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Practice Matters

Is Semaglutide the Key to the Fight Against “Globesity”?

The obesity epidemic was described by the World Health Organization (WHO) as “globesity” in 2001, and the numbers continue to worsen (Khemka et al., 2016; Kamal et al., 2024). In 2022, an estimated 2.5 billion (43%) adults were overweight and 890 million (16%) of those individuals were obese correlating to 1 in 8 worldwide living with obesity (WHO, 2024). By 2030 that number is expected to be more than one billion individuals or 17.5% of the world population will be obese. Obesity is a significant issue for the United States as more than 2 in 5 adults are obese with an estimated \$173 billion in healthcare costs being attributed to obesity and related health consequences (Centers for Disease Control and Prevention [CDC], 2024b). Due to the continued increase in obesity rate, the Faith Community Nurse (FCN) can serve a pivotal role in helping patients understand obesity, diseases associated with increased weight, and lifestyle changes to decrease weight and improve health.

Obesity is defined as a body mass index (BMI) of 30 or greater (WHO, 2024). BMI is a calculation using an individual’s height and weight [weight (kg)/height(m²)] and is considered along with assessment of health risks in the diagnosis of overweight and obesity (National Institute of Child Health and Human Development [NICHD], n.d.; WHO 2023). See table 1 for BMI designations of those 18 years of age and older.

Table 1

BMI Categories (Adults ≥18 years of age)

BMI	Category
Below 18.5	Underweight
18.5-24.9	Healthy weight
25.0-29.9	Overweight
30 and above	Obesity
>40	Morbid obesity

Adapted from “How are Obesity & Overweight Diagnosed?” by NICHD, (<https://www.nichd.nih.gov/health/topics/obesity/conditioninfo/diagnosed>).

The link between obesity and noncommunicable diseases (NCDs) is irrefutable with obesity being a risk factor for hypertension, stroke, coronary artery disease, diabetes type 2, some cancers (e.g., breast, colon), musculoskeletal disorders, and respiratory disease (Kamal et al., 2024; WHO 2023). During the COVID-19 pandemic, individuals who were overweight and obese were twice as likely to be hospitalized with a greater risk for severe illness and mortality (CDC, 2024a; Kamal et al., 2024; WHO, 2023). This risk of severe illness worsens with increasing BMI in addition to those with chronic lung disease, cancer, stroke or cerebrovascular disease, heart conditions, or diabetes. Obesity management guidelines suggest that a 5% reduction in body weight may prevent the development of NCDs (Ruseva et al., 2024).

Obesity Management

The cause of obesity is multifactorial, and the management of obesity is a challenge for individuals as well as medical professionals. Some experts point to evolutionary changes as a cause for our current obesity issues (Martinez-Gomez & Roberts, 2022). The *thrifty gene hypothesis* theorizes that during periods of food scarcity those whose metabolism adapted passed those genes to future generations and may be related to the occurrence of metabolic adaptations to weight loss leading to weight regain.

Lifestyle Changes

According to the 2013 American Heart Association, American College of Cardiology, and The Obesity Society guideline to attain weight loss, a decrease in caloric intake is required (Jensen et al., 2014). Suggested caloric targets of 1200 to 1500 kcal/d for women and 1500 to 1800 kcal/d for men or a 500 kcal/d or 750 kcal/d or 30% energy deficit are recommended. Dietary approaches are varied and should be based on the individual. The Mediterranean diet can be beneficial long-term, the low carbohydrate diet can improve glycemic control in those with diabetes, and high protein diets improve lean muscle mass and satiety (Yurista, et al., 2023). A diet of whole grains, lean protein, fruits, vegetables, fiber-rich foods while restricting refined sugars and alcohol is also encouraged.

The connection between the gut microbiota and obesity has been established indicating that a gut microbiota lacking diversity is a forerunner to obesity (Liu et al., 2021). Dysbiosis is the imbalance of gut microbiota. This can include a decrease in diversity or an imbalance in harmful and beneficial bacteria. The gut microbiota influences appetite, energy absorption, fat storage, circadian rhythm, and chronic inflammation, all of which contribute to obesity. A diverse gut microbiota is crucial for the maintenance of metabolism and energy balance. The gut microbiome may be enriched with a low-fat diet, limiting animal products, and increasing fruits and vegetables (Cunningham et al., 2021).

Probiotics and prebiotics play important roles in symbiosis of the gut microbiota (Ballini et al., 2023). Probiotics are good bacteria, often taken as a supplement, which balances the gut microbiota. Probiotics are also found in many dairy products such as yogurt and cheese. Prebiotics occur through digestion of fibrous foods, often vegetables, and support the growth of probiotics in the gut. Examples of prebiotics include onions, asparagus, wheat, artichoke, oats, soybeans, chicory root, and non-digestible carbohydrates. Prebiotics can also be found in supplements, often in combination with probiotics.

Physical activity not only burns calories but also improves cardiovascular health, builds lean mass, and supports weight loss maintenance (Elmaleh-Sachs et al., 2023). Physical activity should be adapted to the individual's medical health and abilities but in general recommendations suggest 150 to 300 minutes per week of moderate or 75 to 150 minutes per week of vigorous activity for all individuals. Resistance training or strength training are required to build and maintain muscle mass. Encouraging individuals to be active throughout the day such as parking further away, taking the stairs, and intermittent activity is encouraged.

