Are Non-prescription Medications Needed for Weight Control?

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At any one time large numbers of people are attempting to control their weight. Women are the principal consumers of weight-control programs. Their options, outside the prescription drug market and surgical treatment, include diets and diet books, exercise alone or with supervision in exercise facilities, dietary supplements, group programs, doctors, dietitians, psychologists, and other health-care professionals. Non-prescription products available to help people control their weight cover a wide range, including herbal dietary supplements, diet drinks and portion-controlled foods, meal replacements, and low-carbohydrate diets and foods. The introduction of orlistat as an over-the-counter (OTC) product will provide the only Food and Drug Administration (FDA)-approved product for weight loss currently in that category since phenylpropanolamine (PPA) was withdrawn by the FDA. The FDA approval process is considerably more expensive than allowing untested herbal supplements to be marketed without testing, but the added safety evaluation by the FDA will reduce the risk of disastrous outcomes that have plagued many approaches to weight control. Support for a place for orlistat as an OTC product includes the inadequacy of current programs, empowerment of the public, lower cost, and bringing pharmacists into weight-control programs. The downside includes improper use of OTC orlistat that may not result in achieving individual expectations.

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Are OTC medications needed for overweight persons?

A new product for the treatment of overweight persons has recently been marketed. This article will explore the question of whether Americans need an OTC medication to help them lose weight. I will argue that the current epidemic of overweight has serious potential consequences and that the current medical model of treatment has limitations and is not the only approach to the problem. I will also argue that overweight people, as a major segment of the population, deserve to have effective OTC preparations that have been approved by the FDA. Although this approval process is more expensive than marketing untested herbal products that do not have FDA approval, the reassurance that the product is safe and effective is worth the extra cost. If a drug is to be available in supermarkets, drug stores, pharmacies, and health-food stores, it must be safe, effective, and reasonably inexpensive. If it satisfies these conditions, it can play an important role in empowering some segments of the overweight population in dealing with their problem. The rationale for this approach is that medications provided through the usual medical channels are expensive, and are generally used with a "medical model" of disease prevention. These medical costs are not usually covered by most prescription insurance plans. By providing medications in pharmacies and other outlets, the pharmacist can become more involved as a source of information.

Many overweight people believe that they themselves can solve their weight problem with "self-help" strategies. In one study (1), 70% of overweight people indicated that they were unlikely to see a physician to help them with weight loss because most (52%) believed they could do it themselves. There is also a belief that their doctor does not have the time to be of much help and that doctors may not have the expertise. This article will examine the use of non-prescription strategies that can be used by members of the public to help them address the problem of being overweight. In this article, obesity and overweight will be defined using the BMI cutoff points recommended by the National Heart, Lung, and Blood Institute. Overweight is a BMI between 25 and 29.9 kg/m^2 and obesity is a BMI ≥30 kg/m^2 (2).

Obesity is a chronic, relapsing disease

Obesity is a chronic, relapsing disease that is increasingly prevalent (3–5). It is a stigmatized disease (6). In the United States, overweight has been called an "epidemic." It has gotten this appellation because it now affects nearly two thirds of the adult population and a growing number of children (3,7–9). The World Health Organization has also labeled overweight as an "epidemic" because worldwide it may

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affect >300 million people (10). It is a chronic problem, because weight reduction over an extended period of time has been very difficult to achieve for all but a few people. When the efforts to lose weight are terminated or slackened, the body weight tends to rise to the level from which weight loss started or even higher.

Stigma of obesity

Stigma against overweight adults occurs in educational institutions, place of employment, in health-care centers, and elsewhere. One group that used the Medical Outcomes Study Short-form Health Survey (SF-36) demonstrated that overweight people presenting for treatment at a weight-management center had profound abnormalities in health-related quality of life (11). Higher BMI values were associated with greater quality-of-life effects. Overweight women appear to be at greater risk of psychological dysfunction, when compared to overweight men; this is potentially due to increased societal pressures on women to be thin (12).

