating "feast days"), calorie restriction (75% of energy needs every day), or a no-intervention control. The trial involved a 6-month weight-loss phase followed by a 6-month weight-maintenance phase.

MAIN OUTCOMES AND MEASURES The primary outcome was change in body weight. Secondary outcomes were adherence to the dietary intervention and risk indicators for cardiovascular disease.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00960505

JAMA Intern Med. doi:10.1001/jamainternmed.2017.0936
Published online May 1, 2017.

ADF did not produce superior adherence, weight loss or weight maintenance vs CER



Weight loss phase:
ADF: 25% fast days, 125% feed days
DCR: 75% daily

Weight maintenance phase:
ADF: 50% fast days, 150% feed days
DCR: 100% daily

- ADF: n=34, DCR: n=35, 44 years, 34 kg/m^2
- Food provided for first 3 months to ADF and DCR
- Weight loss ADF: 6%, DCR: 5.3% at 12 months

Trepanowski J, JAMA 2017

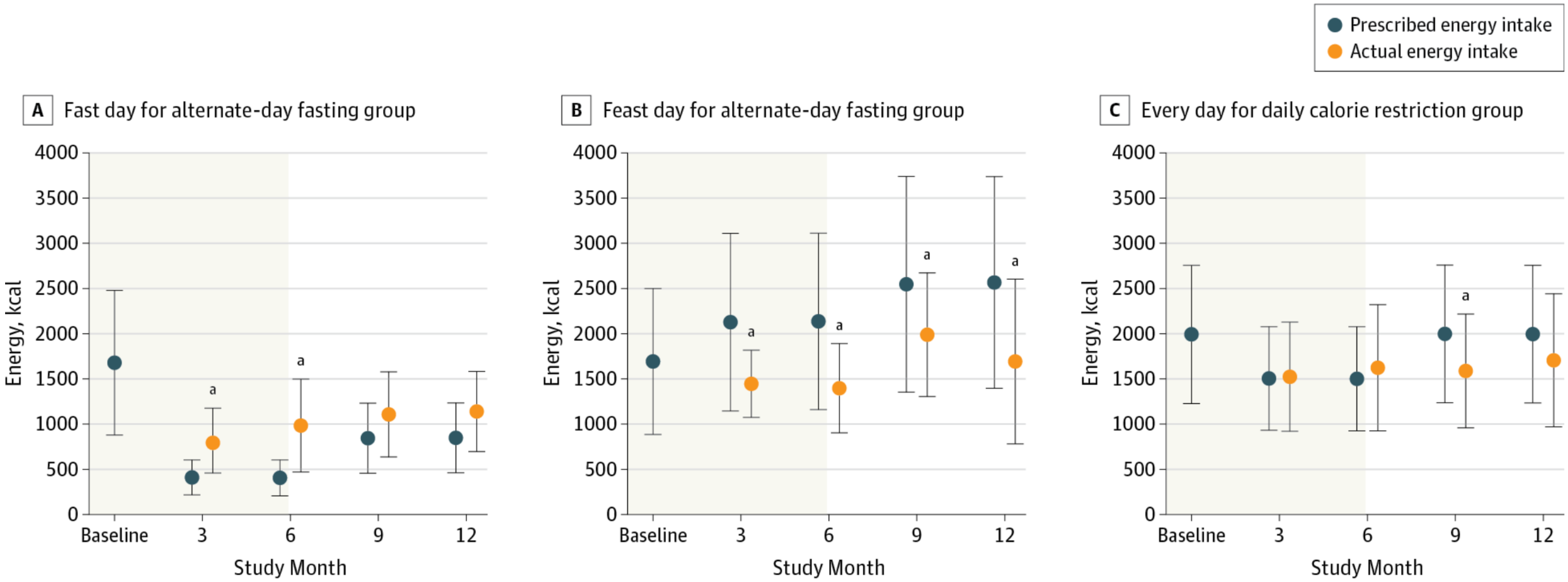
ADF did not produce superior cardioprotection vs CER

No significant differences between groups at 6 or 12 months:

- Blood pressure
- Heart rate
- Triglycerides
- Fasting glucose
- Fasting insulin
- Insulin resistance
- C-reactive protein

