# GLP-1s: A HEALTHCARE REVOLUTION?

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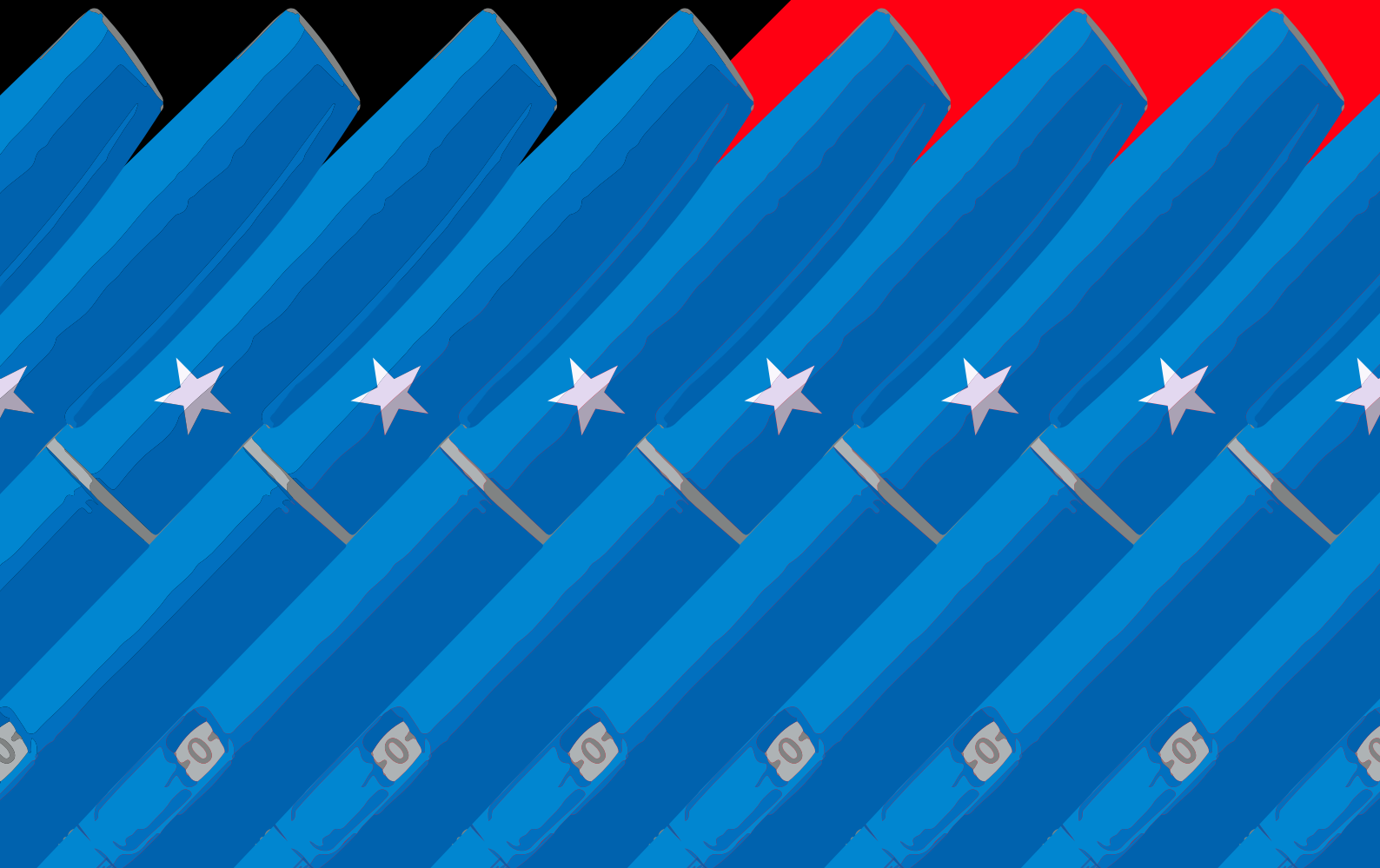
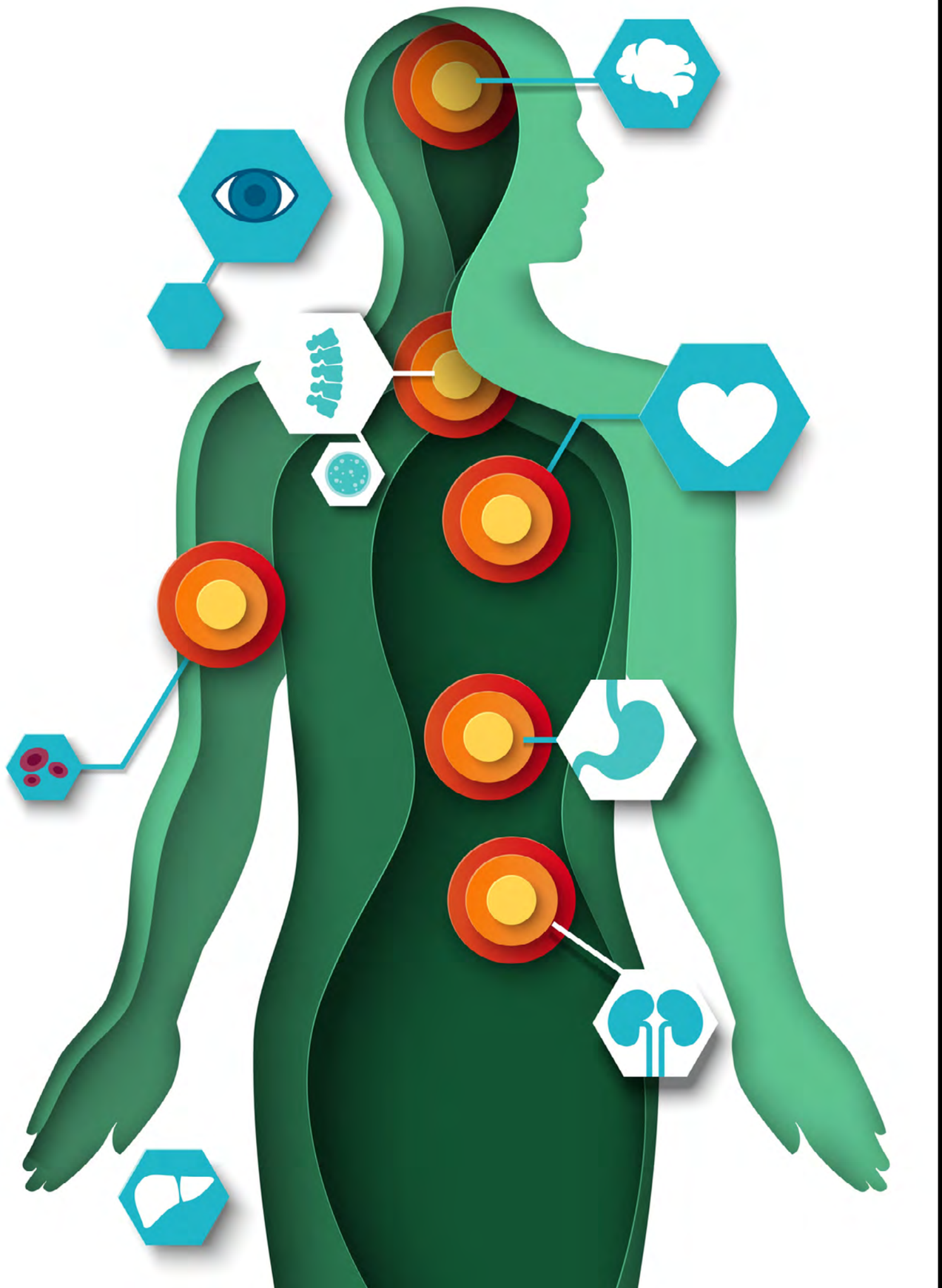




