DIETING SUCCESS: HOW YOU CAN HELP YOUR PATIENTS SUCCEED!

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DISCLOSURE/OFF LABEL DISCUSSION

- Dr. White has no ties to the pharmaceutical industry through speaking, stock ownership, or other arrangement which could provide a real or perceived conflict of interest for this lecture.
- Dr. White has written a book on the topic of metabolic adaptation and ways to overcome it. Sales of the book would directly financially benefit him. You can use the information in this presentation to educate patients and refer them to the trial referenced in the lecture. You do not have to refer people to the book entitled The Part Time Diet: Conquer the Weight Loss Plateau.
- There will be no off label discussion of prescription or over the counter drugs in this lecture. However, there will be a discussion of natural products and food and while the information is referenced, has not been evaluated by the Food and Drug Administration.

OBJECTIVES:

- At the conclusion of this lecture the successful learner will be able to:
  - Describe metabolic adaptation, its physiological underpinnings, and its implications for dieters
  - Describe the potential risks associated with Yo-Yo dieting
  - Describe the part-time diet philosophy and the tenets of successful part-time dieting approaches
  - Define why true dietary breaks are needed and not just altering intensities of continuous dieting
  - Identify metabolic boosters and define the magnitude of their effects
  - Identify drugs that can subvert weight loss and some therapeutic alternatives

METABOLIC ADAPTATION

Plateau occurred at 12.4% body weight loss.

Tremblay A. In J Obes 2013;37:759-64.

SELF ASSESSMENT QUESTION 1

1. What does exercising do to the loss of calorie burn associated with continuous calorie restriction?
   a) Enhances it
   b) Attenuates it
   c) Has no impact

Tremblay A. In J Obes 2013;37:759-64.
**METABOLIC ADAPTATION RELATED TO HUNGER**

Association Between Increases in Hunger (VAS on Y Axis in mm) and Thermogenesis (in kcal/day)

Tremblay A. In J Obes 2013;37:759-64.

**THYROID HORMONE IN NORMAL PEOPLE**

<table>
<thead>
<tr>
<th>Source</th>
<th>Thyroid gland (100%)</th>
<th>Thyroid Gland (30%)</th>
<th>T4 Peripheral Conversion (70%)</th>
<th>T4 Conversion (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posancy</td>
<td>++</td>
<td>++++++</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**RELATIONSHIP BETWEEN T4 AND T3 IN ANOREXIA NERVOSA**

METABOLIC ADAPTATION


**DIETING AND T3 HORMONE IN NORMAL WEIGHTED INDIVIDUALS**

Impact of Calorie Restriction Over the Long-Term on Body Weight (Kg)

CALERIE Study Group 2015
- 318 nonobese people randomized to 2 years of 25% calorie restriction or regular eating

**CALERIE STUDY: IMPACT OF CALORIE RESTRICTION ON METABOLISM AND THYROID HORMONES**

<table>
<thead>
<tr>
<th>Dieting</th>
<th>Baseline</th>
<th>Treatment</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories Consumed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(kcal/day)</td>
<td>12 mo: -20</td>
<td>24 mo: -4</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>RIE (kcal/day)</td>
<td>12 mo: -1</td>
<td>24 mo: -7</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>TDIE (kcal/day)</td>
<td>12 mo: -30</td>
<td>24 mo: -26</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>T3 (ng/dL)</td>
<td>12 mo: -8</td>
<td>24 mo: -18</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>TSH (mIU/L)</td>
<td>12 mo: -0.02</td>
<td>24 mo: -0.15</td>
<td>P=0.04</td>
</tr>
</tbody>
</table>

**IMPACT OF LOW AND VERY LOW CALORIE RESTRICTION IN OBESE PATIENTS ON THYROID HORMONE AND METABOLISM**

**YO-YO IS A NO-NO (AND AN UH-OH)**

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted HR w/ 95% CI</th>
<th>Adjusted HR w/ 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Coronary Event</td>
<td>1.06 (1.03-1.09)</td>
<td>1.04 (1.02-1.07)</td>
</tr>
<tr>
<td>Any Cardiovascular Event</td>
<td>1.05 (1.03-1.08)</td>
<td>1.04 (1.02-1.07)</td>
</tr>
<tr>
<td>Death</td>
<td>1.08 (1.06-1.11)</td>
<td>1.09 (1.06-1.11)</td>
</tr>
</tbody>
</table>

For each movement of body weight of 1.5 to 1.9 kg in the TNT trial (Up or Down), the risk of developing coronary events (heart attack, angina), cardiovascular events (coronary + stroke + TIA), or dying is significantly increased.