Trepanowski J, JAMA 2017

Prescribed vs Actual Energy Intake in the ADF and CER Groups



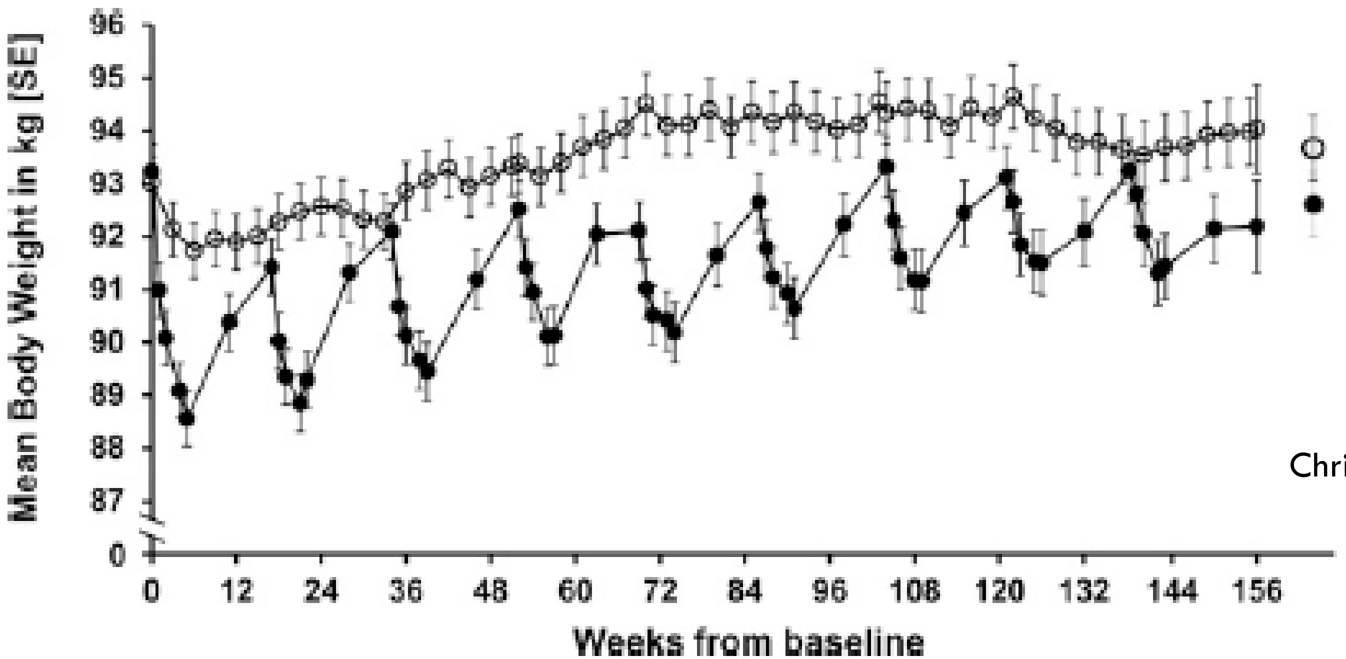
- Dropout rate: ADF: 38% and DCR: 29%

Trepanowski J, JAMA 2017

INTERMITTENT ENERGY RESTRICTION AS A WEIGHT MAINTENANCE DIET

Use of TMRD as weight maintenance

- Patients with knee osteoarthritis previously completed a lifestyle intervention trial and achieved 10% loss of initial body weight.
- Participants were randomly assigned to:
  - IF with meal replacement products for 5 wk every 4 mo for 3 year
  - Daily meal replacements of 1–2 meals for 3 year



Christensen, AJCN 2017

SYSTEMATIC REVEIWS AND META-ANALYSES

Contents lists available at ScienceDirect

Molecular and Cellular Endocrinology

journal homepage: www.elsevier.com/locate/mce

Do intermittent diets provide physiological benefits over continuous diets for weight loss? A systematic review of clinical trials

Radhika V. Seimon [a], Jessica A. Roekenes [a], Jessica Zibellini [a], Benjamin Zhu [a], Alice A. Gibson [a], Andrew P. Hills [b], Rachel E. Wood [c], Neil A. King [d], Nuala M. Byrne [c], Amanda Sainsbury [a,*]

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ABSTRACT

Energy restriction induces physiological effects that hinder further weight loss. Thus, deliberate periods of energy balance during weight loss interventions may attenuate these adaptive responses to energy restriction and thereby increase the efficiency of weight loss (i.e. the amount of weight or fat lost per unit of energy deficit). To address this possibility, we systematically searched MEDLINE, PreMEDLINE, PubMed and Cinahl and reviewed adaptive responses to energy restriction in 40 publications involving humans of any age or body mass index that had undergone a diet involving intermittent energy restriction, 12 with direct comparison to continuous energy restriction. Included publications needed to measure one or more of body weight, body mass index, or body composition before and at the end of energy restriction. 31 of the 40 publications involved 'intermittent fasting' of 1–7-day periods of severe energy restriction. While intermittent fasting appears to produce similar effects to continuous energy restriction to reduce body weight, fat mass, fat-free mass and improve glucose homeostasis, and may reduce appetite, it does not appear to attenuate other adaptive responses to energy restriction or improve weight loss efficiency, albeit most of the reviewed publications were not powered to assess these outcomes. Intermittent fasting thus represents a valid – albeit apparently not superior – option to continuous energy restriction for weight loss.

IER appears equivalent to conventional diets for multiple health outcomes…

- Weight loss (3–5 kg after ~10 weeks)
- Waist and hip circumference
- Fat loss (including visceral adipose tissue)
- Loss of fat free mass
- Improvements in glucose homeostasis
- Dropout rates - no clear evidence that easier to adhere/follow

Seimon R Mol Cell Endocrinol 2015

nutrients

MDPI

Review

Weight-Loss Outcomes: A Systematic Review and Meta-Analysis of Intermittent Energy Restriction Trials Lasting a Minimum of 6 Months

