THE COLLEGE OF FAMILY PHYSICIANS OF CANADA

LE COLLÈGE DES MÉDECINS DE FAMILLE DU CANADA

At a Loss for Weight Loss?

Scaling down the evidence for primary care

June 8, 2021

Conflicts of Interest

All speakers are employees of the College of Family Physicians of Canada.

Adrienne Lindblad, BSP, ACPR, PharmD

Speaker's honorarium from ACFP, Alberta Pharmacists Association, North of 44 Primary Care Symposium

Casual Pharmacist, Alberta Health Services

Betsy Thomas, BSc Pharm

Casual COVID immunizer for Alberta Health Services

No other conflicts to declare

Samantha Moe, BSc Pharm, PharmD, ACPR

No conflicts of interests

Joey Ton, BSc Pharm, PharmD

Speaker's honorarium from ACFP

No other conflicts to declare.

Danielle Perry, RN, MSc

Speaker's honorarium from ACFP, PEICFP, Dalhousie CPD

Correctional Services of Canada.

This program has not received financial or in-kind support.

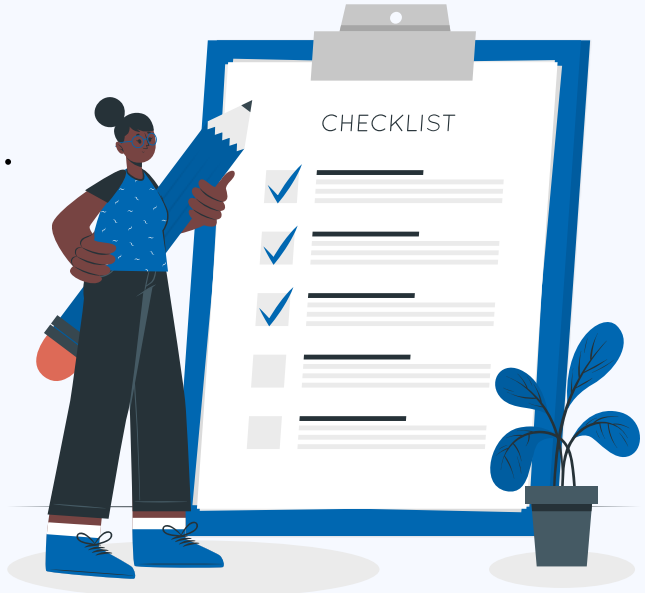
Learning Objectives

By the end of this presentation, participants will be able to:

1) Describe the evidence for non-pharmacological interventions for weight loss (exercise, diet, water, motivational interviewing).

2) Describe the evidence for pharmacological interventions for weight loss (supplements, naltrexone/bupropion, GLP-1 agonists).

3) Apply these strategies to a patient case.



Let's meet Frank.

- 42-year-old man in your practice for several years
- In the past, Frank has not been interested in discussing weight loss.
- Today, Frank tells you his good friend had a heart attack. He's visiting out of concern for own health.
- Vitals and bloodwork within acceptable ranges
- Weight: 100 kg
- You mention weight loss could have a significant impact on his health, and Frank is interested in discussing further.

What options would you recommend for patients like Frank?

Put your answer in the chat.

What is the impact of exercise on weight loss?

Exercise vs control:

Adults who were overweight/obese:

- Weight loss~1.5-2kg over 12mo (2-4 RCT, 270-598 pts)[1,2]

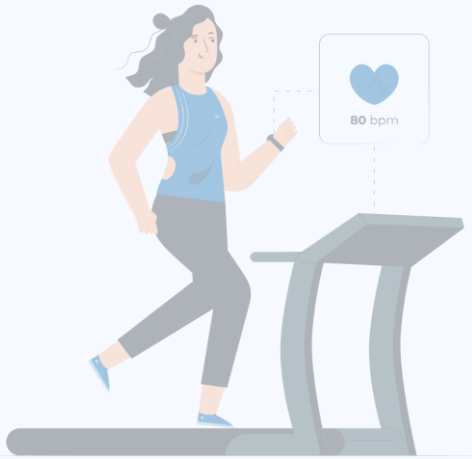
Postmenopausal women who are obese:

- Weight loss ~3.5kg over 12mo (3 RCT, 730 pts)[3]

Specific exercises: (overweight/obese):

- Aerobic exercise: ~1.5-2kg over 6-12mo (14 RCT, 1847 pts)[4]
- Circuit training: ~4-5 kg over 2-12mo (9 RCT, 837 patients)[5]

Bottom Line:
In a general population of adult patients who are overweight/obese, exercise may decrease weight by 1.5-4kg over 2-12months.



1. Cochrane System Rev 2006, Issue 4. Art. No.:CD003817. 2. CMAJ Open 2014. DOI: 10.9778/cmajo.20140012. 3. Menopause 2018; 25(7): 772-82. 4. Obes Rev 2019; 20: 1642-50. 5. Am J Med 2011; 124: 747-55.

