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# Persistence of newer anti-obesity medications in a real-world setting

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ABSTRACT

*Aims:* Evaluate real-world data on persistence with anti-obesity medications (AOMs) and explore associated patient factors.

*Methods:* Truven Health MarketScan® data were analyzed to evaluate utilization of AOMs approved for long-term use between 4/2015 and 3/2016. Kaplan-Meier survival analyses were used to evaluate treatment persistence. A multivariate analysis was performed to identify associations between persistence and relevant factors.

*Results:* In total, 26,522 adult patients were identified as newly prescribed naltrexone/bupropion (44.0%, mean age 47.1, 80.5% female), lorcaserin (24.8%, 48.5, 79.3%), phentermine/topiramate extended release (15.8%, 46.7, 82.2%) or liraglutide 3.0 mg (15.4%, 46.9, 72.4%). At 6 months, 41.8% of patients were still on liraglutide 3.0 mg, compared to 15.9% lorcaserin ($p < 0.001$), 18.1% naltrexone/bupropion ($p < 0.001$), and 27.3% phentermine/topiramate ($p < 0.001$). After adjusting for baseline factors, patients on liraglutide 3.0 mg had significantly lower risk of discontinuation compared to those on lorcaserin (HR = 0.46, $p < 0.0001$), naltrexone/bupropion (HR = 0.48, $p < 0.0001$), and phentermine/topiramate (HR = 0.64, $p < 0.0001$) over the course of follow-up (mean follow-up duration, 342–427 days). Older age, male gender, having hyperlipidemia, and no prior phentermine use were associated with higher persistence. Over 95% of study patients had commercial insurance.

*Conclusions:* In a real-world setting, patients on liraglutide 3.0 mg had the highest persistence rate of the four AOMs studied.



## 1. Introduction

Obesity (BMI $\geq$ 30 kg/m$^2$) is a chronic disease that represents a major public health concern given its prevalence, associated morbidity, and resulting cost burdens on society [1]. Obesity affects over one-third of the US population [2], is a leading cause of preventable death worldwide, and has been linked to a multitude of diseases, including atherosclerotic heart disease, stroke, type 2 diabetes, hypertension, dyslipidemia, non-alcoholic fatty liver disease, and 40% of cancer diagnoses [3–5]. Despite available safe and effective pharmacotherapy options to augment lifestyle interventions consisting of

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nutritional and physical activity improvements, obesity prevalence remains sharply above the Healthy People 2020 goal of 30.5% [3]. In fact, if recent incidence trends continue, it is estimated that close to half of the global population will have obesity by the year 2020 [6].

Obesity treatment guidelines uniformly address clinician responsibility to assist patients with weight reduction through a foundation of lifestyle modification composed of improved diet and increased physical activity, behavior counseling, and clinical support. However, lifestyle intervention alone is generally insufficient to result in meaningful and persistent weight reduction in most patients [7]. The clinical approach to obesity treatment mimics that of hypertension, which is based on the addition of appropriate pharmacotherapy onto a foundation of lifestyle plan recommendations (e.g., reduced-salt diet, increased physical activity). Adjunctive pharmacotherapy with weight-loss medications can result in greater and more sustained weight loss when compared with lifestyle modifications alone [4,8].

