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Transitions in Obesity – an opportunity for GLP-1 drugs?

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ABSTRACT

Obesity is a major contributor to ill health. Until recently, the number of individuals developing obesity has continued to rise, contributing to the global burden of many common and serious conditions including premature cardiovascular disease, type 2 diabetes (T2D), and some cancers. However, in 2023 in the United States (U.S.), evidence suggests that there has been a decline in the number of obese adults. One factor to which this reduction has been attributed has been the introduction of a new class of drugs for the treatment of obesity and T2D, known as Glucagon Like Peptide-1 Receptor Agonists (GLP-1 RA's). These drugs are undoubtedly effective in promoting weight loss [1], and clinical outcomes have been favorable ([2-6]), including reducing the risk of progression to T2D in adults with obesity and prediabetes [7] as well as beneficial effects on lowering the burden of cardio-renal disease. Although there have been many studies of the clinical benefits of GLP-1 drugs, there have been fewer focusing on their economic effectiveness. There is also a paucity of published research into the potential of stratifying and targeting individuals with T2D and/or obesity into sub-populations to produce a focused financial return on investment. Our analysis of US commercial claims data shows that many patients transition between different categories of obesity over time; only the highest obesity class (BMI 40.0 and over) show persistency in the highest class over time, indicating that the focus of treatment with GLP-1 RAs should be on the severely obese.

Background and Aim

There continues to be considerable interest in and praise for a new class of drugs for the treatment of obesity and type 2 diabetes (e.g, Semaglutide with the brand name Wegovy and Tirzepatide with the brand name Mounjaro). GLP-1 RAs are undoubtedly effective in promoting weight loss [1], and clinical outcomes have been favorable ([2-6]), including reducing the risk of progression to T2D in adults with obesity and prediabetes [7]. In recent guidance published by the American Diabetes Association, for adults with T2D and established or high risk of atherosclerotic cardiovascular disease, the treatment plan should include GLP-1 RAs. Similarly, this class of drug is also recommended for adults with T2D who have heart failure with preserved ejection fraction, chronic kidney disease, and/or metabolic dysfunction–associated steatotic liver disease[8,9]. Proponents of widespread use of GLP-1 drugs point to the fact that their use will need to continue, often for the lifetime of the patient, but will reduce the severity of cardiac and metabolic conditions, resulting in cost reduction over time. Currently, data from trials of GLP-RA's are available for 72 weeks and show high rates of attrition from the treatment[10-12]. However, GLP-1 drugs are too new for data to be available to show long-term reductions in co-morbid disease severities and patient costs. As a corollary, the risk of regaining weight after cessation of treatment [13] would likely have a further negative effect on the health economics.

A June 2024 survey conducted by the International Foundation of Employee Benefit Plans [14] reported that employer coverage of GLP-1 drugs is up 8% since fall of 2023 and approximately 33% of companies are now offering GLP-1 drug coverage for both diabetes management and weight loss, although no employers cover GLP-1 drugs for obesity only. In contrast, there are increasing reports of payers and employers dropping coverage of the drug because the combined effect of high obesity prevalence and high cost threatens payer budgets[15]. For example, North Carolina ceased paying for obesity drugs from April 2024[16] in its state health plan. Beckers Payer Issues reported in June 2024 [17] that Blue Cross Blue Shield of Minnesota will cease coverage of GLP-1 drugs in its large group plan in 2025, while Beckers Hospital Review similarly reported in July 2024 that several health systems have also either ceased or reduced coverage [18]. However, there has been limited research examining the final return of investment in stratifying individuals with T2D and/or obesity into subgroups. Therefore, the aim of this study is to evaluate the economic impact of individuals transitioning between different categories of obesity and the use of GLP-1 RAs.

Prior Studies of cost-effectiveness

Although clinical results have generally been favorable for GLP-1 RAs, there has been less discussion about their cost-effectiveness, particularly for payers in the U.S. health system. It is generally believed that reduction in obesity and accompanying co-morbidities will reduce costs sufficiently to offset the cost of the drugs. A report from the World Obesity Federation [19] suggested that the cost of excess weight from associated comorbidities could amount to 4 trillion, or 3.0 % of global GDP by 2035. It would seem, therefore, that a drug that results in significant weight-loss would pay for itself. In a recent article, Thorpe and Joski [20] estimated that average potential savings from weight loss among adults with a baseline BMI of 30 kg/m^2 were between $670 and $2,849 per year for Commercially-insured patients, depending on the degree of weight reduction, and between $1,262 and $5,442 for Medicare patients. However, given an annual list price for Tirzepatide and Semaglutide respectively of $10,000 and $13,500 before discounts and rebates, these levels of savings are unlikely to provide a positive return on investment for most patients. A recent expert report by the Institute for Clinical and Economic Review[21] (ICER) concluded "The cost effectiveness of treatment for obesity with GLP-1 RAs in patients without diabetes exceeds commonly used thresholds….the health-benefit price benchmark range for Semaglutide is $7,500 to $9,800 per year; this would require a discount from the wholesale acquisition cost of 44-57%." Manufacturer discount and rebate information is not publicly available; our best estimate of the maximum price reduction available to commercial payers such as employers is 50%, making economic effectiveness of the drugs marginal at best.