What about exercise in the context of diet change?

What is the impact of dietary changes on weight loss?

Diet versus control:

- General population: weight loss 4.7kg favoring diet over 12 months (8 trials, 913 patients)[1]
- Postmenopausal patients with obesity: 6.5kg over 3-12 months (5 trials)[2]

Diet changes can help with weight loss (4.5-6.5kg weight loss over 3-12 months)…

… and likely has a bigger impact than exercise

Diet vs exercise:

- General population: mean difference 3.6 kg favoring diet over 3-12 months (1 SR, 15 trials, 2247 patients)[1]

Is there an additive effect if you add exercise to a diet regimen?

A modest additive benefit ranging from 0.5-2.0 kg over 3-24 months[1,3,4]

Does intensity of exercise matter?[1]

It depends. In the absence of diet changes, more weight loss with high-intensity exercise than low-intensity (1.5kg over 3-12 months).

Difference not persist if diet changes are added.

1. Cochrane System Rev 2006, Issue 4. Art. No.:CD003817. 2. Menopause 2018; 25(7): 772-82. 3. J Acad Nutr Diet 2014; 114; 1557-1568. 4. Obesity Reviews 2009; 10: 313-23.

Fad Diets

https://www.allposters.com/-sp/Veterinarian-Diet-Posters_i6122972_.htm

Ketogenic Diet

•Most relevant systematic reviews compared to low-fat diet:

1) 13 RCTs, n=1577. At 12-24 months, keto:
- Lost 0.9 kg more; Drop-outs 13-84%

2) 11 RCTs, n=1369. At 6-24 months, keto:
- Lost 2.2 kg more, but results inconsistent (no difference if focus on higher quality studies)

2018 RCT, n=609. At 1 year:
- No difference in weight loss (~5-6kg both groups).
- Patient genotypes had no impact on weight loss.
- Individual weight change varied -30 to +10kg.

Bottom Line: At best, keto helps patients lose ~2kg more than low-fat diet at 1 year (highest quality=no difference). Weight loss peaks ~5 months, but not sustained. An individual's weight change can vary -30 to +10kg with any diet. No RCTs on mortality or CVD. 23andme won't help

TFP #220; Sept 24, 2018.

Intermittent Fasting vs Continuous Dieting

- Example "Intermittent fasting": reduce intake by 75%/day (eg 500kcal/d for 2 days/week); "continuous dieting": reduce by 25%/day
- Systematic review: 9 RCTs at least 6 months in duration, 981 patients:
  - No difference in weight loss (range 2.1-26.6kg) after 6 months-2 years
- 6 Newer RCTs:
  - 5/6: no difference between groups (5-9kg)
  - 1 RCT, 51 men, 11kg lost vs 3kg (continuous diet), but only study completers included
- **Bottom Line: Although inconsistently defined, intermittent fasting (example 500 kcal/day for 2 days/week) and continuous dieting (~25% reduction in caloric intake daily) result in similar weight loss, usually ~5-9kg at 6 months-1 year. Discontinuation rates with both diets is up to ~60%.**

TFP #247; Nov 12, 2019

Water for weight loss

Evidence: 2 randomized controlled trials

RCT#1

Weight-stable adults with no underlying health conditions (N=48, 12 weeks, Baseline Weight: 91 kg)

- Compared a hypocaloric diet + 500 ml water prior to each meal versus hypo diet alone

	Baseline	12 Weeks	
Water	93.2 kg	85.8 kg	*-7.4 kg*
Control	89.9 kg	84.4 kg	*-5.5 kg*

Weight loss was ~2kg greater in the water group (p<0.001) over 12 weeks.

Dennis EA, Dengo AL, Comber DL, et al.; 2010;18(2):300-7.

Water for weight loss

Evidence:

RCT#2

Patients with obesity (BMI≥30) recruited from general practices (N=84, 12 weeks, Baseline Weight: 93kg)

- Compared adding 500 ml of water, 30 minutes prior to meals VS an attention control

	Baseline	12 Weeks	
Water	92.2 kg	89.8 kg	*-2.4 kg*
Control	93.5 kg	92.3 kg	*-1.2 kg*

Weight loss was ~1kg greater in the water group (p=0.028) over 12 weeks.

Parretti HM, Aveyard P, Blannin A, et al. Obesity. 2015;23(9):1785-91.

Water for weight loss

Evidence:

RCT#2

Patients with obesity (BMI≥30) recruited from general practices (N=84, 12 weeks, Baseline Weight: 93kg)

- Compared adding 500 ml of water, 30 minutes prior to meals VS an attention control

Proportion of patients who lost ≥5% of their body weight at 12 weeks

Intervention:27%
Control: 5%

NNT 5

Parretti HM, Aveyard P, Blannin A, et al. Obesity. 2015;23(9):1785-91.

