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PERSPECTIVE

Dietary supplements and alternative therapies for obesity: A Perspective from The Obesity Society's Clinical Committee

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Abstract

In this Perspective Statement from The Obesity Society, the Clinical Committee discusses the use of weight loss supplements in the United States and the lack of regulatory oversight and rigorous testing of their efficacy and safety. A number of products and services claiming to promote weight loss are directly marketed to individuals with obesity and those wanting to lose weight. These products are not regulated as "drugs" by the Federal Drug Administration but, rather, are treated as dietary supplements if ingredients are "generally regarded as safe," requiring little or no testing to show efficacy or safety. Health care providers should be aware of the lack of evidence and deficiencies in regulatory oversight of dietary supplements marketed for weight loss. Regulatory authorities should protect consumers by ensuring accurate and safe marketing claims and preventing promotion of unproven and potentially unsafe products and claims.

INTRODUCTION

Approximately 42% of adults in the United States are affected by obesity and are at risk for adverse health outcomes (1). Between 2013 to 2016, 49% of US adults reported attempting to lose weight within the preceding 12 months (2). Several well-studied interventions such as dietary modifications, behavior therapy, pharmacotherapy, and surgery are effective for weight management (3-5), yet many barriers exist to implement these interventions (6). As a result, many patients struggling to lose weight and/or maintain weight loss turn to over-the-counter dietary supplements and/or alternative therapies (e.g., acupuncture) to achieve their goals, in part because of exaggerated claims of their efficacy. In this Perspective Statement from The Obesity Society (TOS), we discuss the systematic review of weight loss dietary supplements in this issue of *Obesity* and the lack of regulatory oversight to establish safety and efficacy of such supplements in the United States (7).

Numerous products/services promoting weight loss are directly marketed to individuals wanting to lose weight through supermarkets and online purveyors. These products are not regulated by

the Federal Drug Administration (FDA) like prescription antiobesity medications but rather are treated more leniently as "dietary supplements." To comply with the Dietary Supplement Health and Education Act of 1994, manufacturers of these products cannot legally claim that a dietary supplement will diagnose, cure, treat, or prevent a disease, but "structure-function" claims are permitted. Thus, a supplement can be marketed as having potential benefit to an organ/body system, thereby implying health benefits (8).

Federal oversight of dietary supplements is modest and insufficient. The Office of Dietary Supplements publishes dietary supplement fact sheets and an ingredient/label database, funds analytical research of supplement ingredients, and maintains a searchable product website (Computer Access to Research on Dietary Supplements Database) (9). The FDA also monitors for good manufacturing practices and mandates that new dietary ingredients demonstrate safety prior to marketing. Misleading claims can be prosecuted by the Federal Trade Commission (FTC), but this is a process of limited impact, given that thousands of products are continually brought to market, overwhelming FTC's capacity. Although these activities may give an appearance of supervision and surveillance, federal regulations do not authorize the FDA to evaluate product efficacy prior to sales, nor does the FDA require product standardization between batches. Some recommendations have been published to address quality control issues raised in clinical trials of dietary supplements; for example, some products have been shown to contain inconsistent concentrations of the labeled dietary supplement, and others have been found to be adulterated with unsafe, unlabeled, and sometimes banned ingredients (10, 11). The National Center for Complementary and Integrative Health has put forth the CONsolidated Standards of Reporting Trials (CONSORT) 2010 guidelines to improve randomized controlled trials (RCTs) of dietary supplements (12); however, these recommendations are optional rather than required.

In contrast to the limited approval process for dietary supplements, the FDA requires rigorous preclinical and clinical studies to approve prescription antiobesity medications (Figure 1) (13). Moreover, ongoing surveillance continues after approval. Thus, some prescription antiobesity medications (e.g., sibutramine) have been withdrawn from the market after identification of unanticipated adverse events during the postmarketing phase (14). Ongoing surveillance for adverse safety outcomes is yet another critical gap that is not part of dietary supplement regulation.

