

The Obesity Pandemic—How Did We Get Here?

Margaret Malone

On a daily basis, we are reminded of the increasing prevalence of obesity in adults and children and of the negative impact on the health of the nation from obesity-related comorbid disease. Over the past 25–30 years, the proportion of the US adult population defined as obese (BMI >30 kg/m²) has increased and now includes around one-third of the population. In children, there has been a two- to threefold increase in overweight and obese individuals over the same period. This latter trend is of particular concern, because these children are destined to become the next generation of adults with metabolic syndrome and many obesity-related diseases. The number of adolescents being treated for type 2 diabetes is greater than ever before. Unless this trend can be reversed, it has been speculated that they will be the first generation likely to have a shorter lifespan than that of their parents.¹ Despite such overwhelming evidence, the healthcare profession and the government have been slow to respond to the need to develop and implement a long-term, multifaceted approach to weight management.²

Where Have We Been?

Until the early 1980s, drug therapy for obesity consisted primarily of the use of thyroid hormones, treatment based on a premise that obese individuals must have subtle or overt hypothyroidism. Other agents in use from the 1940s to the 1960s included combinations of amphetamine-like agents with digoxin, diuretics, and thyroid hormones (so-called rainbow pills).³ A high incidence of adverse effects that included hypertension, myocardial toxicity, and addiction eventually limited the use of these combinations.

In 1992, a major change occurred when the fenfluramine–phentermine (fen-phen) combination was introduced following a long-term study in a relatively small number of individuals. Many patients were prescribed fen-phen through reputable and not so reputable sources. In

1996, reports of primary pulmonary hypertension were followed in 1997 with reports of valvular heart disease, which led to the withdrawal of fenfluramine and dexfenfluramine. Pharmacists were involved in tracking and contacting the huge numbers of patients who had received these therapies to advise them to discontinue the medication and to follow up with their healthcare providers to schedule echocardiographic studies. Other over-the-counter (OTC) medications that have since been withdrawn include phenylpropanolamine, due to its association with hemorrhagic stroke, and dietary supplements including ephedra alkaloids, due to hypertension, tachycardia, stroke, and seizures. Clearly, these unexpected and serious adverse effects, the cost involved in drug development, and the potential risk of failure or drug withdrawal after reportedly safe use in clinical trials have curbed the enthusiasm of the pharmaceutical industry for developing new obesity agents. These problems also negatively affected the attitudes of healthcare professionals, payers, and patients toward the therapeutic management of obesity.

Where Are We Today?

Beyond the dispensing of drugs, pharmacist involvement in the management of obesity has been very limited until quite recently. The introduction of orlistat in the late 1990s and the recent introduction of the OTC dosage form of orlistat have provided pharmacists an opportunity to become very involved in the counseling of obese patients. The expected weight loss associated with orlistat therapy is around 5–10%, although gastrointestinal effects that include loose stools, fecal urgency, and oily discharge are common. Adherence to orlistat therapy is significantly compromised when patients do not understand the dietary restraints that are needed.

Sibutramine is the only other weight loss medication currently licensed in the US for long-term use and has weight loss effects similar to those that occur with orlistat. Multiple potential drug interactions with monoamine oxidase inhibitors, selective serotonin-reuptake inhibitors, cimetidine, erythromycin, and alcohol can be identified and resolved by pharmacists. Common adverse effects associat-

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ed with sibutramine include dry mouth, headache, constipation, and insomnia. Sibutramine increases blood pressure in some individuals and should be carefully monitored.

Significant progress has been made since the discovery of leptin in 1994. Leptin did not prove useful in humans apart from the few exceptions who had leptin deficiency. However, it led to the ongoing discovery of many neurohormonal pathways and identification of genetic markers that regulate appetite and adiposity. Many new drug developments target different modulators of these pathways, especially those that include ghrelin, the melanin-concentrating hormone receptor, and the cannabinoid receptor (eg, rimonabant, which recently failed to gain FDA approval), with the future outcome being combination therapy with multiple agents.⁴ These new therapeutic agents are in the pipeline and will require novel dosage forms and counseling, which in turn will provide further pharmacy-based opportunities.

Bariatric surgery, including restrictive gastric procedures, gastric banding, and gastric pacing, continues to expand rapidly and requires pharmacists to provide patient care both before and after surgery to ensure that medication management and supplement intake are appropriate. The first bariatric procedures were performed about 50 years ago. Some of the early surgeries, such as jejunoileal bypass, required that pharmacists provide patients with multiple mineral and vitamin supplements to overcome deficiencies incurred due to the surgery. Roux-en-Y gastric bypass also has a malabsorptive component, but it is less severe than that with the older procedures, although significant for some nutrients, especially vitamin B₁₂, calcium, iron, and zinc. Pharmacists should not only be aware of the various surgical interventions for weight loss and their potential impact on drug and nutrient absorption but also should be involved with bariatric treatment center teams.

Where Do We Need to Go?

There have been several reports from pharmacists who are involved in ambulatory and community pharmacy settings for obesity programs, including behavioral modification and lifestyle counseling. This is encouraging but far from widespread. Although national pharmacy organizations have supported some limited programming at meetings and other continuing education offerings, such programs need to be expanded. Two programs in common use include the LEARN (Lifestyles, Exercise, Attitudes, Relationships, and Nutrition) manual and the Active Living Everyday program. There are few studies and limited information on drug dosing in obesity, which is an area in

which pharmacists could become very involved. Meetings of The Obesity Society (NAASO) are attracting record numbers of participants from all healthcare disciplines as the need to develop expertise in the management of obesity is recognized. More pharmacists should consider attending and becoming members of this leading obesity organization.

Where Will We Be in 20–40 Years?

Ideally, the obesity pandemic will have resolved within the next 20–40 years, people will have adopted a healthy lifestyle, and children will live longer than their parents. The worst-case scenario would be if few significant changes were made in the next 10–20 years, forcing the US healthcare system to deal with a massive number of patients (currently children and adolescents) who have multiple obesity-related comorbidities. For example, in 2002, the US projection for direct medical costs solely for the treatment of diabetes was \$92 billion. If even a modest percentage of these costs were diverted to prevention programs in which healthcare providers, including pharmacists, were paid for weight management services and patients were appropriately reimbursed, we might be in a much better place.

The underlying principle of weight control appears simple: to achieve energy balance and weight maintenance, energy intake should equal energy expended. However, the complexity of the modern-day environment and culture in the US, including unlimited access to food, increased sedentary lifestyles, and reduction in physical activity, plays a major role in the obesity pandemic. There are many unanswered questions relating to the best approach and optimal timing for weight loss interventions; my hope is that pharmacists will become fully involved in these potentially exciting and fulfilling opportunities to improve the health of the nation.

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