New Drug Therapies for the Treatment of Overweight and Obese Patients

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Background: Obesity is a serious and costly disease that is growing in epidemic proportions. Obesity-related hospitalizations have nearly tripled from 1996 to 2009. If the current trend in the growth of obesity continues, the total healthcare costs attributable to obesity could reach $861 billion to $957 billion by 2030. The American Medical Association has officially recognized obesity as a disease. Obesity is a public health crisis affecting approximately more than 33% of Americans and costing the healthcare system more than $190 billion annually.

Objectives: To review the 2 new drugs that were recently approved by the US Food and Drug Administration (FDA) for the treatment of obesity, lorcanerin HCl (Belviq) and phentermine/topiramate (Qsymia) and their potential impact on the treatment of obese patients.

Discussion: Lifestyle modification is the first and mainstay treatment for obesity. Antiobesity drugs are indicated as adjuncts to a healthy, low-fat, low-calorie diet and an exercise plan. Currently, 4 drugs are approved by the FDA for the treatment of obesity, 2 of which were approved after June 2012. These 2 drugs, Belviq and Qsymia, have added new tools for the treatment of obesity. In addition to reducing body mass index, these drugs have been shown to reduce hemoglobin A1c levels in patients with diabetes and blood pressure levels in patients with hypertension, as well as to decrease lipid levels in patients with hyperlipidemia. This article reviews the drugs’ mechanisms of action, evaluates landmark clinical studies leading to the FDA approval of the 2 drugs, their common side effects, and the benefits these new drugs can provide toward the management of the obesity epidemic that are different from other medications currently available.

Conclusion: The weight loss seen in patients who are using the 2 new medications has been shown to further improve other cardiometabolic health parameters, including blood pressure, blood glucose levels, and serum lipid levels. Based on clinical trials evidence, it is likely that many obese patients could benefit from these therapies, if used appropriately.

Obesity is a serious and costly disease, and 154.7 million Americans aged ≥20 years are obese or overweight.1 Of these, 78.4 million US adults are categorized as having a body mass index (BMI) of ≥30 kg/m².1 Worldwide, the rate of obesity has nearly doubled since 1980.2 According to the World Health Organization estimates, in 2008 more than 1.4 billion adults aged ≥20 years were classified as overweight (BMI, 25-29.9 kg/m²), and more than 200 million men and nearly 300 million women were classified as obese.2

Ethnicity and Sociocultural Factors

Obesity, ethnicity, and socioeconomic status are closely intertwined. Non-Hispanic blacks tend to have the highest age-adjusted rates of obesity (49.5%) compared with Mexican Americans (40.4%), all Hispanics (39.1%),...
and non-Hispanic whites (34.3%). With regard to socioeconomic status, among non-Hispanic black men and Mexican-American men, those with higher incomes are more likely to be obese than those with low incomes. Higher-income women are less likely to be obese than women with a lower income. There is also a trend showing that educated women (ie, who have college degrees) are less likely to be obese than less-educated women.

According to the recent reports from the National Health and Nutrition Examination Survey (NHANES), the prevalence of obesity has increased among adult men and women between the 1988-1994 NHANES III and the 1999-2000 NHANES. Although the increases have been statistically significant in all racial and sex groups, the longitudinal data related to the development of obesity indicate that the rise in obesity rates in US women has been greatest in non-Hispanic African Americans, followed by Hispanics, and finally Caucasians.

In addition, by age 29 years, the mean BMI of African-American women was >30 kg/m², which is the cut-off point for obesity. Similar trends were observed in men; however, for African-American men, the acceleration in weight gain did not occur until after age 30 years. The exception to the data related to the increase in obesity among minorities is Asian Americans.

Although obesity is more common in African Americans than in white Americans, the effect of obesity on mortality is more lethal for the latter group. It has been reported that nonsmoking white men and women without a history of disease who were at the highest BMI had a significantly higher risk of mortality than their average-weight counterparts (relative risk, 2.58 and 2.00, respectively); a similar association was not seen in African Americans.

Environmental influences, such as abundance of food, food marketing, and access to food from restaurants and large-scale supermarkets, may contribute to the promotion of overweight and obesity. Other cultural differences related to sedentary lifestyle and socioeconomic status, including work environment and cultural expectations, may also play a role in the overall increase in obesity. Evidence suggests that there may also be factors associated with genetic differences to support these trends of increasing BMI. The general consensus is that overweight and obesity are truly multifactorial in nature.