A recent cross-sectional economic study [22] indicates that the positive economic opportunity for GLP-1 RAs is limited to high obesity levels and certain clinical diagnoses. As is the case for most cost-effectiveness studies, this study was limited to one year i.e., patient outcomes were not tracked over multiple years, allowing for analysis of neither the long-term beneficial effects of weight reduction on health, nor the side effects of the drugs or their persistency. However, this previous study did show significant differences between patient cost trajectories as BMI increased; significantly, for many patients and for a wide range of BMI levels, costs were relatively flat. The implication of these cost trajectories is that for different levels of obesity and for many diagnoses, reducing BMI would not lead to sufficient savings to pay for the commercial cost of GLP-1 drugs at present price levels. In conclusion, given the published weight reduction in the range of 15%-20% with these drugs, there is insufficient reduction in their healthcare costs for individuals with a baseline BMI between 30-40 kg/m^2. A recent study by Gleason et al[23,24] found one-year median persistency of about 75% for Semaglutide, and lower rates of persistency for other weight-loss drugs. Clearly, long-term studies of the effectiveness of the drugs that take into account persistency, side-effects and long-term health improvement are needed.

Data

Data for patients with diagnoses of obesity were extracted from claims data in the period 2017-2019 in the Merative dataset, a widely used source of commercially-insured payer utilization and cost data.[i] The authors' previous study analyzed the 2019[ii] costs of US Commercially-insured patients at different levels of obesity (as measured by BMI[iii]) and co-morbidities in the Merative dataset. This prior study represented a cross-sectional analysis of the relationship between levels of obesity and annual patient costs, for different categories of co-morbidities. The cross-sectional analysis did not consider patient treatment modalities of their condition(s), nor did it follow patients over multiple years.

Methodology

Given the conclusion of our 2023 study and the apparent growing reluctance of payers to fund sustained use of GLP-1 drugs, we investigated the extent to which longitudinal analysis of patient obesity states could assist in focusing treatment on certain sub-populations. We therefore performed additional analysis of patient transitions between BMI states in the 2017-9 obesity data, a time-period that both avoids complications of Covid 19 and the introduction of GLP-1 drugs to treat obesity. For this analysis, we limited the study to young adults at least 20 years of age who were eligible in a claims database for at least 6 months per year. Members were required to be continuously enrolled during 2017-2019 period. As this study relied on claims data, BMI information was derived using a series of ICD-10 codes (see the Appendix table). In scenarios where members had multiple BMI levels corresponding to different obesity classes, the maximum level recorded for the year was used. Finally, BMI levels were grouped into 4 classes: patients are classified as overweight (BMI 27.0 to 29.9), Class I (BMI 30.0 to 34.9), Class II (BMI 35.0 to 39.9) and Class III (BMI 40 and over). A total of 26,796 patients with records in 2017-9 were analyzed.

LONGITUDINAL ANALYSIS

For this analysis we examined transitions between classes of Obesity in patients between 2017 and 2019. We observed how members transitioned from one obesity class to another and ultimately used these observed counts to estimate the transition matrix each year. Applying a Markov-chain process to the analysis allows us to project the ultimate state of a constant obesity population over two years. Using this method, the transition matrix for a multi-year period is calculated by multiplying the single-year transition matrices, assuming the transitions are independent across years. Table 1 shows an example of 1-year transitions:

Table 1: Transitions between Obesity states between 2017-8

Transitions 2017-2018					
Counts	2018				TOTAL
2017	Overweight	Class I	Class II	Class III	
Overweight	3,119	913	70	20	4,122
Class I	768	7,027	1,381	65	9,241
Class II	99	914	4,671	891	6,575
Class III	53	126	679	6,000	6,858
	4,039	8,980	6,801	6,976	26,796
Rates	2018				
2017	Overweight	Class I	Class II	Class III	
Overweight	76%	22%	2%	0%	100%
Class I	8%	76%	15%	1%	100%
Class II	2%	14%	71%	14%	100%
Class III	1%	2%	10%	87%	100%
	15.1%	33.5%	25.4%	26.0%	100%

Table 1 shows that 76% of overweight patients remain overweight after one year; the remaining 24% transition to higher obesity classes, with 2% for example becoming Class II. Within the year some patients regress to Overweight: 8% of Class I patients, for example, end the year at the lower BMI level.

