Obesity and Beyond

The Surprising Reach of GLP-1s

Citi GPS: Global Perspectives & Solutions
October 2024

Adam Spielman
Head of Health and Consumer
Citi Global Insights

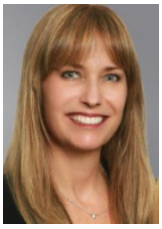
adam.spielman@citi.com

Filippo Falorni, CFA
U.S. Beverages and HPC
Citi Equity Research

Thomas Palmer, CFA
U.S. Food Manufacturers
Citi Equity Research

Heejin Lim
Korea Consumer, Retail and MedTech
Citi Equity Research

Anjolaoluwa Odunsi
Health and Wellness
Citi Global Insights



Diane Wehner, CFA
Senior Portfolio Manager, Healthcare
Citi Global Wealth

Nathan Weinstein, CFA
Global Healthcare Analyst
Citi Global Wealth

Jim Hollingshead
CEO
Insulet

Prashant Agrawal
Founder and CEO
Impact Analytics

Mick Farrell
CEO
ResMed

Carlos M Nunez, MD
Chief Medical Officer
ResMed

OBESITY AND BEYOND

The Surprising Reach of GLP-1s

GLP-1 ‘wonder-drugs’ have crashed into the collective consciousness in recent months. Claims about easy weight loss have clogged our social media feeds. A tribe of followers has emerged. A hype cycle has developed.

What’s the substance behind the hype around these drugs--which have in fact been around for several years? And what impact could they have on the global battle against obesity and beyond, in places you might not have thought about yet?

In this Citi GPS report we’ll look at some of these questions, laying out the scale of the global obesity problem, describing how GLP-1 drugs work, and examining their potential to be part of the long-term solution.

And we’ll sketch out potential usage profiles and the resultant impacts across a range of sectors including healthcare, food and beverages and fashion.

We’ll also hear from several experts to help present a rounded view of current thinking around GLP-1s and the way ahead.

It’s clear that GLP-1s also have many profound medical benefits beyond reducing obesity. There is evidence that they can help with a range of chronic diseases, including cardiovascular and kidney disease. There are also suggestions they could have a role to play in treating dementia, and addictive behavior such as alcohol and nicotine abuse.

The pharma industry is taking note, and the development pipeline of new drugs looks robust.

At present, the impact of GLP-1 drugs on other industries is limited as only 25 million people take them. But that number will probably be hundreds of millions in a few years and the impact of this massive potential growth is another question at the heart of this report.

We’ll look at how these new drugs will in fact increase demand for medical services and the treatment of obesity related diseases - partly because people who use them will live longer, and partly because they’re more likely to go to the doctor.

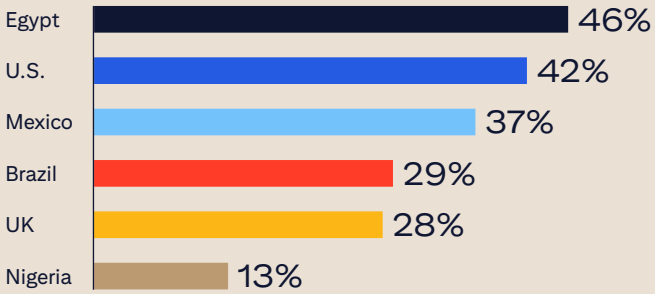
At the same time, they risk reducing demand for food and beverages companies, as users find they want to eat a lot less.

For some the jury is out on the long-term viability and desirability of GLP-1 drugs. This report is designed to bring academic rigor and insight, with an eye on commercial implications and impact, to this healthy debate.

GLP-1s: Obesity & Beyond

Obesity is a global problem

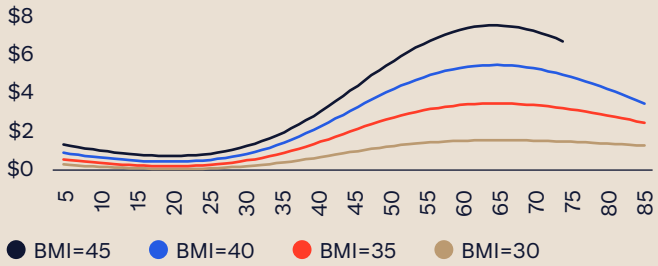
% of adults with obesity, 2022



Source: Lancet, Feb 2024.

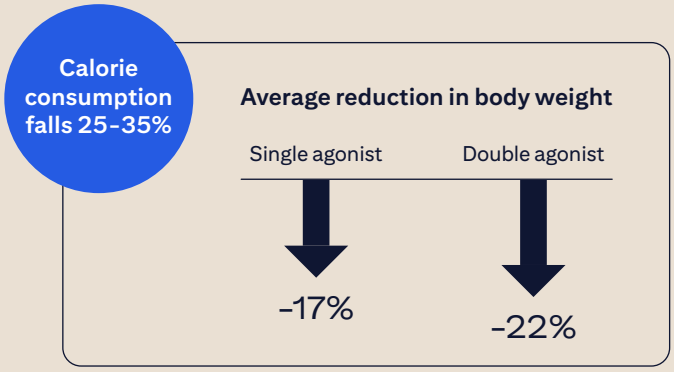
Obesity damages body over decades

Incremental Annual Healthcare Costs by BMI, US
Extra cost per person, vs people with BMI of 22 ($ in 000s)



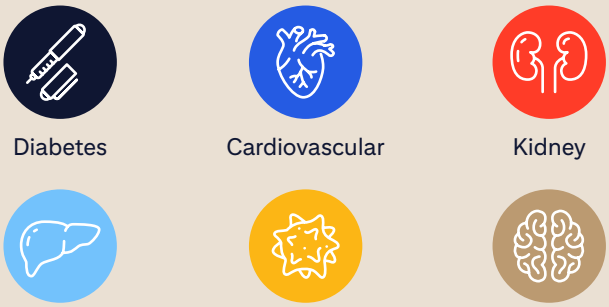
Source: PlosONE, Mar 21.

GLP-1s cut calorie intake leading to weight loss



Source: NEJM.

GLP-1s help fight many diseases



100+ drugs under development

Future anti-obesity drugs target

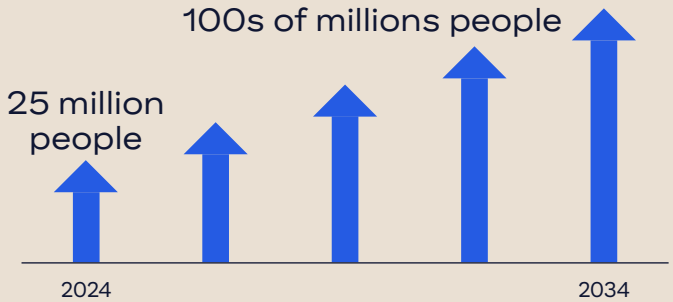
Side effects
- Less bad gastro-intestinal effects
- Reduced muscle loss

Effectiveness
- Greater weight loss
- Greater reduction in co-morbidities

Convenience
- Less frequent injections
- Pill-based

Manufacturing capacity limited but growing fast

Global manufacturing capacity of GLP-1s



Source: Lancet, Feb 2024.

Possible Implications if GLP-1s Reach 100s of Millions

Individuals	Short-term	Increased life expectancy for people with obesity-related diseases. Individuals feel better about their bodies.
	Long-term	More years of healthy life; reduction in numerous chronic diseases.
Economy	Mid- to long-term	Increase in healthy middle-aged work force → more tax revenue. Obesity cuts labor force output by ~2% in many developed countries. 0.5-1% of GDP could be reclaimed if GLP-1s cut obesity by a lot.
Healthcare	Short-term	Demand is likely to expand. GLP-1s could slow the progression of chronic disease but don't cure it, and reduce risk of death. For existing patients, this means acuity will increase more slowly but demand is likely to last for more years. Some procedures will become possible that weren't previously. Individuals likely to engage more with the health system.
	Long-term	Fewer patients will develop chronic diseases in the future.
	Ultra long-term	Increased expenditure on elderly owing to longer life spans.
Medical aesthetics	Short- to mid-term	Participants expect GLP-1s to boost the medical aesthetics marketing.
Health plans	Mid-term	GLP-1s prescribed for the co-morbidities of obesity are likely to increase life expectancy but thereby increase total medical expense. For younger patients, the dilemma is around funding products that provide lifestyle benefits in the near-term, but with prospect of health benefits on a multi-decade view.
Food & Beverages	Short- to mid-term	Switch in consumption from quantity to quality. If 50% of obese Americans took GLP-1s, national calorie consumption reduces by ~5% (= -$400bn in food sales).
Tobacco & Gaming	Short- to mid-term	Reduction in addictive behaviors implies reduced demand.
Apparel Retail	Short- to mid-term	Increased demand with a move to smaller clothing sizes.

Contents

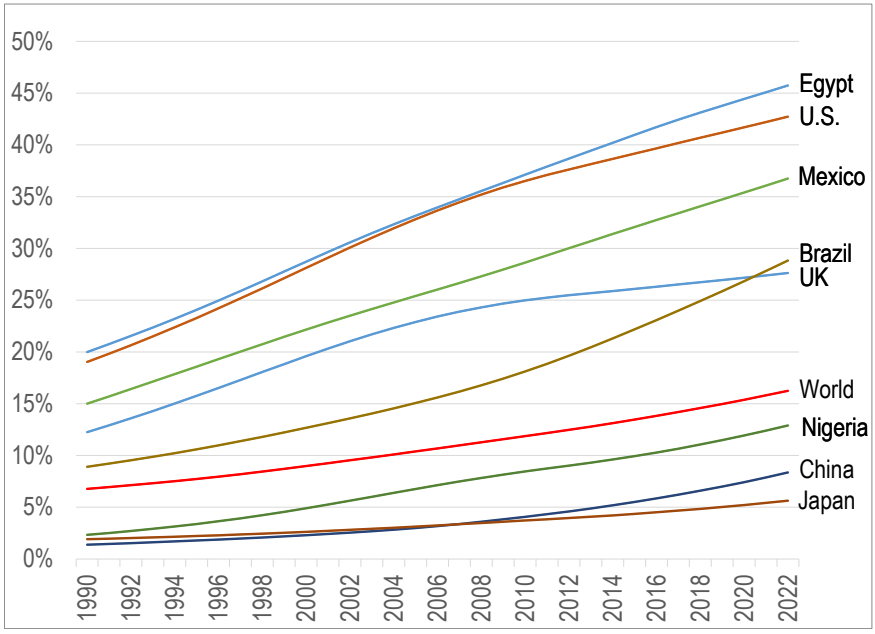
Main points

1. Obesity

GLP-1s are a class of anti-obesity drugs that have been shown in large clinical trials to cut people's weight, sometimes by 20% or more.

- **Obesity is an increasingly serious problem globally.** About 3 billion adults are overweight, of which 1 billion are obese, according to figures from medical journal The Lancet. Roughly 75% of American adults are now overweight, of which more than 40% are obese. About 21% of American children are obese.

Figure 1. Growth of obesity in selected countries, 1990-2022



Source: Lancet, Feb 2024: Worldwide trends in underweight and obesity.

GLP-1s have been used to treat diabetes since 2005. Their use for weight-loss is much newer.

- **Obesity gradually damages all the tissues in the human body.** The damage to the body's organs -- most importantly the heart, brain, pancreas and kidneys -- accrues over decades, and is mostly irreversible. Obesity also causes musculoskeletal problems. The OECD estimates that in the next 30 years, obesity will cause nearly 60% of all diabetes cases, 18% of cardiovascular disease, 11% of dementia and 8% of cancer.

Figure 2. Healthcare Costs per American, by BMI category

Annual healthcare costs for adults (aged 20-85), normalized for age, race, education etc

Weight Category		Annual Costs	Rebased
Underweight	BMI<18.5	$4,420	105
Healthy Weight	18.5<BMI<25	$4,190	100
Overweight	25<BMI<30	$4,810	115
Moderate Obesity	30<BMI<35	$5,670	135
Intense Obesity	BMI>35	$7,290	174

Based on >175,000 anonymized MEPS respondents, 2011-16. Excludes pregnant women.

Source: PlosONE: Mar 2021: Association of BMI with healthcare expenditures in the U.S..

- **Obese people not only have a lower life expectancy, they also live more of their life in ill-health**. The healthcare costs for an American with a BMI of 35 -- averaged over a lifetime -- is almost 75% more than the costs for an individual deemed to be of healthy weight.

- **Obesity is reducing economic output by about 2% in most developed economies**, according to OECD modeling. This is due to a combination of reduced output and absence from work due to obesity related health issues.

2. How GLP-1s work and what they do

- **GLP-1s cut people's weight significantly.** They have been used to treat diabetes since 2005 but have become much more significant in the past couple of years as their anti-obesity properties have become widely publicized. They mimic the hormones produced in an individual's gut that tell the brain that the person is full, among other things. People who take the latest generation of drugs reduce their calorie intake by about 25-35%, shifting away from calorie-dense food in particular. In a large-scale clinical trial, obese non-diabetics using semaglutide for 72 weeks lost about 15-16% of their weight on average. In a separate trial for tirzepatide, non-diabetics lost an average of 22% of their weight. People with diabetes lost, on average, about 5% less in both trials.

- **These drugs provide many additional medical benefits.** These drugs slow the progression of many important chronic diseases, including cardiovascular, kidney and fatty liver diseases. Tirzepatide has been shown to reduce the risk of overweight individuals developing diabetes by more than 90%. Scientists do not fully understand the biological mechanisms that are driving these benefits, but plenty of trials show they are real. GLP-1s can also reduce the risk of many cancers. There is also evidence they help to slow the development of Alzheimer's and may even halt Parkinson's**.** In addition, they appear to reduce addictive behavior: many GLP-1 users say they drink less alcohol, for example, and it appears GLP-1s reduce nicotine intake.

- **The side effects appear to be generally tolerable, if unpleasant.** The most frequent are gastro-intestinal problems like nausea. These drugs have been used by millions of people since 2005, so it seems unlikely that new side effects will emerge for the existing products. Another issue is the loss of reduced muscle mass.

- **Away from clinical trials, many users stop taking GLP-1s after a few months.** If users stop taking GLP-1s, they tend to regain most of the weight they lost. Only 7% of participants pulled out of the clinical trial that showed semaglutide is safe and effective for treating obesity because of the side effects. Real world behavior seems quite different, however, with more than half of new GLP-1 patients stopping use within a year. We think this is partly due to their cost and limited availability, and partly due to the side effects of the current generation of GLP-1s.

- **More than 100 new GLP-1s are being developed,** with the aim of reducing the side effects, making variants that are more convenient to take (for example as pills), or making them more effective, for example by further reducing the risk of particular diseases. This doesn't mean, however, that 100 new anti-obesity drugs will be approved, still less reimbursed.

3. Factors that will determine the scale of their impact

- **Demand for GLP-1s is driven as much by people wanting to look and feel better as by strictly medical factors.** GLP-1s are unique because they have compelling lifestyle motivations and compelling medical ones. According to a Citi survey -- summarized in Figure 15 on page 18 -- more Americans take GLP-1s to lose weight because they want to look or feel better than they do to treat a specific medical issue.

Figure 3. The continuum of motivations for taking GLP-1s

Source: Citi GPS

- **At the moment GLP-1s' real-world impact is limited as global manufacturing capacity is enough for only about 25 million people.** Partly as a result, prices are high, and it is often hard to get reimbursement. In America, Wegovy's list price is currently about $16,000/year, for example. More than 100 million adults there are obese. If half started using GLP-1s, with an average discount of 50% vs. the list price, the total cost would be roughly $400 billion, equivalent to about 8% of the national healthcare budget.
- **However, we believe global capacity will be in the hundreds of millions in the coming years, and prices for some GLP-1s will become much more accessible.** The main manufacturers are increasing capacity as rapidly as they can, and new competitors are likely to enter the market. One firm said it would sell vials (without injector pens) at half price to uninsured individuals. Generic versions of semaglutide are due to become available in China in two years and in Europe and the U.S. in 7-8 years. Liraglutide (an older GLP-1 which is injected daily) has just gone off-patent, and the first generics are entering the market.

Figure 4. Citi GPS Scenarios for global GLP-1 usage in 5-10 years

Scenario	Description	Assumptions
Low growth *Unlikely*	GLP-1s grow, but modestly 50 - 100 mln people reduce weight significantly globally	No reduction in prices so most of the incremental capacity goes unused. Current generation of clinical trials/ new products are mostly disappointing. Lifestyle demand fades as GLP-1s become unfashionable.
Consistent growth *Most likely scenario*	100-300 mln people reduce weight significantly Meaningful change in obesity trends in the rich world	Assumes capacity increases at incumbents as planned and new entrants add further capacity, along with generics in China in 2026 and Europe/ Japan /US in 2031/32. Prices fall for current generation of GLP-s as better products get approved. More reimbursement.
Widespread adoption *Possible, but assumes everything goes right*	More than 300 mln people lose meaningful weight Obesity falls in many countries	Capacity increases as planned, then further expansion on top. Clinical trials live up to expectations. Pill-based GLPs become widely available, increasing demand and making manufacturing easier. Prices for some products drop significantly, reflecting intense competition and then generics

Note: These scenarios are around number of people who might lose a substantial amount of weight thanks to GLP-1s. They do not all have to be taking GLP-1s at any one time.

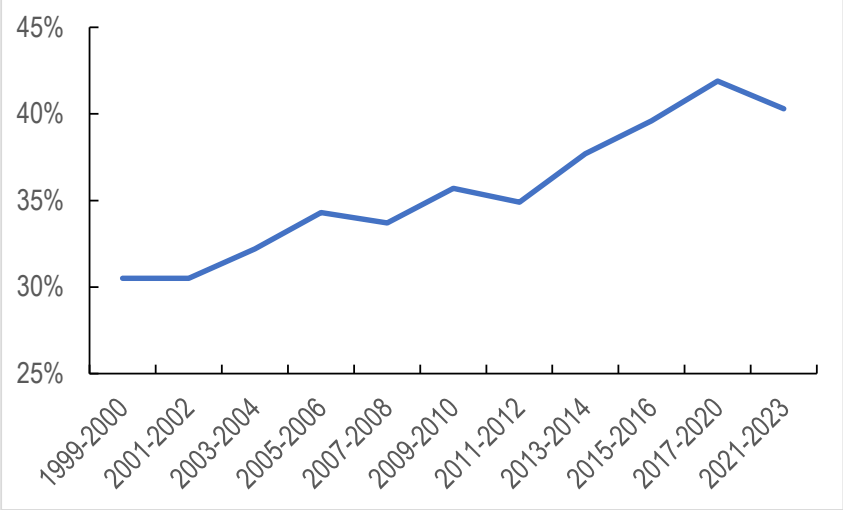
Source: Citi GPS

Figure 4 sets out what we regard as plausible scenarios for global usage of GLP-1s over the next 5-10 years. One of the biggest uncertainties is around pricing: How far will manufacturers lower prices on the existing generation of GLP-1s as improved versions become available? How will they balance public health vs revenue maximization? Will all the planned manufacturing capacity actually get used? In addition, there is the question of how long the average user will continue to take the drugs for.

- **We expect the market will bifurcate**, with some products focused on the lifestyle/ self-pay market, and others aimed at the medical / reimbursement market. We expect the self-pay products to compete mainly on enabling consumers to achieve a target weight with minimal side effects, and the reimbursement products to focus more on reducing co-morbidities. We expect more price competition in the self-pay segment.

- **There is already data suggesting GLP-1s are lowering obesity rates in America.** In September, the CDC published data that showed that the overall rate of adult obesity had fallen for the first time.

Figure 5. % of American adults with obesity (BMI>30)



Source: National Center for Health Statistics

4. How different industries are likely to be affected

GLP-1s are likely to make waves in many areas, but the effects are likely to develop over decades.

It would be easy -- but wrong -- to say that lower levels of obesity will rapidly solve the problems of obesity-related diseases -- for example for type 2 diabetes, chronic kidney disease and fatty liver disease. Clinical trials show GLP-1s don't cure such diseases -- rather they slow progression and reduce mortality.

- **On a human level:** For people with serious obesity-related diseases, for example late-stage kidney disease, GLP-1s extend life expectancy in large part due to lower risk of heart attacks and stroke. Long-term there could be an increase in the years of healthy life, to the extent that GLP-1s reduce obesity in the population. People using GLP-1s for life-style reasons are likely to feel better and look thinner, which in turn is likely to help many individuals' mental well-being[1]. Long-term, GLP-1s will probably increase the years of healthy life of many individuals.