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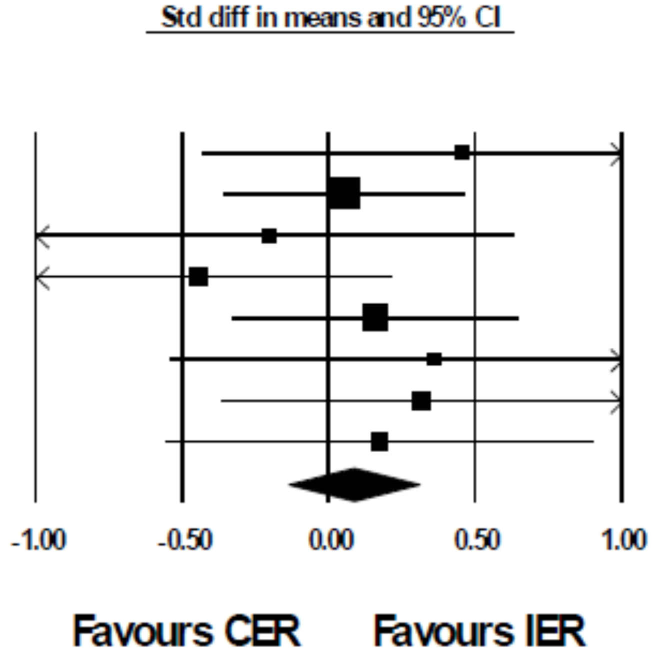
Received: 15 March 2016; Accepted: 2 June 2016; Published: 8 June 2016

Abstract: The aim of this systematic review and meta-analysis is to summarise the effects of intermittent energy restriction on weight and biological markers in long term intervention studies of >6 months duration. An electronic search was performed using the MEDLINE, EMBASE and the Cochrane Library databases for intervention trials lasting 6 months or longer investigating the effects of intermittent energy restriction. A total of nine studies were identified as meeting the pre-specified criteria. All studies included an intermittent energy restriction arm, with six being directly compared to continuous energy restriction. A total of 981 subjects were enrolled and randomised, with weight loss observed in all intermittent energy restriction arms regardless of study duration or follow up length. Eight interventions in six trials were used for the meta-analyses, with results indicating neither intermittent or continuous energy restriction being superior with respect to weight loss, 0.084 ± 0.114 (overall mean difference between groups $\pm$ standard error; $p = 0.458$). The effects of intermittent energy restriction in the long term remain unclear. The number of long term studies conducted is very limited, and participant numbers typically small (less than 50 completers), indicating the need for larger, long term trials of 12 months or more, to be conducted in order to understand the impact of intermittent energy restriction on weight loss and long term weight management. Blood lipid concentrations, glucose, and insulin were not altered by intermittent energy expenditure in values greater than those seen with continuous energy restriction.

Effect of IER on weight loss in the long-term (> 6 months)

Studyname	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
Arguin	0.455	0.455	0.207	-0.437	1.347	0.999	0.318
Harvie	0.055	0.212	0.045	-0.361	0.471	0.260	0.795
Hill	-0.204	0.428	0.183	-1.043	0.636	-0.475	0.635
Keogh	-0.444	0.338	0.114	-1.106	0.219	-1.313	0.189
Wing	0.160	0.251	0.063	-0.331	0.651	0.639	0.523
Rossner (Men)	0.362	0.463	0.215	-0.546	1.270	0.781	0.435
Rossner (Women) study 1	0.320	0.351	0.123	-0.367	1.008	0.914	0.361
Rossner (Women) Study 2	0.174	0.374	0.140	-0.559	0.907	0.465	0.642
	0.084	0.114	0.013	-0.139	0.308	0.742	0.458



- Weight loss difference between groups: **0.084 ± 0.114 kg**
- Similar improvements in circulating lipid profile
- Similar improvements in glucose homeostasis
- Similar dropout rate