In this issue of *Obesity*, members of the Clinical Committee of TOS examined the evidence surrounding dietary supplements and other alternative therapies for weight loss (7). More than 20,000 (20,504) citations involving 53 supplements and products were identified; the quality and efficacy claims of these publications were examined. Full review of manuscripts was performed for 14 products with at least five published RCTs. Serious methodological limitations in the design and execution of these studies were found when compared with FDA requirements for drug evaluation (13) (Table 1). Despite the poor quality of these studies with high degrees of bias, most still failed to show efficacy of the product they were testing. For each study that showed positive results, still others found limited or no weight loss effects or clinically relevant metabolic responses. Yet these are the studies that are often used to support manufacturers' claims of "clinically proven" in their marketing. The selection criteria chosen for the full review of dietary supplements and alternative therapies were very permissive, yet only 14 out of 53 products had more than five published RCTs according to a priori inclusion/exclusion criteria. Several popular and widely used products (e.g., human chorionic gonadotropin, raspberry ketones, nicotinamide adenine dinucleotide, vitamin infusions) did not even meet the predefined number of published RCTs to be eligible for inclusion in the review.

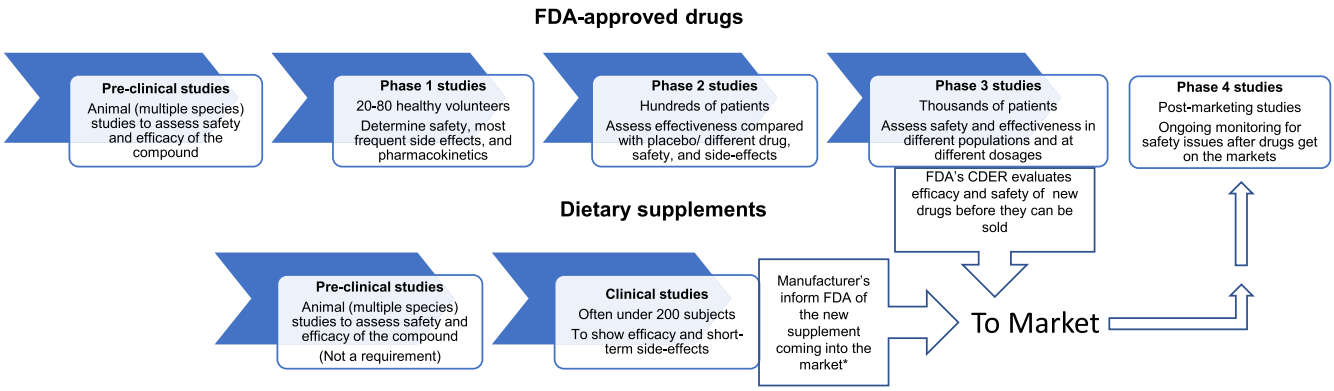

FIGURE 1 Infographic comparing FDA requirements versus the process for dietary supplements. CDER: Center for Drug Evaluation and Research ensures that drug are effective and health benefits outweigh their known risks. *Manufacturers and distributors of dietary supplements and dietary ingredients are prohibited from marketing products that are adulterated or misbranded. Generally, the notification must include information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing a new dietary ingredient will reasonably be expected to be safe under the conditions of use recommended or suggested in the labeling. FDA is responsible for acting against any adulterated or misbranded dietary supplement product after it reaches the market. However, FDA does not evaluate efficacy of dietary supplements. Adapted from: US FDA Drug Approval Process Infographic.

TABLE 1 Comparison of FDA guidance for approval of prescription weight loss medications to studies of dietary supplements evaluated in systematic review[a,b]

Key criteria	Prescription medicines	Dietary supplements
Study design	Randomized, double-blind, placebo-controlled trials.	Usually unblinded with high degree of bias.
Target population and recruitment criteria	Required to be representative of US population (age, BMI, ethnic groups, and comorbidities).	Young healthy individuals with no weight-related comorbidities; BMI lower than average US population.
Sample size	Several thousand individuals (≥4,500) are recruited in phase III trials based on power calculations to establish safety and efficacy.	Small (often under 200 subjects). No report of power calculations.
Trial duration	≥1 year.	Often few weeks to less than 6 months.
Statistical design	Rigorous statistical analyses are conducted emphasizing data transparency. Intention to treat analyses are conducted.	Results often not analyzed or reported in a standardized fashion; tendency to publish only positive findings irrespective of primary trial objective.
Efficacy criteria	Mean weight loss ≥5% over placebo group or proportion of subjects who lose ≥5% of baseline body weight is ≥35% in active drug group and approximately double the proportion who lose ≥5% in the placebo group.	None.
Secondary end points of interest	Blood pressure, pulse, lipids, glucose, glycosylated hemoglobin (as indicated), waist circumference, and quality of life.	Variable, often none.
Publication process	Publications after thorough peer-review process.	Published in low-impact, low-circulation journals with unspecified peer review process.