Figure 6. Summary of possible implications for selected sectors

Sector	Time Horizon	Summary impact
Individuals	Short-term	Increased life expectancy for people with obesity-related diseases Individuals feel better about their bodies
	Long-term	More years of healthy life; reduction in numerous chronic diseases
Economy	Mid- to long-term	Increase in health middle-aged work force → more tax revenue. The OECD estimates obesity cuts labor force output by ~2% in many developed countries. If GLP-1s can reduce obesity meaningfully, maybe 0.5%-1% of GDP could be reclaimed.
Healthcare	Short-term	Demand is likely to expand. GLP-1s can slow the progression of chronic disease but don't cure it and reduce risk of death. For existing patients, this means acuity will increase more slowly but demand is likely to last for more years. Some procedures will become possible that weren't previously. Individuals likely to engage more with the health system.
	Long-term	If GLP-1s reduce total obesity, then fewer patients will develop chronic disease in future years & decades.
	Ultra long-term	Increased expenditure on elderly owing to longer life spans.
Health plans	Mid-term	GLP-1s prescribed for the co-morbidities of obesity are likely to increase life expectancy but thereby increase total medical expense. For younger patients, the dilemma is around funding products that provide lifestyle benefits in the near-term, but with prospect of health benefits on a multi-decade view.
Food & Beverages	Short- to mid-term	GLP-1s cut calorie consumption by 25-35% within months, implying that if half of obese Americans took GLP-1s, national calorie consumption would fall by ~5%. Reduction in calorie consumption implies a switch in consumption, from quantity to quality.
Tobacco & Gaming	Short- to mid-term	Reduction in addictive behaviors implies reduced demand.
Apparel Retail	Short- to mid-term	Increased demand with a move to smaller clothing sizes.

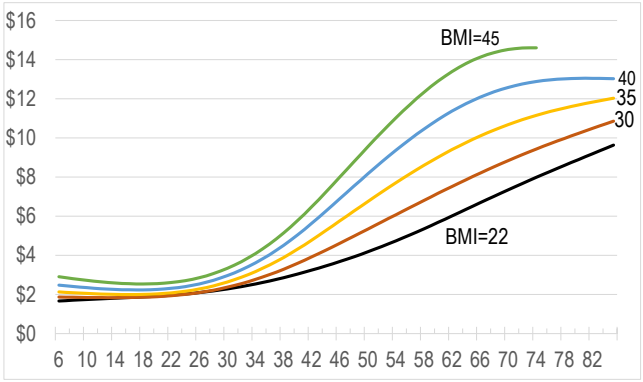
Source: Citi GPS, Citi Global Insights

GLP-1s are likely to have an effect on lifestyle, the global economy, the healthcare system and consumer companies.

- **Economy:** In a scenario where GLP-1s benefit a large number of people, there could be a *gradual* increase in the available labor force in their late middle age due to reduction in musculoskeletal issues and chronic diseases, boosting both GDP and tax revenue. We estimate that if GLP-1s achieve the *Consistent Growth* scenario or better, they could boost GDP by 0.5%-1%.

[1] There is a strong (two-way) association between obesity and poor mental health (Source: CDC).

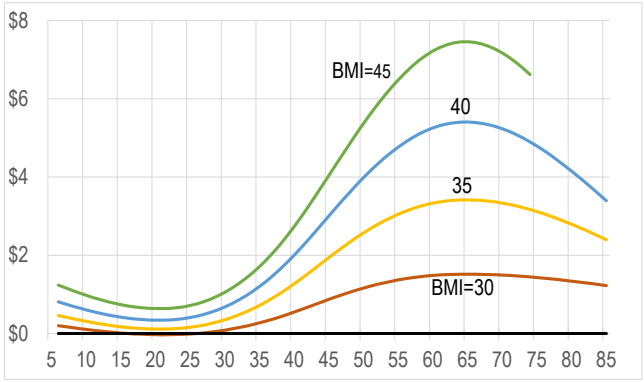
Figure 7. Average Annual Healthcare Costs by Age and by BMI (USA, 2011-16. $ in 1,000s)



Based on 175,726 individuals' health records, 2011-16

Source: : PlosONE: Mar 2021: Association of BMI with healthcare expenditures in the U.S..

Figure 8. Incremental Annual Healthcare Costs by BMI (USA. $ in 1,000s, relative to average costs for people with BMI=22)



Based on 175,726 individuals' health records, 2011-16

Source: PlosONE: Mar 2021: Association of BMI with healthcare expenditures in the U.S..

- **Demand for healthcare provision (1 to 4 years):** We think demand for therapeutics in most obesity-related areas will actually increase in the short- to medium-term as GLP1-s become more widespread. GLP-1s slow the progress of obesity-related disease, keeping people alive for longer, but they don't repair whatever damage has already been done. However, demand in any particular therapeutic area will depend on the balance between negative and positive factors:
  - Patients on GLP-1s are likely to move up the acuity curve more slowly, and this will reduce demand and expense. Treating a patient with stage 3 CKD, for example, is easier (and cheaper) than treating a patient with stage 4 or 5 CKD.
  - On the other hand, patients are likely to live for longer, which means they will require more cumulative treatment. In the example of CKD, the patient may well still advance to stage 4 and then 5, just more slowly than before. In addition, some treatments - for example knee replacements -- that were previously ruled out due to excessive weight may become possible.
  - There is increasing evidence that obese people are more likely to interact with the healthcare system if GLP-1s are an option.

  Many companies that supply products for obesity-related conditions say that so far, GLP-1s have actually been a positive. Insulet supplies insulin pumps, and when we spoke to the CEO, Jim Hollingshead, he said: "We were somewhat surprised but what we see in the claims data – people who start on a GLP-1 are more likely to also initiate insulin within a 12-month period compared to the group who are not on GLP-1s. It's counter-intuitive, but very clear. And if they stop the GLP-1, they are even more likely to start insulin."

- **Demand for healthcare provision (long-term):** The greatest promise of GLP-1s is for people who haven't developed chronic diseases. If people can either shed excess weight before they have become ill, or never become obese in the first place, then those people are much less likely to develop obesity-related diseases. But these are long-term savings. Figure 8 implies that if someone in their 20s loses weight -- and keeps the weight off --then the greatest savings are likely to occur about 30 years later.

- **For health plans / insurance** -- There is the question of who is going to pay for the drugs. These drugs are (currently) expensive, and users need to take them indefinitely. And as we've said, we believe that in the near term, GLP-1s are likely to increase the costs of treating obesity-related diseases, not reduce them.

  In the long-term, the main savings from reducing obesity will occur when the individuals are in their late middle age. Plans for individuals who are younger than this will therefore to find ways of funding the increased cost, without necessarily seeing any of the savings.

- **Employers.** Will employers seek to attract employees by offering to pay for GLP-1s? But at what cost? Employers may be able to ensure some (mostly middle aged) people stay in the work force who may otherwise have to leave. One issue is that obesity is most prevalent in less educated parts of the workforce, implying many people most likely to use this benefit would be in less value-added roles.

GLP-1 cuts users' calorie in-take quite rapidly and reduce addictive behaviors; in contrast the health benefits take years to accumulate.

- **For food, beverage and tobacco companies.** Clinical trials show that obese adults without diabetes who use of the current generation of GLP-1s reduce their calorie intake by about 25-35% for within a few months of starting. The scale of impact is therefore determined by how many people actually use the drugs.

  More than 100 million American adults are obese currently, and a further 80 million are overweight, according to CDC. If you took a scenario in which 55 million took these drugs and lowered their calorie intake by an average of 30%, total calorie consumption in the U.S. would fall by about 5%.[2]

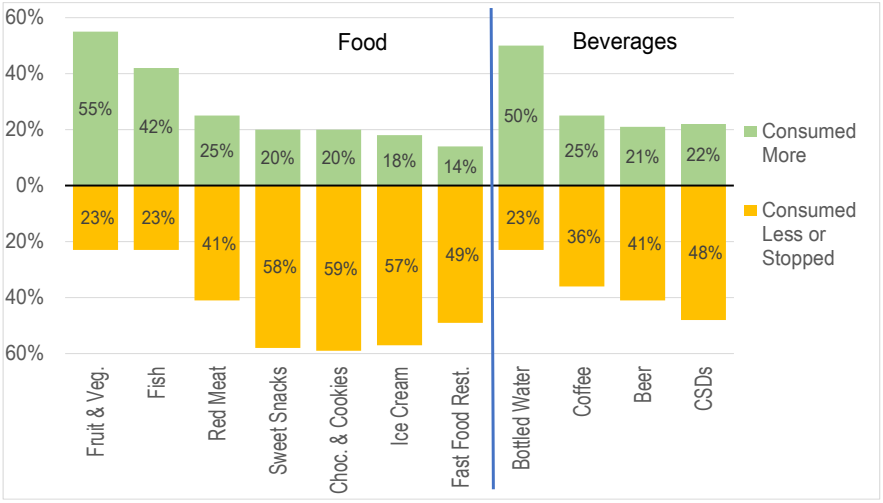
  GLP-1 users seem to avoid calorie-dense foods, while increasing consumption of fresh and healthy food. Citi's Innovation Lab conducted a survey of almost 500 American adults who were using GLP-1s to reduce their weight. Figure 9 shows that, on balance, users said they had increased their consumption of fruit and veg and bottled water, but reduced their consumption of chocolate, cookies, ice cream, sweet snacks and carbonated soft drinks.

See page 62 for a summary of the clinical trials that quantify the reduction in calories consumed by users of the latest generation of GLP-1s

  There is also evidence that GLP-1s help curb addictive behaviors -- whether that is abuse of nicotine, opioids or even compulsive shopping[3]. It is estimated that about 1% of Americans are addicted to gambling. If GLP-1s do become widespread, it is therefore quite possible that the tobacco and gaming industries will also be affected to an extent.

[2] About 22% of the U.S. population is under 18. This calculation assumes none of them take GLP-1s That said, 21% of American 5- to 19-year-olds are also obese.
[3] NIH, 28 Aug 2022; NIH,16 Jul 2013

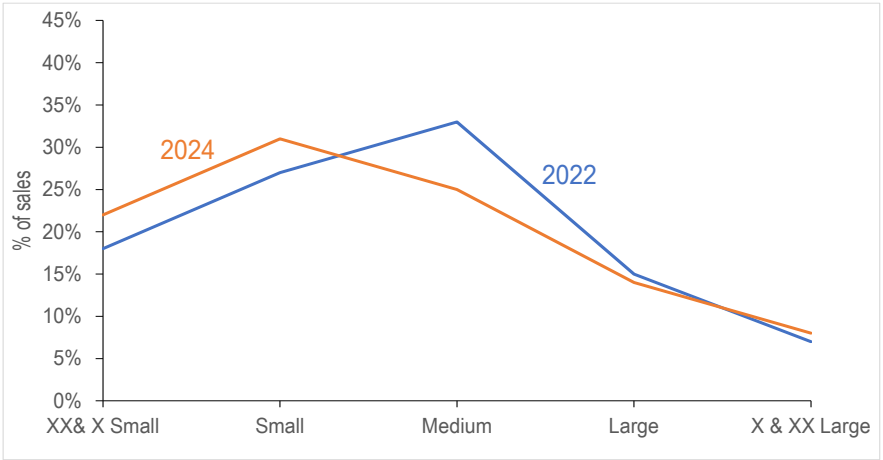
Figure 9. Change in Consumption Reported by GLP-1 users



N=499. Survey in November 2023. CSDs: Carbonated Soft Drinks
Source: Citi Innovation Lab

- **Clothing retail:** Overall we expect GLP-1s to increase demand. As individuals become happier with their bodies, we believe they are more likely to buy more clothes. Some high-end fashion retailers simply do not make XL sizes. However, retailers will have to adapt their ranges to smaller size. GLP-1s are already changing the average size of women's clothing bought in Manhattan. "Getting this right – or wrong – likely will be the difference between profit and loss for many companies," Prashant Agrawal, CEO of Impact Analytics, told us.

Figure 10. Sizing Curve for Women's Fashion, Madison Avenue, 2022 vs 2024YTD



Product: Women's button front long-sleeve shirts
Source: Impact Analytics

What do we mean by "overweight" and "obese"?

Throughout this report we use the standard medical definitions for terms like "healthy weight", "overweight" and "obese". These are based on the Body-Mass Index, or BMI.

$$BMI = \frac{Weight\ in\ kg}{(Height\ in\ meters)^2}$$

The cut offs for the various terms are shown Figure 11-- in simple terms, an adult is "overweight" if their BMI is above 25, and obese if it's above 30. [4]

Figure 12 translates BMIs and the various cutoffs into terms which may be easier to understand, using both the metric system and traditional U.S. measures. It illustrated the relevant weight ranges for someone of 1.75m or 5 ft 9 (which is the height of the average American man) and 1.63m or 5 ft 4 (which is the height of the average American women). It shows that if someone is 1.63m/ 5 ft 4, they would be classified as overweight if they weighed more than 66kg/ 146 lbs, and obese if they weighed more than 79kg /175 lbs.

No-one we have spoken to believes BMI is a perfect measure of obesity, but the ease of calculation does mean it's useful for population-level analysis.

"Overweight" and "obesity" are defined by BMI.

We believe the calculation is somewhat simplistic but nonetheless useful.

Figure 11. Definition of under-, healthy, and over-weight, and obesity for adults by BMI used by CDC

	BMI
Underweight	<18.5
Healthy weight	18.5-25
Overweight	25+
Obese	30+
Severely Obese	40+

Note: We use these definitions in this report unless otherwise noted

Source: CDC

Figure 12. Weight categories for individuals of 1.75m (=5 ft 9) and 1.63m (=5 ft 4)

	Weight Category			
Height	**Healthy**	**Overweight**	**Obese**	**Severely Obese**
Meters	**Kilograms**			
1.75m	57-77 kg	77+ kg	92+ kg	123+ kg
1.63m	49-69 kg	66+ kg	79+ kg	106+ kg
U.S.	**Pounds**			
5 ft 9	125-169 lbs	169+ lbs	203+ lbs	271+ lbs
5 ft 4	108-146 lbs	146+ lbs	175+ lbs	233+ lbs

Source: Citi GPS

[4] A cut-off of 30 was chosen for "obesity" in adults because it seemed to correlate with a significant increase in the risk of certain diseases --- at least for people with European ancestry. Recent research shows, however, the risk of developing type 2 diabetes for a given BMI might be significantly higher for people with other backgrounds. Evidence for this came from an analysis of about 1.5 million people living in England. This found that for the equivalent risk of developing diabetes in White people with a BMI of 30, the BMI cut-off for people with Indian ancestry is a BMI 24, with Chinese or Arab ancestry it's 27, and with Black ancestry it's 28. (Source: Lancet Diabetes & Endocrinology May 2021: *Ethnicity-specific BMI cutoffs for obesity based on type 2 diabetes risk.)*

The problem of obesity

More and more people have become increasingly overweight in the last few decades. About 43% of all adults are now overweight globally, including 16% who are obese. By contrast only 7% of the world population is underweight. [5]

Childhood obesity is also increasing rapidly: 27% of all children aged 5-19 in Chile are now considered obese, and in the U.S. 21% are.

Obesity causes profound ill-health

Obesity results in fatty deposits throughout the body, which in turn leads to chronic inflammation. Over the years, the body's organs don't function as effectively as they should. Damage to the pancreas, for example, leads to diabetes; damage to the heart leads to cardiovascular disease; and damage to the brain leads to dementia. And even if someone loses weight, the damage isn't repaired. (The liver is the only organ that can regenerate itself.)

Obesity is also linked to many cancers, musculoskeletal problems, depression and obstructive sleep apnea.

The OECD estimates that in the next 30 years, obesity will cause nearly 60% of all diabetes cases, 18% of cardiovascular disease, 11% of dementia and 8% of cancer.[6]

Figure 13. Number of people suffering from main chronic diseases associated with obesity

Condition	Population Affected (Mlns)
Chronic Kidney Disease	700
Type 2 Diabetes	540
Cardiovascular Disease	520
PAD (Peripheral Arterial Disease)	200
Alzheimer's	85
Heart Failure	65
MASH (Fatty Liver Disease)	25

Source: Novo Nordisk CMD, March 2024

In the U.S. specifically, more than 100 million people are obese. Figure 28 on page 41 shows that of these, about 22 million have type 2 diabetes, 12 million have atherosclerotic cardiovascular disease (or ASCVD), and 7 million have late-stage kidney disease.

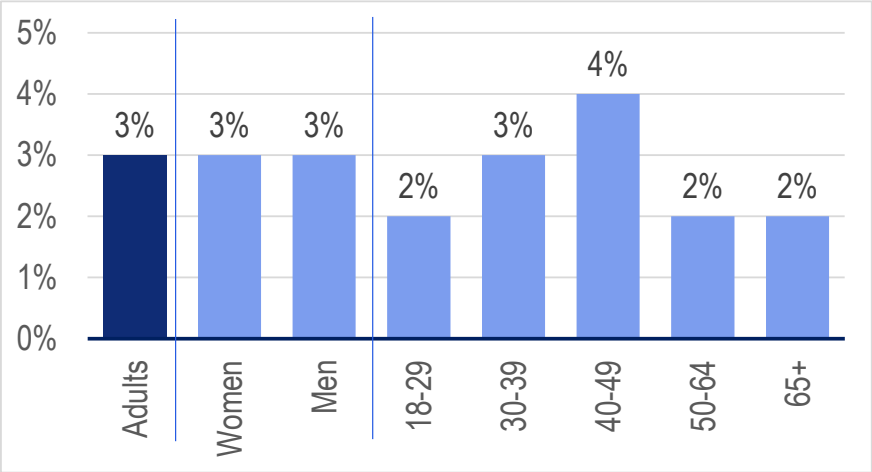
Perhaps it is not surprising that obesity cuts life expectancy: a severely obese 40-year-old can expect to live about 8-9 years less than their healthy-weight contemporaries.[7] For the individuals concerned, it may be more worrying that they can expect to live a higher percentage of their (shortened) lives in ill-health and with limited mobility. On average, obese people suffer 1.6 more years of their life having difficulty with washing and dressing themselves. [8]

[5] See *Worldwide trends in underweight and obesity,* Lancet, Feb 2024
[6] OECD: The Heavy Burden of Obesity.
[7] See: Lancet Diabetes & Endocrinology 2018: Association of BMI and mortality.
[8] J of Gerontology 2021: Impact of Smoking and Obesity on Disability Free Life Expectancy.

What will determine the number of people who benefit from GLP-1s?

This report focuses on the implications of GLP-1s, and those will depend on how many people end up using them, among other factors. Currently, about 3% of Americans are using them for weight loss, according to Gallup.

Figure 14. % of American adults who say they use GLP-1s for weight loss



Data from March 2024. Survey of 5,577 adults
Source: Gallup

The eventual number of users will hinge on many imponderables, including the level of demand (for both medical and life-style reasons); the affordability (which in turn hangs on both pricing and reimbursement policies); and what new products come to the market. However, the factor that is constraining current consumption is manufacturing capacity, so that is where we turn to first.

Capacity

Currently consumption is limited by global manufacturing capacity -- but there are plans to increase this to serve hundreds of millions of people.

Only about 25 million patients are using GLP-1s currently. There isn't manufacturing capacity to make more, and hence there have been widespread shortages.

Both of the leading manufacturers – Novo Nordisk and Eli Lilly -- have committed many billions of dollars to expand capacity. Furthermore, generic versions will enter the market when the drugs lose patent protection. At the end of June, Teva said it was launching a generic version of liraglutide -- a once-a-day injected GLP-1 authorized for diabetes and sold under the brand name Victorza. Semaglutide will lose patent protection in China in 2026, in Europe in 2031, and in the U.S. in 2032.

Our central scenario is that the current capacity of the main existing providers will be able to supply over 200 million people. However, it is quite possible that they accelerate their plans, or that they fail to meet their current targets. We also expect plenty of other companies to start making GLP-1s, both new products and generics, as we explain on page 19. Therefore, our central scenario is that in 10 years, global capacity for GLP-1s will be for many hundreds of millions.

Demand for lifestyle usage

The "lifestyle" motivations for taking GLP-1s are extremely strong, at least currently.

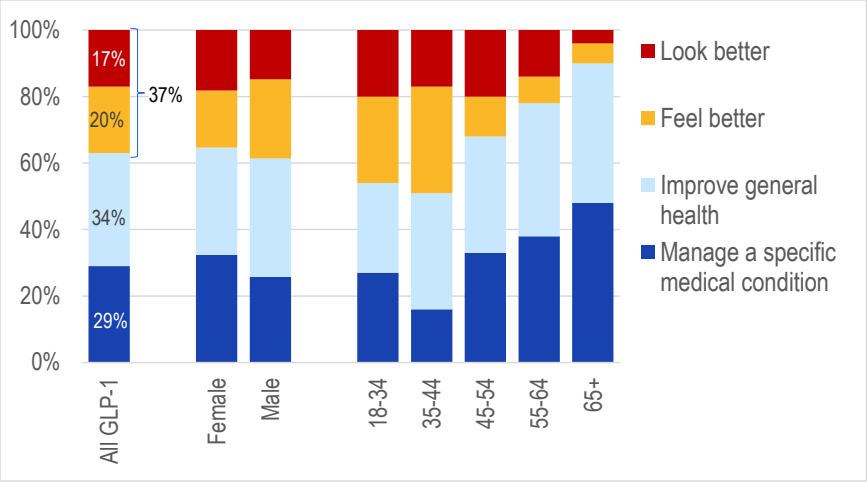
But we believe it is hard to predict how this will evolve over 5-10 years.

The GLP-1 class of drugs is unique because there is a continuum of strong motivations for taking them, from treating a specific medical condition (e.g. type-2 diabetes with obesity); through trying to become healthy; to simply trying to look thinner.