Intentional weight loss reduces the stigma and improves the quality of life (13). Severely overweight patients, who lost an average of 43 kg through gastric bypass demonstrated improvements on all domains of the SF-36 to such an extent that their scores after weight loss were equal to or better than population norms (14). In contrast, an increasing BMI may lead to psychological distress (15). Central adiposity has also been associated with the risk of a depressive mood (16). In a study of 497 patients with BMI >40 kg/m^2, who were preparing for bariatric surgery, the Beck Depression Inventory assessment of depression was >16 (depressed) in 53% of the subjects, with an average value of 17.7. Higher scores were found in obese women, young patients, and those with poor self-image (17). After weight loss, depression scores improved significantly, with an average score of 7.8 one year after surgery and 9.6 four years after surgery.

Stigma or social disapproval is a major reason for wanting to lose weight. Because women who are overweight are particularly stigmatized, it is understandable why the large majority of individuals seeking to lose weight are women.

Health hazards of weight gain

It is well known that being overweight increases many health risks (18). These undesirable health outcomes include early death, diabetes, gall bladder disease, heart attack, stroke, osteoarthritis, and some forms of cancer. Although these medical diseases pose a significant health cost to the individual and to society, for most people the reason for seeking weight loss is to improve their quality of life and to look better in the eyes of others. There is simply no reason to view potential health benefits as the major reason why most people seek help in losing weight. If it were so, equal numbers of men and women would be present in most weight-loss programs, and that is simply not the case. Yet, except for "exercise" and "diets done on their own," more women chose other treatment options (19). Moreover, the detrimental health effects on women take longer to manifest themselves—witness the substantially longer life expectancy for women at comparable body weights.

Benefits of weight loss on life expectancy

A considerable body of data document that weight loss improves a number of the intermediate risk factors for disease (2,10,20). Documentation that intentional weight loss reduces mortality is scantier. In one study of intentional vs. unintentional weight loss, Williamson and colleagues reported a 20% reduction in all-cause mortality rate among 15,069 women with related health conditions, who were followed from 1959–1960 to 1972. Most of this was attributable to a reduction in cancer-related deaths. Mortality related to diabetes was reduced 30–40%. In women with no preexisting illness (N = 28,388), intentional weight loss of ≥20 lb in the previous year was associated with a 25% reduction in all-cause mortality (21). Using a different data set, the Williamson group (22) conducted a prospective analysis of 12-year mortality among 4,970 overweight individuals aged 40–64 years, with diabetes, and enrolled in the American Cancer Society Prevention Study I. Intentional weight loss was reported by 34% of the cohort and resulted in a 25% decrease in total mortality and a 28% reduction in cardiovascular disease and diabetes mortality. A weight loss of 20–29 lb (9.1–13.1 kg) was associated with the largest reductions in mortality. Similar results were reported from a follow-up of the National Health Interview Survey that included enough subjects to link 20,439 deaths to the National Death Index. In this group, with a 9-year follow-up, those reporting intentional weight loss had a 24% lower overall mortality rate compared to individuals not trying to lose weight (23). In a follow-up of individuals who had bariatric gastric-bypass surgery, Flum and colleagues noted a modest overall survival benefit associated with the procedure, suggesting again that "intentional" weight loss could reduce overall mortality (24).

There can be both medical and cosmetic (self-image) benefits to weight loss. However, they do not necessarily occur together. For example, a 10% weight loss, which would be clinically significant for a 300 lb (145 kg) person, would only reduce the body weight by 30 lb (13.6 kg) to 270 lb (122.7 kg)—a weight change that many people might not notice. At the other extreme, a 10% weight loss for an individual weighing 150 lb (68.2 kg) would decrease weight to 135 lb (59 kg), which would have a very positive impact on self-image. We also know that cosmetically significant weight losses may not produce clinically significant effects. After liposuction that removed about 7% of body weight, primarily as subcutaneous fat, there were no improvements in the health-related risk factors (25). These distinctions are summarized in **Table 1**.