Clinical and Economic Burden
As of June 2013, the American Medical Association has officially recognized obesity as a disease based on the belief that “recognizing obesity as a disease will help change the way the medical community tackles this complex issue that affects approximately 1 in 3 Americans.” Obesity is a public health crisis affecting more than 33% of American adults and costing the healthcare system more than $190 billion annually. Obesity affects many health issues and is associated with a range of cardiometabolic health issues, which exacerbate costs. Obesity-related conditions include heart disease, stroke, type 2 diabetes, and certain types of cancer (eg, endometrial, colon, and breast cancers). Overweight and obesity are linked to more adult deaths worldwide than underweight. For example, 65% of the world’s population lives in countries where overweight and obesity are more death-related than underweight (including all high-income and most middle-income countries).

Obesity-related hospitalizations have nearly tripled from 1996 to 2009. In 2009, there were approximately 2.8 million hospital stays for which obesity was either the primary or secondary diagnosis. The overall associated cost was a staggering $33.4 billion, or roughly 10% of aggregate hospital costs in 2009. If the current trends in the growth of obesity continue at this pace, the total healthcare costs that are attributable to obesity could reach between $861 billion and $957 billion by 2030.

KEY POINTS

- In 2013, the American Medical Association has officially recognized obesity as a disease.
- Obesity prevalence is growing in epidemic proportions and is a risk factor for a wide range of other cardiometabolic diseases.
- Obesity-related hospitalizations have nearly tripled from 1996 to 2009.
- If the current growth trend of obesity continues, total healthcare costs attributable to obesity are projected to reach up to $957 billion by 2030.
- By mid-2012, 2 new drugs—lorcaserin HCl (Belviq) and phentermine/topiramate (Qsymia)—were approved for the treatment of obesity.
- In addition to reducing body mass index, these drugs reduce hemoglobin A1c levels in patients with diabetes, blood pressure levels in patients with hypertension, and decrease lipid levels in patients with hyperlipidemia.
- The ability to manage obesity and other associated cardiometabolic risk factors is an important development in the treatment options for obese or overweight patients, especially those with other cardiovascular comorbidities.
- Based on clinical trials evidence, it is anticipated that many obese or overweight patients who have access to these therapies could benefit from them, if used appropriately.
accounting for 16% to 18% of healthcare expenditures in the United States. In 2006, the per-capita medical spending for patients who are obese was $1429 (42%) greater than for normal-weight patients.

Treatment of Obesity

The mainstay of treatment and prevention for overweight and obesity remains making sensible and healthier diet choices as well as regular physical activity. But these often are not enough, as can be seen by the growing rates of obese Americans. Antiobesity drugs are indicated as adjuncts to a reasonable diet and an exercise plan.

From 1996 until 2012, only 2 drugs—orlistat (Xenical) and phentermine HCl (Adipex-P)—were approved by the US Food and Drug Administration (FDA) for the treatment of overweight and obesity. However, orlistat has multiple gastrointestinal side effects, including flatulence and fecal urgency, and phentermine HCl has multiple cardiac side effects, including palpitations, hypertension, and tachycardia. This makes these 2 drugs difficult for patients to take, and they are only ideal for a select subpopulation of patients.

Recently, 2 new drugs—phentermine and topiramate extended release (PHEN/TPM ER; Qsymia; VIVUS) and lorcaserin HCl (Belviq; Arena Pharmaceuticals)—have been approved by the FDA for the treatment of obesity. This article reviews their mechanisms of action, evaluates landmark clinical studies leading to their approval by the FDA, and discusses the common side effects, and the potential benefits that these drugs can provide in the management of the obesity epidemic.

Phentermine/Topiramate (Qsymia)

Qsymia was approved in July 2012 by the FDA for the treatment of obesity. Consisting of a combination of phentermine and topiramate, Qsymia is indicated for use in addition to a low-calorie diet and increased physical activity for adults with an elevated BMI of ≥30 kg/m² (ie, obesity) or ≥27 kg/m² (ie, overweight) with at least 1 obesity-related condition.