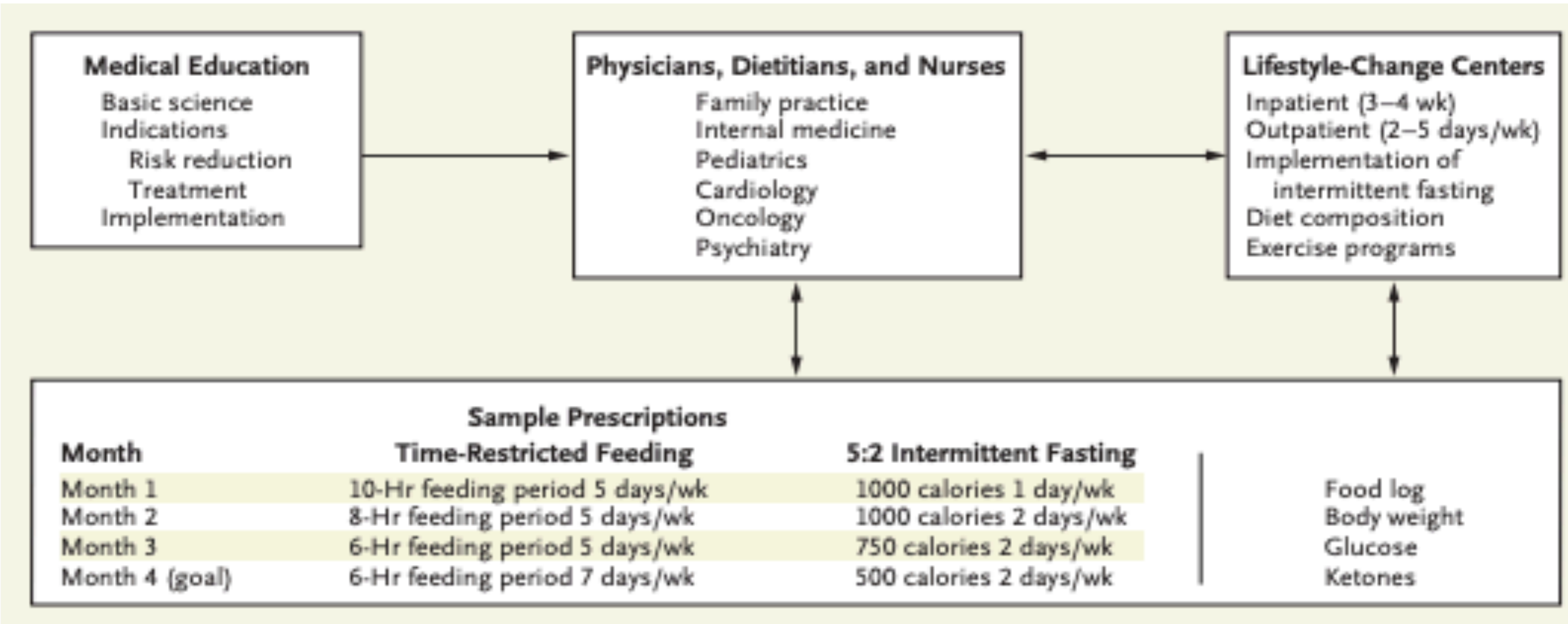
Headland M Nutrients 2016

Summary

- Valid option for weight loss
- Some individuals may prefer IER to daily restriction
- Provides another tool for the management of overweight/obesity
- Benefits for many health conditions, diabetes mellitus, CVD
- No studies report serious adverse events, no evidence of disordered eating/unhealthy diets - no long-term evidence

Clinical consideration

People may experience hunger, irritability, and a reduced ability to concentrate during fast days but disappear



Rafael de Cabo NEJM 2019

SEVERE ENERGY RESTRICTION

JAMA Network Open.

Original Investigation | Nutrition, Obesity, and Exercise

Effect of Weight Loss via Severe vs Moderate Energy Restriction on Lean Mass and Body Composition Among Postmenopausal Women With Obesity
The TEMPO Diet Randomized Clinical Trial

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Abstract

IMPORTANCE Severely energy-restricted diets are the most effective dietary obesity treatment. However, there are concerns regarding potential adverse effects on body composition.

OBJECTIVE To compare the long-term effects of weight loss via severe vs moderate energy restriction on lean mass and other aspects of body composition.

DESIGN, SETTING, AND PARTICIPANTS The Type of Energy Manipulation for Promoting Optimum Metabolic Health and Body Composition in Obesity (TEMPO) Diet Trial was a 12-month, single-center, randomized clinical trial. A total of 101 postmenopausal women, aged 45 to 65 years with body mass index (calculated as weight in kilograms divided by height in meters squared) from 30 to 40, who were at least 5 years after menopause, had fewer than 3 hours of structured physical activity per week, and lived in the Sydney metropolitan area of New South Wales, Australia, were recruited between March 2013 and July 2016. Data analysis was conducted between October 2018 and August 2019.

INTERVENTION Participants were randomized to either 12 months of moderate (25%-35%) energy restriction with a food-based diet (moderate intervention) or 4 months of severe (65%-75%) energy restriction with a total meal replacement diet followed by moderate energy restriction for an additional 8 months (severe intervention). Both interventions had a prescribed protein intake of 1.0 g/kg of actual body weight per day, and physical activity was encouraged but not supervised.

MAIN OUTCOMES AND MEASURES The primary outcome was whole-body lean mass at 12 months after commencement of intervention. Secondary outcomes were body weight, thigh muscle area and muscle function (strength), bone mineral density, and fat mass and distribution, measured at 0, 4, 6, and 12 months.

Key Points

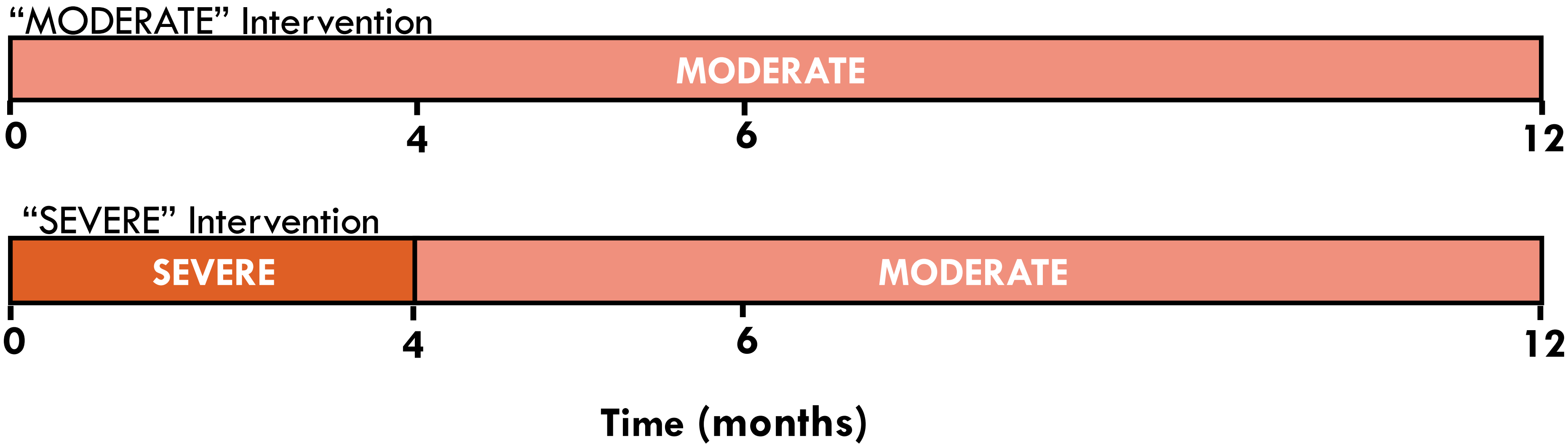
Question What are the long-term effects of severe vs moderate energy restriction on lean mass and other aspects of body composition?