It appears that more Americans currently take GLP-1s to look or feel good than to treat specific obesity-related medical conditions. Citi's Innovation Lab surveyed about 500 Americans using GLP-1s to reduce their weight about their main motivations. Figure 15 shows that more are doing so because they believe the drugs will help them look good or feel healthy, than to treat a specific medical condition.

More Americans are currently taking GLP-1s for lifestyle reasons than to manage a specific weight-related medical condition.

Figure 15. Main motivations for taking GLP-1s



n=499. Universe = American adults using GLP-1s to reduce their weight. Survey conducted November 2023
Source: Citi GPS

Will the demand for "lifestyle" usage remain strong in five or ten years? It is certainly possible to argue that it won't be, because many consumer habits swing into, and then out of, fashion. In the future, people may focus more on GLP-1s' side effects such as reduced muscle mass.

But there are also good reasons to believe demand for lifestyle purposes will continue to grow. The desire to look attractive is fundamentally embedded in humans, and it's hard to imagine that being a healthy weight will go out of fashion. Furthermore some of the next generation of GLP-1s are designed to substantially reduce the side effects.

Our base assumption is that "lifestyle" demand will continue to grow, as the drugs become cheaper and more convenient. We note there is no sign of a slowdown in the growth of Botox, which in some ways is comparable, as it is an FDA approved drug that is used for cosmetic reasons. However we do think there is a great deal of uncertainty here.

Demand for medical purposes

We expect there will be increasing evidence that GLP-1s help with a wide range of very common diseases.

Where we see uncertainty in the outlook for lifestyle usage, we believe there is likely to be more and more demand from medical purposes, because clinical trials are providing more and more evidence that GLP-1s reduce the risk of several important diseases in overweight individuals, including type 2 diabetes, and cardiovascular and kidney diseases -- where millions of people are impacted. Further trials are being conducted around dementia and MASH (or fatty liver disease).

In addition, there is some evidence that GLP-1s may reduce the risk of dementia. A Phase 2 study[9] has indicated that a relatively old GLP-1 (lixisenatide) stops the progression of Parkinson's[10]. Novo is spending something in the order of $50-100 million sponsoring a Phase 3 trial to see if semaglutide delays Alzheimer's. This level of investment suggests optimism towards achieving a favorable outcome.

We believe that over time, the market will become increasingly segmented. We believe some drugs will be aimed mainly at the "medical" market, where the emphasis will be on the evidence of reduction in diseases associated with obesity and payments will be reimbursed from insurance; meanwhile other drugs will be aimed mainly at the self-pay "lifestyle" market, with the emphasis on achieving a target body weight with minimal side effects.

Time on prescription

Another question is how long users keep taking GLP-1s for. To be really effective, they need to be taken indefinitely. According to Novo, users prescribed its GLP-1s for diabetes use them for an average of about 4 years, whereas users of Wegovy – the version of semaglutide prescribed for obesity – have an average time on prescription of 6 months.[11] Novo management argue that when supply improves, the average time on prescription will increase too. "We are confident that over time, the stay time will improve more towards 12 months and beyond," Doug Langa, head of North America, said in the 2Q24 earnings call.

Our central assumption is that persistence *will improve over time, as we expect that many of the factors that are lowering it will ease, including the high price and the poor availability. However the most important driver of better persistence is likely to be new products with reduced side effects or which are more convenient. Many people find it hard to take drugs over the long term, as* Figure 16 *shows. We are hopeful that eventually GLP-1s will do much better than this, because the motivations – for both medical and lifestyle reasons – are so powerful. Unlike with a drug for HIV, GLP-1s users can see in the mirror if their weight is under control.*

---

[9] Phase 2 trials are designed to provide good evidence but aren't regarded as conclusive. They generally involve a small number of hundreds of participants. Phase 3 trials are designed to provide statistically convincing proof. As a result, they are larger -- usually involving thousands of participants -- and are therefore much more expensive.
[10] NEJM, April, 2024: Trial of Lixisenatide in early Parkinson's Diseases.
[11] An analysis of 4,000 commercially insured individuals who were prescribed GLP-1s for weight loss in 2021, and who didn't have diabetes, found only 32% were continuing to take GLP-1s at after 12 months. The 1-year persistence rate was higher for semaglutide (47%) than liraglutide (19%). (See Journal of Managed Care & Specialty Pharmacy May 2024. Real-world persistence to GLP-1s among obese commercially insured adults without diabetes.) Separately, Insulet commissioned an analysis of diabetes patients' insurance claims. It found 55% of T2D patients who initiated GLP-1 therapy discontinued within a year.

Figure 16. % of patients adhering to medications after 12 months	
Diabetes	~50%
HIV	~50%
Asthma	~40%
Psoriasis	~30%
Source: Novo Nordisk	

New products

New products are likely to drive growth as more convenient and more effective products are likely to be approved in the coming years.

Another factor that ought to increase usage of GLP-1s is innovation. Currently more than 100 GLP-1 drugs are being developed,[12] although that certainly does NOT mean that 100 new GLP-1 drugs will come to market. Nonetheless we expect a series of new products, which promise either reduced side effects, or greater convenience, or an increase in the rate of weight-loss.

- **Fewer side effects/ issues**: Some biotechs are working on GLP-1s that have additives to help individuals preserve muscle mass; others have weight loss drugs that they believe will generate fewer gastrointestinal issues -- like nausea, vomiting and diarrhea -- than the current generation.
- **Greater convenience**: Currently GLP-1s require users to inject themselves weekly.[13] It looks likely, however, that solutions will become available in the next 5-10 years that either allow monthly injections or move to pills. Many companies have candidate pill-based GLP-1s in clinical trials, for example Novo and AstraZeneca.
- **Greater power**: Many of the drugs currently being tested promise greater power. For example, a Phase 2 trial implies Novo's CagriSema product is likely to cut people's weight by at least 25% in a year.[14]
- **Stronger impact on co-morbidities:** Some companies appear to be angling their drugs as being particularly effective at tackling certain co-morbidities. For example, Boehringer Ingelheim believes survodutide may be confirmed as the best-in-class treatment for MASH.

Our central case is that a variety of new (and differentiated) products will become available, but most will be priced at a premium. Meanwhile the price on the "old" versions (like Ozempic) will be cut, in a similar fashion to the pricing policy for new iPhones. We think this approach would allow the manufacturers to maximize revenues while ensuring that it would increase the number of users of large populations that benefit from GLP-1 drugs technology.

[12] https://www.statnews.com/2024/02/26/obesity-liver-disease-mash-wegovy-zepbound-drug-tracker/

[13] The current generation of GLP-1s all use large molecules that break down in the stomach, which is why they have to be injected. Furthermore, they are hard to combine with other small-molecule treatments, for example for cardiovascular diseases. It is true that a pill-based version of semaglutide has been approved for diabetes (branded as Rybelsus), but this (1) requires the user to take the pills before they have eaten or drunk anything in the morning, and to wait a further 30 minutes before consuming anything afterwards; and (2) uses a much larger dosage of semaglutide than the injected version.

[14] Lancet Aug 23: Efficacy and safety of co-administered once weekly cagrilintide and semaglutide.

New side effects

GLP-1s have been used for nearly two decades for diabetes so it's unlikely that new, medically-significant side effects will emerge for the existing drugs.

Demand could be dampened substantially if dangerous new side effects emerge. In medical terms we believe this is unlikely for the established drugs, however, because GLP-1s have been used for diabetes for almost two decades.

Life-style usage is newer, and likely to be more fickle. We therefore see more risk. For example, we can imagine a situation that if people cycle on and off these drugs over several years, then the loss of muscle could get worse, as people might lose muscle and fat every time they take GLP-1s, but add only fat when they came off them.

Generics

Generic versions of semaglutide will become available in China in 2026, in Europe and the U.S. in 2031-32 -- so in less than a decade the prices of the Ozempic/ Wegovy are likely to drop very substantially.

Typically, the price of drugs falls by 70-90% when patents expire and generics enter the market. This will occur first with semaglutide -- which goes off patent in China in 2026, in Japan and Europe in 2031 and in the U.S. in 2032.

Dr Reddy's is one of largest manufacturers of generics, and the company's CEO, Erez Israeli, has made his intentions clear: "We want to market this product on time in all the markets as the patent expires." We therefore expect widespread availability of much cheaper versions of semaglutide to become available, starting in China in about two years, and reaching America in eight years.

Pricing

We expect the price of GLP-1s to fall, but it's hard to know how much.

Another important -- and hard to predict -- variable is the price of these drugs, and how that might change over time. Currently GLP-1s are expensive for users. However, we believe the level the drug suppliers have set them at reflects the (currently) limited manufacturing capacity as much as anything else. Over time, prices of (some) GLP-1s are likely to fall, but no-one knows by how much.

In the U.S., the list price for Wegovy is about $16,000/ year and for Zepbound is about $13,000/ year. The complicated American system of rebates, reimbursement and co-pays for drugs means that few people pay anything like this amount, but still many people struggle to afford them. In previous years, average achieved prices have been falling at about 10-15% a year.

In late August, one company said it would start selling its GLP-1 in vials (as opposed to injector pens) at half price. The offer is currently limited to individuals who do not have insurance and who have on-label prescriptions – in other words who are using it to treat obesity, rather than for lifestyle reasons.

Other countries

In other countries the price appears to be substantially cheaper -- for example in the U.K., the list price for Wegovy is £2,100/ year for the NHS -- but in practice there is little supply.

Retail prices are often quite different from list prices, and they are hard to compare internationally, because the way rebates and insurance works varies by market. However, when KFF did a survey of prices advertised on the web last August -- summarized in Figure 17 -- the differences were striking. Semaglutide retailed for ten times less in the UK, Australia and France than it did in the U.S.

Figure 17. List price of semaglutide by country

	$ cost	Index (US =100)		$ cost	Index (US =100)
U.S.	$936	100	Netherlands	$103	11
Japan	$169	18	UK	$93	10
Canada	$147	16	Australia	$87	9
Germany	$103	11	France	$83	9

Note: Based on web searches, Aug. 15, 2023..
Source: Peterson-KFF

What will happen to pricing?

The question remains, however: *What will happen to pricing in the future?*

It is possible that the price for some GLP-1s will fall enough so that hundreds of millions of people can afford them -- otherwise there would be no point in investing billions of dollars to build all that capacity. If some companies making GLP-1s are aiming mainly at the self-pay market, they are likely to treat GLP-1s as a consumer product, which implies price segmentation to maximize sales.

One reasonably likely scenario is that GLP-1s will follow the model that has become common with mobile phone handsets, whereby new generations are priced at a premium, while the older products (like semaglutide) are priced at increasingly lower levels.

On the other hand, historically pharma companies have set prices in order to maximize dollar-revenue, not maximize the number of people able to access the medicines. It is therefore possible that prices will remain sufficiently high that many people will not be able to access them, at least until generics become available.

We think it is most likely that prices of some GLP-1s will fall considerably from where they are -- even if the newest and most convenient versions remain expensive. We expect some of the least expensive GLP-1s to be targeted at the lifestyle/ self-pay market, because many consumers there will be price sensitive.

Reimbursement

Health plans are increasingly likely to offer reimbursement for prescriptions of GLP-1s to protect against disease.

While the drugs remain expensive, most (potential) users will rely on reimbursement from some sort of health plan. In America, in the commercial sector, 34% of plans provide coverage for GLP-1s for both diabetes and obesity, 57% for diabetes only and 19% for neither.[15] However Medicare (which covers Americans aged over-65) doesn't currently provide reimbursement for drugs prescribed only to reduce weight.

In addition, if the drugs get cheaper, reimbursement for pure weight loss is likely to become more common.

Many health plans are struggling with the immediate cost. One example is the North Carolina health plan, which covers for more than 750,000 state employees. It stopped reimbursing GLP-1s this April. Last year the plan paid more than $100 million for GLP-1s for more than 25,000 individuals, more than it spent on treating cancer.

As we've said, however, there is increasing evidence that GLP-1s provide protection against several important diseases, including cardiovascular and chronic kidney diseases and diabetes. We therefore expect increased reimbursement for this sort of use. Medicare, for example, has already announced that it will cover Wegovy when it is prescribed for heart health.

Furthermore, to the extent that there are significant falls in the price of GLP-1s it will become more attractive for employers and health plans to offer some reimbursement simply to reduce people's weight.

[15] IFEBP June 2024: Employer Coverage of GLP-1 Drugs on the Rise

Scenarios for usage

We predict the most likely scenario for GLP-1 usage is consistent growth resulting in 100-300 million people reducing their weight in the next decade.

In the previous section, we discussed the factors that may drive more or less people to use GLP-1s. Based on them, we offer the following scenarios on a ten-year view.

1. **Low growth**. GLP-1s grow, but only modestly. 50-100 million people reduce weight significantly by 2034.
   - No reduction in prices so most of the incremental capacity goes unused. Current generation of clinical trials/ new products are mostly disappointing. Lifestyle demand fades as GLP-1s become unfashionable.
   - Our assessment: *Unlikely*
2. **Consistent growth.** 100-300 million people reduce weight significantly by 2034, implying meaningful change in trend lines in obesity in the developed world.
   - Doesn't necessarily imply hundreds of millions using GLP-1s at any one time.
   - Assumes capacity increases at the incumbents as planned, plus new, as yet unannounced capacity from new entrants and widespread use of generics. This scenario requires effective prices fall for semaglutide and similar products as better GLP-1s get approved, and more reimbursement as prices fall.
   - *We think this is the most likely scenario.*
3. **Widespread usage.** More than 300 million people benefit from GLP-1s, with obesity starting to fall in many countries.
   - The planned capacity increases get built on time, and further expansion is launched. The clinical trials of the NextGen products live up to expectations. In particular, pill-based GLPs become widely available, increasing both demand and making manufacturing easier. Prices for at least some products drop significantly, reflecting more intense competition. Widespread reimbursement, at least for cheaper GLP-1s.
   - *This scenario assumes everything goes well for GLP-1s.*

Citi Investment Management view of GLP-1s

Diane Wehner, CFA
Senior Portfolio Manager, Healthcare
Citi Global Wealth

Nathan Weinstein, CFA
Global Healthcare Analyst
Citi Global Wealth

How big is the opportunity for obesity?

It's difficult to overstate the enormity of the problem of obesity, which has been referred to as an epidemic. For example, in data furnished by Novo Nordisk, the number of people living with diabetes, globally, was pegged at 537 million, whereas the number with obesity was a staggering 813 million.

The obesity opportunity should not be viewed in isolation. For example, there is material overlap between obesity, type two diabetes, atherosclerotic cardiovascular disease, and heart failure, among others. As a result, alleviating obesity with GLP-1s can have positive implications for patients, leading to better outcomes in challenging disease categories and comorbidities, particularly those involving the cardiovascular system.

To what extent is the GLP-1 story about diabetes vs obesity?

GLP-1s were initially developed for the treatment of type 2 diabetes. According to Novo, only 15% of the world population of diabetics are achieving good control of their disease. While that seems low, it actually represents significantly greater penetration of therapeutic interventions than in obesity -- just 2% of obese people are treated medically.[16] Our view is that breakthroughs with the GLP-1 agents are creating a de novo anti-obesity medication (AOM) class that is in the early-stages of a multi-year uptake cycle. This is likely to have positive ramifications in terms of the participating companies' revenue growth rates.

The two main companies have leveraged their GLP-1 armamentarium in such a way that the same API can serve both segments (diabetes and obesity) albeit under different brand names: *Zepbound* and *Wegovy* for weight loss and *Ozempic* and *Mounjaro* for diabetes, among others. We look to both markets as a source of growth, with the obesity market to serve as an important driver of differentiated growth during the next chapter of the GLP-1 story.

What is limiting volumes at the moment? How is this likely to change?

This is an insightful question given the relevance of volume limitations in the GLP-1 market. Based on the enormity of the unmet medical need, we've endeavoured to focus on the key hurdles to ungate future GLP-1 script (Rx) growth. On this basis, two recurring themes viewed as obstacles to volume growth are: (1) production capacity and (2) access.

In terms of the former, both the main companies have been investing billions of dollars into expanding their manufacturing capacity -- expanding existing production facilities, building new facilities, and acquiring companies to take ownership of their manufacturing footprint. Novo Nordisk, for example, announced the acquisition of a contract development and manufacturing organization for $11bn in February.

[16] Source: Novo Nordisk

In part, the extent of the manufacturing investment is due to diabetes and obesity being mass market indications involving hundreds of millions of people globally, which means they exist at a different scale than most other medical categories. Another important driver of the high capex costs is that injectable GLP-1s involve multiple simultaneous processes such as peptide production, injector device manufacture, and fill/finish, all of which need to be done to the satisfaction of regulators' exacting standards. Further, time is of the essence when it comes to scaling, as biopharmaceutical companies have only a limited period of intellectual property (IP) exclusivity in which to earn a return on investment on approved drugs.

As of August 19, 2024, a search of the FDA drug shortages database indicates that semaglutide is currently in shortage, with availability limited for the lowest dosage strength (0.25mg/.5ml) of Wegovy. Likewise, tirzepatide shows as being in a shortage, currently, although no specific dose level is indicated. The manufacturers, to their credit, have tried to protect the availability of the higher dose levels of their GLP-1s, to ensure access for patients with greater medical need.[17]

As the ongoing manufacturing investment results in expanded capacity, it is likely to increase availability and help grow Rx. Future oral GLP-1 drugs could further alleviate pressure on the supply chain.

Can new entrants challenge the duopoly?

Over the next ~3-5 years, we do not expect the GLP-1 duopoly to be materially disrupted. Longer-term, given the enormity of the opportunity, it's reasonable to assume that additional competitors will enter the market. Companies that wish to challenge the existing duopoly will have to not only develop a promising drug (or series of drugs) but solve for production at scale. While other large pharmaceutical companies may have existing production capacity which could be retooled for GLP-1s, small biotechnology companies with one or two promising agents but no meaningful capex budget may find their best path-to-market is via being acquired.

What about other key stakeholders?

We're currently witnessing the formative years of the GLP-1 obesity treatment market, and as such it's hard not to wonder whether alignment between key stakeholders (patients, providers, payors, and drug developers) will be realized. Each of these stakeholders has a role to play and a likely desire to partake in the incentives which include improved health outcomes and monetary upside.

Signposts to watch as GLP-1s experience mass uptake include: (1) pricing dynamics, including ASP compression (prices decline as uptake scales to many millions of patients), (2) coverage decisions (and whether they're based on a holistic appreciation for long-term benefits rather than a focus on near-term costs), (3) innovation, with numerous injectable, oral, and API combinations being developed, and 4) a broader issue regarding the role of the pharmaceutical industry in society, and in particular whether the policy landscape will remain conducive to drug development (which is, by its nature, risky, expensive, and time consuming).

[17] FDA Drug Shortages. FDA.
https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm

The science behind GLP-1s

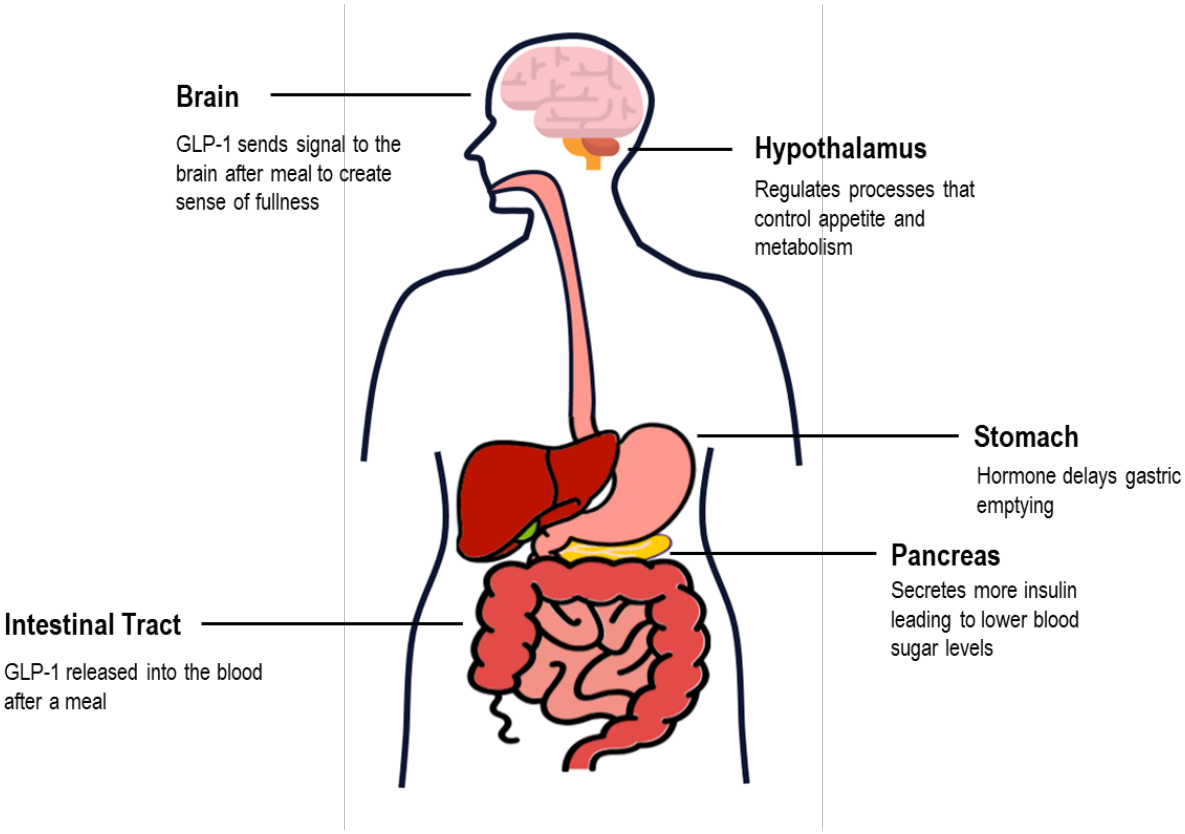
GLP-1s drugs work by reducing the appetite

It is well known that more and more people have become overweight, and that this leads to numerous health issues. The good news, however, is that this new generation of drugs -- the GLP-1s -- can reduce people's weight by 15-25%, and also reduce the risk of many obesity-related diseases.