Risks associated with efforts at weight control

Use of weight-control strategies can be risky. **Table 2** summarizes a number of the unintended consequences that have plagued the introduction of new approaches for weight control. Many treatments have been associated with unintended therapeutic outcomes. The use of thyroid hormone produced hyperthyroidism. Dinitrophenol produced neuropathies and cataracts. Amphetamine was addictive. Fenfluramine produced a form of valvular heart disease. These

Table 1 Clinically effective and cosmetically effective weight loss

Type of procedure	Percent weight loss and actual weight change	Is this weight loss clinically significant?	Is this weight loss cosmetically significant?
Diet/Exercise	10% from 300 to 270 lb	Yes	No
	10% from 200 to 180 lb	Yes	Probably No
	10% from 150 to 135 lb	Yes	Yes
Liposuction	7% from 220 to 200 lb	No	Probably No
	7% from 160 to 149 lb	No	Yes
Surgery (gastric bypass)	40% loss from 264 to 165 lb	Yes	Yes

Table 2 Unintended consequences of antiobesity treatments

Year	Drug	Consequence
1892	Thyroid extract	Hyperthyroidism
1932	Dinitrophenol	Cataracts, neuropathy
1937	Amphetamine	Addiction
1967	Rainbow pills (digitalis, diuretics)	Arrhythmias, death
1971	Aminorex	Pulmonary hypertension
1985	Gelatin diets	Cardiovascular deaths
1997	Phen/Fen (phentermine + fenfluramine)	Valvulopathy
1998	PPA (phenylpropanolamine)	Strokes
2003	Ephedra (Ma huang)	Heart attacks, stroke

unintended and unwanted side effects indicate a need for caution when introducing new treatments, unless the risk of the new treatment is very low. Because overweight is so highly stigmatized, any effective treatment will have to be made available to improve quality of life and self-image. Thus, both non-prescription and prescription drugs to treat overweight must have very high safety profiles. One downside of an OTC medication is that it may be improperly used and that the unrealistic expectations of individuals may not be met. Moreover, by removing the physician from the equation, some of the potential comorbidities may not be detected and treated. In a free society such as ours, however, the balance weighs in favor of empowering consumers to make choices that meet their own needs in an environment where those choices are reasonably safe.

Individual expectations

Before initiating any program of weight control, an individual must be ready to make the changes needed to facilitate weight loss. Anyone entering the grocery store, pharmacy, or health-food store in search of help in losing weight has already reached a decision about trying to do something about excess body weight. One complaint about medications for weight control is that they frequently fail, that is, they do not produce continuing weight loss that meets the individual's expectations and are thus labeled as "no good" (26). A plateau in response to treatment occurs with every treatment; thus, we need a better interpretation for the plateau of body weight. Overweight is not curable but can be controlled in many ways. When a program of weight control is stopped, weight is regained. This is similar to what happens to patients with hypertension who are treated with drugs and who stop taking their antihypertensive drugs, and to patients with high cholesterol who stop taking their cholesterol-lowering drugs. In each case, blood pressure or cholesterol rises. Like the problem of excess body fat, these chronic diseases have not been cured, but rather palliated. When efforts at weight control are stopped, the risk factor recurs and so does body fat (27).

Criteria for successful weight loss

A decrease in body weight of 5–15% from baseline improves most comorbidities associated with overweight in individuals who are at high risk (20). People who are ready to lose weight and have a reasonable expectation for their weight loss, are ready to begin a weight-control program. An ideal outcome is a reduction of body weight to a BMI below 25 kg/m^2, with no weight gain thereafter. This is rarely achieved and is unrealistic for most people; thus, they need guidance in accepting a realistic goal, usually a weight loss of 5–15%. This is where package materials and/or pharmacists can help. A satisfactory outcome is a maintenance of body weight over the ensuing years. A good outcome would be a loss of 5–15% of initial body weight and regain no faster than the increase in body weight of the population (0.5 kg/year). People who achieve this should be applauded. An excellent outcome would be weight loss of >15% of body weight. An unsatisfactory outcome is a loss of <5% with regain above the population weight (28).