Water for weight loss- Context

Equivalence trials try to prove that two interventions are equal rather than one being better than the other.

Equivalence RCT (N=303, 12 weeks; non-nutritive sweetened beverages versus water)

- Over 12 weeks, the water group lost **~4kg** compared to **~6kg** with NNS beverages
- Proportion of patients losing ≥5% body weight: **64%** (diet beverages) versus **43%** (water) **NNT 5**

3-armed RCT (N=318, 24 weeks; water, diet beverages or attention control)

- No difference between groups at 24 weeks

Peters JC, Wyatt HR, Foster GD. Obesity. 2014;22(6):1415-21; Tate DF, Turner-McGrievy G, Lyons E. Am J Clin Nutr. 2012;95:555-63.

Water for weight loss

Bottom Line

Supplementing standard dietary programs or education with additional water intake (~1500 ml/day) may lead to increased weight loss (~1-2 kg) over 12 weeks.

Similarly, replacing caloric beverages with water or diet beverages may lead to increased weight loss (~2 kg) over 12 weeks.

No adverse events were reported.

Frank: Visit 2

- It has been 4 months since your first discussion with Frank.
- He has started walking every day for 20 minutes and has replaced some of his drinks with water. He tried the ketogenic diet, however, could not maintain the restrictions.
- Today, his weight is down to 97 kg (from 100 kg).
- He wants to try intermittent fasting and asks if he can add a diet supplement that he has heard of.

Which supplement would you like to learn about?

Put your answer in the chat.

- Conjugated Linoleic Acid (CLA)
- Green Tea Extract
- Garcinia Cambogia
- Fibre Supplements

What is it: Conjugated Linoleic Acid (CLA)

What is it?

- Polyunsaturated fatty acids naturally found in animal food products.

What is it believed to do?

- Decrease body fat, increase lean body mass, reduce hunger, improve satiety.

What does it cost?

- $50 for 180 softgels (1 soft gel per meal)

https://www.amazon.ca/Evlution-Nutrition-Conjugated-Supplement-Stimulant-Free/dp/B01HXGY7RU/ref=sr_1_5?crid=24JZK23MZU5IU&dchild=1&keywords=cla+supplement+fat+burner&qid=1622220050&sprefix=cla+supplement%2Caps%2C219&sr=8-5

Evidence: Conjugated Linoleic Acid (CLA)

Systematic Review of 11 RCTs (n=486, BMI 25 to 35, 4 weeks to 26 weeks)

Interventions: CLA 0.6g TID to 2g QID versus Placebo

Body Weight at end of Trial: CLA -1.9kg vs Placebo -2.5kg

Adverse events reported

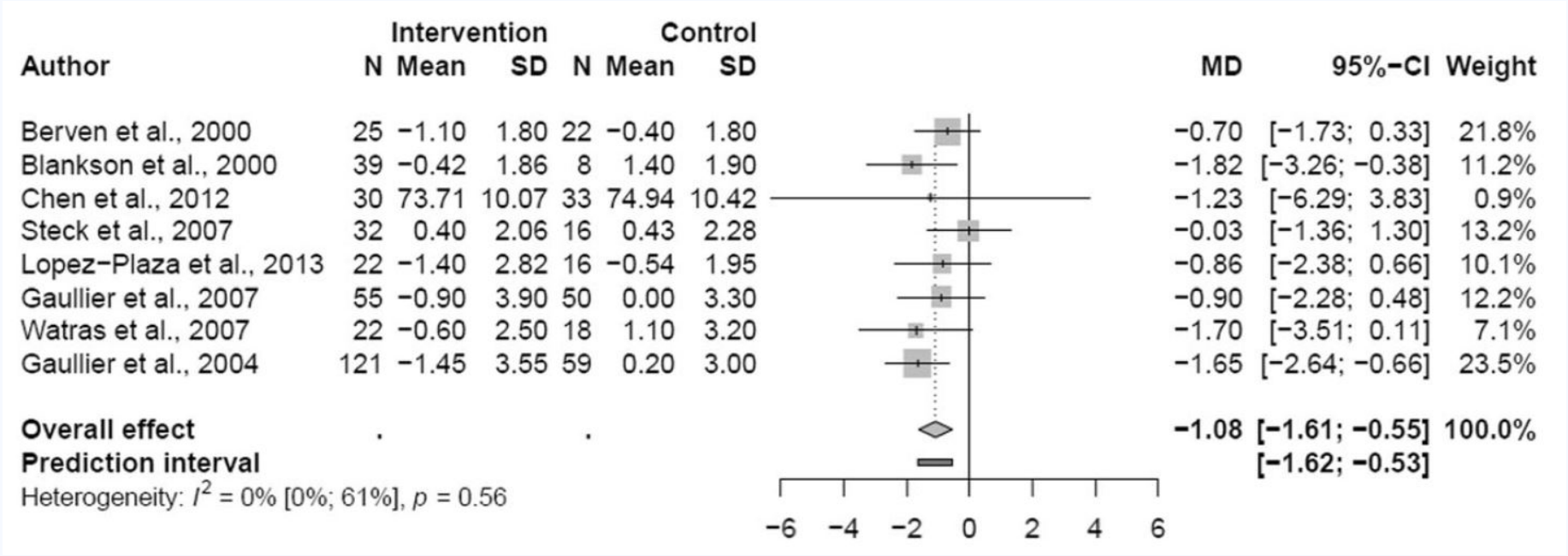
Gastrointestinal related symptoms (gas, bloating, diarrhea) not statistically significant between CLA and placebo but 8/11 RCTs did not report on safety.