Semaglutide

Semaglutide is a glucagon-like peptide 1 (GLP-1) receptor agonist that is indicated to reduce excess body weight and maintain weight reduction long term in adults and pediatric patients 12 years and older with obesity as well as adults who are overweight with at least one weight related comorbidity (Novo Nordisk, 2024b). It is also indicated in combination with reduced calorie diet and increased activity to decrease major cardiovascular events, such as cardiovascular death, myocardial infarction, and stroke. The medication is given the same time weekly by SQ injection in the abdomen, thigh, or upper arm. Dose initiation is 0.25 mg for weeks one through four. Dose escalation begins week five through eight with the dose of 0.5 mg, week nine through 12 with the dose of 1 mg, and week 13 through 16 with the dose of 1.7 mg. Maintenance dosing begins in week 17 and is 2.4 mg. For patients that do not tolerate the 2.4 mg, maintenance dose may be reduced to 1.7 mg.

Semaglutide is contraindicated in individuals that have a personal or family history of medullary thyroid cancer and in individuals with multiple endocrine neoplasia syndrome type 2 (Novo Nordisk, 2024b). Adverse reactions may include acute pancreatitis, increased risk of cholelithiasis and cholecystitis, hypoglycemia, acute kidney disease, hypersensitivity reactions, diabetic retinopathy complications, and suicidal ideation. More common side effects may include nausea, vomiting, diarrhea, constipation, abdominal pain, headache, and fatigue. Use in pregnancy is contraindicated. Semaglutide may cause fetal harm and should be discontinued when pregnancy is recognized. Males and females that are hoping to get pregnant, should discontinue use at least two months before planned pregnancy due to the long half-life.

As Semaglutide can lower blood sugar levels, the risk of hypoglycemia is increased with the use of other diabetic medications such as insulin and insulin secretagogues (Novo Nordisk, 2024b). Semaglutide causes delayed gastric emptying and may decrease absorption of oral medications taken at the same time. Clinical pharmacology trials with Semaglutide 1 mg did not show that absorption of oral medications was affected. Regardless, it is recommended to monitor the effects of oral medications while given with Semaglutide.

Numerous clinical trials have been completed to evaluate Semaglutide. These include the Semaglutide Treatment Effect in People with Obesity (STEP) and the Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (SELECT). The STEP trials have conducted nine separate trials to date to evaluate Semaglutide in the treatment of overweight and obesity (Moiz, et al., 2024). Semaglutide 2.4 mg has clinically shown significant decreases in body weight in obesity in predominantly white populations in STEP 1-5 and 8 trials while STEP 6 trial supported this in east Asian participants (Bergman et al., 2023). Further analysis in STEP 2 indicates that Semaglutide 2.4 mg was not impacted by race or ethnicity. Current trials are being conducted in Brazil, China, Hong Kong, and South Korea to add to the ethnicity component as a possible consideration.

In the STEP trials, the majority of patients reported at least one comorbidity and over 25% had three or more comorbidities (Moiz et al., 2024). Most common comorbidities included dyslipidemia, hypertension, knee osteoarthritis, and obstructive sleep apnea. The SELECT trial showed that overweight or obese patients that had established cardiovascular disease but did not

have diabetes compared to placebo benefited from Semaglutide weekly and demonstrated a 20 percent decreased risk of major cardiac events such as cardiovascular death, non-fatal myocardial infarction, and stroke (Bergman et al., 2023; Moiz et al, 2024). Moiz et al., 2024 concluded that once weekly Semaglutide was associated with decreases in body weight and positive effects on BMI, waist circumference, and blood pressure. Their results support maintenance use of Semaglutide in the treatment of overweight and obese patients without diabetes.

Semaglutide education is essential for patient success (Novo Nordisk, 2024a). Important side effects to be aware of include pain in the abdomen that does not resolve with or without vomiting. These symptoms could be caused by inflammation of the pancreas (pancreatitis) or gall bladder concerns. If the pain is severe, the patient should go to the emergency department for further evaluation. Other potential side effects include low blood sugar in patients with type 2 diabetes, acute kidney injury, nausea, vomiting, reflux, indigestion, constipation, diarrhea, runny nose, allergic reactions (e.g., swelling to face, lips, tongue, throat, difficulty breathing, rash, and rapid heart rate), and depression or thoughts of suicide.

There are many other components of lifestyle changes that will help with patient success in weight loss. The first is increased water intake. Staying hydrated is essential for optimal function and individuals should drink one-half their body weight in ounces of water each day (PBS, 2002). For example, a person who weighs 200 pounds should drink 100 oz of water per day. Next is food intake. While Semaglutide helps slow down digestion to decrease overeating and feeling full, the slow transit of food through the GI track can cause nausea, stomach discomfort, gas, bloating, constipation, or diarrhea (Cleveland Clinic, 2024). It is recommended to eat non starchy vegetables, fruits, lean proteins, whole grains, and healthy fats and eat these slowly to allow the brain to identify that it is full. Satiety (sense of fullness) can take up to 30 minutes after eating before it is recognized by the brain. Along with slow transit of food through the GI track, there can be decreased absorption of vitamin B12. Kanai et al. (2024), suggested weekly Semaglutide treatment can lower vitamin B12 levels and possibly lead to deficiency. Vitamin B12 supports metabolism and energy production which may enhance weight loss (Pedersen, 2024). The addition of vitamin B12 IM can potentially ameliorate nausea and vomiting that can be associated with Semaglutide.

Conclusion

The obesity epidemic continues to worsen, and the introduction of GLP-1 agonist medications is a valuable addition to the treatment of overweight and obesity. Beyond weight loss, these medications can improve other health markers that include lower blood pressure and cholesterol levels, better blood sugar control, and decrease obesity related disease such as major cardiovascular events including myocardial infarction, stroke, and cardiovascular death. While FCNs may not be active in the management of those that are receiving treatment for weight loss, they serve an important role as health educators and health counselors for those in their community. They advocate for a holistic understanding of health that includes physical wellness. Understanding new trends in the management of a disease that contributes to many comorbidities will allow FCNs to create programs to assist their community reach improved health outcomes.

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