Quality of life

As made clear by the comparison of the weight loss needed to achieve clinical significance vs. that needed to achieve a significant improvement in quality of life, the improvement in quality of life is the major driving force in the search for weight control for many if not most overweight people (**Table 1**). As Oliver pointed out, "The greatest share of the market for diet products is not made up of people who are trying to lose 200 lb, but by people who are trying to lose only 20" (29). This has ramifications in many areas. From the health-care perspective, a reduction in comorbidities is desirable for long-term health. Remission of diabetes or hypertension can reduce the costs of treating these conditions, as well as delay or prevent the development of associated diseases (30). Weight loss can also reduce the wear and tear on joints and slow the development of osteoarthritis. Sleep apnea usually resolves after weight loss.

Psychosocial improvement is the driving reason for many people who pursue weight control. Studies of patients who achieved long-term weight loss from surgical intervention comment on their improved social and economic function.

Loss of 5% or more of initial body weight almost always translates into improved mobility, improvement in sleep disturbances, increased exercise tolerance, and heightened self-esteem.

The weight-loss craze

A number of studies document the large number of Americans who are trying to lose weight by dieting or other means. A survey of 1,000 consumers by Opinion Dynamics in August 2005 found that 25% were on a diet to lose weight or to maintain a lower body weight (31). In a report to the weight-loss industry in 2005, Marketdata Enterprises estimated that 71 million Americans were trying to lose weight (31). The successful commercial products in this field vary from year to year, providing room for new entrants and growth of fledglings.

Diet books and the low-carbohydrate diet

Each year a new crop of diet books are published, holding forth some new, magic formula for lifetime success in losing weight. These are used by 34% of those trying to lose weight (1). The first of these English language books was published in the middle of the nineteenth century. The fact that there is a continuing market for new books is a reflection of the old adage "hope springs eternal" (32): "Even though I have failed in the past, this new magic diet will be the one for me now." So, with each winter season, a new crop of diet books appear. Most of these books have little published data to support them. Two trials have compared four popular diets. In one of these trials, there was no difference in weight loss among the groups assigned to any of the diets (33). In the other trial, the low-carbohydrate diet produced significantly more weight loss than the other three diets against which it was compared. In the latter study, all the subjects were women aged 30–50 years. A second, important difference was the larger size of the second study, which gave it more statistical power to detect a difference (34).

One of the common dietary themes has been the low-carbohydrate diet. The publication of three papers in prominent medical journals in 2003 showing greater weight loss with low-carbohydrate diets prompted an explosion of "low-carb" interest and products (35–37). The trajectory for low-carbohydrate foods typifies many of the trends in the weight-loss industry. In 2003, the sales were $889 million and that jumped to $2,237 million in 2004, then fell to $1,947 million in 2005 (31). In spite of this decline in food sales, there is still interest in the low-carb approach, as indicated by the large number of users of two message boards dealing with the problem (http://www.lowcarb.ca has 89,462 members and was 136th in postings; lowcarbfriends.com was 142nd in postings with 56,384 members; ref. 31).

Meal replacements, diet drinks, frozen foods, and diet bars

Meal replacements burst onto the scene in the 1990s, and like other dietary strategies, had a boom followed by an implosion. In one survey, the meal replacements were used by 42% of the respondents. As noted in the *Nutrition Business Journal* (31), the market for meal replacements has fallen 13% in 3 years, from $2.3 billion to $2 billion. Approximately 7% of the 71 million American dieters use meal replacements, down from as high as 24% in the early 1990s, according to BestDietForMe.com. This category was hard hit by the low-carb craze of the past 3 years.