All major obesity management guidelines recommend pharmacotherapy as add-on to lifestyle modification for patients with BMI $\geq$ 30 kg/m$^2$ and for those with BMI $\geq$ 27 kg/m$^2$ who have obesity-related diseases or risk factors [9,10] or when potential benefits outweigh the risks [11]. Prior to 2012, most weight loss pharmacotherapy options were amphetamine congeners with labeling recommendations for short-term use only, typically interpreted as up to 12 weeks. In recent years, the FDA has approved a number of new anti-obesity medications (AOMs), including lorcaserin (Belviq®, Eisai Inc.) and phentermine/topiramate extended release (Qsymia®, Vivus Inc.) in 2012, naltrexone/bupropion (Contrave® Extended Release, Orexigen Therapeutics, Inc.) in 2014, and liraglutide 3.0 mg (Saxenda®, Novo Nordisk, Inc.) in late 2014. These newer medications have no limitations regarding duration of use owing to the nature of obesity as a chronic disease similar to hyperlipidemia and hypertension in which medications are continued indefinitely. A systematic review of clinical trial data reported through the end of 2013 for AOMs approved for long-term use at the time (orlistat, lorcaserin, and phentermine/topiramate) reported greater mean weight loss and an increased likelihood of clinically meaningful weight loss after 1 year of treatment with these AOMs when added to lifestyle measures as compared to placebo [8]. Similar benefits relative to placebo were noted in recently published trials with liraglutide 3.0 mg used for up to 3 years [12] and naltrexone/bupropion used for 1 year [13].

Recent longitudinal data from a large electronic medical records database study [14] confirmed the clinical suspicion that weight cycling is a common phenomenon among individuals with obesity. These findings reaffirm the significant challenge patients experience in achieving and sustaining weight loss. This is compounded by the metabolic adaptations following weight loss that encourage weight regain [15]. Again, similar to treatment of other chronic diseases, medications can be highly effective as a component of a more comprehensive weight loss strategy but are certainly not a cure for obesity. Weight loss is not typically sustained once drug therapy is discontinued, thus adherence and persistence with medication regimens are important determinants of real-world treatment benefits.

As these newer AOMs have been on the market for several years and more patients have been using them, there is a need to assess drug utilization patterns reflective of real life usage. The objective of this study was to evaluate real-world data on persistence with AOM therapies and to explore patient factors associated with persistence patterns.

## 2. Methods

### 2.1. Study design

This was a retrospective analysis of the Truven Health MarketScan® claims databases (Commercial and Medicare Supplemental) with access to more than 130 million de-identified patients. Truven databases is a widely used, proprietary research data source in the US with robust, longitudinal data gathered from diverse sources (employers, health plans, Medicaid, other carriers) and broad geographic representation. Multiple data sourcing allows for the ability to retain patients even when they switch health plans. MarketScan data are fully HIPAA compliant.

The time period for this analysis was January 2014 to September 2016, which was the latest available data from the Truven database at the time of analysis. Eligible patients were adults ($\geq$ 18 years old) who newly initiated treatment (index claim) with an AOM approved for long-term use (lorcaserin, liraglutide 3.0 mg, fixed dose combination naltrexone/bupropion, fixed dose combination phentermine/topiramate) between January 1, 2015 and March 31, 2016. The term "AOM" throughout this paper refers specifically to these four medications approved for long-term use. Use of the index AOM or any of the other long-term AOMs that were a focus of the study was not allowed within a 1-year period prior to the index claim and such patients were excluded. Prior use of orlistat and phentermine was allowed. Orlistat is approved for long-term use but was not included as an AOM of interest because of very low utilization. The March 31 cut-off for index claim inclusion was necessary to allow for 6 months of follow-up data prior to the data collection cut-off of September 2016. At least 12 months prior and 6 months post-index continuous enrollment in a health insurance plan with pharmacy benefits was required.

### 2.2. Data analysis

Patient demographic information included age, sex, geographic region, and insurance type. The following comorbidities were recorded and used to calculate the Charlson Comorbidity Index (CCI) [16] for each patient: AIDS, metastatic solid tumor, moderate/severe liver disease, malignant lymphoma, leukemia, any non-metastatic solid tumor, diabetes with end-organ damage, moderate/severe renal disease, hemiplegia, diabetes without end organ damage, mild liver disease, ulcer disease, connective tissue disease, chronic pulmonary disease, dementia, cerebrovascular disease, peripheral vascular disease, congestive heart failure, and myocardial infarction. Hypertension and hyperlipidemia were additional comorbidities of interest not included in the CCI.