Crit Rev Food Sci Nutr . 2020;60(10):1614-1630. doi: 10.1080/10408398.2019.1584873. Epub 2019 Mar 21.

Evidence: Conjugated Linoleic Acid (CLA)

Systematic Review (8 RCTs, 568 patients, >12 weeks)

- Mean difference -1.1kg (-1.6 to -0.6kg) over placebo.
- Side effects: No significant adverse events versus placebo.



Int J Obes (Lond). 2021 May 11.doi: 10.1038/s41366-021-00839-w. Online ahead of print.

Bottom Line

Evidence for Conjugated Linoleic Acid (CLA) suggests a weight change of about 1.1kg over placebo.

The clinical significance of this change is questionable.

The evidence does not suggest significant adverse events in patients.

What is it: Garcinia Cambogia

What is it?

- Herb derived compound extracted from the plant Garcinia cambogia.

What does it do?

- Reduce fatty acid synthesis, suppress food intake and decrease weight gain.

What does it cost?

- $26 for 60 capsules (2 capsules QD)

https://www.amazon.ca/Garcinia-Cambogia-Suppressant-Non-Stimulating-Metabolism/dp/B07SD3BQXJ/ref=sr_1_5?dchild=1&keywords=weight+loss&qid=1622148293&sr=8-5

Evidence: Garcinia Cambogia

RCT (135 patients, Mean BMI 32, mean 39yo, mean weight 86kg)

- Garcinia Cambogia extract 1000mg TID versus placebo

Change in body weight: G. Cambogia -3.2kg vs Placebo -4.1kg (not statistically significant)

Adverse Events

- No significant differences between treatment and placebo.
- Some adverse events reported in the trial included headaches, upper respiratory tract symptoms, gastrointestinal tract symptoms.

JAMA. 1998 Nov 11;280(18):1596-600.
doi: 10.1001/jama.280.18.1596.

Evidence: Garcinia Cambogia

Meta-Analysis (8 RCTs, 530 patients, mean weight 83kg, mean BMI 31, 8-12 weeks)

- G.Cambogia (166mg/day to 4667mg/day) versus placebo

Change in Body Weight: Mean Difference -1.34 kg (-2.6 to -0.7 kg)

Adverse Events

- None reported

Complement Ther Med. 2020 Aug;52:102451.