Diet drinks have seen a steady increase in consumption for the past three decades. Some of this has been driven by the potential use of diet drinks to prevent weight gain or to help in weight loss. In 1970, there were 2.1 gallons/person of diet drinks and 22.2 gallons/person of regular soft drink consumed. By 1990, use of diet drinks had risen to 10.7 gallons/person, but consumption of regular soft drinks still remained in the lead, with 35.6 gallons/person. Portion sizes available for both regular and diet drinks have increased over the years. It obviously matters in terms of "energy intake" whether the beverage has energy (regular soft drinks) or not (diet drinks, water, and tea or coffee without milk or sugar). To help guide the public in the selection of beverages, a Beverage Guidance panel met and made recommendations based on the health implications of the various available beverages (38).

Herbal products sold under the dietary supplement health and education act

With the passage of the Dietary Supplement Health and Education Act in 1995, the floodgates were opened for many herbal products, in addition to the non-herbal products described above, which are often included in weight-loss programs. A wide variety of dietary supplements have been touted for their potential in fighting overweight. In one survey, they represented 90% of the $1 billion spent on medications for weight control. Ephedra-containing herbal products were early sellers in this class, and >$1 billion/year was allegedly spent on these products at their peak years. Such products might cost a dieter $35.00 per month: it was clear that the public was interested in them. In another study, using a cross-sectional population-based telephone survey of health behaviors from September 2002 through December 2002, Blanck and colleagues (39) estimated that 15.2% of adults (women 20.6% and men 9.7%) had ever used a weight-loss supplement, and 8.7% had used one in the past year (11.3% women and 6.0% men). Almost 10% (10.2%) had used them for ≥12 months and almost one-third (30.2%) had used them in the past year, with nearly three quarters of this group (73.8%) using products containing ephedra, caffeine, and/or bitter orange. In this time period, ephedra/ephedrine products topped the list (55%), followed by chromium, hydroxycitrate, and bitter orange. However, since these data were collected in 2002 before the FDA removed the ephedra products, the order of preference would probably be different now. A scientific basis for the introduction of ephedra (Ma huang) and guarana (a source of caffeine) was available from data testing ephedrine and caffeine as combination therapy, which had been published by Danish investigators (40). Two clinical trials with combinations of herbal ephedra and guarana were published that mirrored the studies with the pure compounds (41). Concerns about safety have led the FDA to try to remove them from the market (42).

There is a "laundry list" of other herbal products that have also been used and that are available in health-food stores and pharmacies (43). Data supporting the claims made for herbal products are often slim and of limited quality. Yet surprisingly, the public believes that they have been reviewed and approved by the US FDA (1). A review of studies conducted using randomized, placebo-controlled, double-blind strategies showed only a few studies that met these criteria. What this means is that the public is purchasing products of variable commercial purity and that the evidence for the effectiveness of these products is scanty or non-existent. Safety is untested. The laws that allow this are clearly a disservice to the public and deprive them of clinical trials demonstrating the safety and effectiveness of products they may plan to use (42). The FDA has taken one important step to correct the manufacturing problem, by requiring, effective 22 June 2007, that dietary supplements meet "Good Manufacturing Practices."

FDA-approved products

At present there are two products approved by the FDA for long-term use in the treatment of obesity and four other drugs approved for "short-term" use. All these drugs, except orlistat, are sympathomimetics or serotonin–norepinephrine reuptake inhibitors. Use of these drugs requires a medical prescription, and all the drugs, except orlistat, are classified as potential drugs of abuse by the Drug Enforcement Agency. A number of randomized, controlled trials support the long-term use of orlistat and sibutramine (44,45). Both these drugs were approved by the FDA >7 years ago. Orlistat is only minimally absorbed into the body, and its side effects are those expected from its mechanism of action, which involves blockade of intestinal lipase.

