## **Redefining Lifestyle to Improve Metabolic Health**

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#### Abstract

Weight loss continues to be a leading lifestyle recommendation to improve metabolic health in those at risk of type 2 diabetes. Initially weight loss does improve hyperinsulinemia, insulin resistance, inflammation, and hyperglycemia. However, these gains are often reversed due to homeostasis hormones that work to replenish lost energy stores. What follows for many patients is rebound weight that is gained back as metabolically harmful visceral fat. For these weight-cycling clients, dieting attempts may actually increase their risk of metabolic disease including type 2 diabetes. Emerging evidence supports alternative life-style interventions to prevent weight gain and improve insulin sensitivity and glucose tolerance. Some of these interventions include: finding and addressing causes of weight gain to prevent continued gain, improving sleep, incorporating vigorous activity into daily life, and eating based on internal cues. These interventions are all evidence-based, helpful ways to prevent and/or treat diabetes. This review discusses ways to diagnose and educate patients to alter their life-style in a more sustainable, homeostasis friendly way that may both help prevent weight cycling and improve metabolic health.

#### A HEALTHY LIFESTYLE WITHOUT PRESCRIBING WEIGHT LOSS

One of the leading approaches to improving metabolic health and thereby preventing diabetes is recommending to individuals that they lose weight.<sup>1,2</sup> However, because of homeostatic responses to energy loss, this lifestyle recommendation may not always lead to desired long-term metabolic health. It is true that in the short term, weight loss can improve insulin sensitivity. Consuming fewer carbohydrates, increasing activity, and/or temporarily reversing leptin resistance by decreasing the size of fat cells can improve glucose tolerance. Leptin is a long-term fullness hormone produced by fat cells that also has euglycemic properties.<sup>3</sup> When leptin signals the hypothalamus that adequate fat stores are present, messages are sent to eat less, expend more energy, and normalize glucose levels. However, too much fat triggers as yet unknown chemical messengers, making the hypothalamus resistant to leptin.<sup>4</sup> While lower leptin levels may improve leptin sensitivity, they also decrease energy expenditure and increase appetite, leading to the starvation response.<sup>5</sup> The body's reaction to weight loss that makes rebound weight gain so likely.

### WEIGHT LOSS LIKELY LEADS TO WEIGHT

## REGAIN AND METABOLICALLY UNHEALTHY WEIGHT CYCLING

While weight homeostasis is very complex, it is similar to many other homeostasis systems where a disruption is met with compensation. Focusing on calories-in and calories-out neglects the impact of energy hormones on the need of the human body to maintain or achieve homeostasis.<sup>6</sup> While the lack of will power is often blamed for weight regain after dieting, it is more likely due to metabolic compensation where hunger and fullness hormones work to prevent or reverse weight loss. These homeostatic forces make keeping weight off especially difficult. Rebound weight gain is often the end result<sup>7</sup>.

Regaining lost weight after a diet often leads to another weight loss attempt. With repetitive loss and gain of 10-50 pounds, a pattern of weight cycling emerges. Weight cycling is a high-risk behavior for the development of Type 2 diabetes (T2D), as regained weight is more metabolically unhealthy because it preferentially deposits as visceral fat.<sup>8</sup> Visceral adipose tissue, as opposed to subcutaneous adipose tissue, produces more inflammatory factors, as well as resistin and visfatin, hormones that are linked to insulin resistance.<sup>9</sup> In summary, while all weight gain can lead to negative metabolic changes, regained weight is especially likely to promote insulin resistance and inflammation. There are a number of things an individual can do to improve metabolic health with little risk of weight cycling. Preventing further weight gain by addressing causes, promoting sleep, engaging in vigorous exercise, and combining intuitive eating can nurture homeostasis rather than disrupting it.