PHEN/TPM ER acts on obesity through the 2 different mechanisms of action of each of its components. Phentermine is a sympathomimetic amine anorectic, which works to antagonize alpha-adrenergic receptors. Catecholamines, such as norepinephrine, are thought to be released into the hypothalamus in response to phentermine. This results in appetite suppression from an increase in blood leptin concentration and consequently in reduced food consumption. Leptin is one of the most important adipose-derived hormones that are manufactured primarily by adipose tissue. Leptin plays a crucial role in appetite, metabolism, and behavior. Other metabolic effects and mechanisms of action may also be involved that are yet unknown.

Topiramate is frequently used as an antiepileptic drug. Topiramate is believed to be beneficial for obesity management by enhancing the activity of neurotransmitter gamma-aminobutyric acid (GABA). GABA functions through its modulation of voltage-gated ion channels and by the inhibition of carbonic anhydrase or AMPA/kainite excitatory glutamate receptors. The exact mechanism of action is still not clear.

Clinical Trials

The 2 studies that have demonstrated the effectiveness of PHEN/TPM ER are the CONQUER (Effects of Low-Dose, Controlled-Release Phentermine plus Topiramate Combination on Weight and Associated Comorbidities in Overweight and Obese Adults) trial and EQUIP (Controlled-Release Phentermine/Topiramate in Severely Obese Adults: a Randomized Controlled Trial). Key features of these trials are listed in Table 1. CONQUER. This was a randomized, double-blind,
placebo-controlled phase 3 trial performed in 93 US centers on 2487 patients who were aged 18 to 70 years with a BMI of 27 to 45 kg/m². Primary end points included the percentage of patients who achieved ≥5% weight loss and the percentage change in body weight. Patients were divided into 3 groups: placebo (N = 994), PHEN/TPM ER 7.5/46 mg (N = 498), and PHEN/TPM ER 15/92 mg (N = 995).

At 56 weeks, results were significantly in favor of the 2 groups of patients taking PHEN/TPM ER, with change in body weight of −8.1 kg (P < .001) and −10.2 kg (P < .001) for PHEN/TPM ER 7.5/46 mg and PHEN/TPM ER 15/92 mg, respectively, compared with −1.4 kg for patients receiving placebo. A total of 62% of the patients taking PHEN/TPM ER 7.5/46 mg and 70% of the patients taking PHEN/TPM ER 15/92 mg (P < .001 for both) achieved at least a 5% weight loss compared with 21% of patients receiving placebo. Of the patients in the 2 groups receiving PHEN/TPM ER, 37% and 48% (P < .001) had a >10% weight loss.

EQUIP. The second trial, EQUIP, was a double-blind, parallel-group study of 91 US sites involving 1267 patients aged 18 to 70 years for a total treatment duration of 56 weeks. The study divided patients into 3 groups: patients receiving placebo (N = 514), PHEN/TPM ER 3.75/23 mg (N = 241), and patients receiving PHEN/TPM ER 15/92 mg (N = 512). All patients had a BMI ≥35 kg/m²; blood pressure (BP) ≤140/90 mm Hg, and were using 0 to 2 antihypertensive medications; triglycerides ≤200 mg/dL, with 0 to 1 cholesterol-lowering medication; and fasting blood glucose level ≤110 mg/dL.

Similar to the CONQUER study, the primary end point was the percentage of patients who achieved at least 5% weight loss. The secondary end point included improvement in any of the complications of obesity, including fasting blood glucose, BP, cholesterol, and waist circumference. The final results were similar to those seen in the CONQUER study.

At the end of 56 weeks, patients in the placebo, PHEN/TPM ER 3.75/23-mg, and PHEN/TPM ER 15/92-mg cohorts lost 1.6%, 5.1%, and 10.9%, respectively, of their baseline body weight (P < .001), including 17.3%, 44.9%, and 66.7%, respectively, of the patients in categorical analysis (P < .001). The PHEN/TPM ER 15/92-mg group also had the highest success in achieving secondary end points.

Clinical Utility
The most common side effects of PHEN/TPM ER identified in both studies were dry mouth, paresthesia, constipation, dysgeusia, insomnia, and dizziness. Of note, generic components of PHEN/TPM ER are available on the market at higher starting doses.

PHEN/TPM ER was studied and compounded in its currently available forms and dosages to minimize the typical side effects that are seen with its individual components (which are available only in the higher doses). No clinical data are available in the literature regarding PHEN/TPM ER’s impact on various BMI ranges than those approved by the FDA. In addition, unlike lorcaserin HCl, no published data are available regarding PHEN/TPM ER’s impact on various races.