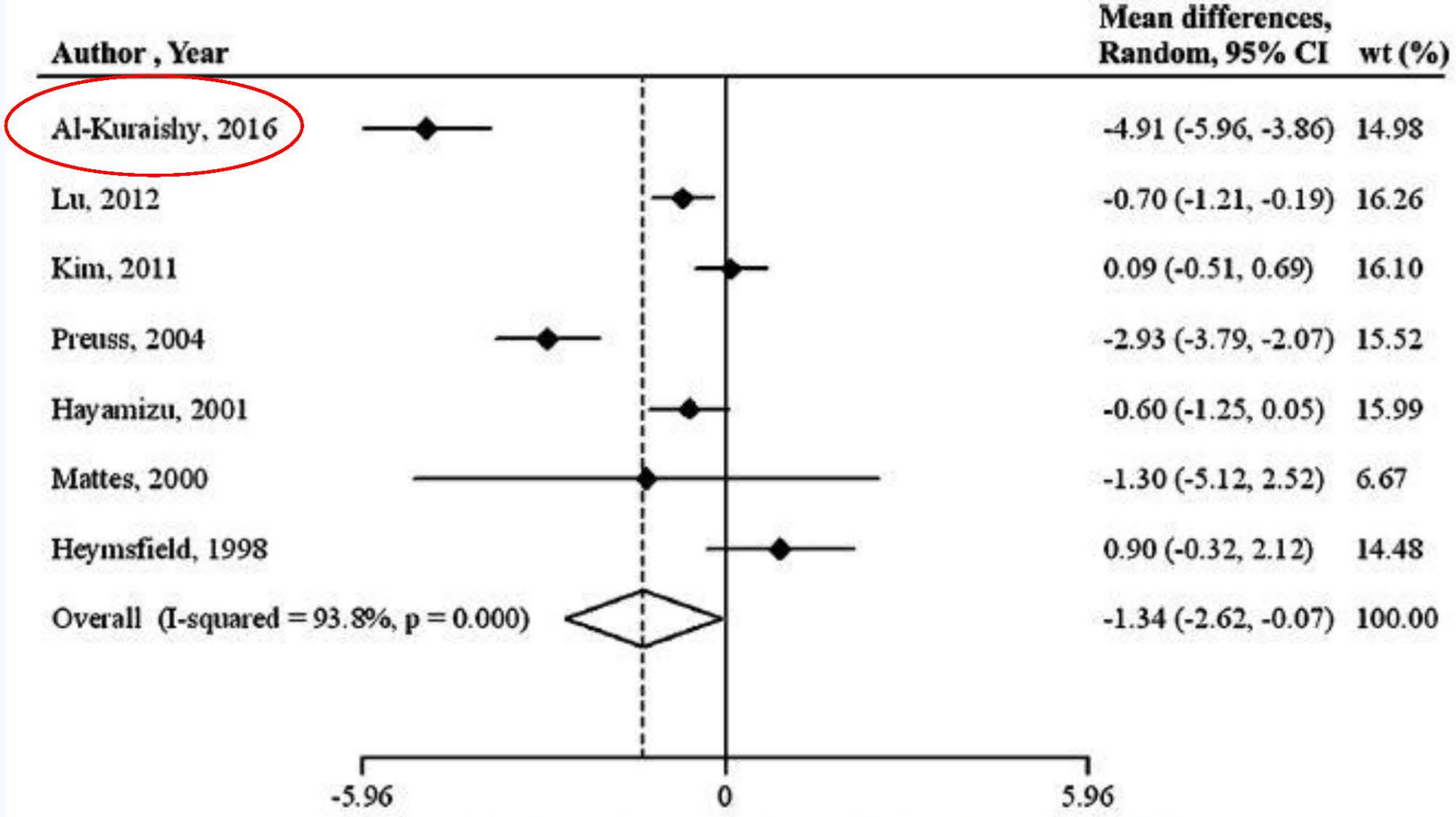


Fig. 2. Forest plot of studies that assessed effect of Garcinia cambogia on body weight.

Complement Ther Med. 2020 Aug;52:102451.

Bottom Line

Highest quality RCT suggests no significant difference between Garcinia Cambogia and placebo.

A meta-analysis suggests Garcinia Cambogia reduces weight about 1 kg more than placebo, but results included a study that should not have been included.

No significant harms found with Garcinia Cambogia.

What is it: Green Tea Extract

What is it?

- Extract from green tea leaves.

What does it do?

- Lose weight and maintain weight loss by increasing person's energy output due to higher concentrations of caffeine.

What does it cost?

- $20 for 60 capsules (1 capsule QD)

https://www.amazon.ca/Garcinia-Cambogia-Suppressant-Non-Stimulating-Metabolism/dp/B07SD3BQXJ/ref=sr_1_5?dchild=1&keywords=weight+loss&qid=1622148293&sr=8-5

Evidence:

Cochrane 2012 (14 RCTs, 1562 patients, baseline weight 68-95kg, BMI 24-32, 12 weeks)

- Green Tea Extract (Included drinks, supplements and tea) vs control

Change in Body Weight: Green tea extract led to an additional loss of 0.95kg compared to placebo.

Adverse Events: No significant adverse events reported within the studies.

Additional Evidence

1 SR (22 studies, 2357 patients, BMI 25-30, duration 2-16 weeks)

- Found green tea reduced weight by about 1.8kg more than placebo

Cochrane Database Syst Rev . 2012 Dec 12;12:CD008650.
Phytother Res . 2020 Oct;34(10):2459-2470. doi: 10.1002/ptr.6697. Epub 2020 May 5.

Bottom Line

Evidence suggests green tea could reduce weight by 1-2kg more than placebo over 3 months.

No significant adverse events seen with this supplement.

What is it: Fibers

Includes:

- Psyllium (Metamucil®)
- Glucomannan (PGX®)
- Many others (Chitosan, Fructans, etc.)

What does it do?

- Soluble fiber that absorbs water and makes you feel fuller.

What does it cost?

- $24 for 200 soft gels (3-6, three times daily)

https://www.amazon.com/Metamucil-Multi-Health-Psyllium-Supplement-Sugar-Free/dp/B003CT2YQY
https://www.amazon.com/Natural-Factors-Daily-Matrix-Softgels/dp/B002HICO48/ref=sr_1_3?dchild=1&keywords=pgx&qid=1622848729&sr=8-3

Evidence

Psyllium

2 RCTs (288 patients, 16 and 52 weeks, 77-91kg):

- No significant weight change vs placebo.
- Side effects: Mainly flatulence experienced with a 1/3 of patients in one of the RCTs.