## Every person in the world is a patient at some point in their lives, making healthcare one of the largest industries in the world.

Our sector has seen many technical advances in recent years, including personalized medicine, wearables and, of course, artificial intelligence, which is now impacting drug discovery, diagnosis and healthcare delivery. However, one of this century's biggest game-changers will likely be a novel drug class that's showing unprecedented success, or the promise of it, in treating some of the world's most prevalent conditions. GLP-1-based drugs ('GLP-1s'), with their unparalleled efficacy and myriad applications, may be sparking nothing short of a healthcare revolution...

## The revolution begins...

GLP-1s were originally developed and approved to treat type 2 diabetes (T2D), but like many other drugs – one example being Viagra, originally indicated in cardiovascular disease but now with widespread use in erectile dysfunction – it became apparent that GLP-1s had clinical benefits in other areas too, most notably obesity. This is because GLP-1-based drugs work by mimicking the effects of the hormone glucagon-like peptide-1 (GLP-1), which regulates appetite, insulin secretion, and glucose metabolism. By activating GLP-1 receptors, these medications reduce hunger, increase feelings of fullness, and improve blood sugar control.

Having gone on to demonstrate great success in trials for weight reduction in people with obesity or in those who are overweight, GLP-1s have now gained regulatory approvals in many markets. In the US today, healthcare professionals and consumers have the option of semaglutide (Wegovy® by Novo Nordisk), liraglutide (Saxenda®, also Novo Nordisk) and tirzepatide (Eli Lilly's Zepbound®). But that's not the end of the story; GLP-1s are showing favorable clinical results in multiple other conditions, both metabolic and non-metabolic. These are explored in more detail in this paper, but it's safe to say we can expect further label extensions for this exciting drug class.

Meanwhile, the weight loss revolution has begun – and it couldn't have happened soon enough. According to the CDC, more than 100 million adults in the US are obese[1], a figure which is rising rapidly. Over 22 million are severely obese. A recent Ipsos study (June 2024) found that no less than 10% of US respondents were currently taking a GLP-1-based medication[2]. While this covers all conditions the agents are licensed for, given the prevalence figures and the growing publicity, we expect GLP-1 use for obesity to massively expand in the near future. Unsurprisingly, given the market direction, earnings for both Novo Nordisk and Eli Lilly increased by over 30% year-on-year in the 12 months up to June 2024[3,4].