The concurrent use of PHEN/TPM ER and other anorexiant or nonselective monoamine oxidase inhibitors have shown to increase the risk of cardiovascular effects (ie, hypertensive crisis) and central nervous system stimulatory effects. PHEN/TPM ER is contraindicated during pregnancy and is unsafe during lactation. The increased risk of oral clefts and other craniofacial defects resulting from exposure to topiramate have been identified by epidemiologic data and in animal studies.

The starting dose for PHEN/TPM ER is 3.75/23 mg once daily for 14 days and is then increased to 7.5/46 mg once daily. Medication must be taken in the morning to prevent possible insomnia at night. The maximum recommended dose is 15/92 mg. If weight loss is <5% in 12 weeks, PHEN/TPM ER must be gradually tapered off by taking 1 capsule every other day for 1 week to prevent the incidence of a withdrawal seizure.

Lorcaserin HCl (Belviq)
Lorcaserin HCl (Belviq) is a novel weight-loss medication that was approved by the FDA in June 2012 for obese patients with BMI ≥30 kg/m² or overweight patients with BMI ≥27 kg/m² and at least 1 of these comorbidities—hypertension, type 2 diabetes, or dyslipidemia.

The mechanism of action is stimulation of satiety centers via selective agonistic action at the 5-HT₂C serotonin receptors, which are found throughout the brain and are thought to reduce hunger by the production of opioid melanocortin neurons in the hypothalamus. Nonselective serotonin agonists, such as fenfluramine, have previously demonstrated significant weight loss in patients, although the side-effect profile included valvulopathy by activation of 5-HT₄ receptors and were therefore withdrawn from the market. Lorcaserin HCl has much greater affinity for 5-HT₂C over 5-HT₄.

Clinical Trials
Lorcaserin HCl was approved by the FDA based largely on 3 major phase 3 trials—Behavioral Modification and Lorcaserin for Overweight and Obesity Management (BLOOM), Behavioral Modification and Lorcaserin Second Study for Obesity Management (BLOS-
Table 2  BLOOM, BLOSSOM, and BLOOM-DM: Evaluating Lorcaserin HCl as an Adjunct to Diet and Lifestyle Modification for Weight Loss

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Medication</th>
<th>Method</th>
<th>Patients, N</th>
<th>P Value</th>
<th>Side effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLOOM</td>
<td>Lorcaserin HCl</td>
<td>10 mg twice daily vs placebo (both with diet and exercise)</td>
<td>3182</td>
<td>&lt;.001</td>
<td>Headache, nausea, back pain, nasopharyngitis</td>
<td>47.5% vs 20.3% achieving ≥5% total body weight loss</td>
</tr>
<tr>
<td>BLOSSOM</td>
<td>Lorcaserin HCl</td>
<td>10 mg twice daily vs 10 mg daily vs placebo (with diet and exercise)</td>
<td>4008</td>
<td>&lt;.001</td>
<td>Headache, nausea, dizziness, fatigue, upper respiratory infection</td>
<td>47.2% vs 40.2% vs 25% achieving ≥5% total body weight loss</td>
</tr>
<tr>
<td>BLOOM-DM</td>
<td>Lorcaserin HCl</td>
<td>10 mg twice daily vs 10 mg daily vs placebo (all with diet and exercise) All patients with type 2 diabetes</td>
<td>604</td>
<td>&lt;.001</td>
<td>Headache, nausea, back pain, nasopharyngitis, symptomatic hypoglycemia</td>
<td>37.5% vs 44.7% vs 16.1% achieving ≥5% total body weight loss</td>
</tr>
</tbody>
</table>

Sources: References 19-21.

SOM), and Behavioral Modification and Lorcaserin for Obesity and Overweight Management in Diabetes Mellitus (BLOOM-DM). Key features of these trials are listed in Table 2.19-21

BLOOM. The BLOOM trial was double blinded and included 3182 obese or overweight adults who were assigned to either lorcaserin HCl 10 mg twice daily for 2 years, placebo for 2 years, or lorcaserin HCl for 1 year and then placebo for 1 year. All patients received diet and exercise counseling once at the initiation of the trial and at each subsequent follow-up visit at 2 weeks, 4 weeks, and monthly thereafter. The primary end points at the end of year 1 were loss of ≥5% body weight, change in weight between baseline and the end of year 1, or loss of ≥10% body weight.