Glucomannan

7 RCTs (617 patients, 5-52 weeks, 77-101kg):

- Change of -1.3kg (-2.5 to -0.1) over placebo

Limiting to RCTs >12 weeks: -0.79kg (-1.3 to -0.26)

- Side effects: One RCT reported more belching, bloating and stomach fullness with treatment which resolved within 3 days. No other significant findings.

Other fiber supplements found no consistent clinical benefit.

Int J Obes (Lond). 2021 May 11.doi: 10.1038/s41366-021-00839-w. Online ahead of print.

Bottom Line

There are a lot of fiber supplements.

Evidence suggests that fiber supplements such as glucomannan and psyllium do not lead to a clinically significant weight loss.

Side effects are limited to various GI effects.

Supplement Conclusion

The evidence for supplements is mediocre and it is unlikely we will get much better.

Extremely hard to isolate an effect to supplements alone when diet can play a large factor as well.

No significant harms have been suggested in evidence; it will come down to shared decision making.

Motivational Interviewing

Motivational Interviewing for Weight Loss

Evidence:

1 Systematic Review and 4 Randomized Controlled Trials

Systematic Review

11 trials, 3636 participants, Baseline BMI 27-38; interviews ranged in:

- Session duration and frequency;
- Delivery method;
- Delivery Person

In ~½ of the included studies, motivational interviewing was offered in conjunction with a behavioural weight management program

Change in body weight (8 RCTs; 1743 participants; 4-18-month duration):
Mean Difference: -1.47 kg ($p<0.01$)

Armstrong MJ, Mottershead TA, Ronksley PE. Obesity Reviews. 2011;12:709-23.

Motivational Interviewing for weight loss

Evidence:

RCT#1

Primary care population with at least one CVD risk factor (N=334; 6 months with 18-month follow up)

- Compared standard information + motivational interviewing (5 in-person sessions by physical activity specialist and dietician) to standard information alone.

No statistical differences between groups at either time points.

Hardcastle SJ, Taylor AH, Bailey MP. Intern Journal of Behavioural Nutrition and Physical Activity: 2013;10:40

Motivational Interviewing for weight loss

Evidence:

RCT#1

Primary care population with at least one CVD risk factor (N=334; 6 months with 18-month follow up)

- Compared standard information + motivational interviewing (5 in-person sessions by physical activity specialist and dietician) to standard information alone.

Pragmatic- participants could only access counsellors during two, 4-hour blocks/week.

Mean # sessions= 2/5

Lost to follow up was high: 123/334 (37%)

Stages of Change: Started and remained at a stage 3 (preparation) throughout the trial (no move to "action")

Motivational Interviewing for weight loss

MCID -1.25 kg

Evidence:

RCT#2

Adults with a ≥20% risk of CVD over 10 years (N=1742; 12 months with 24-month follow-up; three-armed trial)

- Compared motivational interviewing in two settings (group and individual; 10, 40-minute sessions) to usual care

	Baseline	12 months	24 months
Group	85.2 kg	82.6 kg	82.7 kg
Individual	84.2 kg	83.3 kg	83.0 kg
Control	83.7 kg	83.4 kg	83.1 kg

Individual or Group MI versus Usual Care: **~0.5kg more @ 12 months**

No difference between individual and group.

No differences at 24 months.

Ismail K, Stahl D, Baylet A, et al. Health Tech Assess. 2019;23(69)

Motivational Interviewing for weight loss

Evidence:

RCT#3

Women with Type II diabetes (oral medications only) and BMI 27-50 (N=217, 18 months)

- Compared motivational interviewing (5, 45-minute sessions by clinical psychologist) combined with a behavioural weight control program to program alone.

	Baseline	6 months	12 months	24 months
MI	97 kg	92.3 kg	92.2 kg	93.5 kg
Control	97 kg	93.9 kg	94.3 kg	95.3 kg

Weight Loss
-4.7 kg vs -3.1 kg

All time points were significant, in favour of motivational interviewing.

West D, Gore SA, DiLillo V, et al. Diabetes Care. 2007;30:1081-7;

Motivational Interviewing for weight loss

Evidence:

RCT#3

Women with Type II diabetes (oral medications only) and BMI 27-50 (N=217, 18 months)

- Compared motivational interviewing (5, 45-minute sessions by clinical psychologist) combined with a behavioural weight control program to program alone.

	Baseline	6 months	12 months	24 months
MI	97 kg	92.3 kg	92.2 kg	93.5 kg
Control	97 kg	93.9 kg	94.3 kg	95.3 kg

All time points were significant, in favour of motivational interviewing.

RCT#4

Adults with BMI 25-50 (N=398, 18 months, online only, Baseline Weight: 98 kg)

- Same design, except **online.**
- No difference in outcomes between groups.

Motivational interviewing for weight loss

Motivational interviewing may lead to small reductions (~ 0.5 – 1.5 kg) in weight over 6-12 months, however weight loss is likely not maintained following cessation of interviews.

In-person interviews, in combination with weight loss treatment programs, are likely most effective.