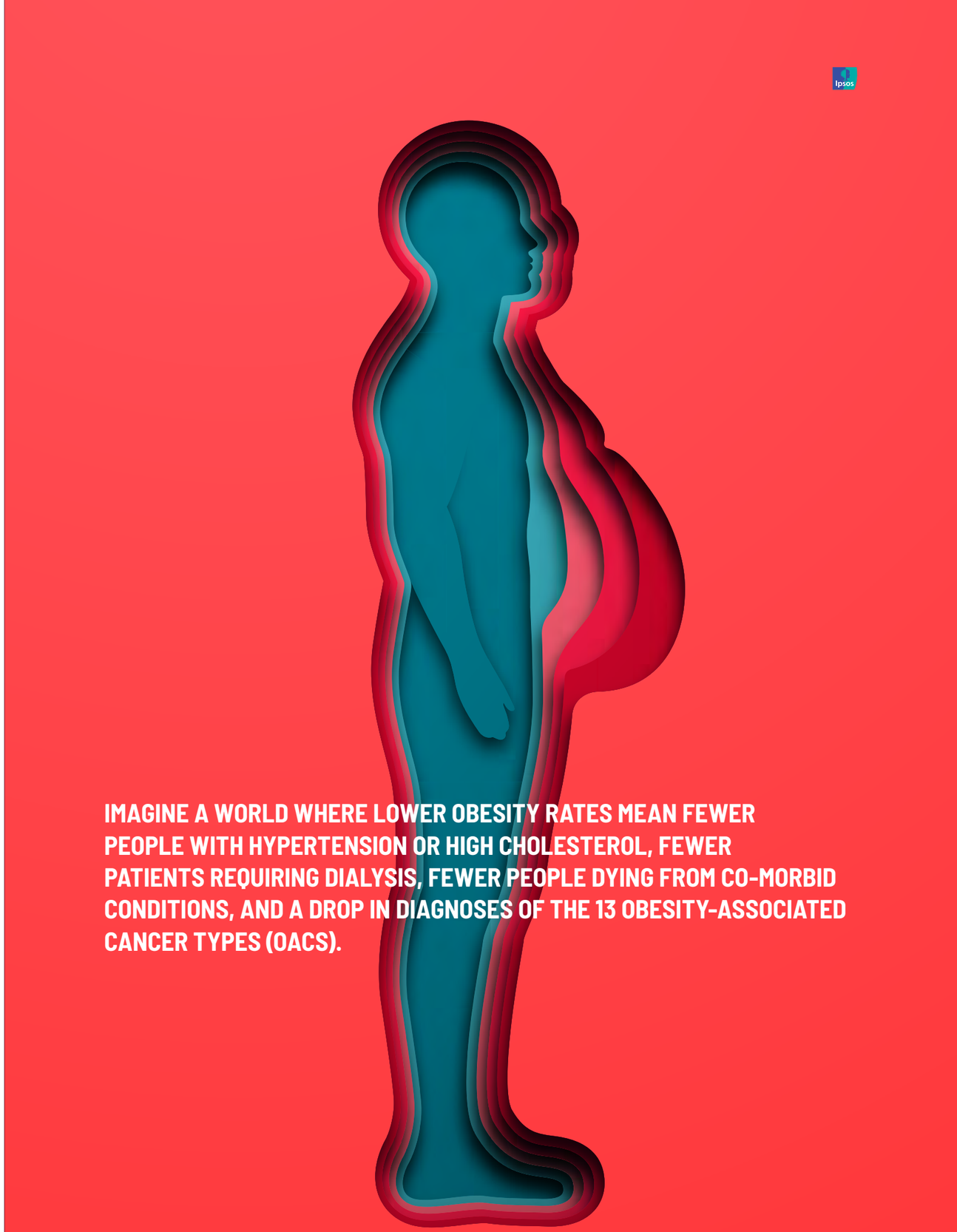
While the potential to treat every person with obesity and T2D is exciting enough, the true impact of all this may be far beyond our current comprehension. We know that obesity is linked to many other common health conditions, including cardiovascular disease, kidney disease, liver disease, and cancer. So, imagine a world where lower obesity rates mean fewer people with hypertension or high cholesterol, fewer patients requiring dialysis, fewer people dying from co-morbid conditions, and a drop in diagnoses of the 13 obesity-associated cancer types (OACs). Taking this a stage further, we would see a huge reduction in the burden of care, far easier access to healthcare, and a dramatic drop in healthcare costs.

Of course, we are a long way from this scenario today. Currently, demand for these drugs is far outweighing supply, leading to shortages for those truly in need. What's more, their high cost is making them prohibitively expensive for many and insurance coverage varies hugely. However, the development of GLP-1s is a clear priority for pharma, garnering huge levels of investment (more on this below), and the global obesity drug market is predicted to reach $105 billion by 2030[5]. Meanwhile, governments and policymakers are increasingly attentive to the situation.

In the following sections, we take a closer look at some of the diseases that could be positively impacted by GLP-1s, both directly and indirectly. And it's certainly not an exhaustive list. One thing is clear, however. Although we are still in the very early stages of the GLP-1 revolution, management of T2D and obesity could be just the start...







**IMAGINE A WORLD WHERE LOWER OBESITY RATES MEAN FEWER PEOPLE WITH HYPERTENSION OR HIGH CHOLESTEROL, FEWER PATIENTS REQUIRING DIALYSIS, FEWER PEOPLE DYING FROM CO-MORBID CONDITIONS, AND A DROP IN DIAGNOSES OF THE 13 OBESITY-ASSOCIATED CANCER TYPES (OACS).**

## Opportunities in Cardiometabolic and Renal Diseases

**Metabolic dysfunction-associated steatohepatitis (MASH)**

MASH – previously known as NASH (non-alcoholic steatohepatitis) – is inflammation of the liver caused by excess fat cells, which causes progressive liver damage. It is often under-diagnosed due to its 'silent' nature in the early stages but is a leading cause of liver-related morbidity and mortality. With only one drug recently approved by the FDA to treat the condition[6], it is an area of high unmet need.