# INVESTIGATING THE CAUSES OF WEIGHT GAIN TO PREVENT CONTINUED GAIN

There are many reasons for undesired weight gain, and the varied causes should be investigated by the clinician. A nonintuitive lifestyle that involves indulging in excess amounts of calorically dense foods, and decreasing physical activity are often reasons why individuals gain weight.<sup>10</sup> However, these behaviors are just some of the reasons for weight gain. Clinicians need to rule out non-behavioral causes before concluding that an indulgent lifestyle is to blame. Emotional states, medications, endocrine disorders, activity-induced pain, and rebound weight gain after dieting are common causes of weight gain that should not be overlooked.

#### Emotional or Stress Eating

Emotional eating often results in consumption of excess food or poor food choices and often leads to weight gain. Beginning a stressful new job or going through a divorce are just two examples of life events that can spur emotional eating. Asking patients if they have noticed a change in their eating habits, and if that coincided with any other changes in their lives, should be part of the history if weight gain has occurred. If the patient acknowledges overriding fullness cues and eating more than usual, the underlying stress, emotional pain, depression, and/or anxiety could be helped in a variety of ways. Cognitive behavioral therapy (CBT), and intuitive eating/mindfulness training are two techniques supported by the evidence.<sup>11,12</sup> While CBT has been the gold standard for emotional eating, referral to a psychotherapist would be necessary. Primary care practitioners, on the other hand, can recommend the use of mindfulness and the if-then strategy of implementation intention<sup>13</sup>. Having patients notice how they feel when they overeat, and log the intention, "'IF' While I am eating 'THEN' I am paying attention to the serving size" is a powerful strategy to remove distractions and help internalize a positive behavior change.<sup>13,14</sup> If not comfortable teaching these strategies advanced practice nurses can refer patients to self-help books, telephone coaching, internet, and smartphone applications (see Table 1).

#### Medications

Some of the biggest contributors to weight gain are often commonly prescribed medications. The leading classes of medications inducing weight gain, in order of severity are: antiepileptics, antipsychotics, antidiabetic agents, glucocorticoids, antidepressants, hormonal contraceptives, antihypertensive agents, and antihistamines.<sup>15</sup> Besides causing weight gain, some of the medications can cause metabolic changes including hyperglycemia and lipotoxicity. Antiepileptics that are more likely to cause weight gain include, carbamazepine, gabapentin, and valproate, whereas, lamotrigine, phenytoin, and topiramate are low risk for weight gain. Among the popular second-generation antipsychotics, olanzapine and clozapine are known to be high risk for severe weight gain, and T2D. The antipsychotic quetiapine poses a moderate risk, and aripiprazole and paliperidone are at low risk for weight gain. Among antidiabetic drugs, insulins and sulfonylureas are associated with moderate to severe weight gain. This gain occurs because insulin's role is to drive glucose into cells. These extra calories are likely to be stored as either fat or muscle, thus increasing the individual's weight. The mechanism of a sulfonylurea is to stimulate the secretion of insulin, thereby acting like an insulin. The basal insulin detemir is associated with less risk of weight gain than regular insulin presumably related to the prolonged duration of glycemic control<sup>16</sup>. Oral hypoglycemics, including GLP-1 agonists and GLT-2 inhibitors can induce weight loss through decreased glucagon and slowed gastric emptying decreasing food intake. These hypoglycemics should replace sulfonylureas as they can potentially induce some weight loss in patients at risk for weight related metabolic disease.15 (See Table 1.)

Glucocorticoids are prescribed to reduce inflammation and are universally associated with both weight gain and metabolic changes including hyperglycemia. While the benefits of short term steroids may outweigh the risks, for longer term usage, non-steroidal anti-inflammatories or disease modifying drugs could be used.15 While the only class of antihypertensives to cause weight gain are beta blockers, both beta-blockers and thiazolidinediones can cause dysglycemia. The two classes of antihypertensives that may prevent weight gain and improve insulin sensitivity are ACE-inhibitors and angiotensin receptor blockers (ARBS). Another potential cause for weight gain includes hormonal contraceptives. Among the biggest offenders for weight gain and dysglycemia are the progestin only injectables or implants.<sup>17,18</sup> The results are more mixed when it comes to combination contraceptives, with some women experiencing no weight gain, or even weight loss, while others can gain