Bottom Line

Frank: Visit 3

- It has been 4 months since you've seen Frank.
- Today's weight: 97 kg (no change)
- Frank has heard about a "new" weight loss drug and wants to know more about his options.

Naltrexone/Bupropion (Contrave®)

Systematic Review (4 RCTs, N=3955, 82% female, 56 weeks, baseline wt ~100kg)[1]

Participants were obese (BMI≥30) OR overweight (BMI≥27) with at least 1 co-morbidity; 1 trial in overweight patients with diabetes

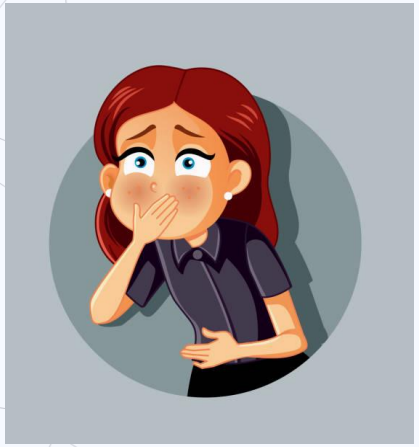
Groups: Naltrexone/Bupropion 32mg/360mg vs placebo (+ lifestyle changes)

Outcomes at 56 weeks:

- **≥5% weight loss**: Naltrexone/Bupropion 53% vs placebo 21% **(NNT 4)**
- **≥10% weight loss**: Naltrexone/Bupropion 29% vs placebo 9% **(NNT 5)**
- **Weight loss** (2 trials reporting): Intervention lost ~ 6 kg (99-93kg) compared to ~1 kg in control (100-99kg)

1. JAMA. 2016; 315(22):2424-34

https://www.mymed.com/medication/contrave-bupropion-naltrexone



Naltrexone/Bupropion (Contrave®)

Withdrawals due to Adverse Events[1]:
29% vs 13% (**NNH 7**)

Significant Adverse Events[2]:
Nausea (31% vs 7%, NNH 5)
Constipation (18% vs 7%, NNH 10)
Headache (12% vs 7%, NNH 20)
Vomiting (10% vs 3%, NNH 15)
Dizziness (9% vs 4%, NNH 10)
Dry Mouth (8% vs 2%, NNH 17)

1. JAMA. 2016; 315(22):2424-34 2. Br J Clin Pharmacol. 2020;86(4):646-667

https://topotcalternatives.com/wp-content/uploads/2018/11/otc-contrave-alternatives.jpg
https://www.istockphoto.com/illustrations/cartoon-of-the-throw-throwing-up

Naltrexone/Bupropion (Contrave®)

Limitations: Industry funded, high dropout rates (~45%)