22.4% of people with the least weight variability had a cardiovascular event versus 36.9% of those with the most variability (quintile 1 vs 5) and a positive relationship across all quintiles (p<0.001 for trend).


**SELF ASSESSMENT QUESTION 2**

2. What does continuous dieting do to resting calorie expenditures each day and to T3 thyroid concentrations?

- a) Reduces calorie expenditure but increases T3 concentrations
- b) Reduces calorie expenditure and decreases T3 concentrations
- c) Increases calorie expenditure and decreases T3 concentrations
- d) Has no effect on either of these items

**PART-TIME DIETING VS. NO DIETING**

- There are tons of observational studies looking at benefits of ritualistic fasting (Ramadan, etc), intermittent fasting, and part-time dieting versus no control (before vs. after), historical control, or non-diet control.
- This data is inherently biased and weak, and I did not put stock in most of this data set, you shouldn't either.
- There are tons of rodent studies looking at mechanisms and effects.
- This data can explain real phenomena but should not be used as proof of the phenomena, too many times animal data showing an effects has not translated into the human trial realm.

**MATADOR TRIAL**

- Minimizing Adaptive Thermogenesis and Deactivating Obesity Rebound (MATADOR)
- 51 obese men
- Diet cut 33% of baseline calories during active diet days
- Byrn NM. In J Obes 2018: 42:129-38

**MATADOR TRIAL: WEIGHT LOSS RESULTS**

- 10.8 more pounds of weight loss (P=0.009) ER = Active, EB = Break

**MATADOR TRIAL OFF DIET WEIGHT LOSS RESULTS**

- Part-Time Dieters gained back 3.0 fewer lbs than the Continuous Dieters
MATADOR TRIAL: REE RESULTS

REE = Resting energy expenditure (# calories burned each day by just living)

<table>
<thead>
<tr>
<th></th>
<th>Continuous Diet</th>
<th>Part-Time Diet</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>9047±737</td>
<td>8619±963</td>
<td>0.48</td>
</tr>
<tr>
<td>16 Weeks Active Dieting</td>
<td>-624±557</td>
<td>-502±481</td>
<td>0.48</td>
</tr>
<tr>
<td>6 Months of Follow-Up</td>
<td>-548±590</td>
<td>-452±494</td>
<td>0.65</td>
</tr>
</tbody>
</table>

REE = Resting energy expenditure

Adjusted REE = Adjusted for decreases in weight

<table>
<thead>
<tr>
<th></th>
<th>Continuous Diet</th>
<th>Part-Time Diet</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>-749±498</td>
<td>-360±502</td>
<td>0.03</td>
</tr>
<tr>
<td>6 Months of Follow-Up</td>
<td>-770±523</td>
<td>-255±515</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Part-Time Dieting Leads to 389 more calories being burned each day over 16 weeks & 515 more calories being burned even at 6 months after the end of dieting. Treadmill walking at 3.5 mph for 1 hour = 356 calories (as per: https://www.livestrong.com/article/308255-calories-burned-per-hour-on-a-treadmill/)

Roman YM. Int J Obes 2018; doi: 10.1038/s41366-018-0204-0.

ROMAN 2018: TRIALS BROKEN UP BY STUDY QUALITY

- Trials using ITT Analyses
  - -3.15 (-6.22 to -0.09)kg additional weight loss (~7 lbs) with intermittent versus continuous dieting
- Trials not employing ITT Analyses
  - +0.98 (-0.36 to +2.32)kg additional weight gain (~2 lbs) with intermittent versus continuous dieting
- These trials had very high attrition rates (people leaving the studies)
  - Keogh 2014 [6.4% attrition in intermittent vs 20% in continuous]
  - Wing 2003 [over 50% attrition in both groups]

Roman YM. Int J Obes 2018; doi: 10.1038/s41366-018-0204-0.