[a]Adapted from: Food and Drug Administration's Obesity Drug Guidance Document: A Short History. Colman E. *Circulation*. 2012;125:2156-2164.
[b]Based on observations reported by Batsis et al. (7).

Annual sales of dietary supplements for weight loss are booming with an industry valued at $30 billion worldwide (15), despite subpar evidence. The use of these products will continue as long as they are allowed to be marketed with the aforementioned limited federal oversight and there is a lack of access to evidence-based obesity treatments. There are numerous obstacles to providing and receiving care for obesity through appropriate means, including lack of adequate insurance coverage for medical visits, FDA-approved obesity medications, and surgical interventions, as well as a lack of providers with expertise in obesity management. The amount reimbursed for medical services delivered often does not cover the organizational costs incurred while providing care for patients with obesity within a multidisciplinary team. This makes the costs of maintaining an obesity management program financially challenging, and the result is a lack of comprehensive programs across the United States. Until our public and private health care systems rise to the challenge of providing appropriate care for patients with obesity, the marketing of these unproven and readily available dietary supplements will continue. In the absence of legislative or regulatory changes, it is unlikely that the predatory "Wild West" of dietary supplements will change.

Our recommendation to clinicians is to consider the lack of evidence for non-FDA-approved dietary supplements and therapies and guide their patients toward tested weight management approaches. Public and private entities should provide adequate resources for obesity management. Finally, we call on regulatory authorities to critically examine the dietary supplement industry, including their role in promoting misleading claims and marketing products that have the potential to harm patients.

CONFLICT OF INTEREST

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REFERENCES

1. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017-2018. *NCHS Data Brief*, no. 360. National Center for Health Statistics; 2020.
2. Martin CB, Herrick KA, Sarafrazi N, Ogden CL. Attempts to lose weight among adults in the United States, 2013-2016. *NCHS Data Brief*, no. 313. National Center for Health Statistics; 2018.
3. US Preventive Services Task Force; Curry SJ, Krist AH, Owens DK, et al. Behavioral weight loss interventions to prevent obesity-related morbidity and mortality in adults: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2018;320:1163-1171.
4. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393-403.
5. Jensen MD, Ryan DH, Apovian CM, et al. AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation*. 2014;129(25 suppl 2):S102-S138.
6. Kaplan LM, Golden A, Jinnett K, et al. Perceptions of barriers to effective obesity care: results from the National ACTION Study. *Obesity (Silver Spring)*. 2018;26:61-69.
7. Batsis JA, Apolzan JW, Bagley PJ, et al. A systematic review of dietary supplements and alternative therapies for weight loss. *Obesity (Silver Spring)*. 2021;29:1102-1113.
8. US Food and Drug Administration. Dietary supplements. Updated August 16, 2019. Accessed March 23, 2021. https://www.fda.gov/food/dietary-supplements
9. Office of Dietary Supplements. Computer Access to Research on Dietary Supplements (CARDS) Database. https://ods.od.nih.gov/Research/CARDS_Database.aspx. Accessed March 23, 2021.
10. US Pharmacopeial Convention. USP Global Public Policy Position: ensuring the quality of dietary supplements. Published 2016. Accessed March 23, 2021. https://www.usp.org/sites/default/files/usp/document/about/public-policy/public-policy-dietary-supplements.pdf
11. Dietary Supplements Quality Collaborative. Advancing quality in the dietary supplement market. https://dsqcollaborative.org/. Accessed March 23, 2021.
12. CONSORT (CONsolidated Standards of Reporting Trials) 2010 guideline. 2010. http://www.consort-statement.org/consort-2010. Accessed March 23, 2021.
13. Center for Drug Evaluation and Research. Guidance for industry developing products for weight management. Published February 2007. Accessed March 23, 2021. https://www.fda.gov/media/71252/download
14. US Food and Drug Administration. FDA requests the withdrawal of the weight-loss drug Belviq, Belviq XR (lorcaserin) from the market. FDA Drug Safety Podcast. Updated February 19. 2020. Accessed March 23, 2021. https://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-requests-withdrawal-weight-loss-drug-belviq-belviq-xr-lorcaserin-market
15. Industry Research. Global weight loss supplements market report, history and forecast 2015-2026, breakdown data by manufacturers, key regions, types and application. Published September 15, 2020. Accessed March 23, 2021. https://www.industryresearch.biz/global-weight-loss-supplements-market-16421571

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