Findings This randomized clinical trial included 101 postmenopausal women with obesity. At 12 months, participants who had undergone severe energy restriction experienced approximately 2-fold greater weight and fat loss, approximately 1.5 times as much loss of whole-body lean mass (proportional to total weight lost), and approximately 2.5 times as much loss of total hip bone mineral density compared with participants who had undergone moderate energy restriction.

Meaning Although severe energy restriction is an effective obesity treatment, caution is necessary when implementing it in postmenopausal women, especially those with osteopenia or osteoporosis.

+ Invited Commentary

Study Protocol



Seimon, JAMA, 2019

Moderate (~30%) energy restriction from baseline requirements

Number of serves from 5 'core' food groups serves to meet energy target and ~1g protein per kg body weight

- Grain (cereals)
- Vegetables
- Fruit
- Reduced fat dairy
- Lean meat/alternatives

Severe (~70%) energy restriction from baseline requirements

+

+

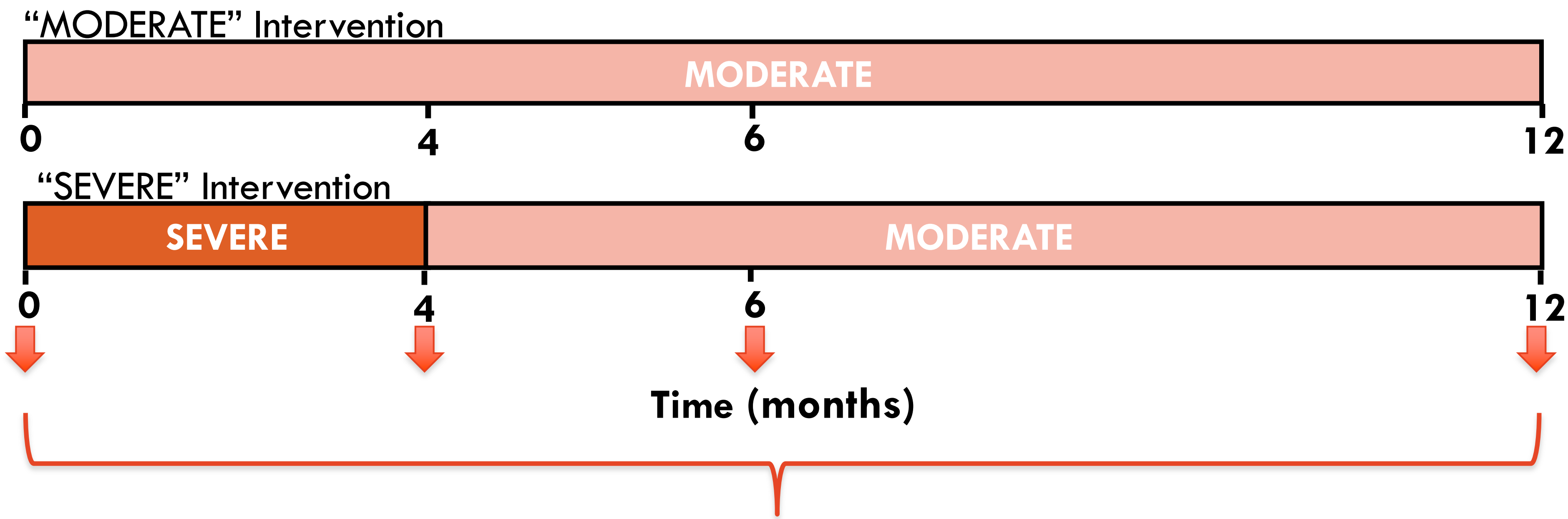
3-4 commercial meal replacement products

Whey protein isolate to meet ~1g protein per kg body weight

2 cups low energy vegetables &

1 teaspoon oil

Study Protocol



Body weight

Fat mass and distribution

Lean mass and function

Bone mineral density

- Prescribed protein intake of 1g/kg of actual body weight per day
- Physical activity was encouraged but not supervised

Seimon R, Healthcare, 2018

Baseline characteristics

	SEVERE ($n = 50$)	MODERATE ($n = 51$)
Age (years)	58.0 ± 4.4	58.0 ± 4.2
Weight (kg)	90.1 ± 9.4	92.4 ± 8.3
Body Mass Index (kg/m^2)	34.3 ± 2.5	34.3 ± 2.5

Data: Mean ± SD

Flow of participants throughout the 12-month trial

101 Underwent randomization

50 Randomized to the SEVERE intervention

4 Discontinued the trial
- **2** Discontinued *during* 4-month SEVERE intervention
  - **1** Felt unwell on testing day
  - **1** Health reasons unrelated to trial
- **2** Discontinued *after* 4-month SEVERE intervention
  - **1** Dissatisfied with diet
  - **1** Lost to follow-up