moderate amounts of weight.<sup>19</sup> In the antihistamine class, diphenhydramine, a sedating drug, can cause weight gain, while the non-sedating loratadine and cetirizine are lower risk options<sup>20</sup>. While not everyone responds with weight gain or metabolic changes, assessing for these changes is critical. The treatment implications for these findings is to start with those medications at the lowest risk for causing weight gain, and if the patient is already on a medication and has gained weight, to consider changing to a weight neutral or weight loss medication in the same class.<sup>15</sup> (See Table 1)

#### Endocrine

Weight gain should prompt investigation into possible endocrine causes, the two most common endocrine disorders associated with weight gain and metabolic changes are Polycystic Ovarian Syndrome (PCOS) and hypothyroidism. Polycystic Ovarian Syndrome (PCOS) has a prevalence in the US of 4 - 12% while the prevalence of hypothyroidism is estimated at 4.6%.<sup>21</sup> PCOS is a complex disorder that overlaps with metabolic syndrome. Ten percent of patients with PCOS are diagnosed during a gynecology appointment due to menstrual complaints, as PCOS causes infrequent menses. Excess weight and virilizing effects may also be a complaint of women with PCOS.<sup>22</sup> However, the metabolic disorders common in PCOS may go unrecognized by women with the disorder. Assessing glucose levels and cardiovascular risk is essential. Metformin can be used both preventively and for prediabetes and is generally considered weight neutral.<sup>22</sup>

Hypothyroidism continues to go underdiagnosed even though most medical histories assess for recent weight gain.<sup>23</sup> While not as metabolically unhealthy as PCOS, excess weight found in undiagnosed or undertreated hypothyroidism can cause leptin insensitivity, putting the patient at risk for T2D. Thyroid stimulating hormone (TSH), has been the gold standard in screening for hypothyroidism. With that being said, a normal TSH tells us only that the pituitary is functioning and the thyroid is producing enough thyroxine (T4) to trigger the negative feedback response. However, most of the body's cells need the more active form of thyroid, triiodothyronine (T3), which requires T4 to be converted into T3. $^{23}$  If T3 is low. hypothyroid symptoms and effects are seen even though the pituitary and the thyroid are working.25 Because fT4 and fT3 need to be deiodinated in the cell there has been a call among holistic endocrine practitioners and scientists to

include fT4 and fT3 in the workup of someone who is symptomatic.<sup>26,27</sup> Hypothyroid patients who become euthyroid often lose weight and improve their lipid profiles.

## "NEW" LIFESTYLE RECOMMENDATIONS THAT CAN IMPROVE METABOLIC HEALTH

#### Sleep

Emerging evidence is finding sleep to be very beneficial in improving metabolic health and thereby preventing diabetes. Assessing for sleep insufficiency in patients who have gained weight is important, as they may need help's figuring out how to sleep longer and deeper. Getting between 7-8.5 hours of sleep a night is needed for optimal health.<sup>28</sup> Shortened sleep duration has been shown to increase cortisol and ghrelin levels, which in turn increases appetite and food intake.<sup>28,29</sup> When sleep is increased, leptin and insulin sensitivity, body mass index (BMI), and glucose tolerance are all improved.<sup>30,31</sup> The biggest contributors of shortened sleep are circadian disturbances like early awakening, poor sleep hygiene, and psychiatric/psychological causes leading to insomnia. Significant metabolic health risks such as occur with less than 6 hours of sleep.<sup>32</sup>