They mimic the effect of the GLP-1 hormone

When someone digests food, their intestines release several hormones - two of the most important are GLP-1 (which stands for "glucagon-like peptide-1") and GIP (which stands for "glucose-dependent insulinotropic polypeptide"). These are sensed by *receptors* in the brain, stomach and pancreas. When these receptors are triggered in the brain, they generate a sense of fullness and hence reduce the desire to eat; when they are triggered in the stomach, they slow the rate at which the stomach empties; and when they are triggered in the pancreas, they help produce insulin, which controls blood sugar and hence diabetes.

Figure 18. How GLP-1 works



Source: Citi GPS

Semaglutide is a “GLP-1 agonist” which means it activates GLP-1 receptors. Tirzepatide is a “double agonist” because it activates both GLP-1 and GIP receptors.

It’s not possible to use the hormone GLP-1 itself as a drug, because the body naturally breaks it down within a few minutes. Drugs like semaglutide work because they combine a fatty-acid “tail” attached to the GLP-1 “head”. The head binds to, and activates, the GLP-1 receptors. The tail protects the head, because it is tough and sticky, slowing down the rate at which the body breaks it down.

“The way that these GLP-1 agents work is that they help people to eat less. You simply consume less calories when you are on this medicine,“ says Lotte Bjerre Knudsen, Novo’s Chief Scientific Advisor. “It's about 30% [less] with semaglutide.”

They typically reduce weight by 10% to 25%

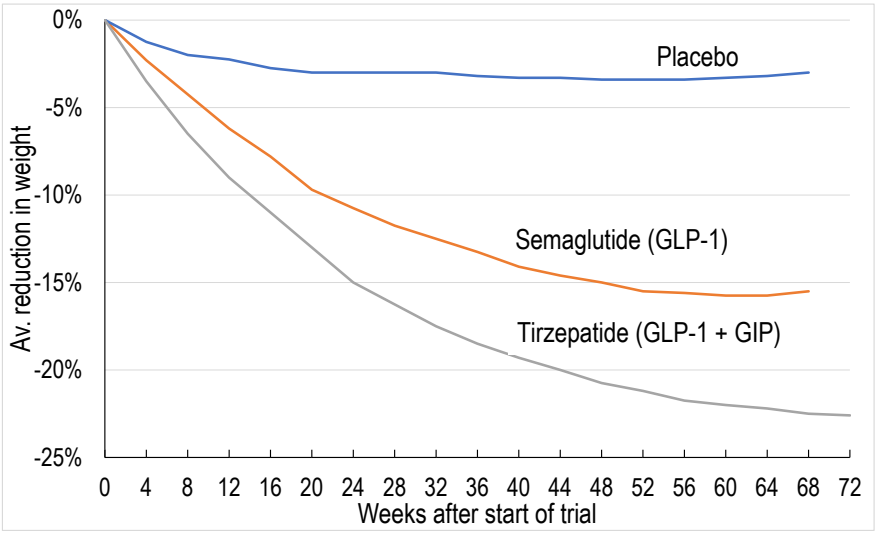
The latest weight-loss drugs are much more effective than previous generations.

Some of the most powerful evidence comes from two trials in which overweight individuals were given either semaglutide (in the Step trials) or tirzepatide (in the Surmount trials), or placebos.

- People using semaglutide once a week, as directed, lost an average of about 17% of their body weight after about 16 months.
- People using tirzepatide lost an average of about 22% of their body weight.
- People using a placebo throughout lost about 3% of their body weight.

Different arms of the same trials showed that diabetics typically lost 5 percentage points less weight than non-diabetics for both drugs.

Figure 19. Average weight loss for people taking either semaglutide or tirzepatide or placebos



This chart combines data from two trials. In both, participants had a starting BMI>30, or >27 with a co-morbidity. Average weight at start = 105 kg / 232 lbs. Excludes diabetics.

Source: NEJM: March 2021 and July 2022

Figure 19 shows the average decline in body weight for people taking high doses of GLP-1s. However some people in the trials took lower doses, and some were much less (or more) responsive than others. In the Surmount 1 trial, of the participants who were on 15mg of tirzepatide, 90% lost at least 15% of their initial body weight, including 40% who lost at least 25%. Another way of looking at the same data is that 10% of participants on this high (15mg) dose lost less than 10% of their initial body weight. Of the participants who were on 5mg tirzepatide, only 50% lost 15% of their body weight.

GLP-1s help with a wide range of chronic diseases

There is growing evidence that GLP-1s help with many obesity-related diseases as well as weight loss. It appears that only part of these benefits are directly due to weight loss – researchers don't yet fully understand the biological method by which these benefits accrue.

In addition to helping drive weight-loss, there is a significant amount of evidence that GLP-1s help with several other important diseases. They were originally approved for **type 2 diabetes** because GLP-1s help stimulate glucose production (as well as reducing the appetite). In addition, there is growing evidence they help with many other obesity-related diseases.

- **Cardiovascular disease:** The Select trial showed impressive evidence that semaglutide improves the outlook for individuals with serious cardiovascular risk.[18]. This was a large trial (about 17,600 people) over a reasonably long period of time (average of 34 months of treatment and 40 months of follow up). The participants receiving the drug had 20% fewer major cardiovascular events, like heart attacks and strokes, than the participants receiving a placebo, and 19% fewer deaths. Figure 21 shows that the gap in death rates steadily increased over time, which implies that if individuals with these risks continue to take semaglutide for more than four years the reduction in fatalities would increase steadily.

GLP-1s have been used to treat diabetes since 2005. It's now known they can also prevent diabetes.

- **Diabetes:** GLP-1s have been approved to treat type 2 diabetes. On top of this, the Surmount trial showed that for adults who are overweight or obese and who have pre-diabetes, those who took a double agonist are more than 90% less likely to develop full-blown diabetes than people using a placebo.

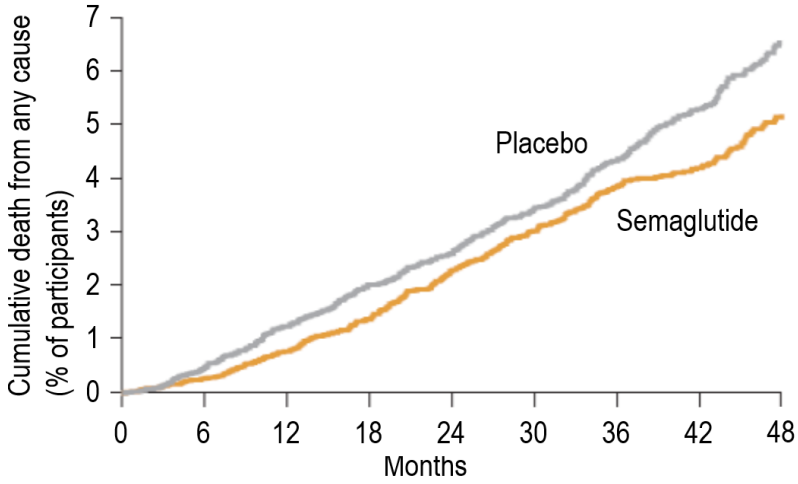
Figure 20. Major Events During the SELECT trial, including deaths and non-fatal CV events like strokes and heart-attacks

	Semaglutide		Placebo		Hazard Ratio
Participants (n)	8803	%	8801		
Death from any cause	375	4.3%	458	5.2%	81%
Death from CV	223	2.5%	262	3.0%	85%
Heart failure[1]	300	3.4%	361	4.1%	82%
Major CV events	873	9.9%	1074	12.2%	80%
~Fatal	223	2.5%	262	3.0%	85%
~Non-fatal heart attack	234	2.7%	322	3.7%	72%
~Non-fatal stroke	154	1.7%	165	1.9%	93%
~Coronary revascularization	473	5.4%	608	6.9%	77%
~Other non-fatal CV events	262	3.0%	325	3.7%	81%

Source: NEJM: Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes, Nov 2023

[18] NEJM Nov 23: Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

Figure 21. Percent of participants dying during SELECT - semaglutide arm vs placebo arm



Source: NEJM: Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes, Nov 2023

- **Chronic kidney disease**: The Flow trial shows that semaglutide also helps with CKD.[19] Flow had 3,500 participants, who had CKD and type 2 diabetes (but were not necessarily overweight). The trial showed that semaglutide slowed down the deterioration in kidney function and reduced the overall death rate by about 20%.

- **MASH/ fatty liver disease:** In a Phase 2 trial, survodutide (which is being developed by Boehringer Ingelheim) demonstrated strong results against MASH. After 48 weeks, up to 83% of people receiving the drug achieved a significant improvement (depending on the dose), vs 18% of people on the placebo.

Early evidence suggests GLP-1s can also help prevent dementia getting worse.

- **Parkinson's:** Lixisenatide is an old GLP-1, approved only for diabetes. However, in a recent Phase 2 study, it stopped the progression of Parkinson's in early-stage patients.

- **Alzheimer's and Dementia:** There is also evidence that GLP-1s can also help with dementia. For example, a retrospective study[20] of 130,000 diabetes patients published in July found that semaglutide was associated with a lower risk of the cognitive issues (such as memory loss) that are often an early sign of dementia. Novo is spending something in the order of $100 million sponsoring two Phase 3 trials to see if semaglutide delays Alzheimer's.

[19] NEJM June 24: Effects of Semaglutide on CKD in Patients with Type 2 Diabetes
[20] Retrospective studies work by studying health records after the event; they are considered much less robust than prospective, randomized controlled trials.

GLP-1s and cancer

There is evidence that GLP-1s reduce the risk of developing obesity-related cancers.

There is also early evidence that GLP-1s do reduce the number of people getting cancer, according to a 10-year *retrospective* study of people with BMIs above 35, some of whom had bariatric surgery, and some took GLP1s.[21] Those with bariatric surgery saw greater weight loss in the first 2 years, but those on GLP-1s had a lower risk of cancer and lower overall risk of death.

Relative to no intervention:

- People who had been given GLP-1s had a 39% lower risk of one of 13 obesity-related cancers and 50% lower risk of all-cause mortality over the 10-year period. (n≈3,200)
- For people who had had bariatric surgery, the risk of cancer was only 22% lower than people who had had no treatment. (n≈11,100)
- People on GLP1s had a 14% lower risk of all-cause mortality than those with bariatric surgery, even though the people who took GLP-1s had lower weight loss.

GLP-1s may also reduce addiction

There is some evidence that GLP-1s may inhibit addictive or compulsive behavior.

On top of the evidence that GLP-1s reduce people's weight and slow the progression of many chronic diseases, there is evidence that they may reduce addictive or compulsive behavior, whether that be abusing alcohol, nicotine, illegal narcotics, gambling, or even biting one's nails.

It appears that GLP-1 and GIP can affect dopamine secretion in the so-called "pleasure" or "reward" center of the brain, inhibiting addictive behaviors.

Alcohol

Probably the best evidence around the impact of GLP-1s on addictions concerns alcohol:

- Studies in rodents and monkeys show that GLP-1 can reduce alcohol drinking, in some cases by as much as 50%.[22]
- A study based on about 68,000 Reddit posts from (human) GLP-1 users found 71% of people who said they drank alcohol had reduced cravings. A sample of individuals (n=158) reported reduced drinking and binge drinking.[23]

The Citi Innovation Lab survey of GLP-1s users showed about 40% were drinking less.

[21] J. of Clinical Oncology May 2024. Comparative risk of cancer risk in GLP-1s vs bariatric surgery.
[22] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6428196
[23] Nature, 28 Nov 2023

"There's really been a large number of clinical and anecdotal reports coming in suggesting that people's drinking behaviors are changing and, in some instances, pretty substantially while taking semaglutide," according to Prof. Christian Hendershot, an addiction researcher at the University of North Carolina.[24] “These reports, for the most part, are anecdotal . . . at the same time, it does seem like there's a pretty strong signal here."

Nicotine

There’s evidence GLP-1s also help with control of smoking. For example, a large retrospective study published in late July analysed the health records of more than 220,000 American smokers with type 2 diabetes. Those who used semaglutide to treat their diabetes where 32% less likely to need medical attention for smoking, relative to other smokers who used insulin.[25] The findings were consistent for regardless of BMI and occurred within 30 days of taking semaglutide. The authors said report that the "The fact that semaglutide (and other GLP-1 receptor agonists) leads to weight loss becomes particularly relevant because smoking cessation is associated with weight gain, which contributes to relapse, particularly in women."

[24] https://www.npr.org/sections/health-shots/2023/08/28/1194526119/ozempic-wegovy-drinking-alcohol-cravings-semaglutide.

[25] Annals of Internal Med, Jul 24: Association of semaglutide with tobacco use disorder.

The side effects are mostly tolerable, if unpleasant

The most common side effects of GLP-1s are gastro-intestinal problems and muscle loss – which are generally tolerable.

All drugs have side effects, and the GLP-1s are no exception. The most common ones are gastro-intestinal problems, for example diarrhea. In addition, the drugs cause the loss of lean muscle mass, which is particularly concerning for the elderly.

Figure 22 shows the proportion of people on one of the main GLP-1s trials suffering from various side effects, and Figure 23 does the same for the main double agonist trial. They show:

- Many more individuals on the GLP-1s had gastro-intestinal problems, for example nausea, diarrhea and vomiting, relative to those people on the placebo;
- There was little substantive difference for other types of side effects -- for example around psychotic issues.

Overall, 7% of participants who were receiving these drugs pulled out of the trial because of the side effects, vs. 3% for the placebos. As we say, the side effects are often unpleasant, but they are tolerable.

Figure 22. Proportion of Step1 participants suffering from various side effects

	Semaglutide (GLP-1)	Placebo
Gastrointestinal	74%	48%
Nausea	*44%*	*17%*
Diarrhea	*32%*	*16%*
Vomiting	*25%*	*7%*
Constipation	*23%*	*10%*
Dyspepsia	*10%*	*4%*
Abdominal pain	*10%*	*6%*
Psychotic Disorders	10%	13%
Cardiovascular Disorders	8%	11%
Nasopharyngitis	22%	20%
Headache	15%	12%
Respiratory infections	9%	12%
Any adverse event	89%	86%
Serious adverse event	10%	6%
Adverse event leading to discontinuation	7%	3%

Source: NEJM: March 2021

Figure 23. Proportion of Surmount1 participants suffering from various side effects

	Tirzepatide (GLP-1 + GIP)	Placebo
Gastrointestinal		
Nausea	32%	9%
Diarrhea	22%	7%
Vomiting	11%	2%
Constipation	14%	6%
Dyspepsia	11%	4%
Abdominal pain	5%	3%
Decreased appetite	10%	3%
Eructation	5%	1%
Severe GI Events	3%	1%
Major depression/suicidal ideation	0.3%	0.0%
Cardiovascular Disorders	0.4%	0.8%
Any adverse event	80%	72%
Serious adverse event	6%	7%
Adverse event leading to discontinuation	7%	3%

Source: NEJM: July 2022

But many people do stop taking GLP-1s

Away from clinical trials, many individuals find GLP-1s more burdensome than these numbers imply. Several sources have reported that fewer than half of Americans who start on GLP-1s continue for more than 12 months. For example, an analysis of 4,000 commercially insured individuals who were prescribed GLP-1s for weight loss in 2021, and who didn't have diabetes, found only 32% were continuing to take GLP-1s at after 12 months.[26] The 1-year persistence rate was higher for semaglutide (47%) than liraglutide (19%).

However, Novo has said the average duration of GLP-1 usage for diabetes patients is about 4 years.

[26] Journal of Managed Care & Specialty Pharmacy May 2024. *Real-world persistence to GLP-1 RAs among obese commercially insured adults without diabetes.*

Large pipeline of drugs under development

Expect GLP-1s that are more effective, more convenient or have fewer side effects.

Beyond the existing GLP-1s, like semaglutide, tirzepatide and liraglutide, about 100 other drugs are under development. The companies behind them hope to improve on the current generation, by creating drugs are that more convenient to take (for example by making them pill-based), reduce muscle wastage or nausea, or that are simply more effective.

As we've said, the existing generation of drugs all mimic GLP-1 and one mimics GIP as well. However, there are several other hormones that play similar roles in the body, and which drugs could potentially harness to encourage weight loss, including amylin, glucagon, peptide YY and GLP-2. Most of the other 100-or-so drugs that are under development target some combination of these as well as (or instead of) GLP-1.

The existing GLP-1 drugs all consist of large molecules, which break down in the stomach, which is why they have to be injected. Furthermore, they are hard to combine with other small-molecule treatments, for example for cardiovascular diseases. And as we've said, they come with important side effects.

There is, therefore, plenty of room for improvement:

- **Greater power**: Some of the drugs currently being tested promise either greater weight or are targeted at certain obesity-related conditions. For example, Novo's CagriSema product looks likely to cut people's weight by at least 25% in a year. Survodutide has shown promising results in treating MASH. Anti-obesity drugs might also be combined with other types of drugs to cut cardiovascular risk, for example statins or PCSK9 inhibitors (which both lower LDL, or "bad", cholesterol in the blood).
- **Less muscle wastage:** Several companies are developing anti-obesity drugs that include elements to promote muscle growth, for example Versanis Bio, CinRx, and Regeneron.
- **Less nausea**: Zealand Pharma is an example of the company working on a drug that mimics amylin to trigger weight loss but with noticeably less nausea than the existing GLP-1s.
- **Greater convenience**: It looks likely that solutions will become available in the next 5-10 years that either allow monthly injections, or (even better) move to a pill-based solution -- at least 27 of the drugs under development are pill-based. One example is danuglipron, a small-molecule, pill-based GLP-1, made by Pfizer.

Amgen has a (large) molecule in phase 2 trials, which is interesting because (1) it requires monthly injections only, and (2) management hopes that users will continue to have a lower weight even after the treatment ends.

A small number of these drugs may obtain approval in late 2025, for example CagriSema, assuming their Phase 3 clinical trial data fulfills the early promise. However it will be several years before others come to the market, and many are likely to fail in their trials. We don't believe there will be 100 anti-obesity drugs on the market, all getting reimbursed.

We do, however, think it is reasonable to look forward to a time when many more GLP-1s are available from more companies, providing greater competition and more capacity. This will allow prescribers and users to tailor their treatment, depending on their individual situation, goals, and tolerance.

Non-medical usage

The lifestyle motivations for taking GLP-1s are just as strong as the medical ones

Many people are interested in using GLP-1s to improve their physical appearance. About 40% of Americans are unhappy with their body weight.

The previous section of this report showed that GLP-1s reduce people's weight significantly and also seem to help with a wide range of chronic diseases. But we think this analysis is half the story, because GLP-1s are at least as much about things like well-being and looking good as they are about specific medical issues.