KEOGH 2014 DIFFERENT DIET LENGTHS

- Continuous Dieting: 1315 kcal/day for 8 weeks
- Part-Time dieting: 1315 kcal/day for 1 week then 1 week break (usual diet) for 8 weeks
- Unlike other studies, this is only 4 weeks of active dieting
- Weight loss of 2 weeks: -3.2±2.1 kg vs. 2.0±1.9 kg (p=0.063)
- So dieting for half as many days resulted in losing 2.6 fewer lbs


SUPPORTING TRIALS: FIRST THREE USED ITT, LAST TWO EXCLUDED BECAUSE DIET INTENSITY CHANGED IF DIET RESULTS WERE NOT SEEN

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Diet Details</th>
<th>Results: Cont vs. Part-Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carter 2016</td>
<td>1553 kcal/day for 12 weeks vs. 597kcal 2 days per week and rest on other days for 12 weeks</td>
<td>-4.0kg vs. -5.0kg (p=NS)</td>
</tr>
<tr>
<td>Harvie 2013</td>
<td>35% weekly calorie reduction every day vs 70% calorie restriction 2 days per week and rest other days for 12 weeks</td>
<td>-3.7kg vs. -5.0kg (p=NS)</td>
</tr>
<tr>
<td>Harvie 2011</td>
<td>35% weekly calorie reduction every day vs. 75% calorie restriction 2 days per week and rest other days for 24 weeks</td>
<td>-4.6kg vs. -5.7kg (p=NS)</td>
</tr>
<tr>
<td>Rustor 1990</td>
<td>300 or 500kcal/day everyday for 4 weeks vs. 500kcal diet 3 times a week for 4 weeks with breaks of 4 weeks in between</td>
<td>Study A: -12.4kg vs. -15.7kg (p=NS) Study B: -15.2kg vs. -22.6kg (p=NS) Study C: -12.8kg vs. -14.8kg (p=NS)</td>
</tr>
<tr>
<td>Arguin 2012</td>
<td>Continued energy restriction for 15 weeks followed by 5 weeks of weight stabilization vs. 15-week dieting followed by 5-week rest periods for 20 total weeks</td>
<td>-7.5kg vs. -1.7kg (p=NS)</td>
</tr>
</tbody>
</table>

REFERENCES FOR TABLE

SELF-ASSESSMENT QUESTION 3

3. What can best be said about intermittent dieting versus continuous dieting in terms of weight loss?
   a) Trials assessing equal number of dietary days using intention to treat methodology found modest additional benefits from part-time dieting
   b) All the trials showed impressive results and intermittent dieting is clearly the best approach
   c) None of the trials found that it made any difference

A CAUTIONARY TALE: RESTS MUST BE RESTS

- In a trial by Wing 1994, obese patients consumed 1,000-1,200 kcal/day for 48 weeks vs. 12 weeks of 400-500 kcal/day followed by 12 weeks of 1,000-1,200 kcal/day for 48 weeks
- In effect low calorie diet versus low calorie alternating with VLCD
- Alternating group cut 25% more calories over the study than the other group

WING 1994 RESULTS (P<0.05 FOR BOTH)

- Better weight loss after first 12 weeks (VLCD vs. LCD)
- Where is the weight loss in either group for 24 weeks, especially the group with 1 additional round of VLCD built in?