The group receiving loracerin HCl lost an average of 5.8 kg compared with a 2.2-kg loss in the control arm. In the treated group, 47.5% achieved the ≥5% weight-loss goal versus 20.3% of patients in the placebo group; 22.6% in the lorcaserin HCl group achieved the ≥10% weight-loss goal versus 7.7% of patients receiving placebo. Patients who were switched to a placebo for 1 year after lorcaserin HCl regained weight and had results similar to the placebo group at the conclusion of the 2-year trial, despite monthly counseling for diet and exercise.

Side effects of patients in the treatment arm that were higher than for patients in the placebo arm included headache, upper respiratory infection, nausea, dizziness, and fatigue. Valvulopathy was not increased in either treatment arm.

BLOSSOM. The randomized, placebo-controlled, double-blind BLOSSOM trial included 4008 patients who were aged 18 to 65 years and were obese (BMI, 30.45 kg/m²) or overweight (27.29 kg/m²) with comorbid risk factors. Patients were assigned to lorcaserin HCl 10 mg twice daily, lorcaserin HCl 10 mg once daily, or to placebo for 1 year; all patients received counseling on diet and exercise.

The twice-daily treatment group lost 5.8 kg compared with 4.7 kg and 2.9 kg in the groups receiving 10 mg once daily and placebo, respectively. The total patients achieving ≥5% total weight loss were 47.2% in the twice-daily treated group versus 40.2% and 25%, respectively, in the groups receiving 10 mg once daily and placebo; the rates of achieving 10% total weight loss among the groups were 22.6%, 17.4%, and 9.7%, respectively. Men lost more total weight (6 kg) in the once-daily dosed cohort than in the twice-daily dosed cohort (5.6 kg), and Caucasians lost more weight than Hispanics or African Americans.

Side effects that occurred more frequently in the active treatment groups compared with the group receiving placebo included headache, upper respiratory infection, nausea, dizziness, and fatigue. Valvulopathy was not increased in either treatment arm.

BLOOM-DM. The BLOOM-DM trial included 604 patients aged 18 to 65 years with a BMI of 27 kg/m² to 45 kg/m² and with type 2 diabetes who were being treated with metformin, a sulfonylurea, or both. Patients were randomized to placebo or to lorcaserin HCl 10 mg once daily or to lorcaserin HCl 10 mg twice daily for 1 year. The mean starting hemoglobin (Hb) A₁c was 8.1%. Of the patients who completed the study, the weight loss was 1.9 kg in the placebo group, 5.6 kg in the once-daily loracerin group, and 5.9 kg in the twice-daily loracerin group. The patients’ mean HbA₁c decreased by 0.5%, 1.0%, and 1.1%, respectively.
Approximately 50% of the patients in the active treatment groups reached an HbA1c of <7% versus only approximately 25% of patients in the placebo group.21 Adverse events were similar to previous trials; however, symptomatic hypoglycemia was more common in the group receiving lorcaserin HCl (8.4%) than in the group receiving placebo (6.3%). New valvulopathy occurred in 0.5% of patients receiving placebo and in 2.5% and 2.9%, respectively, of patients in the once- and twice-daily–treated groups, respectively, which was not statistically significant. This should be followed closely, because these data indicate a possible trend toward dose-related new valvulopathy. Patients who had baseline valvulopathy had no significant increase in disease between groups.21

Clinical Utility
Overall, these trials demonstrated significant weight loss compared with placebo in approximately 50% of the patients, with reduction in cardiovascular risk markers such as BP, low-density lipoprotein cholesterol (LDL-C), C-reactive protein (CRP), fasting glucose, and HbA1c.19-21 The side effects that were higher in the treatment arms compared with in the placebo arm varied, but included headache, nausea, back pain, upper respiratory infection, dizziness, and fatigue.

Of note, echocardiography at the beginning and end of the trials did not show a statistically increased rate of valvulopathy in any of the trials. Given the slightly higher rate of symptomatic hypoglycemia, it is sensible to reassess and consider decreasing the dosages of other hypoglycemic agents for patients who are actively losing weight with lorcaserin HCl.19-21

The recommended dose of lorcaserin HCl is 10 mg twice daily for 12 weeks, then continue in patients who lose ≥5% of body weight; otherwise discontinue.17,18

Discussion
Obesity has increased in prevalence throughout the past decade. The adverse conditions associated with obesity include type 2 diabetes, hypertension, and dyslipidemia. These conditions can lead to additional ailments, such as stroke, vascular disease, and neuropathy.