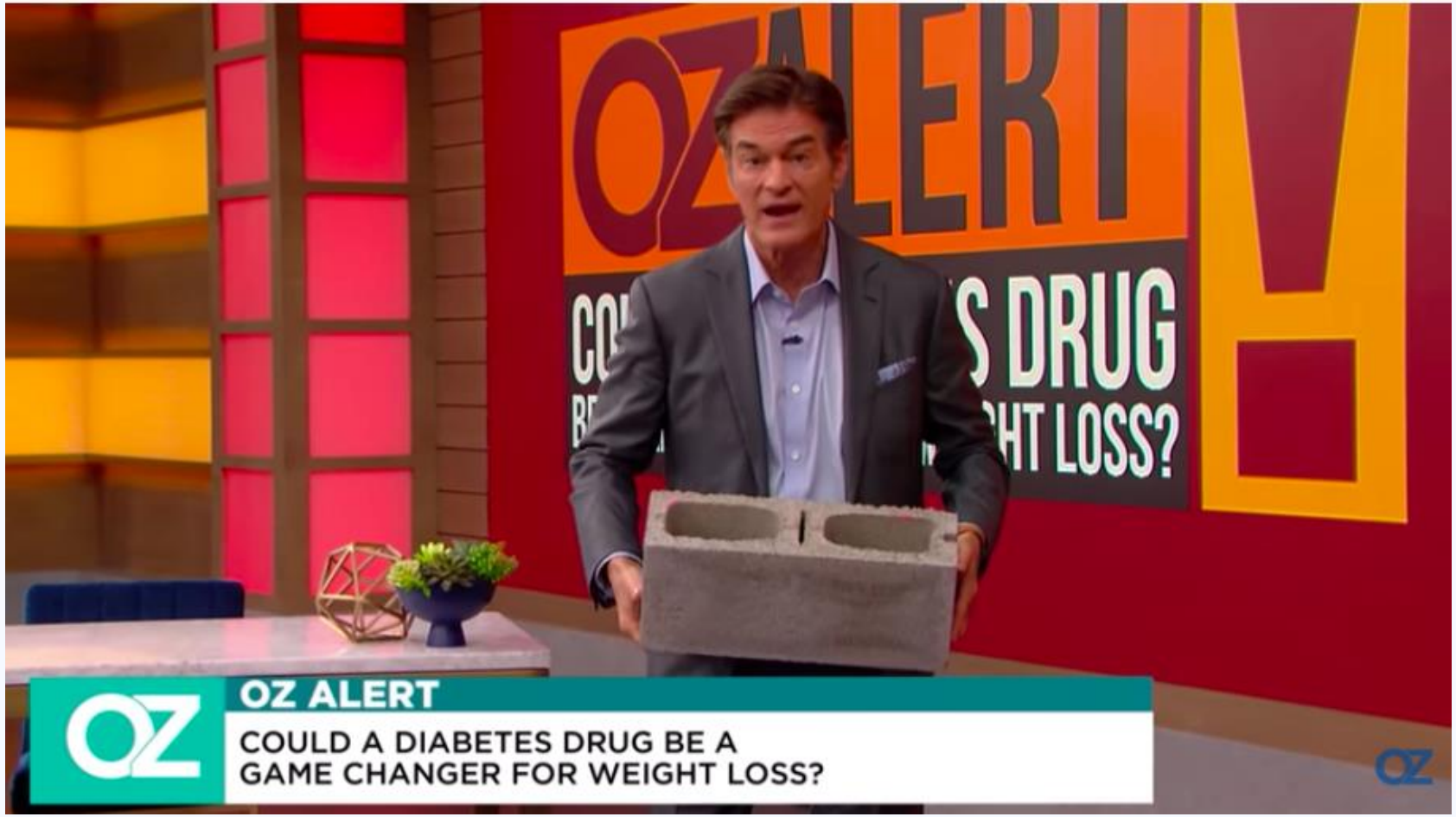
Cost: $275 + dispensing fees per month

Bottom Line:

Over 56 weeks, **53%** of patients taking naltrexone/bupropion achieved a ≥5% loss in body weight, compared to **21%** in control (**NNT= 4**). Withdrawals due to adverse events were significantly greater with naltrexone/bupropion (**29%**) compared to placebo (**13%, NNH=7**).

https://www.goodrx.com/blog/heres-how-to-save-on-weight-loss-medication-contrave/

GLP-1 agonists



Semaglutide

- 4 industry-sponsored RCTs, 2.4mg SC weekly (with lifestyle). Baseline weight ~100kg. DM and non-DM. After 68 weeks:
  - Average weight loss: 10-15% (2-3% placebo)
  - Proportion who lost >5% body weight: 70-80% (30% placebo), NNT=2
  - Lost >10%: ~50-70% (8-12% placebo)
- 2.4mg versus 1mg: mean weight loss 10% versus 7%
- Withdrawal RCT: after 20 weeks treatment, randomized to continue or stop. After 48 weeks:
  - 7% weight regain
- AE:74% GI vs 48% (placebo), NNH=3
  - Withdrawal due to AE: 7% vs 3%, NNH=25
  - Cholelithiasis: 2.6% vs 1.2%, NNH=71

Upcoming TFP. NEJM 2021;384:989-1002, JAMA 2021;325:1403-13, Lancet 2021;397:971-984, JAMA 2021;325:1414-25

Liraglutide

- 2 large industry-sponsored RCTs, Liraglutide 3mg SC daily, mean weight 106kg, ~4500 participants
  - Weight loss: ~3-5% at 1 year
  - Lost >5% body weight: 67% vs 27% (placebo), NNT=3
  - Lost >10%: 33% vs 11% (placebo), NNT=5
- Weight regain once stopped
- Withdrawal for AE: 10% versus 4% (placebo), NNH=17
- Semaglutide vs Liraglutide (semaglutide sponsored): 6-14% versus 8% liraglutide.

TFP #168. August 15, 2016. Lancet 2018;392:637-49

GLP-1 Bottom Line

- Semaglutide and liraglutide both effective for weight loss, with mean weight loss ~3-15% (dose dependent).
  - ~70% lose at least 5% of body weight NNT=2-3
- Semaglutide may be slightly better than liraglutide at higher doses (example, if real: 220-pound person, final weights: ~190 vs 200 pounds)
- Both drugs require dose titration
- Up to 75% of patients experience GI adverse effects
  - about 10% stop for adverse effects
- Cost and availability could limit use.

Frank: Revisited

One month later…

- Frank continues to walk 3-4 times per week and has been following the intermittent fasting diet, although has occasional lapses.
- He recently started liraglutide 3mg SC daily. He is having some nausea but is willing to continue to see if it improves.
- You plan to follow up with Frank in 3 months.

Summary: Weight Loss

- Encourage patients to find a diet they can stick with.
- Advise physical activity 3-5x per week for 30-60 minutes.
- Increase water intake.
- Naltrexone/bupropion can reduce weight by 5-10% over ~ 1 year.
- GLP-1 agonists can reduce weight by 10-15% over ~1 year.

Questions?

SM

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