GLP-1s are currently being studied for their potential to treat this condition, as they may help reverse steatohepatitis, lower cardiovascular risk, and reduce liver fat content and liver enzymes. It is very likely to be the next indication for GLP-1s, with phase III trial results expected for semaglutide in Q4 2024[7].

**Chronic kidney disease (CKD)**

Statistics from the International Society of Nephrology estimate that approximately 850 million people worldwide are affected by CKD[8], a condition in which damaged kidneys cannot filter the blood efficiently. Coupled with an increasing mortality rate and sources citing as many as 9 out of 10 individuals unaware that they have CKD[9], it is a major global health concern.

Diabetes plays an extremely detrimental role in the incidence of CKD (40% of people with diabetes are estimated to develop it[10]) and mortality rates increase in those with diabetes when kidney disease is also present[11]. Given GLP-1s' role in treating diabetes, a positive impact on CKD and its repercussions has been seen in research. In the FLOW trial, semaglutide reduced the risk of major kidney disease events in patients with both diabetes and CKD[12]. In fact, the trial was stopped prematurely due to meeting efficacy criteria that warrants doing so!

Taking this a step further, what if the treatment of diabetes that leads to a reduction in CKD cases ultimately translates to fewer patients needing a transplant following kidney failure? As of March 2024, 89,101 people in the US were recorded as actively waiting for a kidney transplant[13]. If GLP-1s can slow CKD progression at the very least, and prevent it from occurring at the very most, the world of dialysis and kidney transplantation would dramatically change.