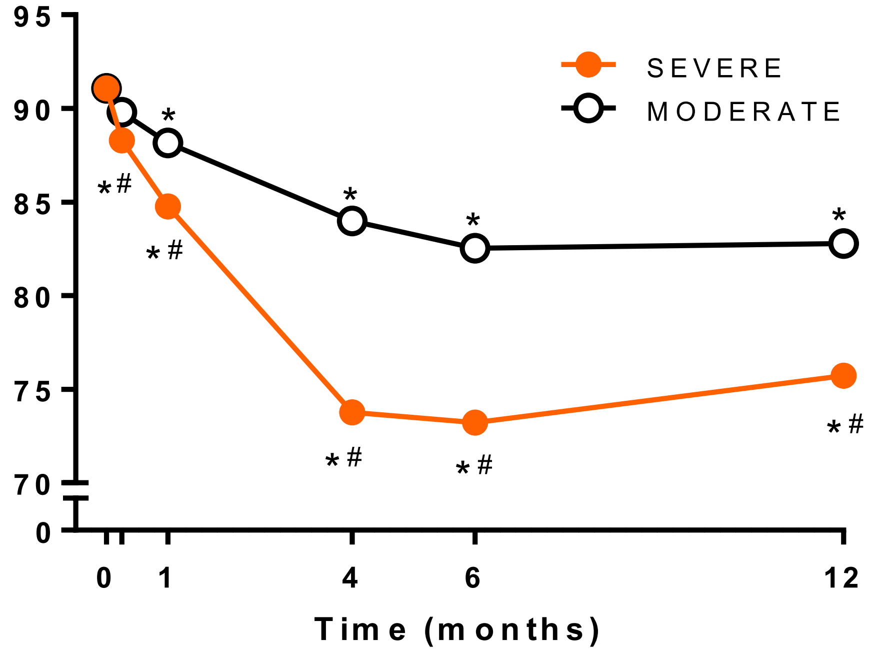
46 Completed 12-month SEVERE intervention

51 Randomized to the MODERATE intervention

12 Discontinued the trial
- **5** No longer able to commit
- **5** Dissatisfied with diet/weight loss
- **1** Lost to follow-up
- **1** No reason provided

39 Completed 12-month MODERATE intervention

Change in body weight (kg)