Figure 24. The continuum of motivations for taking GLP-1s

Source: Citi GPS

The "lifestyle" motivations to lose weight can be extremely strong

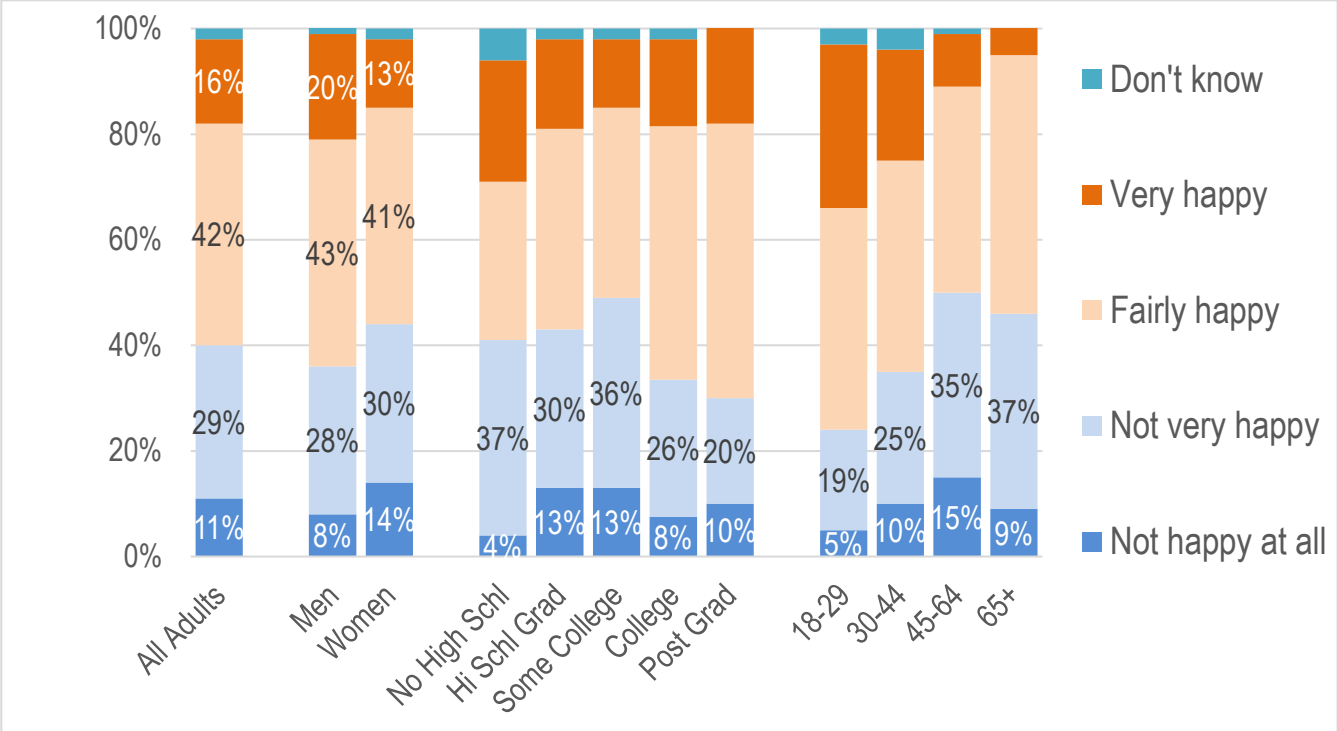
One of the most fundamental drivers of behavior is the desire to look attractive. Global sales for personal care and beauty products easily exceed $600 billion, and sales for apparel top $1.5 trillion. The global market for medical aesthetic procedures is about $200 billion, according to Frost and Sullivan, and is growing at about 11% annually.

About 40% of Americans are unhappy with their weight and body image, according to YouGov. The number is slightly higher for women than men and for the middle-aged, as Figure 25 shows. Last year 45% of Americans said they would be interested in taking safe and effective weight loss drugs.[27]

[27] KFF Health Tracking Poll, July 2023.

Figure 25. Happiness with body weight, and image American adults

In general, how happy, if at all, would you say you are regarding your own weight and body image?



n=1,016. Feb 2024

Source: Citi GPS

Citi survey shows lifestyle motivations are as important as traditional medical ones

In a survey, more people were taking GLP-1s to look or feel good than for strictly medical reasons.

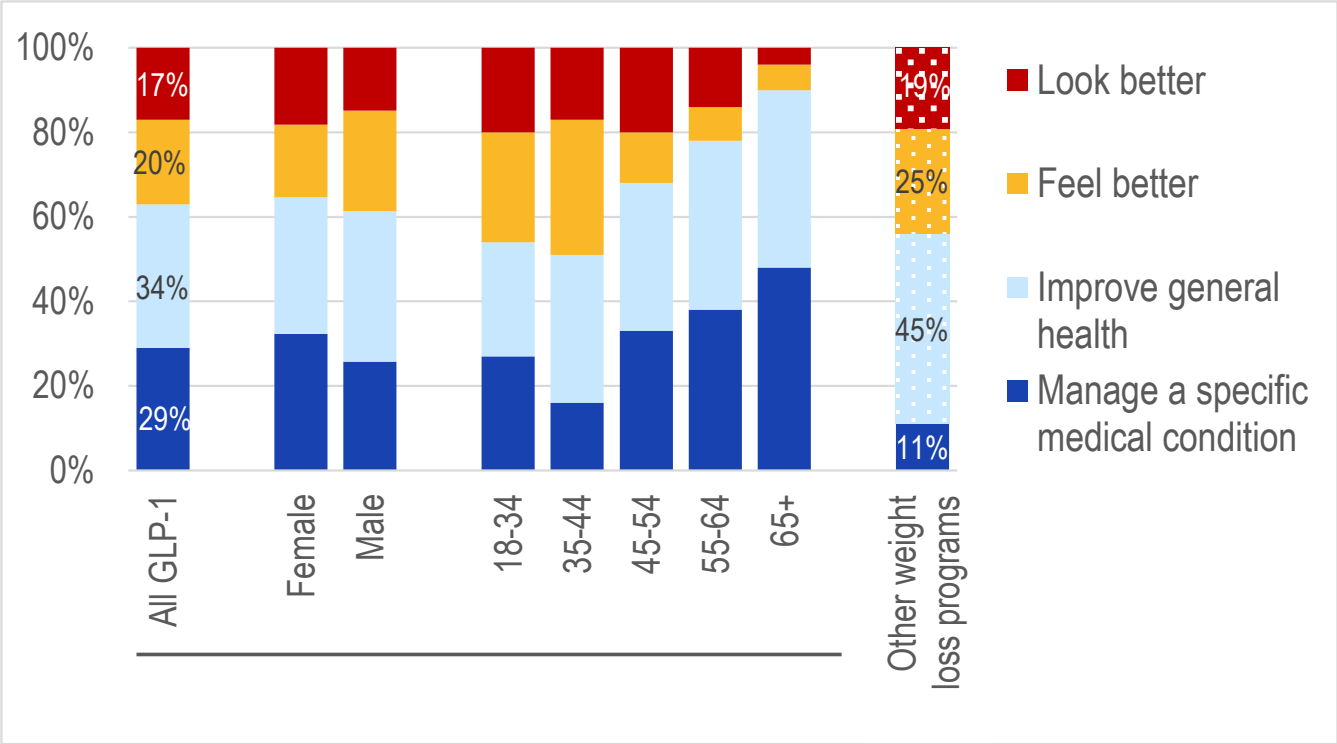
The point that lifestyle motivations for taking GLP-1s to lose weight are at least as important as medical ones, was encapsulated by Jimmy Kimmel at the Oscars ceremony last year when he joked: "Everybody looks so great. When I look around this room, I can't help but wonder 'Is Ozempic right for me?'"[28]

This argument is backed up by a survey of 1,000 Americans, conducted by the Citi Innovation Lab in November last year. Half of the participants were using GLP-1s to lose weight, and half were using other methods, for example special diet plans. One of the questions was around the main motivations for using the GLP-1s (or other weight-loss methods); Figure 26 shows the results.

For the GLP-1 users, 29% of respondents said they were taking the GLP-1s for a specific medical condition, 34% said they wanted to improve their overall health, but more (37%) said they were doing so to feel or look better -- with younger Americans more likely to do so.

[28] https://www.youtube.com/watch?v=GoM-64EkchU

Figure 26. Main motivations for taking GLP-1s



n=1,000. Universe = American adults who wish to lose weight, either with GLP-1s or other methods
Source: Citi Innovation Lab

Impact on the medical industry

Much of the damage from obesity evolves slowly but irreversibly

To understand how GLP-1s are likely to affect the medical industry, it is necessary to understand how obesity is linked to disease.

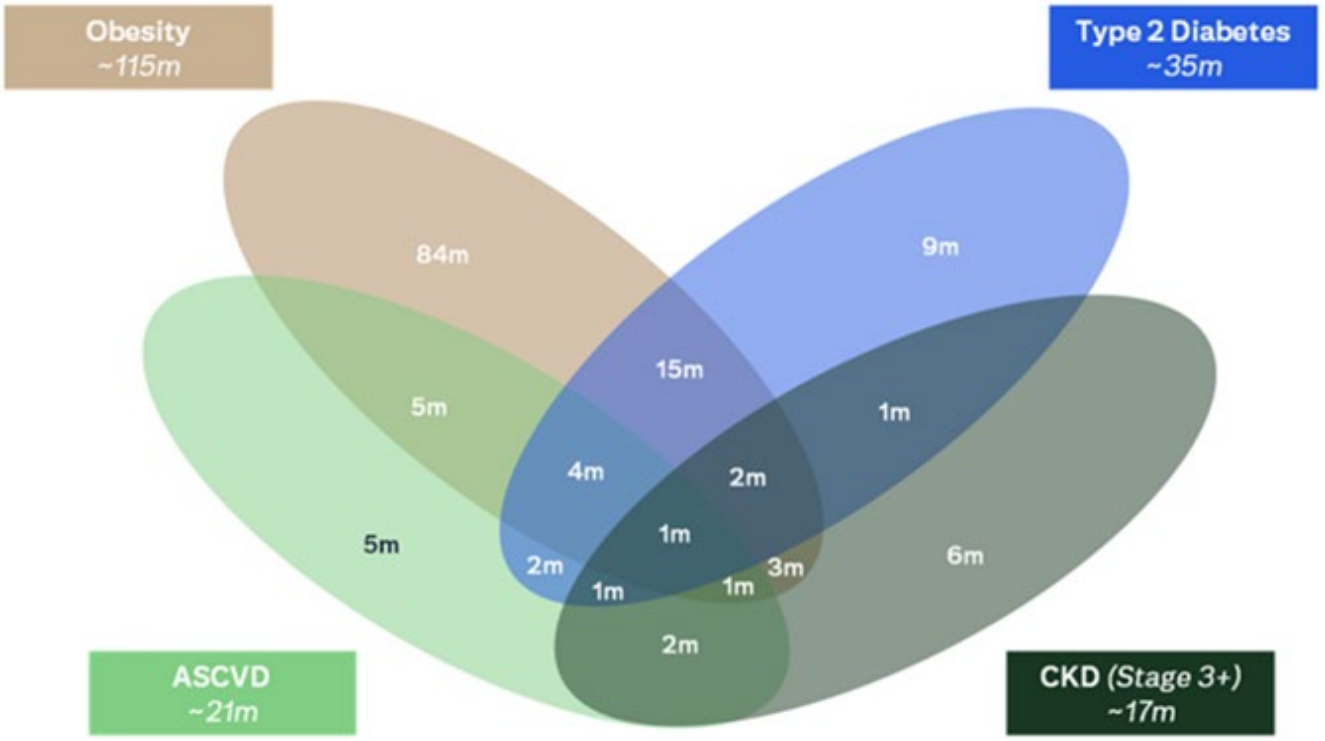
Obesity isn't a disease in itself: no-ones dies of obesity. However there are a large number of obesity-related diseases, for example type 2 diabetes, chronic kidney disease and fatty liver disease. These develop through the *slow* build-up of what is *usually irreversible* damage to various systems in the body. With type 2 diabetes, the body becomes progressively less able to regulate blood sugar properly; with kidney disease the body becomes progressively less able to filter the blood.

Figure 27. Number of people suffering from main chronic diseases associated with obesity

Condition	Population Affected (Mlns)
Chronic Kidney Disease	700
Type 2 Diabetes	540
Cardiovascular Disease	520
PAD (Peripheral Arterial Disease)	200
Alzheimer's	85
Heart Failure	65
MASH (Fatty Liver Disease)	25

Source: Novo Nordisk CMD, March 2024

Figure 28. Overlap between obesity, diabetes, cardiovascular disease and late-stage chronic kidney disease within the U.S.



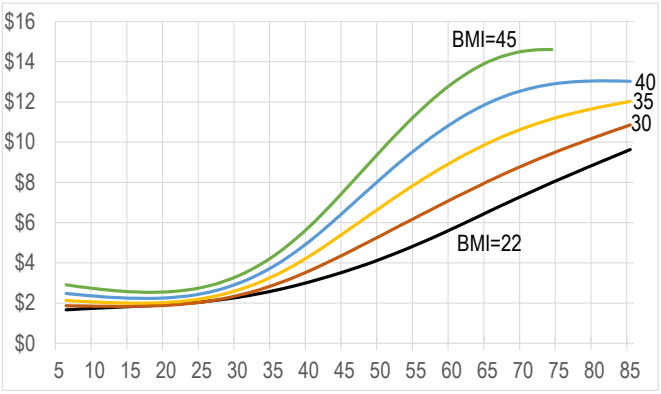
Source: Novo Nordisk CMD, March 2024

We emphasize the word *slow* because it can take several decades for the damage to be done. The damage is *usually irreversible* because no organ in the human body can repair itself, except the liver. As we have highlighted, the Select and Flow trials showed semaglutide is effective in fighting (for example) cardiovascular and chronic kidney disease. However, it doesn't actually cure people -- it slows down the deterioration.

The relationship between age, obesity and medical costs

The point that obesity slowly damages the body becomes clearer once one considers the relationship between age and obesity, and healthcare expenditure. The best data we have seen comes from an analysis of the U.S. Medical Expenditure Panel Survey (or MEPs) and controls for potentially confounding effects in the relationship with BMI. The headline data is summarized in Figure 29 and it shows the unsurprising results that both the cost of healthcare increases with age (after about 30), and that overweight individuals require more healthcare dollars.

Figure 29. Av Annual Healthcare Costs by Age and by BMI ($ in 1,000s

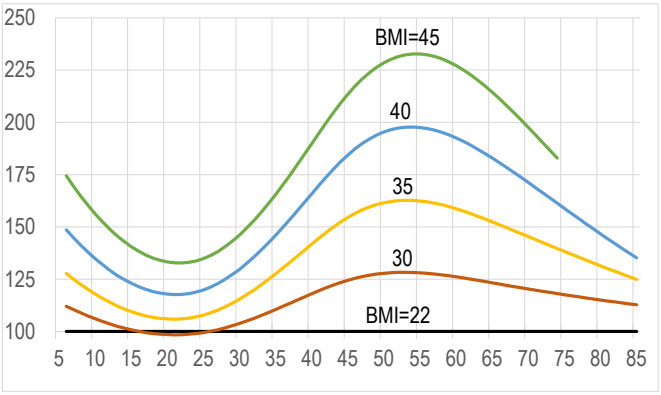


Source: PlosONE: Mar 2021: Association of BMI with healthcare expenditures in the U.S..

- Figure 29 provides detailed averages of healthcare expenditure, by age and by BMI
- Figure 30 show the incremental cost relative to those with BMI=22, in relative and absolute terms
- These charts are based on the medical records of almost 176,000 Americans
- The data comes from 2011-16, so the absolute expense is likely to be materially higher now, but the conclusions are likely to be unchanged
- They do not attempt to show what would happen if someone's BMI dropped, say from 40 to 22.

Figure 30. Relative Healthcare Costs by BMI

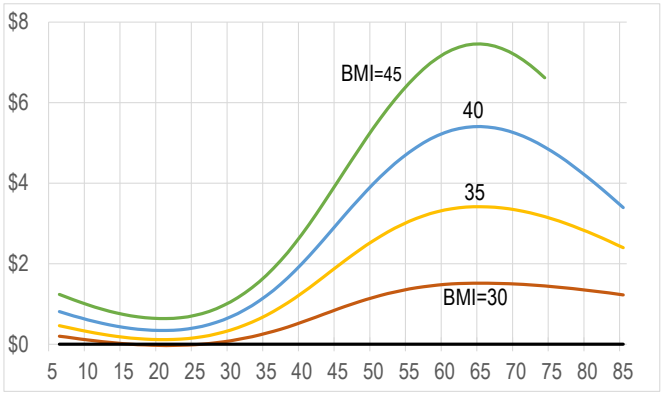
(Rebased. BMI of 22 =100)



Source: PlosONE: Mar 2021: Association of BMI with healthcare expenditures in the U.S..

Figure 31. Incremental Annual Healthcare Costs by BMI

($ in 1,000s relative to average costs for people with BMI=22)



Source: Citi GPS, PlosONE: Mar 2021: Association of BMI with healthcare expenditures in the U.S..

These charts are based on historic data. They don't show what would happen if someone's BMI fell, say from 45 to 30.

We think the bottom two charts -- which show the incremental cost of (long-term) obesity -- are much more interesting.

- For people below the age of about 30-35 the incremental healthcare needs of even severely obese individuals is really quite modest, especially when measured in absolute terms. *This reflects the point that obesity harms the body only very gradually.*
- For people between the ages of 45 and 75, the incremental medical needs of the severely obese are very large. *By middle age the harm created by obesity frequently results in diseases that few healthy-weight individuals face.*
- In old age, obese individuals continue to require more healthcare, but as a percentage of the cost of healthy-weight individuals this is much less pronounced than at age 55. On average, a 55-year-old with a BMI of 40 requires the same medical expenditures as a 85-year-old with a BMI of 22. *In old age, the cell structures of even healthy-weight individuals have deteriorated, so the difference that high BMIs make is reduced.*

The charts do not show what happens if individuals lose weight

It is vital to remember, however, that these charts compare the historic cost of people with different BMIs. *They can't be relied on to show what would happen to healthcare expenditure if someone moved from a BMI of 45, say, to 30 or 22.* There has been no historic research on the medical needs of people who were obese or severely obese, and then dropped to a lower BMI. This rarely happened before GLP-1s were invented.

On the other hand, the clinicals trials we discussed earlier in the report do show what happens when someone takes a GLP-1. Both the Flow trial -- which focused on people with type 2 diabetes and kidney disease -- and the Select trial -- which focused on overweight people with cardiovascular disease -- showed that for people in these categories, taking semaglutide reduced death rates by about 20%. However, there was no sense or expectation that GLP-1s would actually cure these diseases.

There's a critical distinction between those who have developed chronic disease and those who haven't

The two points we have made-- that the problems accrue *slowly*, but that they are *generally irreversible* -- means there is a vital distinction between those obese individuals who have already developed chronic, obesity-related diseases, like type 2 diabetes, and chronic kidney disease, and those who haven't.

- **People who have already developed a chronic disease:** The fact that GLP-1s *slow* the progression of obesity chronic diseases means treatment can be delayed, but it likely to last longer.
- **People who haven't yet developed chronic disease:** The greatest promise of GLP-1s is for people who haven't developed chronic diseases. If GLP-1s mean that people can either shed excess weight before they have become ill, or never become overweight, then the risk of these diseases falls very, very significantly.

What this all means for healthcare companies

Short- to mid-term: demand is likely to increase

In the short- to mid-term (say 1 to 4 years), we believe demand for medical care for people with obesity-related diseases will increase, although there are puts and takes:

Factors that will reduce demand for medical care

- **Patients using GLP-1s are likely to move up the acuity curve more slowly**. For kidney patients, for example, semaglutide may delay the need for dialysis by two or three years, according to Dr Sagar Nigwekar, a professor at Harvard.[29]

Factors that will increase demand for medical care

- **Patients are likely to live longer**, which means both that they are more likely to live long enough that their symptoms reach a stage when intense medical intervention is required, and also are likely to require more cumulative treatment. To continue with the kidney disease example: under the current treatment pathways (which don't include GLP-1s), of the people who reach stage 3 CKD, more than 90% die before they reach stage 5, when dialysis or a kidney transplant is always necessary.
- **Some treatments which were previously ruled out due to excessive weight may become possible**, for example in knee replacement surgery.
- **Obese patients using GLP-1s are more likely to interact with the healthcare system** it seems. ResMed -- the largest company focused on sleep apnea -- says its data shows patients with a GLP-1 prescription are more likely to initiate and continue with therapy.

In the coming pages, we analyze three areas of healthcare in detail – diabetes, kidney care and obstructive sleep apnea, including an interview with a sector-leading CEO. The CEOs of Insulet and ResMed, companies in automated insulin delivery and devices for sleep apnea, both say that GLP-1 are boosting demand.

Long-term: demand may fall

If GLP-1s mean that people can either shed excess weight before they have become ill, then the risk of these diseases falls significantly in the following decades.

On a 5+ year view, there may well be a reduction in spending in some categories. If there are fewer obese individuals, then (with a multi-year lag) we would expect fewer people to suffer from many chronic diseases, including cardiovascular disease, chronic kidney disease, and diabetes. (Obese people are prone to many chronic diseases in middle age -- for example CKD. Figure 31 showed that if someone in their 20s loses weight -- and keeps the weight off --then the greatest savings are likely to occur about 30 years later.) Furthermore, the Surmount showed that for adults who are overweight and have pre-diabetes, those taking a double agonist reduce their risk of full-blown diabetes by more than 90%.

On a multi-decade view, demand may rise again

On a multi-decade view, costs might rise again, as people live longer. A reduction in obesity will both reduce healthcare spend on each individual in middle age, but also increase average longevity, which will tend to increase spending.

[29] See page 54 for a further discussion

Most research on the subject suggests these two effects will roughly balance. One recent academic paper attempted to model the healthcare costs in England, where the obese population to move to BMI below 25 -- and the conclusion was that the two effects would roughly cancel out.[30]

GLP-1s for lifestyle usage vs GLP-1s for medical indications

We have argued that the GLP-1 market may well become increasingly bifurcated. If this does occur in practice, the impact on the rest of the health industry is likely to be counterintuitive. **Medically-focused GLP-1s are likely to increase health spending** because they will prolong the lives of individuals who need expensive therapies. **Lifestyle-focused ones offer the best chance of reducing medical expense** in the long term because they offer the hope of reducing or eliminating obesity in individuals before it causes significant tissue damage.