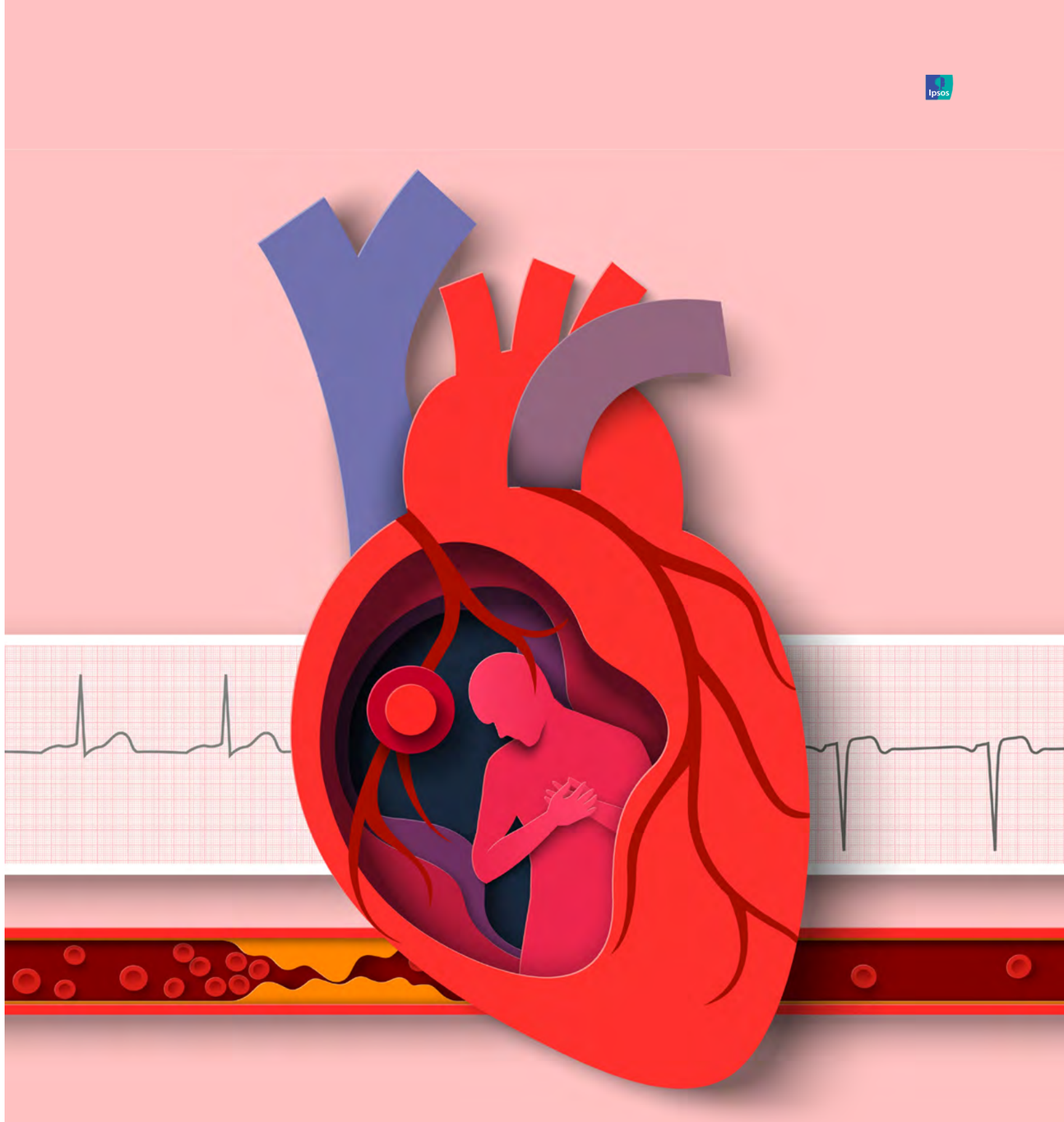
**Heart failure (HF)**

Chronic heart failure (CHF) is a progressive condition in which the heart muscle is unable to pump enough blood to meet the body's needs. Patients are categorized into two main groups depending on their left ventricular ejection fraction (the amount of blood pumped out of the ventricle): those with reduced ejection fraction (HFrEF) and those with preserved ejection fraction (HFpEF).

CHF can be caused by a number of factors, including many of those where GLP-1 agents are being used or studied. Obesity is known to increase the risk of heart failure – especially HFpEF, with figures showing that approximately 80% of HFpEF patients are considered overweight or obese[14]. Currently, semaglutide and tirzepatide are being studied as potential treatments for HFpEF and have been shown in trials to reduce the risk of HF events and cardiovascular death[15,16].







**OBESITY IS KNOWN TO INCREASE THE RISK OF HEART FAILURE. CURRENTLY, SEMAGLUTIDE AND TIRZEPATIDE ARE BEING STUDIED AS POTENTIAL TREATMENTS FOR HFpEF AND HAVE BEEN SHOWN IN TRIALS TO REDUCE THE RISK OF HF EVENTS AND CARDIOVASCULAR DEATH.**

## Opportunities in Neurodegenerative Diseases, Cancer & Beyond

Clearly, GLP-1s are likely to broaden treatment options for the cardiometabolic disease arena and related comorbidities. There is also evidence for them to treat conditions that have arisen as a result of obesity, and their influence on the brain has sparked research into their potential for treating neurodegenerative diseases and addiction.

**Alzheimer's disease (AD)**

GLP1-s are already showing promise in Alzheimer's disease (AD). Semgalutide is currently part of a 3-year phase III investigation to assess its effectiveness in early AD[17], while phase 2b data for liraglutide shows a reduction in cognitive decline by as much as 18%[18].

Lending credence to the hypothesis that AD may represent a brain-specific form of diabetes (due to a shared commonality of mechanisms associated with insulin resistance[19]), analysis of T2D patients found that GLP-1s were associated with a lower risk of dementia compared to other diabetic drug therapies[20]. By dual-benefitting the sizeable – and growing – population of people living with diabetes and/or AD, the GLP-1s could offer both a therapeutic and preventative drug option for people in this cohort.

**Obstructive sleep apnea (OSA)**

OSA is a chronic disease in which breathing repeatedly stops and starts during sleep, and which can lead to serious health complications if left untreated, e.g., heart disease, high blood pressure, and T2D. Because excess weight around the throat and airways can cause tissues to collapse and airways to block, people who are overweight or obese are more likely to develop the condition.