WING 1994: WHY DIETS PLATEAU AND REAL BREAKS ARE NEEDED

VARIABLE CONTINUOUS DIETING VERSUS STEADY CONTINUOUS DIETING

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Calories Consumed</th>
<th>RSE or BMI Effects</th>
<th>Activity Calories Required</th>
<th>Weight Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&gt;100 kcal/day</td>
<td></td>
<td>&gt;150-300 kcal/day</td>
<td>&gt;7 lb/week</td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td>&gt;3 lb/week</td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td>5-7 kcal/day</td>
<td>&gt;3 lb/week</td>
</tr>
<tr>
<td>120 kcal/tablespoon</td>
<td>&lt;80 kcal/day</td>
<td>0</td>
<td>1.7 kcal/day</td>
<td>&gt;3 lb/week</td>
</tr>
<tr>
<td>32 kcal</td>
<td>0</td>
<td></td>
<td>1.7 kcal/day</td>
<td>&gt;3 lb/week</td>
</tr>
<tr>
<td>2 kcal</td>
<td>&gt;30 kcal/day</td>
<td>0</td>
<td>1.7 kcal/day</td>
<td>&gt;3 lb/week</td>
</tr>
<tr>
<td>0 kcal</td>
<td>0</td>
<td></td>
<td>1.7 kcal/day</td>
<td>&gt;3 lb/week</td>
</tr>
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<td>0 kcal</td>
<td>0</td>
<td></td>
<td>1.7 kcal/day</td>
<td>&gt;3 lb/week</td>
</tr>
</tbody>
</table>

Stimulants double or triple risk of mental, GI, and heart rhythm ADEs!

REFERENCES

Roman YM, Int J Obes 2018; doi: 10.1038/s41366-018-0204-0.
### DIETARY SUPPLEMENTS FOR WEIGHT LOSS

- FDA reports 317 “natural” weight loss aids sold from 2007 to 2016 secretly contain prescription drugs
- Sibutramine, sibutramine, fenfluramine
- All banned by the FDA because of proven cardiovascular risks
- Phenolphthalein and loop diuretics
- Dehydration and hypokalemia risk, phenolphthalein has possible cancer risk as well
- Non-FDA approved antidepressants (depressants)
- Risk of serotonin syndrome when combined with other serotonin-enhancing drugs
- Muscle rigidity, high body temperatures, seizures, muscle and kidney damage


### FEELING MORE FULL

- Vinegar Chili Peppers Water Slowly Digestible Starch
- Resistant Starch
- Low Carb Vegetables


### SELF ASSESSMENT QUESTION 4

4. What can best be said about metabolic boosters?

- a) Aside from exercise, their impact on enhancing calorie burn or weight loss is very small and cannot overcome metabolic adaptation on their own
- b) They are the “missing link” in our quest to lose weight
- c) They actually suppress the number of calories burned each day instead of increasing it

### CHEMICALS THAT INCREASE WEIGHT

- Things that release or mimic cortisol
- Sleeplessness/sleep apnea—Good sleep hygiene or CPAP
- No blue spectrum light before bed, no reading emails before bed, bed just for sleeping, sleeping when tired
- Corticosteroids—Use topical varieties, adjuvants, and alternatives to lower systemic steroid dose
- Insulin and sulfonylureas—Metformin, sitagliptin, exenatide are alternatives
- THC—Lower THC varieties for medicinal purposes, reducing recreational use


### CHEMICALS THAT INCREASE WEIGHT

- Things that block histamine-1 receptors
- Antihistamines (diphenhydramine, fexofenadine, cetirizine, etc)
- Antipsychotics (Huge increases in weight) – Zyprexa and aripiprazole are alternatives
- Antidepressants (tricyclics, mirtazapine) – Ziprasidone, quetiapine, duloxetine are alternatives
- Antihistamines
- Valproic acid, Lamictal – Topiramate is an alternative
- Progestosterone stimulators
- Medroxyprogesterone – Newer birth control pills and IUD methods have lower risk


### CONCLUSIONS

- Healthy eating is important for overall health—whether or not you lose weight
- Mediterranean and DASH eating plans have most evidence of health benefits
- Vegetarian and DASH eating plans have most evidence of health benefits
- Losing weight is hard
- Initial weight loss is a false weight loss
- Continuous dieting advantages future weight loss through metabolic adaptation
- "Metabolic adaptation is highly responsive to recent caloric exposure"
- Exercise increased fiber intake and goal keeping are important keys to weight loss
- Exercise (including intermittent fasting) lasting less than three days a week or dieting for a week or two before taking a rest week or two in a row is not a way to ensure weight loss over a longer period of time
- Longer-term options need to firmly establish the metabolic sensitiveness (especially WOMEN) are very sensitive
- Gaining weight after dieting is easier to do than losing it was
- Low cheat meals adaptation can help maintain
- Practicing weight maintenance during rest days can help
- Yo-yo dieting may be risky