Case studies

We illustrate these points in the following sections examining how GLP-1s have impacted care in three common obesity-related conditions: (1) type 2 diabetes; (2) chronic kidney disease; and (3) obstructive sleep apnea.

The T2D and CKD are similar in some ways because they both result from irreparable damage to one of the body's main functions, and this usually has been made much worse by obesity over many years. In both cases, GLP-1s help both indirectly (by reducing obesity) and directly. In the case of diabetes, it's because GLP-1s help trigger insulin production in the pancreas; in the case of CKD, it's because GLP-1s slow the deterioration of kidney function, presumably by reducing inflammation in the kidney[31].

Sleep apnea is rather different because it doesn't result from a deterioration in the body's biochemical processes. It is generally triggered by a narrowing of the airway, which in turn is usually related to the buildup of fat. Sleep apnea can be cured by slimming, unlike diabetes and CKD.

In each case, one might expect GLP-1s to reduce demand for services related to these issues. However in each case, the main companies involved say -- rather unexpectedly -- that if anything GLP-1s are increasing demand, at least for now.

[30] Diabetes Obes. Metab. April 2024: Counting the lifetime cost of obesity:
[31] The Flow trial showed this effect kicked in for semaglutide users, regardless of weight loss.

Case Study: Diabetes and GLP-1s

Type 2 is the most common type of diabetes, accounting for about 90% of cases. It's also the type where GLP-1s are highly relevant, partly because it is usually triggered by excess body weight, and partly because GLP-1s can be used to treat it. T2D occurs when the body progressively produces less insulin, or stops responding properly to insulin, or both. T2D is often associated with obesity, a poor diet and physical inactivity. It's usually managed through lifestyle changes, drugs, and insulin therapy.

Diabetes is an increasingly important public health issue: about 415 million people globally have the disease, and the total is increasing with obesity. In the U.S., about 38 million people (=12% of the population) have diabetes, of which 30 million have been diagnosed. A further 98 million adults (=38%) have pre-diabetes, which means their glucose levels are higher than they should be, but not high enough to be classified as diabetic.

Excess weight is the main driver of type 2 diabetes: 90% of people diagnosed with T2D worldwide are overweight or obese. Each 5-point increase in BMI increases the risk of developing T2D by 2.5 times.[32]

If fat builds up in the pancreas, the beta cells can gradually loss the ability to produce insulin. Furthermore, fat appears to release "pro-inflammatory" chemicals that make the body less sensitive to insulin by disrupting insulin-responsive cells.

However other factors can also be important, including age, sex and ancestry. According to research carried out in the UK, people of South Asian heritage are up to 6 times more likely to have T2D than the average of the local population.[33]

How is it treated?

Treatment goals for diabetes typically include achieving and maintaining target blood sugar levels (measured by "HbA1c"[34]) and preventing or delaying further complications (for example cardiovascular or kidney disease). HbA1c is the average blood glucose level for the last 2-3 months. People with a figure above 6.5% are classified as diabetic. People with an HbA1c of 5.7%-6.4% are classified as pre-diabetic.

Beyond life-style changes (in other words losing weight and increasing physical activity) there are several therapeutic approaches:

- The first-line drug is usually metformin. This works by lowering glucose production in the liver and improving insulin sensitivity. It's cheap and well-tolerated.
- Second line drugs include SGLT-2 or DPP-4 inhibitors[35], or GLP-1s, depending on the patient's specific conditions.

In severe cases, people with type 2 diabetes will use insulin, which requires both monitoring glucose levels, and injecting insulin. In rich countries, this is increasingly done with continuous glucose monitors and insulin pumps.

[32] https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(17)30068-3/fulltext
[33] https://www.diabetes.co.uk/south-asian/
[34] HbA1c stands for glycated hemoglobin. It's sometimes shortened to A1c.
[35] SGLT-2: Sodium-glucose transport protein 2. DPP-4: Dipeptidyl peptidase 4.

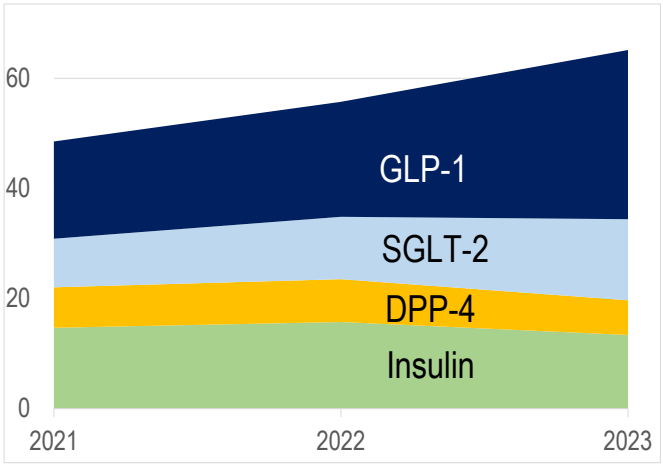
What has the impact of GLP-1s been so far?

GLP-1s have been used for T2D for a long time: the FDA approved the first -- exenatide (which is sold as Byetta) -- back in 2005. However, the class received a lot of extra publicity in June 2020 when Novo Nordisk said that semaglutide resulted in an weight loss of 15% over 68 weeks, implying it was an effective treatment for obesity. There was more publicity in August 2023 when Novo announced that semaglutide also substantially reduces the risk of heart attacks and stroke.

GLP-1s have taken share within the market for diabetes drugs

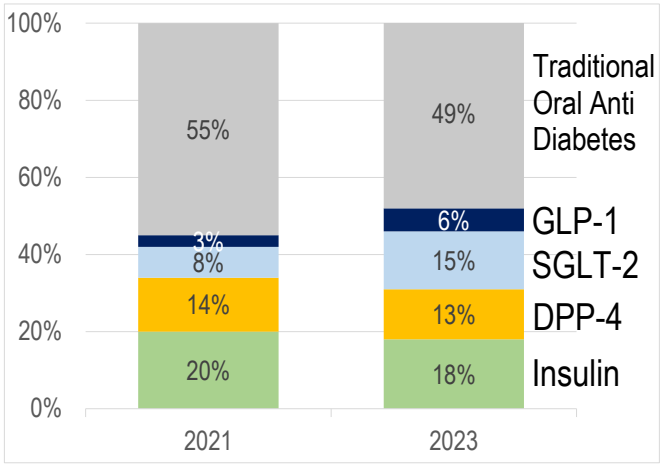
In some senses, GLP-1s are just another (particularly effective) class of drugs for diabetes, which have the side effects of weight loss and protection from heart disease, and where new products have become steadily better over time. They are often used in combination with other drugs, most often SGLT-2s. GLP-1s have also increased adherence.

Figure 32. Anti-diabetes drugs sales ($ in blns)



Global. Branded drugs only.
Source: Citi GPS

Figure 33. Anti-diabetes drugs volume share



Global. Includes generics. Based on prescriptions
Source: Citi GPS

As a result, GLP-1s have steadily been taking share from other drugs, in an expanding market.

GLP-1s have increased demand for MedTech products

Despite GLP-1s' success in treating type 2 diabetes, the most important MedTech companies in the space say that if anything their business has been boosted.

Continuous Glucose Monitors

Abbott and Dexcom are two of the makers of continuous glucose monitors, and both say that even if a diabetic patient is using a GLP-1, they will get a better reduction in HbA1c if they also use a CGM. They say that in addition, demand for CGMs increase when patients switch to GLP-1s.

Clinical results

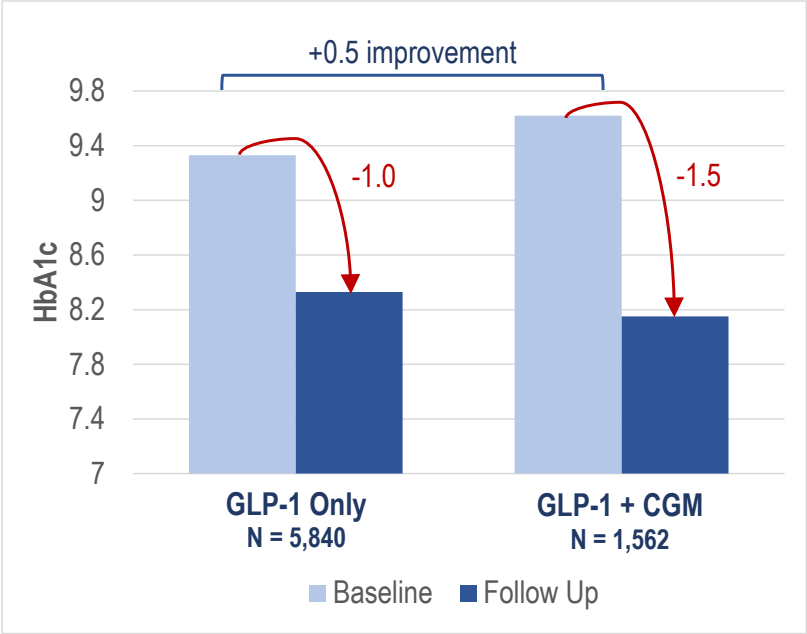
From a clinical perspective, GLP-1s and CGMS are mutually reinforcing.

Abbott says that in the U.S. more than 40% of diabetic patients using its most popular CGM -- the FreeStyle Libre -- also use GLP-1s. We don't think this is particularly surprising given the increasing use of GLP-1s by people with diabetes.

The company emphasises that GLP-1s and CGMs are mutually reinforcing in terms of clinical results. Abbott's research shows:

- People with Type 2 diabetes who use GLP-1s and have an HbA1C ≥8%, and then start using an Abbot FreeStyle Libre CGM, see a significant improvement in their HbA1C after six months, irrespective of GLP-1 duration, GLP-1 type or insulin therapy type. (The average decline was 1.5%.) [36]
- Diabetics had a greater reduction in HbA1c when using GLP-1 and FreeStyle Libre technology together (-2.4%), compared to using GLP-1 alone (-1.7%).

Figure 34. Glycemic control for GLP-1 users with and without CGMs



Source: Dexcom

Dexcom's data -- illustrated in Figure 34 -- also shows better A1c reductions for people with T2D who use GLP-1s and CGM, rather than GLP-1s alone.

Business impact

They are also mutually reinforcing in terms of sales.

From a business perspective it is equally important that GLP-1s usage appears to increase demand for CGMs, and vice versa. According to Abbott's data:

- Diabetics who use GLP-1s wear their CGM on more days per month than people who don't use GLP-1s.
- Diabetics who use a CGM take their GLP-1s more regularly than those who don't use CGMs.

"What we discovered was that people who were using [the FreeStyle Libre continuous glucose monitors] and GLP-1s were using more of both of the products," CEO Robert Ford said in an interview.[37]

[36] https://abbott.mediaroom.com/2024-03-06-Real-World-Data-Show-Abbotts-FreeStyle-Libre-R-Systems-and-GLP-1-Medicines-Work-Better-Together-for-People-with-Type-2-Diabetes

[37] https://www.cnbc.com/video/2023/10/18/we-dont-see-weight-loss-drugs-impacting-medical-devices-sales-says-abbott-ceo-robert-ford.html

Dexcom's CEO, Kevin Sayer, has also said that prescriptions for CGMs increased when patients started using GLP-1s, as these devices provide valuable real-time data that helps in personalizing and adjusting treatment plans. This integration can lead to better glycemic control and more informed decisions regarding lifestyle and medication adjustments.[38]

Insulin pumps

Insulet specializes in insulin pumps, and it too has said that even though GLP-1s help the body produce insulin, the growth of usage has turned out to be beneficial to the company. The CEO, Jim Hollingshead, told us: "We were somewhat surprised but what we see in the claims data is that people who start on a GLP-1 are more likely to also initiate insulin within a 12-month period compared to the group who are not on GLP-1s. It's counter-intuitive, but very clear. And if they stop the GLP-1, they are even more likely to start insulin."

But GLP-1s *are* likely to reduce demand in the long-term

As we have said, GLP-1s appear to have increased demand for diabetes services so far. However, in the long-term it seems unlikely that will continue to be the case. As we have mentioned, the Surmount trial showed that for obese and overweight individuals with prediabetes, those who used tirzepatide were more than 90% less likely to develop full blown diabetes than those using a placebo. We think this is a highly significant finding, given that 75% of American adults are overweight or obese, and 38% have prediabetes.

[38] https://www.dexcom.com/en-us/all-access/clinical-corner/benefits-of-glp-1-drugs

Interview with Insulet

We interviewed Insulet's CEO, Jim Hollingshead, recently. The full interview is here but we have included edited highlights below.

Jim Hollingshead, CEO, Insulet

Insulet develops, manufactures and distributes insulin management systems for diabetic patients. Their award winning OmniPod is a tubeless, waterproof automatic insulin delivery system.

If a diabetes patient is using GLP-1s, how do products like CGMs or insulin pumps help?

Both Abbott and Dexcom have published data that show using CGMs in the context of GLP-1 therapy is beneficial. That's because CGMs allow you to see your blood glucose and how it is progressing over time. When physicians prescribe CGMs in parallel with GLP-1s, it's terrific because they show both patients and physicians the data, so they can manage the condition better.

You can see in the clinical data and in the claims data that a lot of people on GLP-1s do not have well controlled glycemia – so CGMs can really help.

We have just published the results of the largest ever trial for automated insulin delivery in the type 2 space. We're really proud of it, partly because it was representative of the actual insulin market for type 2 in the U.S. The clinical results were fantastic. We had an average A1C reduction of 0.8 in the population of people with A1C of 7 and higher. The worse your baseline A1C, the more improvement you got.

More than half of the sample, 55%, were on a GLP-1. Those patients got the same benefit. So what that says is insulin delivered through Omnipod 5 benefits people with or without a GLP-1.

Don't GLP-1s reduce the number of people using insulin therapy?

Counter-intuitively, it's the over way around. We've just published a big study in conjunction with Optum Health [based on insurance claims] – and we found that people on GLP-1s were more than twice as likely in the next 12 months to also initiate insulin therapy. That finding was really counter to market expectation, but it's clear and robust result in the data. And we also found that if patients discontinued GLP-1 in the first three months, they were even more likely to initiate insulin.

Why do GLP-1s actually increase the use of automated insulin delivery?

I'm speculating here, but I think physicians understand that insulin and GLP-1s are good companion therapies, and when somebody reaches a level where their blood glucose is out of control, they need to escalate down that down. More and more we're seeing GLP-1s and insulin being initiated in roughly the same time period.

In the past, one of the reasons why doctors have avoided prescribing insulin is that people living with type 2 diabetes are usually heavy. They're trying to manage their weight – and insulin therapy usually increases your weight. And so to docs, it's sort of like "I don't want to put you on insulin because I'm telling you to manage your weight, and it's a countervailing effect."

Do GLP-1s bring patients into the healthcare system that might otherwise have avoided it?

There's a lot of shame that people feel with obesity; there's a lot of shame people feel about their diabetes. I don't have any stats for it, but I think it's very plausible that the shame barrier has kept people out of clinic, yes.

People ought not to feel that way. If shame is the barrier to getting appropriate care, then we have to break that down. Type 2 diabetes is biochemical condition; people need therapy; and we want to be a big part of providing that. That's why we're so focused on ease of use and discretion with our wearable disposable patch pumps.

What happens if GLP-1s reduce obesity and hence lower demand for Insulet?

The first thing I would say is that would be a huge benefit to society. Everybody working at Insulet gets out of bed every day to help people with diabetes.

But it's the scale of the issue that makes it really daunting. Globally there's more than 500 million people living with diabetes – and it'll be 1 billion soon. More than 30 million people have been diagnosed with Type 2 diabetes in the U.S., and people think there's about 9 or 10 million who have Type 2 diabetes and don't know it. They haven't been in the clinic so they're undiagnosed. If they slide through that progression and they end up on insulin, it'll be like an avalanche. There's just a pile of snow on the top of the mountain that's slowly sliding downhill.

If there was a silver bullet, it would definitely be better. But none of the current therapies actually repair the pancreas.

How have GLP-1s changed Insulet's strategy?

Actually, we haven't changed our strategy at all. It was surprising to our investors in the fall when we came out and said that GLP-1s are not impacting our business.

I'll point to three things which gave us confidence back in the fall. The first thing is demand for our products are very high. Second, when you look at claims data in the U.S., you see GLP-1s have gone up like a hockey stick but insulin [demand] is flat. Third, when you look at statistics on control and A1C levels across the population over the whole span that GLP-1s have been on the market, the number is just pegged at 14% of people who have an A1C over 9. So GLPs haven't improved the high-end control, and that's the population that will definitely be prescribed insulin.

So we've said GLP-1s haven't impacted us.

Kidney disease and GLP-1s

Chronic Kidney Disease, or CKD, is another area where healthcare professionals think GLP-1s could have an impact, particularly in delaying its progression. Roughly 37 million American adults have CKD, most of whom are unaware they have it.

CKD is the term used when kidneys function less well than they should -- it lumps together about 60 different specific diseases. If left untreated, CKD generally progresses over time, going up the five stages. (Stage 5 – kidney failure -- is also known End Stage Renal Disease, or ESRD.) Unfortunately, there is no cure for CKD -- once a kidney is damaged, it can't be repaired.

Diabetes, high blood pressure, obesity and heart disease are the main risk factors. However excess body weight is also very important: each 5-point increase in BMI results in about a 50% increase in the risk of developing CKD, according to a study of roughly 280,000 participants in the UK Biobank.[39]

However, the vast majority of patients who reach Stage 3 die before they get to Stage 5 -- most frequently from cardiovascular diseases.

What has the impact of GLP-1s been so far?

So far GLP-1s have been relevant for CKD because they reduce obesity, help with obesity and reduce cardiovascular risk. However, the Flow trial showed that semaglutide directly reduces risk in CKD too -- so we believe that (some) GLP-1s will be used directly for CKD patients in future. It is important to note however that semaglutide has NOT yet received approval for treating CKD.

The Flow trial showed GLP-1s can help with CKD

Novo Nordisk's Flow trial[40] is the first dedicated kidney outcome trial for GLP-1s. Just over 3,500 people with type 2 diabetes and CKD were injected with 1mg of semaglutide or a placebo, with a median follow-up of 3.4 years. The study shows patients treated with semaglutide experienced a 24% relative risk reduction in a composite measure of kidney-disease related events. For the participants using semaglutide:

Flow showed semaglutide helps with CKD, well beyond what could be driven by the reduction in body weight.

- The risk of a drop in the eGFR[41] of 50% or more was 27% lower
- The slope of eGFR was less steep, indicating a slower worsening of CKD
- Initiation of kidney replacement therapy (e.g. dialysis or transplant) was lowered by 16%
- All-cause mortality was 20% lower. This was driven by a 29% reduction in the risk of death from cardiovascular causes, which is the main risk; the reduction in the risk of death from kidney causes was only 3%.

In summary, Flow implies that semaglutide will be extremely useful for treating CKD, first because it slows the rate of progression, and second because it reduces the

[39] J of Am Soc Nephrology: 2021 Conventional and Genetic Evidence on the Association between Adiposity and CKD.
[40] NEJM 2024: Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes.
[41] eGFR (estimated glomerular filtration rate) is one of the main measures of kidney function.

risk of death of CKD patients. The Flow trial looked at a fairly high risk group of patients. During the trial, in the placebo group, almost 2.8 times more participants died (16%) than started kidney replacement therapy (6%).

Our colleagues in Citi Equity Research recently hosted a call[42] to analyse the data with Dr. Sagar Nigwekar, who specializes in kidney care at Massachusetts General Hospital and is Assistant Professor of Medicine at the Harvard Medical School. He predicts that when semaglutide is approved for CKD, it will become an important treatment option, but only for certain patients.

Impact on dialysis

We expect that in the next few years, the effects of GLP-1 that increase the usage of dialysis will if anything more than offset the effects that decrease usage.

On the negative side, GLP-1s are likely to delay dialysis. “I would expect the average age of dialysis in the U.S. will go up by 2 or 3 years” for patients using GLP-1s, Dr. Nigwekar said in the Citi call. But he also emphasized the data in Flow that showed patients are likely to live longer. Furthermore, he said GLP-1s are likely to ensure that the patients that do start dialysis are generally slimmer and healthier.

[42] Discussion with US nephrologist on GLP1s post detailed FLOW data - Video Webcast

Sleep Apnea and GLP-1s

What is sleep apnea?

Obstructive sleep apnea -- or OSA -- is another important condition that is linked to obesity, and where GLP-1s could make a big impact.

OSA occurs when there are repeated interruptions in breathing during sleep. These happen when excessive relaxation of the throat muscles causes the airway to become too narrow or collapse completely, blocking the flow of air into the lungs. Sleep apnea can lead to daytime tiredness, cognitive impairment, and worsening cardiovascular and metabolic health.

The severity of sleep apnea is measured using the Apnea-Hypopnea Index (AHI), which is the average number of apnea (pauses in breathing) and hypopnea (shallow breathing) episodes per hour of sleep. Sleep apnea is diagnosed where the AHI reaches 5 or more events per hour. Sleep Apnea is classified as severe when there are more than 30 episodes an hour.