OTC products differ from the herbal products sold under the Dietary Supplement Health and Education Act in having FDA approval for their claims. Until 1998, PPA was the principal ingredient in OTC weight-loss pills. This drug is an α-adrenergic agonist that reduces food intake in experimental animals and produces vasoconstriction in human beings. It was this latter effect that made it so useful in cold remedies. There are short-term studies showing that it lowered body weight in human clinical trials. PPA was marketed under many trade names along with additional ingredients whose effectiveness in weight control was not known. Because PPA constricts small vessels, it was also an ingredient in many of the head-cold and sinus-relief products. Concern that PPA could increase blood pressure and lead to stroke prompted a case–control study to examine the relation of use of PPA in either cold medicines or for weight loss to the risk of stroke. This study, with all its design limitations, was published in a very prestigious medical journal (46) and led the FDA to withdraw PPA from the market for weight loss, cold, and sinus preparations. The relationship of PPA to risk of stroke was in reality very low risk indeed—between 1 in 100,000 and 1 in 1 million. If all drugs were required to meet this level of safety, it is unlikely that any further drugs would ever be approved for weight control.

A low dose of orlistat has been approved by the FDA as an OTC aid for overweight people who want to control weight. It will be the only FDA-approved OTC product in the weight-loss field. At 60 mg, three times a day, it is half of the dose used in the prescription form of orlistat. In a 2-year trial with orlistat used for FDA approval, the 60 mg, three times a day, dose produced weight loss at 1 year that was 8.6% below baseline, compared to 6.6% for the placebo and 9.7% for the 120-mg, three-times-a-day dose (**Figure 1**). In a 4-month trial in mildly overweight patients (BMI 25–28 kg/m^2), it increased weight loss 50% above that seen in the group receiving diet and placebo (**Figure 2**; ref. 47).

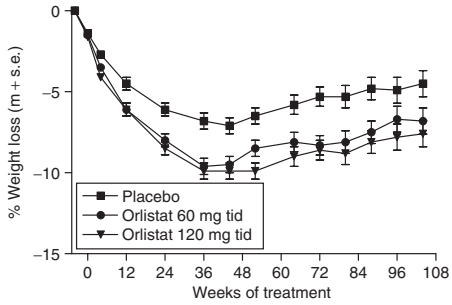

Figure 1 Percent change in body weight over 2 years in obese participants randomized to a double-blind, placebo-controlled trial. During the first year, the participants ate a diet calculated at 600 kcal/day below their energy needs. During the second year, the diet was planned to maintain initial weight loss. (Data redrawn from Rössner S, Sjöström L, Noack R, Meinders AE, Noseda G. Weight loss, weight maintenance, and improved cardiovascular risk factors after 2 years treatment with orlistat for obesity. European Orlistat Obesity Study Group. *Obes Res* 2000;8:49–61.)

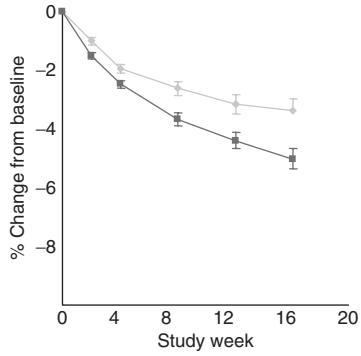

Figure 2 Effect of orlistat on body weight in overweight individuals. In this study, overweight individuals with a BMI between 25 and 28 kg/m^2 were randomized to placebo or orlistat 60 mg, three times a day, with a structured weight-loss program for all participants. Weights were collected for only four months (adapted from ref. 47).

Conclusion

This article has examined whether there is a need for OTC drugs as part of the strategy for weight control. I conclude that for many people the stigma of obesity is a sufficient reason to lose weight and that lower cost, safe, and effective medications available over the counter would assist in this process.

DISCLOSURE

The authors declared no conflict of interest.

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