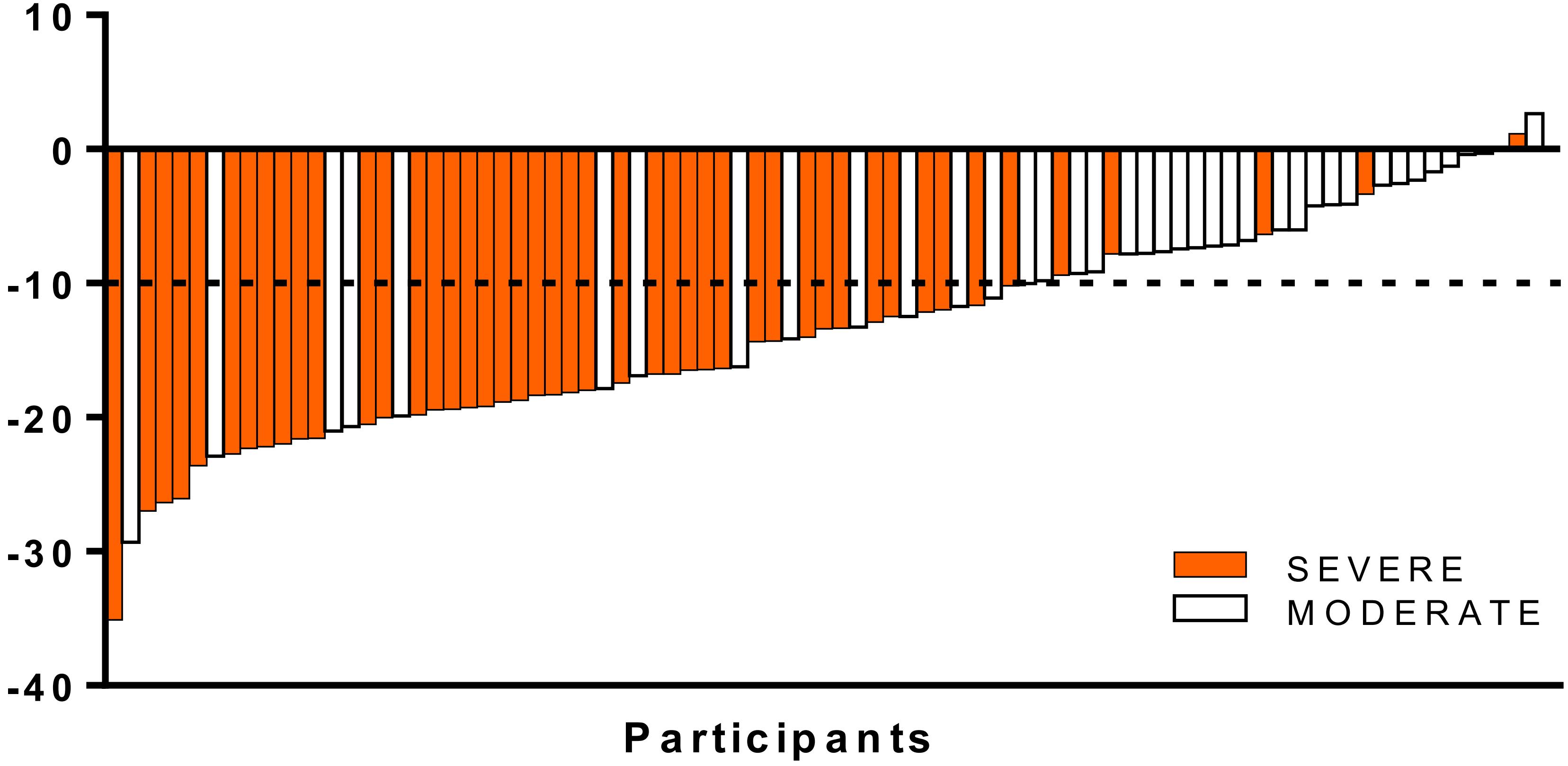


Data: Mean ± SEM

* vs 0 months, $P < 0.05$; # vs MODERATE, $P < 0.05$

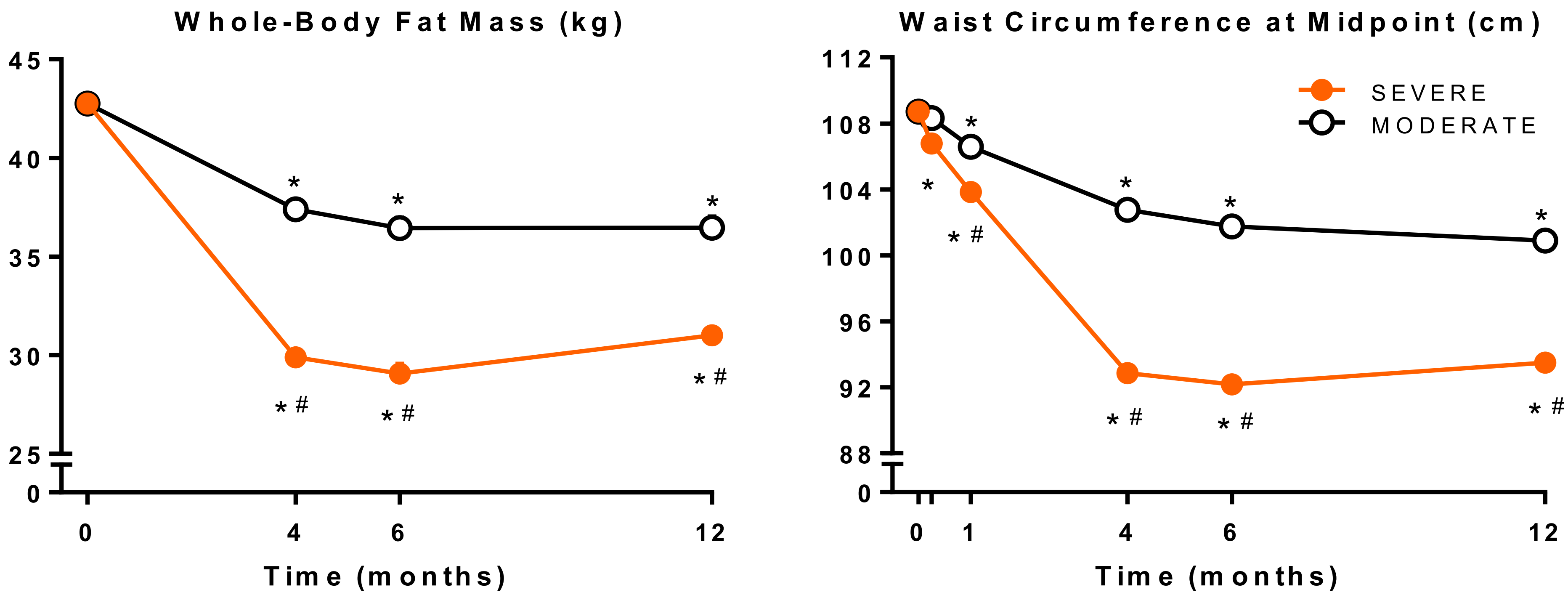
Seimon, JAMA, 2019

Change in body weight (%) at 12 months



Seimon, JAMA, 2019

Fat Mass and Distribution

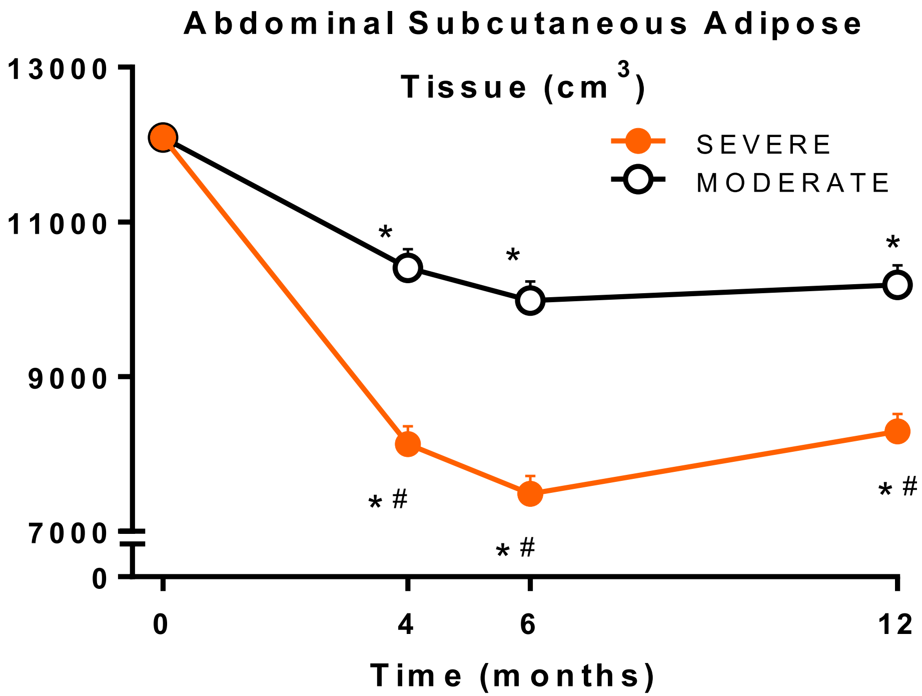


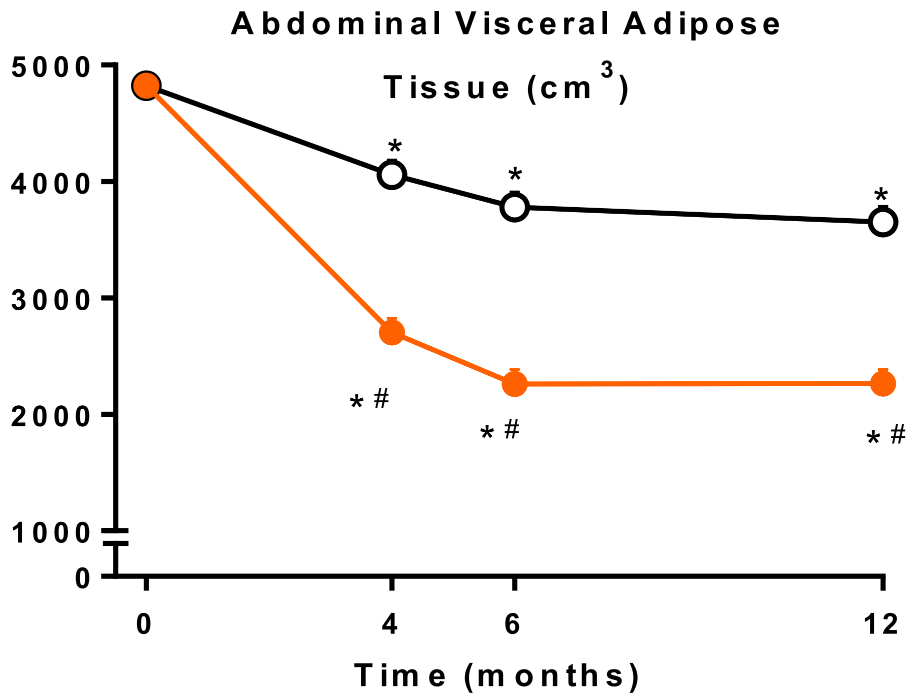
Data: Mean ± SEM

* vs 0 months, P < 0.05; # vs MODERATE, P < 0.05

Seimon, JAMA, 2019

Abdominal Fat Mass

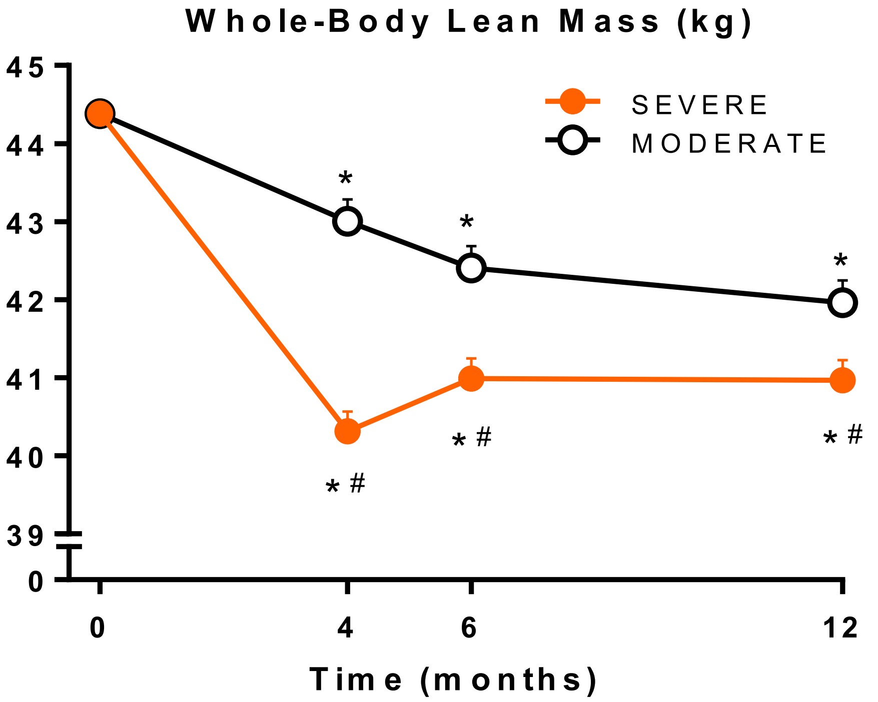




Data: Mean ± SEM
* vs 0 months, $P < 0.05$; # vs MODERATE, $P < 0.05$

Seimon, JAMA, 2019

Lean Tissue



Data: Mean ± SEM

* vs 0 months, P < 0.05; # vs MODERATE, P < 0.05

Seimon, JAMA, 2019

Summary

Compared to moderate energy restriction over a 12-month period, severe energy restriction resulted in:

- ~2 times more weight loss (2.5-3 times more likely to lose 10% body weight)
- ~2 times more fat loss, abdominal adipose tissue volume
- ~1.5 times more loss of lean mass (albeit proportional to total weight lost)
- More likely to remain in the trial