Figure 35. Sleep Apnea Severity Classification by AHI Index

	AHI Index
Normal	<5
Mild	5-15
Moderate	15-30
Severe	>30

Source: CDC

Sleep apnea affects very roughly 1 billion people worldwide, and the number is growing.[43]

Being overweight or obese is an important risk factor for obstructive sleep apnea, because extra fat deposits around the neck can narrow the airway, contributing to airway collapse.

However, we have seen many different estimates of exactly how tight the link is:

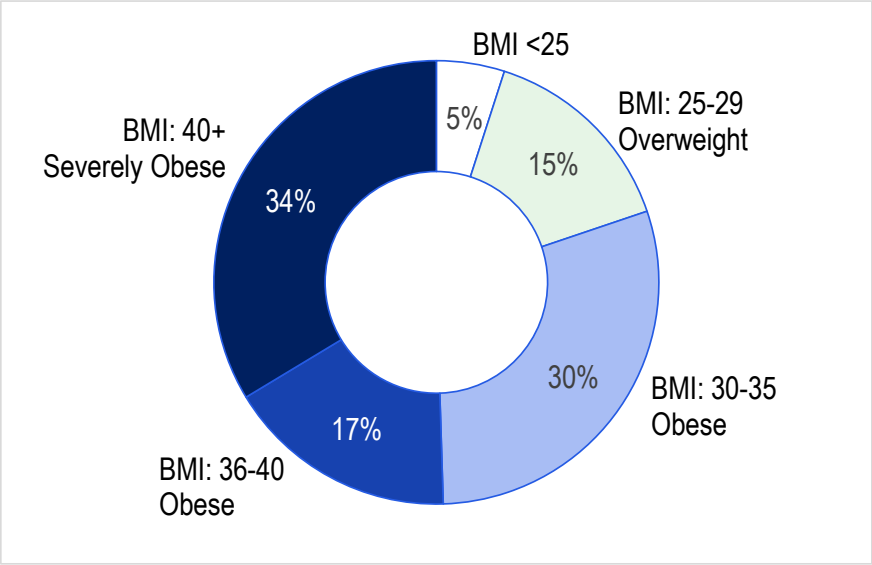
- According to one recent study, around 34% of adults with mild OSA; 43% with moderate OSA and 54% with severe OSA are obese.[44] However, other studies give higher and lower numbers.
- An analysis of the insurance claims of almost 8 million Americans with OSA, showed that 80% were obese at time of diagnosis, of which 34% were severely obese. (See Figure 36.)
- Among individuals with severe obesity, estimates for the prevalence of OSA range from 55% to 90%.[45]

[43] Global prevalence and burden of obstructive sleep apnea: a literature-based analysis

[44] Sleep May 24: Prevalence of Obesity in Obstructive Sleep Apnea

[45] Obesity Surgery May 2003: Obstructive Sleep-Related Breathing Disorders in Patients Evaluated for Bariatric Surgery

Figure 36. OSA Patients by BMI at time of diagnosis



N = 7.97 million
Source: Discovery Healthcare via Inspire Medical

As with type 2 diabetes and chronic kidney disease, sleep apnea has no cure but lifestyle changes such as weight management are recommended to treat the symptoms. Weight loss is strongly linked to improvement in OSA in people who are overweight or obese.[46] On average every kilogram (=2.2 pounds) of weight loss leads to a reduction in AHI of 0.8 events/hour.[47]

What about GLP-1s?

Surmount OSA showed a double agonist is very helpful, as it cuts the AHI events/hour by around 50-60% but doesn't totally cure sleep apnea.

The Surmount OSA clinical trial provides the most detailed evidence.[48] It enrolled individuals with moderate to severe sleep apnea, with most at the severe end, and most were significantly obese. At the start of the trial the average AHI was about 51 events/hour, and the average BMI was 39. After 52 weeks:

- Patients taking tirzepatide but *not* using CPAP saw an average reduction of about 25 AHI events an hour (or 51%) from 52 events/hour to 26, vs. an average reduction 5 AHI events/ hour for the placebo group;
- Patients taking tirzepatide and using CPAP, saw an average reduction of about 29 AHI events an hour (or 59%) from 50 events/hour to 20, vs an average fall of 6 AHI events/hour for the placebo group.

In short, the average patient using the GLP-1 moved from really severe sleep apnea to moderate sleep apnea -- an important improvement but not a complete solution.

Nonetheless the largest company in the sector – ResMed -- argues that GLP-1s are actually driving demand up, partly because more obese individuals who were reluctant to interact with the healthcare system now have a reason to do so.

[46] See Interactions Between Obesity and Obstructive Sleep Apnea and Weight Loss Is Integral to Obstructive Sleep Apnea Management
[47] Ibid.
[48] For the full results, see NEJM June 24: Tirzepatide for the Treatment of Obstructive Sleep Apnea

Interview with ResMed

We recently interviewed ResMed's CEO, Mick Farrell and Dr. Carlos Nunez, chief medical officer. The full interview is here. Below are edited highlights.

Mick Farrell, CEO, ResMed

Carlos M Nunez, MD, Chief Medical Officer, ResMed

ResMed is a medical devices company specialising primarily in the obstructive sleep apnea market.

What's the relationship between obesity and obstructive sleep apnea?

Carlos M. Nunez: There are often numbers that are thrown around that make you believe that the majority of patients with obstructive sleep apnea also have obesity, but that's not the case.

The latest, and actually the largest, epidemiologic study looking at the question: "What is the percentage of patients with obstructive sleep apnea who have obesity" was presented a few months ago at the American Academy of Sleep Medicine. It showed that even in severe sleep apnea, less than half of the patients also have obesity.

There is tremendous overlap between obesity and sleep apnea that we cannot ignore, but we have to keep it in perspective. The two are different: one's a disease; and one's a condition. They both deserve to be treated because they are different things.

How important is losing weight in treating OSA?

Carlos M. Nunez: Losing weight is an important part of managing sleep apnea. There is absolutely a connection between the two, and they have to be treated at the same time. If you look at the literature when patients are treated with both CPAP therapy for their obstructive sleep apnea and you actively manage their weight, they have the best chance of having the best outcomes.

Mick Farrell: When you look at the Surmount OSA trial in detail, it showed very few of the patients [using the GLP-1 drug] got to an AHI below 5. Bariatric surgery is far more effective at lowering weight than these new drugs, and 95% of patients that had sleep apnea before [bariatric surgery], still have it afterwards.

A weight loss drug or a surgery for bariatric surgery does not change your DNA. It does not change your gender, and it doesn't change the distance genetically that you have between your tongue and your uvula.

What's the impact of GLP-1s on demand for sleep apnea solutions?

Mick Farrell: We have been tracking 811,000 subjects, over 12 months, and now over 24 months, and we're going to continue. And we're seeing that [those who use GLP-1s have] a 10.7% higher start rate on positive airway pressure [PAP] therapy.

After one year, we see patients using GLP-1s are 310 basis points higher, when it comes to buying masks, accessories, tubing, humidifiers. And at 24 months, demand for resupply separates even further – it's 530 basis points higher for a GLP-1 patient's resupply rates [than for OSA patients who don't use GLP-1s].

Look at the real evidence. Look at our last four to eight to twelve quarters of growth. And by the way, watch us the next four, eight or twelve quarters.

Why do people takings GLP-1s use more OSA therapy?

Carlos M. Nunez: The primary care physician is most likely to see these patients. Some are showing up for the first time in years, saying " I hear about these miracle new drugs. Help me out, Doc. What can I do here?" Well, the doctor's going to treat the entire patient. No physician in their right mind is going to say; "I'm going to put you on a GLP-1 and hopefully in a year you will have lost enough weight that your other issues will have gone away."

Mick Farrell: They [GLP-1s] are bringing patients into the funnel. These patients are getting some treatment for their diabetes, their obesity and other aspects. Their residual apnea is so high they're motivated patients.

I think in the long run, GLP-1 drugs will be a very useful drugs. I think they'll bring more patients into the funnel, because there's this aesthetic improvement like Botox had, that you have this physical reduction in how you look. You feel fitter, look fitter. And that's a motivation. We have been trying for 35 years to motivate the billion people who [suffer from sleep apnea] to come into the channel.

Our biggest competitor, for 35 years since the company was started, was lack of education and awareness and the fact that the person suffering is in a subconscious state.

What happens if, in future, GLP-1s grow to such an extent that obesity rates start to fall?

Mick Farrell: The TAM in 2050 might be slightly lower – maybe by single digit percentages -- but the flow of patients for every year between now and 2050 is going to improve because this class of medicines brings people into primary care. They get these prescriptions and they get diagnosed with other diseases including sleep apnea and insomnia.

We've run the numbers on this. We're sort of data nerds here. We took a forecast, a very conservative forecast, of aging and the increase of obesity. And then we put the maximum impact of GLP-1 drugs and the conclusion was that in 2050 there will be between 1.2 billion and 1.4 billion patients with obstructive sleep apnea – assuming GLP-1s are free to everybody who wants them.

I'm optimistic the GLP-1 drugs, because of the aesthetic improvement that they bring, will bring more patients into the healthcare funnel than high blood pressure meds. I think there's a tailwind coming for ResMed from GLP-1s.

The Medical Aesthetics Market and GLP-1s

Heejin Lim
Korea MedTech
Citi Equity Research
heejin.lim@citi.com

The global market for medical aesthetics is worth around $200 billion currently, according to Frost & Sullivan, and is growing at about 11% compound. In 2023, about 56% of the procedures were non-surgical– which includes injectables and energy-based procedures, but they accounted for only about 27% of the dollar value. We estimate the non-surgical medical aesthetics segment will grow at a 3-year CAGR of 17%, to $71 billion by 2026E, driven by anti-aging and fat reduction.

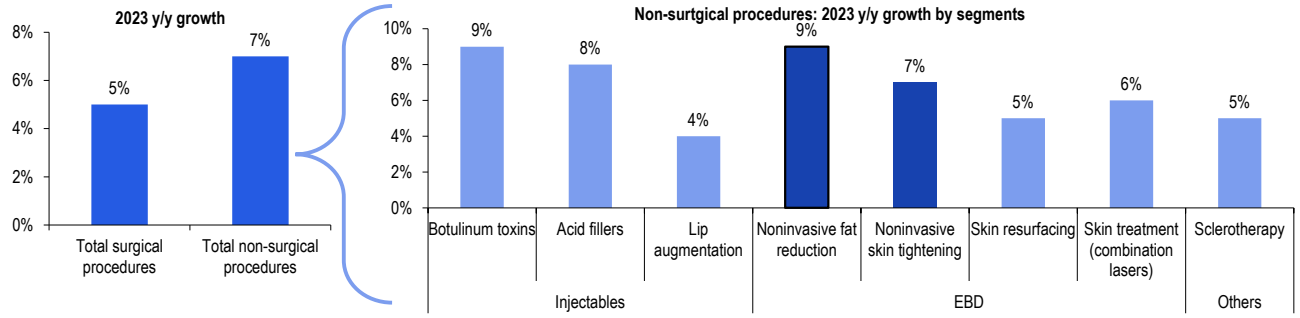
GLP-1s likely to boost the medical aesthetics market

We recently surveyed 320 medical practitioners in the non-surgical sector in the four most important markets – the U.S., China, Korea and Brazil – to see how they expect the industry to develop.

The doctors told us that on, balance, they expect GLP-1s will have a positive spillover impact on medical aesthetic practices. Partly this is because rapid weight loss increases patients' needs for non-surgical skin tightening. There is some evidence this is already happening in the U.S. for example. Last year non-invasive fat reduction grew 9% and skin tightening procedures rose 7%.

In addition, the doctors believe the weight-loss theme will create a virtuous cycle of continued demand.

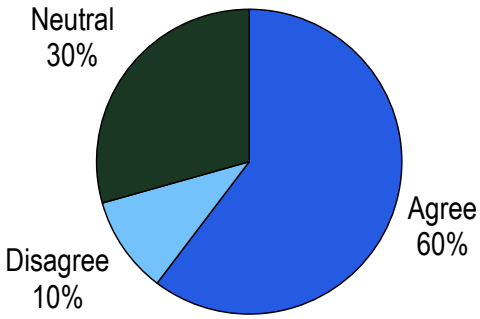
Figure 37. Medical Aesthetic Market Growth, 2023



Source: ASPS, Citi Research

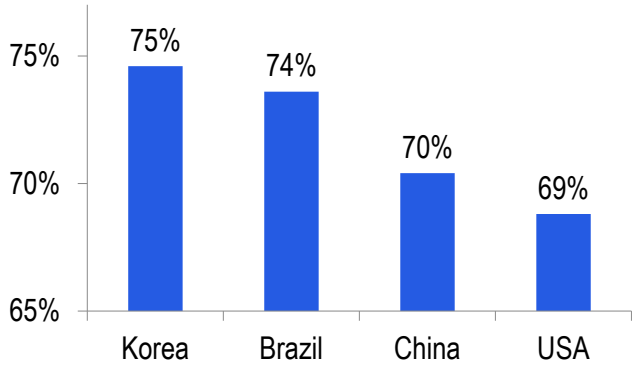
In our survey, 60% of the doctors agreed that weight-loss-related drugs or supplements have had a positive impact on business (vs. 10% who disagreed). The Korean doctors were the most positive.

Figure 38. Do you agree weight-loss drugs are having a positive impact on business?



Source: Research Innovation Lab

Figure 39. Av. Expectation (0% = very negative, 100% = very positive)



Source: Research Innovation Lab

Impact on consumer companies

Weighing the impact on food, beverage and tobacco companies

The latest generation of GLP-1s have been shown to cut calorie consumption for non-diabetic obese adults by about 25-35%.

Whereas we believe that GLP-1s are likely to boost demand for many healthcare companies, some potential negatives for food, beverage and tobacco companies should be examined.

The latest generation of GLP-1s cut calorie consumption for non-diabetic obese adults by 25-35% within a few months, clinical trials show, which implies lower food and drink volumes. GLP-1s also seem to reduce addictions, which means they may also hurt nicotine and gaming.

So far only about 3% of American are using these drugs for weight loss, Figure 14 shows, implying about a 1% of reduction in calorie consumption, assuming each of these people have reduced their calorie intake by 30%. However, if the number of GLP-1 users does increase significantly, then the impact is likely to be material.

When GLP-1s are used for diabetes, they are given in much lower doses, implying a much smaller decline in calorie consumption. Currently more than 85% of GLP-1 prescriptions are for diabetes. We expect, therefore, that as the use for weight loss increases, the impact on food and beverage companies is likely to greater (per GLP-1 user) than in the past.

Currently volume trends for food, beverage and tobacco in the U.S. are compatible with a hit from GLP-1s. For example, total food volumes fell by about 1% in America in the 12 months to July 27, Nielsen reported. The main companies blame this principally on the increase in the cost of living, but a GLP-1 impact can't be ruled out.

Food companies can adapt by offering products with smaller portion sizes but more protein and fiber. GLP-1s users also want hydration and products that help soothe gastric discomfort.

There are some positives for the food industry of course. GLP-1s users say they eat more fresh vegetables, fruit and fish. And some companies are developing products especially for GLP-1 users. Herbalife, for example, has said it will make a range of high protein products targeted at GLP-1 users.

Mattson, a food development consultancy, has conducted research focusing on how large companies should adapt their offerings for GLP-1 users. It concludes that users want products that offer:

- Smaller portions
- Hydration
- Increased protein (to address the loss of lean muscle)
- Soothing for nausea and gastric discomfort

Justin Shimek, CEO of Mattson, said: "I think these medicines are both a risk and opportunity for the food industry, but clearly we believe that this is going to be a time of disruption."[49]

[49] https://www.ift.org. May 2024

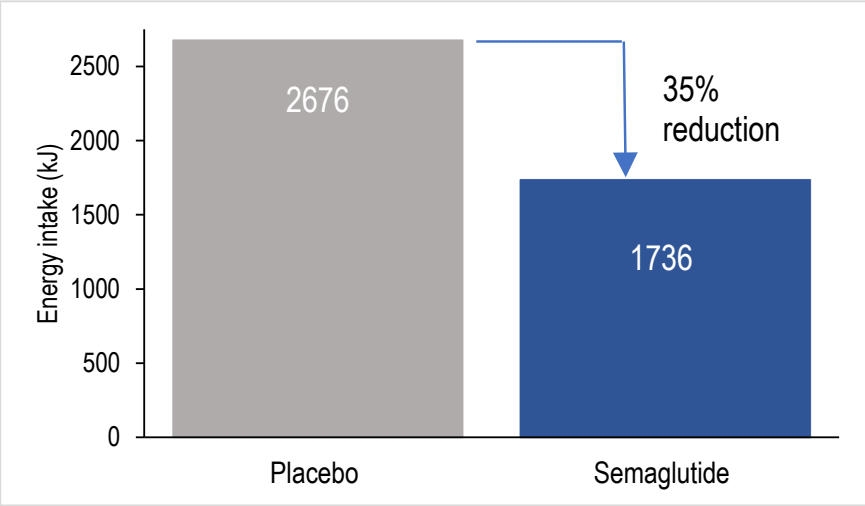
The latest generation of GLP-1s cause a cut in calorie consumption by 25-35% within months

Two clinical trials show that the latest generation of GLP-1s cuts energy consumption by about 25-35% after a few months in non-diabetic obese adults.[50]

Figure 40 summarizes the headline results of the first trial – which excluded people with diabetes.

Figure 40. Average calorie consumption during buffet style lunch 20 weeks after using semaglutide or a placebo

2.4mg semaglutide vs placebo, after 20 week use. n=72



Source: Diabetes Obes Metab.. 2021: Effect of semaglutide once weekly on energy intake, appetite, & control of eating.

The historic real-world impact of GLP-1s may understate their future impact

It is important to remember that this research explicitly excluded people with diabetes. We suspect the calorie reduction for diabetics would be considerably lower for two reasons, although we don't have any hard clinical data:

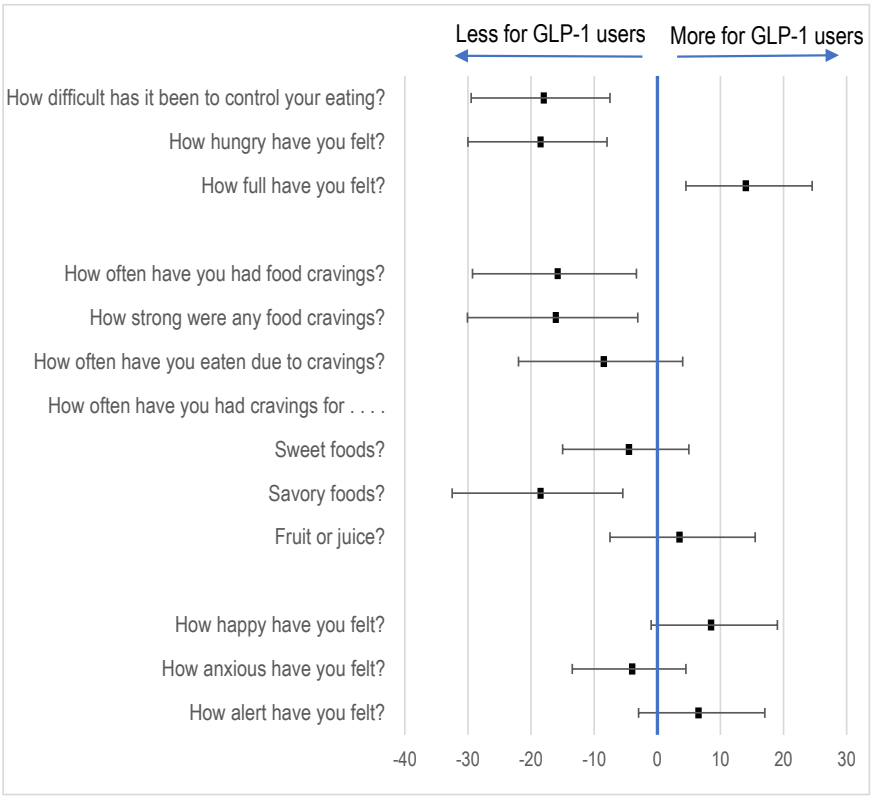
- GLP-1 prescriptions for diabetes use smaller doses. For example, when semaglutide is prescribed for diabetes, it's sold as *Ozempic*, and comes in a 1.0mg dose; when it's sold for weight-loss, as *Wegovy*, and comes in a 2.4mg dose.
- Diabetics typically lose very roughly 5% less body-weight than non-diabetics for the same dose.

[50] Diabetes Obes Metab.. 2021*: Effect of semaglutide once weekly on energy intake, appetite, & control of eating.* And Diabetes Obes Metab. 2017 *Effects of once-weekly semaglutide on appetite, energy intake and control of eating.*

Currently, fewer than 15% of people taking GLP-1s are receiving prescriptions for weight loss. As capacity increases, we expect this percentage to increase significantly, implying the average weight loss per user will probably increase.

Figure 41. Attitudes to eating and food

2.4mg semaglutide vs placebo, after 20 weeks. n=72



Source: Diabetes Obes Metab.. 2021: Effect of semaglutide once weekly on energy intake, appetite, & control of eating.