Sleep hygiene can help getting to sleep on time as well as sleeping more deeply. Patients should be apprised of the need to avoid caffeine 7 hours, and alcohol 2 hours before bedtime. Also turning off of "blue light" an hour before bedtime is a good way to help increase the natural sleep hormone melatonin.33 For patients who still find it difficult to fall asleep or stay asleep, recommending melatonin supplements can help.<sup>34</sup> If restorative sleep still evades the patient, it is important to assess for obstructive sleep apnea (OSA), a major disruptor of deep, restful sleep and is associated with obesity.<sup>35</sup> Obstructive sleep apnea can be dealt with in traditional ways by prescribing a sleep study and a consultation with a sleep specialist. However, for those clinicians working with uninsured patients who report excessive daytime sleepiness, and snoring associated apnea, recommending a 30 degree wedge be placed under the top half of the mattress could be very helpful.<sup>36</sup> (See Table 2)

#### Exercise

The knowledge that exercise improves cardiometabolic health is not new, however, recent studies show that even short bouts of vigorous exercise can promote metabolic health.<sup>37,38 39,40</sup> Increasing the heart rate to 85% of maximum (220 – age) as few as 10 minutes daily or 18 minutes several times a week may be sufficient to see improvement in

aerobic health and leptin sensitivity <sup>41,42</sup>. Vigorous dancing, hiking, playing tag or water games, bicycling up hill, are some of the ways to improve metabolic health. Smartphone apps can help keep patients active.<sup>43,44</sup> While moderate exercise also benefits health, putting in the required 10,000 steps a day may be difficult for working parents or those with activity-induced pain in lower extremities. For those with more time and unable to walk for exercise, video game console sports, such as Nintendo Wii tennis, baseball, or boxing can be done at home. Rowing machines, and other upper body activities could be done either moderately or in vigorous bursts (See Table 2).

Decreasing physical activity could also result in weight gain. There are many reasons for this besides preferring to sit on the sofa and watch television. Reduced activity could be a result of fatigue, chronic pain, old injuries, or newly developing arthritis.<sup>45</sup> For those suffering from pain, referral to an appropriate specialist may be indicated. Physical therapy can also help to maximize their mobility and find exercise that is also enjoyable, sustainable, and suitable for their limitations.

#### Intuitive Eating

Research shows that threats to health, such as lack of food, sleep, or long periods of exertion, are perceived by homeostatic sensors as threats to human survival.<sup>39,40</sup> Dieting which often requires ignoring hunger, may be perceived as a threat, whereas intuitive eating, which honors internal cues is perceived as reassuring to the body<sup>14</sup> This alternative approach to dieting was started by lay health writers in the 1980's and has dieticians more likely to use intuitive eating than restrictive practices.<sup>14,46</sup> By having patients make sure they have healthy and delicious food available for when ideal hunger sets in (neither starving nor hardly hungry) so they can eat until they are satisfied is key for intuitive eating.<sup>46</sup> Whether an advance practice nurse or a nutritionist helps guide the patient, this non-dieting approach to eating helps patients replace an antagonistic relationship with the body for a nurturing one.<sup>14</sup>

### SUMMARY

Emerging evidence is revealing real but invisible compensatory mechanisms that make weight loss difficult to maintain. With the recognition that some patients may be especially susceptible to the risk of weight regain, and that regained weight secretes metabolically unhealthy hormones. Advance practice nurses are in a prime position to promote effective lifestyle changes that can prevent metabolic disease with minimal risk of weight regain and weight cycling.<sup>48,49,50</sup>

Investigating why patients have gained weight, finding out how there are sleeping, and what they do for exercise could be very helpful in recommending targeted, evidence-based lifestyle changes. Sleep reduces hunger evoking hormones like ghrelin and cortisol, while exercise re-sensitizes the hypothalamus to leptin, a known antidiabetic hormone.<sup>51,52</sup>

Also beneficial is finding out what cues a patient to eat, or begin a meal, as well as what motivates them to stop eating. Having patients eat based on internal cues prevents both the starving and the splurging responses than can occur when hunger is ignored. Helping patients focus on these metabolically healthy behaviors are also often easier to comply with than overriding a powerful survival cue like hunger. Lifestyle that incorporates activities that help restore leptin and insulin sensitivity can go a long way to improving metabolic health and thereby preventing a major cause of global morbidity and mortality, T2D.

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