

offered to patients at the highest risk (eg, those newly diagnosed with cancer), patient education is provided, and institutional guardrails are established regarding data privacy (eg, health care systems never receive credit data and only the patient navigation

teams receive the results of the credit screen). Open conversations combat stigma; escalating costs of living and medical services demand a paradigm shift in the detection of financial hardship to improve cancer care affordability and outcomes.

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Muscle Mass, Fragility, Weight Loss, and Cancer Treatment

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Obesity is associated with an increased risk of dying of cancer.¹ These data suggest that finding methods to promote weight loss might serve as a means to decrease cancer mortality, an important task given that 74% of adults in the US have overweight or obesity.² An emerging treatment gaining popularity is glucagon-like peptide-1 (GLP-1) receptor agonists. An analysis of initial studies confirms their effectiveness for weight loss, with an average weight loss of 4.6 kg and waist circumference reduction of 4.6 cm.³

However, focusing solely on weight loss fails to account for overall body composition, which includes muscle mass and fat mass. Decreased muscle mass is associated with both an increased risk of cancer and death due to cancer, along with frailty, falls, morbidity, and overall mortality.⁴ Although muscle mass is commonly lost during weight reduction methods, GLP-1 inhibitors promote profound decreases in appetite and food consumption, with muscle loss rates approaching 40%.⁵ This number is considerably higher than traditional approaches to weight loss, such as dietary changes with or without exercise; exercise remains the standard of care to limit muscle loss during a period of weight loss. With regard to GLP-1-induced weight loss, the concomitant loss of muscle mass may be exacerbated by nutritional deficiencies and protein underconsumption, both exceedingly concerning in populations with cancer at risk for muscle loss, frailty, and decreased physical function.

As muscle mass correlates with a decreased risk of cancer, improved outcomes, and longevity in the healthy population, the question must be posed as to whether using GLP-1s to solve the issue related to excess body fat might mask another, possibly more insidious,

problem of muscle loss, including frailty, falls, and future morbidity and mortality. Are we trading a current problem for a future, possibly greater, issue? Additionally, the problem of muscle loss during concurrent fat loss could be worsened by a lack of lifestyle changes and future regain in body weight, which is often mainly fat mass. Thus, one could lose considerable muscle mass while taking these medications, only to gain future fat mass back with little gain in muscle. Since sarcopenia—the loss of muscular strength and mass—is associated with an increased risk of dying from cancer and with the association of low muscle mass with a wide range of worse oncologic outcomes, we express caution regarding pharmacologic weight loss in those with cancer.⁶

The most successful method to lose body fat and maintain or gain muscle mass is through nutritional optimization combined with adequate resistance training. This approach has been shown to be both safe and effective in patients with cancer.⁷ The benefits of nutrition and exercise expand beyond improvements in body composition, showing an improvement in quality of life, anxiety, depression, strength and mobility, balance and fall risk, and, most recently, survival.⁸ In other words, changes in dietary and exercise habits promote overall health and well-being with minimal downside, besides soreness and small risk of injury. Yet neither is part of standard cancer care and rarely does insurance cover this approach, while GLP-1 inhibitors are now covered by most insurance providers, showing a clear predilection toward pharmaceutical weight and health management vs optimizing one's lifestyle.

We acknowledge the difficulty in behavioral modification and challenges with implementing these changes, such as time constraints, the current food environment, and unfamiliarity with train-

ing regimens, among others. Yet lifestyle modification, however difficult, offers the only option that provides a multitude of benefits while mitigating potential adverse effects when confronting the problem of obesity and its associated comorbid conditions, including cancer.

If we, as a field, continue to favor pharmacologic solutions to answer lifestyle problems, we can expect downstream medical issues requiring additional short-term fixes. Perhaps, much like with osteoarthritis, where an individual must fail physical therapy before further treatment, we should first encourage a tiered

approach before turning to medications with unknown long-term safety.

Although many individuals will not succeed with behavioral and lifestyle modifications, we stress that they should first be directed to lifestyle changes, which we argue should be promoted and covered by health plans as first-line therapy. With backing from insurance, we envision an incentive structure that will promote the creation and widespread adoption of structured exercise and nutrition programs for people living with cancer. Only after these interventions have failed should we consider pharmacologic management.

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