In addition to diet and exercise, both PHEN/TPM ER and lorcaserin HCl have shown promising results in reducing body weight compared with placebo when used for 1 year. For patients in whom traditional diet and physical activity are unable to reduce their BMI, implementation of these medications may be beneficial (Table 3). The use of these new drugs should not be a substitute for tradition-

<table>
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<tr>
<th>Table 3</th>
<th>Characteristics of Phentermine/Topiramate Extended Release and Lorcaserin HCl</th>
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</thead>
<tbody>
<tr>
<td>Drug characteristics</td>
<td>Qsymia (Phentermine/topiramate extended release)</td>
</tr>
<tr>
<td>Indications</td>
<td>An adjunct to a low-calorie diet and increased physical activity in adults with an initial BMI of ≥30 kg/m² or ≥27 kg/m² in the presence of at least 1 weight-related comorbidity</td>
</tr>
<tr>
<td>Dosage forms</td>
<td>3.75/23 mg, 7.5/46 mg, 11.25/69 mg, 15/92 mg</td>
</tr>
<tr>
<td>Administration</td>
<td>3.75/23 mg daily for 14 days then increase to 7.5/46 mg; discontinue or increase dose if 3% weight loss is not achieved after 12 weeks or discontinue if 5% weight loss is not achieved after 12 weeks on maximum daily dose of 15/92 mg</td>
</tr>
<tr>
<td>Outcome</td>
<td>66.7%-70% of patients achieved ≥5% weight loss on maximum daily dose of 15/92 mg</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Pregnancy, glaucoma, hyperthyroidism, within 14 days of taking MAOIs, hypersensitivity to sympathomimetic amines</td>
</tr>
<tr>
<td>Adverse reactions</td>
<td>Paresthesia, dizziness, dysgeusia, insomnia, constipation, dry mouth</td>
</tr>
<tr>
<td>Drug interactions</td>
<td>Oral contraceptives, central nervous system depressants including alcohol, MAOIs, non–potassium-sparing diuretics</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; MAOI, monoamine oxidase inhibitor.
Sources: References 15, 16, 19-21.
New Drug Therapies for Obesity

Dr Nguyen have no conflicts of interest to report.

Dr Mahgerefteh, Dr Vigue, Dr Freestone, Dr Silver, and

Author Disclosure Statement

References


The Modern Epidemic of Obesity

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The modern epidemic of obesity represents a huge problem for healthcare providers and payers in the United States, let alone for obese patients. The prevalence of obesity has truly exploded since the early 1980s, when a panoply of causative factors aligned together almost at once to turn the tide against the previously trim physique of the average American.

PATIENTS: The early 1980s saw the widespread introduction of high-fructose corn syrup—a very calorie-dense food additive that has become ubiquitous in all of our diets—into many of our daily foods and drinks. Restaurant portions began to increase at approximately the same time, because restaurant owners sought to justify higher prices by heaping larger servings of food onto their customers' plate.

The same period further witnessed the advent of the home computer, which made it possible for Americans to entertain themselves for endless hours, and with little physical effort. Cable television and video games, too, came along at that time, as well as the advent of the video cassette recorder, all conspiring to keep people further glued to their TV screens for longer periods of time. All of these technical achievements facilitated the ability to be entertained at home for long hours, without the need to move as much as before.

Couple this with a growing parental paranoia about allowing children to play unattended in their neighborhoods, and we have a perfect storm of increased caloric intake and decreased physical activity.

PAYERS/PROVIDERS: Therefore, we need help. The adverse health consequences of obesity are legion, including increased risks of diabetes, heart disease, malignancies, arthritis, depression, as well as other health conditions. Previously approved weight-loss medications have been very disappointing, to say the least, and they have often been toxic as well.

We are now, one hopes, in a new era of obesity management, with the recent approval of 2 new medications, which were approved last year by the US Food and Drug Administration as adjunct to diet and exercise. These novel agents that are described in detail in the review article by Mahgerefteh and colleagues may help patients and providers to effectively fight back against the obesity epidemic in the United States.

The data from clinical trials are promising for these 2 new agents. Time, and real-world data, will tell whether these can be duplicated outside of clinical trials, and if these medications are indeed able to live up to the promises they offer.