We performed the same analysis on the 2018-9 data; results (not shown) are similar to those of 2017-8, leading us to conclude that in a largely untreated population the obese population transitions form a homogeneous Markov process. Homogeneity in the Markov process allows us to project forward a population over a number of years. As an example, in Table 2 we show the result of projecting the 2017 population to their state at the beginning of 2020.

Table 2: Distribution of the 2017 Obese Population at Beginning of 2020

2017-20	**Overweight**	**Class I**	**Class II**	**Class III**
Overweight	57.6%	34.0%	5.2%	1.2%
Class I	15.4%	61.0%	20.6%	3.0%
Class II	3.9%	22.9%	54.4%	21.0%
Class III	1.9%	5.3%	16.8%	77.8%

Table 2 shows that, with the exception of Class III obesity, there is considerable movement both to higher and lower levels of obesity. Only 57.6% of patients classified as overweight in 2017 remain overweight 2 years later; the remaining 42.4% transition to higher levels of obesity. Of the Class II obese patients in 2017 a similar percentage (54.4%) remain Class II, while 26.8% regress to lower BMI classes (a fraction (3.9%) to overweight). 21.0%, however, transition to Class III. The experience of Class III obese patients is different: 77.8% remain in the highest BMI category while only 22.2% regress to a lower category.

Projecting this analysis forward for more years (not shown) illustrates the fluidity of the overweight and Class I and II populations, and the "stickiness" of the Class III population

Table 3: Patient Costs by Class, 2017-9

COST	2017	2018	2019
Overweight	$ 1,005	$ 1,089	$ 1,404
Class I	$ 787	$ 859	$ 951
Class II	$ 961	$ 1,038	$ 1,113
Class III	$ 1,275	$ 1,437	$ 1,515

Cost Analysis

There are economic implications of the transition analysis as well Note that in Table 3, costs have not been normalized for patient co-morbidities. The costs in Table 3 are noteworthy in several respects: Overweight patients tend to be higher cost than Classes I and II, a finding that is somewhat consistent with our earlier paper that showed the flat trajectory of costs over the Class I and II range with an increase below BMI 30. Of significance for the present analysis, however, are the costs of Class III patients. Taken together with the persistency of patients at BMI levels 40 this analysis indicates the necessity to focus on the treatment of these patients. Secondarily there is a relatively high transition probability from Class II to Class III, which suggests that modeling the Class II population to find those at risk of transition to Class III could also be cost-effective.

Conclusion

Although there is a great deal of evidence showing the clinical benefits of GLP-1 for adults and young people with type 2 diabetes and/or obesity, data are beginning to emerge that show that widespread use of GLP-1 drugs may not be economic at current drug pricing levels. Longitudinal data will be required to demonstrate reduction in disease severity and related cost. In the meantime, payers will require that the use of GLP-1 drugs will need to be part of a broader suite of obesity treatments, with drug therapy focused on those patients whose treatment will prove cost-effective.

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Appendix

Obesity Definitions	ICD-10 Code	ICD-10 Definition
BMI >27	Z6828	Body mass index (BMI) 28.0-28.9, adult
	Z6829	Body mass index (BMI) 29.0-29.9, adult
	Z6830	Body mass index (BMI) 30.0-30.9, adult
BMI > 30	Z6831	Body mass index (BMI) 31.0-31.9, adult
	Z6832	Body mass index (BMI) 32.0-32.9, adult
	Z6833	Body mass index (BMI) 33.0-33.9, adult
	Z6834	Body mass index (BMI) 34.0-34.9, adult
	Z6835	Body mass index (BMI) 35.0-35.9, adult
	Z6836	Body mass index (BMI) 36.0-36.9, adult
	Z6837	Body mass index (BMI) 37.0-37.9, adult
	Z6838	Body mass index (BMI) 38.0-38.9, adult
	Z6839	Body mass index (BMI) 39.0-39.9, adult
	Z6841	Body mass index (BMI) 40.0-44.9, adult
	Z6842	Body mass index (BMI) 45.0-49.9, adult
	Z6843	Body mass index (BMI) 50.0-59.9, adult
	Z6844	Body mass index (BMI) 60.0-69.9, adult
	Z6845	Body mass index (BMI) 70 or greater, adult
Overweight	-	BMI 27-29.9
Class I Obesity	-	BMI 30-34.9
Class II Obesity	-	BMI 35-39.9
Class III Obesity	-	BMI ≥40

[i] Real world evidence. Merative. www.merative.com/real-world-evidence.
[ii] Analysis was limited to 2019 to avoid complications from Covid.
[iii] See Appendix for ICD-10 diagnosis codes.