GLP-1s may increase demand for fresh food

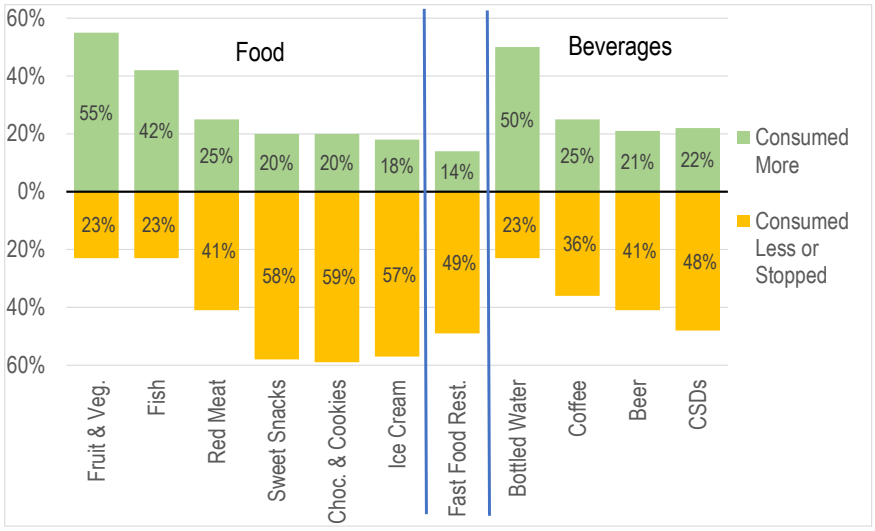
GLP-1s reduce the appetite by mimicking the hormones that tell the body it has just eaten. It is therefore unsurprising that users report fewer food cravings. However, it also appears that GLP-1s help users eat more healthy food.

In both the trials we just mentioned, the participants were asked about their attitudes toward eating -- and in both the participants taking semaglutide said they were less hungry, had fewer food cravings, and were more able to control their food intake. So far, so expected. However, people on GLP-1s were less interested in savory food than sweet food, and if anything, they were more interested in consuming fruit and juice, as Figure 41 shows.

This finding is supported by a survey we commissioned of nearly 500 American adults who were using GLP-1s to lose weight. Figure 42 shows that many more said they had increased their consumption of fresh fruit and vegetables and water as a result.

Figure 42. GLP-1 users mostly say they consume more fresh fruit & vegetables, and bottled water, but less unhealthy food

Since taking GLP-1s have you consumed more or less of each item?



N=499. Survey conducted Nov 2023. CSDs = carbonated soft drinks. Fast food restaurants = restaurants with drive thru.

Source: Citi Innovation Lab

Food & Beverages – The view from Equity Research

Filippo Falorni, CFA
U.S. Beverages, HPC Lead Analyst
Citi Equity Research

Tom Palmer, CFA
U.S. Beverages, HPC Lead Analyst
Citi Equity Research

For the Packaged Food & Beverage sector, the peak of market worries around the impact of GLP-1 drugs was reached in the second half of 2023. During the period, the market became increasingly worried about the impact of GLP-1 drugs used for weight loss on consumer purchasing behaviors in the Food & Beverage space. Market concerns were heightened by a Walmart comment on October 5th reported by several news articles, indicating GLP-1 users were buying less units and less calories, which drove large declines in Food & Beverage stocks on the day and in the following months.

Worries around GLP-1 impacts coincided with a general slowdown in Food & Beverage volumes for public companies, which we believe were mainly driven by other factors, including: (a) a general slowdown in U.S. consumer conditions, particularly among lower-income cohorts after several years of high price increases from CPG companies; (b) the impact of the year-on-year reduction in SNAP benefits among lower income cohorts; and (c) consumer trade-down leading to a shift in volumes from branded players to private label options.

In February 2024 we published a note titled "Market Not Yet Losing Appetite for GLP-1 Impacts, Should It?" including a Citi Innovation Lab survey of ~500 GLP-1 users, compared it to a sample of ~500 consumers under other weight loss regimens. As discussed in the note, we view the near-term impact on calorie consumption and food & beverage volumes as manageable amounting to <100 bps per year over the next 5 years and building to ~1.5% by 2035. If the pace of adoption of GLP-1 were to be faster than expected and broader across the globe, we would expect CPG companies to more aggressively focus on changing their portfolios to adapt to the new consumer environment (similar to what many Beverage companies did with zero-sugar product offerings as sugar reduction became front-and-center in the minds of consumers).

While the longer-term potential on consumption is still unclear and likely several years out, we expect stock performance to potentially still be impacted by news on GLP-1 in the near-term. Specifically, we believe two areas of news could potentially have negative impacts on Food & Beverage stocks: (1) advancements on the development of a pill format for GLP-1 drugs by drug manufacturers; and (2) updates on health insurance coverage of those drugs for weight loss and/or lowering of the cost of the drugs for consumers.

At a sector level, in the Packaged Food space we see particular risk for categories with already low underlying consumption trends because even an incremental 1-2% volume decline over the next decade could mean eventual industry oversupply and erode pricing power (e.g., center store meals). We see more risk for companies that derive the majority of their sales from the U.S. and have elevated exposure to snacks and/or prepared meals. We see lower risk in the Beverage space as we view beverage consumption as more tied to social interactions, less reduction in consumption and spending levels by consumers on GLP-1 drugs relative to food/snacking based on our survey results, and more international exposure of beverage companies. (We see lower risk in emerging markets.)

GLP-1s and fashion

We think that if GLP-1s usage does become substantially more widespread as we expect, it could be a positive for overall clothing sales. Partly this is because people will need to buy new clothes as their body shape changes. However we believe the more important effect is likely to be that those individuals who are happier with their bodies are more likely to buy more fashion.

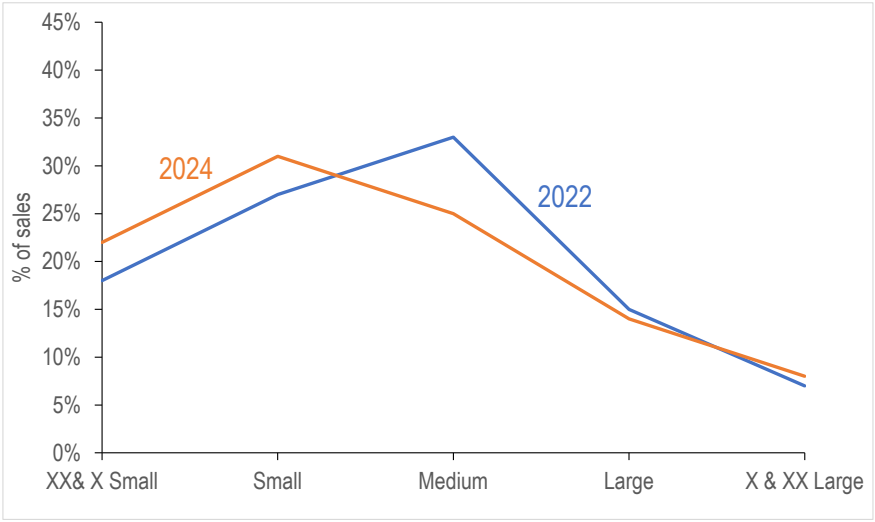
“Fashion will definitely benefit from GLP-1s,” Prashant Agrawal, founder and CEO of Impact Analytics, a retail-focused data insights company, told us. “But the companies that will benefit will be the ones that adapt their sizing – and plenty of retailers get this badly wrong.”

Some of the biggest gainers are likely to be the very high-end fashion companies, Mr. Agrawal told us, because they don’t make clothes in XL sizes.

There is already evidence that clothing sizes are falling

If people are taking GLP-1s and losing weight, one would expect them to buy new, smaller clothes, in part to show off their new, leaner bodies. One of the areas with the greatest use of GLP-1s for weight loss is in the Upper East side of Manhattan, particularly among women.[51] Impact therefore analyzed sizing curves for women’s fashion sales among the tony stores on Madison Avenue -- and found a significant shift in sizing since GLP-1s have commonly used for weight loss.

Figure 43. Sizing Curve for Women's Fashion, Madison Avenue, 2022 vs 2024YTD



Source: Impact Analytics

Retailers typically operate on thin margins, and they often order their inventory many months in advance. Getting the sizing curve right – or wrong – can easily make the difference between a profit and a substantial loss.

[51] Impact Analytics says 44% of NY’s GLP-1 prescriptions go to people who do not have type 2 diabetes -- and 75% of these individuals are female.

Interview with Impact Analytics

Impact Analytics provides data-driven insights to help retailers optimize supply chain and merchandizing. We interviewed Prashant Agrawal, founder and CEO. The full interview is here.

Prashant Agrawal,
Founder and CEO of Impact Analytics

Impact Analytics advises retail and CPG companies on supply chain issues, based on AI derived insights.

How will GLP-1s affect fashion retail?

Overall GLP-1s are great for fashion, because you have revenge shopping.

People want to lose weight. They're going to find ways to do this. And they say "I've lost weight. I can buy stuff that I haven't bought before, and I'm going to go out and do it." You feel more comfortable with your body. You want to do things and buy things you didn't buy before.

Two caveats to that - one a positive, and one a negative. So the negative one first, is returns. When you have e-commerce and you start to lose weight, you'll end up buying two to three sizes, because you don't know exactly what you fit in, and that actually hurts bottom line. This is less of a problem for brick-and-mortar stores.

The second piece, and I think this is for luxury, luxury often is not sized up, and you have pent-up demand for people that are losing weight to go in and buy stuff that they couldn't buy before. So on the margins, for sure, luxury fashion will benefit from this.

Overall, GLP-1s are a positive. To take advantage of that positivity, you need to be ahead of the size curve. Retailers need to ask "Where are we seeing the shifts? How is it different by product type, color, all of these things, by location?"

Is there any evidence that GLP-1s are impacting fashion retailers?

We looked at New York, specifically Midtown and the Upper East Side because this is the epicenter of GLP-1 drug use. What we saw was actually a little bit startling. We looked at size curves in 2022, '23 and '24. And what we saw is size curves move to the left. People shifting from double XL to medium, from XL to small. This is a five to 10% shift towards the left in that size curve. That’s startling because over the years, in the U.S., you’ve seen size curves shifting rightwards as people got heavier.

In terms of retail and fashion, this skews heavily towards women, at least what we've seen in the U.S. in our data.

And outside New York?

GLP-1 usage will be different by different states, different countries. You look at the Middle East and Australia and New Zealand. The US is not the only country that has an obesity problem. And some of the other places that do, specifically in the GCC are wealthy, and they will find a way to GLP-1 drugs at the end of the day. And for GCC countries, it could have a bigger impact than almost anywhere in the world.

How important are changing sizes?

So just to step back, retail has gotten size curves wrong for a long time. You can walk into any store, and you'll always wonder, "Why do they have so many extra smalls, or why do they have too many double XLs?"

I was just in London, in a large retailer, quite famous, and looked at the pants [trousers for UK readers]. The mathematics of this is quite hard, because you're actually buying so many SKUs that retailers tend to order the same sizes for white, beige and black. But it's a fact that if you're heavier, you're more likely to buy black pants. So this store had ended up with too much black XS, but lots of double XLs in white. That's today without GLP-1s, and that's hurting their profit margins.

You see promos, markdowns, clearance. If you're a retailer with a billion dollar sales, if you're going to miss your size curves by 3%, that's a $20 million bottom line impact.

Size curves are something you usually have taken your eye off of. You may visit it every three, four, five years. But GLPs are a big deal. This is going to be something gradual over '25, '26, '27. So, you need to monitor if you're a retailer, every six months. You've got to get ahead of it.

Do retailers get this?

This isn't rocket science, is it? If people lose weight, they will then obviously reduce their clothing sizes. But while that seems very obvious, we haven't seen fashion retail wake up to this fact. They need to buy correctly and that means extrapolating what GLP-1 drug usage will do to these size curves over time.

Conclusions

This report has covered a lot of ground, including the science behind this new and exciting class of drugs. Three of the main points are:

- **It is quite possible that usage will grow into several hundreds of millions of people in the next 5-10 years.** The impact of these drugs will depend on how many people use them. Currently it's about 25 million people globally, because that is the global manufacturing capacity. However, we believe it is quite possible that future usage will be many times this level.
  - The pharma industry is investing billions of dollars into expanding capacity. Novo Nordisk (the smaller of the two currently dominant players) says it is investing in order to supply 50-100+ million patients.
  - More than 100 new GLP-1s drugs are under development.
  - Demand for this class of drugs is utterly different from any other because it's driven both by extremely strong lifestyle reasons and extremely strong medical reasons. In our survey of Americans who are using GLP-1s to lose weight, more are doing so to look thin or feel healthy than for a specific medical reason.
- **For the health industry, GLP-1s are likely to increase demand for the next few years.** GLP-1s slow the advance of many obesity-related diseases, which means people with these diseases who use the drugs are likely to live longer. In addition, more obese are interacting with the healthcare system, because it can finally offer them a useful therapy.
- **For food and beverage companies, total consumption may fall more than some expect.** Clinical trials show that individuals taking GLP-1s to lose weight reduce their calorie consumption by 25%-35%. If demand does grow to, for example, 15% of the population, that would imply a roughly 5% drop in the national calorie intake. Demand for certain sectors – eg protein and vegetables – may grow, however.

As our premier thought leadership product, **Citi Global Perspectives & Solutions (Citi GPS)** is designed to help readers navigate the most demanding challenges and greatest opportunities of the 21st century. We access the best elements of our global conversation with senior Citi professionals, academics, and corporate leaders to anticipate themes and trends in today's fast-changing and interconnected world.

All Citi GPS reports are available on our website www.citigroup.com/global/insights/citigps

[Cross Border Payments 24x7](#)
Faster, Simpler, Smarter
October 2024

[Global Giving](#)
Generosity and the Economics of Philanthropy
October 2024

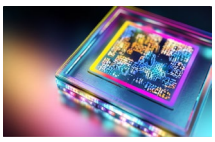
[Sustainable Transitions: Unleashing the Power of Treasury](#)
Unleashing the Power of Treasury
August 2024

[Hard to Abate Sectors and Emissions II](#)
The Road to Decarbonization
July 2024

[Embracing Demographic Transition](#)
Health and Wealth in an Aging World
July 2024

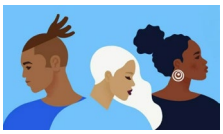
[AI in Finance](#)
Bot, Bank & Beyond
June 2024

[What Machines Can't Master](#)
Human Skills to Thrive in the Age of AI
May 2024

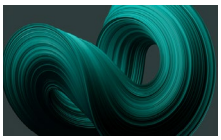


[Disruptive Innovations X](#)
Ten More Things to Stop and Think About
May 2024

[Future of Healthcare](#)
The Oxford Prescription
May 2024



[Closing the Racial Wealth Gap](#)
Restating the Economic Case
April 2024



[Supply Chain Financing](#)
Building Resilience
January 2024

[Unlocking Climate and Development Finance](#)
Creating Bankable Projects
December 2023

[Food, Water, and Climate Change](#)
Solutions for Tackling this Critical Nexus
November 2023

[APEC Economic Outlook](#)
Navigating Shifting Dynamics
November 2023

[Supply Chains](#)
Lessons Learned Helped by New Technology
November 2023

[Food Security](#)
Solutions for a Perfect Storm
November 2023

Treasury Leadership
Does It Matter?
November 2023

Philanthropy and the Global Economy v3.0
Perspectives on the Future of Giving
October 2023

Supply Chain Technology
Improving Efficiency, Resilience, and Transparency
October 2023

Technology at Work v7.0
The Third Phase of Globalization
October 2023

Africa
A New Growth Model
October 2023

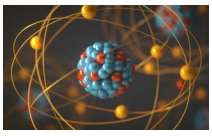
Skills That Pay
The Returns from Specific Skills
October 2023

Future of Cross-Border Payments
Who Will Be Moving $250 Trillion in Next Five Years?
September 2023

Unleashing AI
The AI Arms Race
September 2023

Hydrogen
A Reality Check on the Hydrogen Craze
August 2023

Quantum Computing
Moving Quickly From Theory to Reality
July 2023



Future of Nuclear Energy in a Low-Carbon Environment
Fission and Fusion Advanced Reactors to Prevail
July 2023

Voluntary Carbon Market
A Critical Piece of the Net Zero Puzzle
July 2023

Economic and Social Mobility
The Role of Business in Improving Outcomes
June 2023

Sustainable Ocean Economy
Charting a Prosperous Blue Future: Risk to Resilience
June 2023

Asia as a Time Machine to the Future
Seven Areas Where Asia Gives Insights Into the Future
May 2023

Money, Tokens, and Games
Blockchain's Next Billion Users and Trillions in Value
March 2023

The Cyber Problem
Causes and Consequences of the Rise in Cyber Skill Demand
March 2023

The Creator Economy
Getting Creative and Growing
March 2023

Generative AI
ChatGPT and Search
February 2023

Supply Chain Finance
Uncertainty in Global Supply Chains Is Going to Stay
January 2023

If you are visually impaired and would like to speak to a Citi representative regarding the details of the graphics in this document, please call USA 1-888-800-5008 (TTY: 711), from outside the US +1-210-677-3788

IMPORTANT DISCLOSURES

This communication has been prepared by Citigroup Global Markets and is distributed by or through its locally authorised affiliates (collectively, the "Firm"). This communication is not intended to constitute "research" as that term is defined by applicable regulations, though it may contain thematic content that has been or may be contained in research reports. Unless otherwise indicated, any reference to a research report or research recommendation is not intended to represent the whole report and is not in itself considered a recommendation or research report. The views expressed by each author herein are their personal views and do not necessarily reflect the views of their employer or any affiliated entity or the other authors, may differ from the views of other personnel at such entities, and may change without notice.

You should assume the following: The Firm may be the issuer of, or may trade as principal in, the financial instruments referred to in this communication or other related financial instruments. The author of this communication may have discussed the information contained herein with others within the Firm and the author and such other Firm personnel may have already acted on the basis of this information (including by trading for the Firm's proprietary accounts or communicating the information contained herein to other customers of the Firm). The Firm performs or seeks to perform investment banking and other services for the issuer of any such financial instruments. The Firm, the Firm's personnel (including those with whom the author may have consulted in the preparation of this communication), and other customers of the Firm may be long or short the financial instruments referred to herein, may have acquired such positions at prices and market conditions that are no longer available, and may have interests different or adverse to your interests.

This communication is provided for information and discussion purposes only. It does not constitute an offer or solicitation to purchase or sell any financial instruments. The information contained in this communication is based on generally available information and, although obtained from sources believed by the Firm to be reliable, its accuracy and completeness is not guaranteed. Certain personnel or business areas of the Firm may have access to or have acquired material non-public information that may have an impact (positive or negative) on the information contained herein, but that is not available to or known by the author of this communication. The Firm shall have no liability to the user or to third parties, for the quality, accuracy, timeliness, continued availability or completeness of the data nor for any special, direct, indirect, incidental or consequential loss or damage which may be sustained because of the use of the information in this communication or otherwise arising in connection with this communication, provided that this exclusion of liability shall not exclude or limit any liability under any law or regulation applicable to the Firm that may not be excluded or restricted.

The provision of information is not based on your individual circumstances and should not be relied upon as an assessment of suitability for you of a particular product or transaction. Even if we possess information as to your objectives in relation to any transaction, series of transactions or trading strategy, this will not be deemed sufficient for any assessment of suitability for you of any transaction, series of transactions or trading strategy.

The Firm is not acting as your advisor, fiduciary or agent and is not managing your account. The information herein does not constitute investment advice and the Firm makes no recommendation as to the suitability of any of the products or transactions mentioned. Any trading or investment decisions you take are in reliance on your own analysis and judgment and/or that of your advisors and not in reliance on us. Therefore, prior to entering into any transaction, you should determine, without reliance on the Firm, the economic risks or merits, as well as the legal, tax and accounting characteristics and consequences of the transaction and that you are able to assume these risks.

Financial instruments denominated in a foreign currency are subject to exchange rate fluctuations, which may have an adverse effect on the price or value of an investment in such products. Investments in financial instruments carry significant risk, including the possible loss of the principal amount invested. Investors should obtain advice from their own tax, financial, legal and other advisors, and only make investment decisions on the basis of the investor's own objectives, experience and resources.

This communication is not intended to forecast or predict future events. Past performance is not a guarantee or indication of future results. Any prices provided herein (other than those that are identified as being historical) are indicative only and do not represent firm quotes as to either price or size. You should contact your local representative directly if you are interested in buying or selling any financial instrument, or pursuing any trading strategy, mentioned herein. No liability is accepted by the Firm for any loss (whether direct, indirect or consequential) that may arise from any use of the information contained herein or derived herefrom. Although the Firm is affiliated with Citibank, N.A. (together with its subsidiaries and branches worldwide, "Citibank"), you should be aware that none of the other financial instruments mentioned in this communication (unless expressly stated otherwise) are (i) insured by the Federal Deposit Insurance Corporation or any other governmental authority, or (ii) deposits or other obligations of, or guaranteed by, Citibank or any other insured depository institution. This communication contains data compilations, writings and information that are proprietary to the Firm and protected under copyright and other intellectual property laws, and may not be redistributed or otherwise transmitted by you to any other person for any purpose.