The weight loss potential of GLP-1s could certainly lead to a reduction in sleep apnea; this notion has been supported by data released by Eli Lilly in April 2024, demonstrating tirzepatide's success in reducing the severity of sleep apnea by almost two-thirds across two studies[21].

**Cancer**

Obesity is a known major risk factor for many different types of cancer, with thirteen types of malignancies specifically identified as OACs[22]. A study that analyzed the electronic health records of patients with T2D found that those treated with GLP-1s had a significant risk reduction in ten of these thirteen cancer types[22].

More than 684,000 OACs are recorded in the US each year[23]. If we imagine a hypothetical scenario where the number of cases was reduced by just 5% as a result of a decrease in obesity, it would equate to 34,200 fewer people receiving a cancer diagnosis. With the average cited cost of cancer treatment at $150,000 per patient[24], this would mean a financial saving to the US healthcare system of more than $5 billion. And that's just one country – what could be achieved globally?





**Addiction**

Addiction can take many guises, with alcohol and drug abuse being two of the most well-known. A report issued by the World Health Organization cited 2.6 million deaths worldwide in 2019 due to alcohol, and 600,000 deaths caused by psychoactive drugs[25].

Currently, GLP-1 agents are being studied as a potential treatment for addiction because they may help reduce cravings, reduce the rewarding properties of addictive substance abuse, and help reduce relapse. Research is still ongoing, but preclinical studies showed a reduction in relapse to heroin- and fentanyl-seeking behavior in rats[26]. Other studies suggest that the effects of GLP-1s on addiction are mediated through dopamine signaling[27]. This will certainly be a very interesting space to watch.

**GLP-1 AGENTS ARE BEING STUDIED AS A POTENTIAL TREATMENT FOR ADDICTION BECAUSE THEY MAY HELP REDUCE CRAVINGS, REDUCE THE REWARDING PROPERTIES OF ADDICTIVE SUBSTANCE ABUSE, AND HELP REDUCE RELAPSE.**

## The Opportunity & Outlook for Pharma

As touched upon earlier, given the potential of these drugs to prevent and treat so many conditions – with perhaps some still to be discovered – many pharma companies are investing heavily in the development of next-generation GLP-1 agents. These include:

| Mono-agonists | Dual agonist | Triple agnonist |
|---|---|---|
| GLP-1, e.g. semaglutide | GIP/GLP, e.g. tirzepatide (GIP = gastric inhibitory polypeptides) | GLP1/GIP/GcgR (GcgR = glucagon receptor) |

Aside from the societal benefits, the financial incentives for their doing so are huge. We talked about an overall increase in earnings of the two key players in the obesity market right now, but if we focus on the earnings from their GLP-1 agents specifically, this industry-wide investment is not unexpected. Novo Nordisk reported a 55% jump in second quarter sales of Wegovy[28], while Eli Lilly's US revenue from Zepbound for Q2 2024 was $1.24 billion[29].

While these two companies are the current 'winners' with the first entrants to the obesity market, Pfizer, Amgen and Boehringer Ingelheim are hot on their heels – and more will follow. Given the numerous conditions and millions of patients who can be positively impacted by these agents, any pharma company with an effective drug in the GLP-1 class can win. And companies don't necessarily have to focus on weight-loss alone to realize success, e.g., Regeneron and Altimmune are concentrating on medications that also help preserve lean muscle mass during the GLP-1 weight loss journey. As remarked upon earlier, the global obesity drug market is predicted to reach $105 billion by 2030, and with over 335 companies currently involved in the development and application of GLP-1s - including technology vendors and start-ups[30] - there is a very big picture to get involved in.

Turning our attention back to the even bigger picture, it is ultimately society who will win. As this paper has shown, these advances have the potential to massively improve health outcomes while generating significant cost savings across the entire healthcare system. Increased access to GLP-1 therapies (including optimized manufacturing and supply processes) will reduce the strain on healthcare systems by decreasing the overall number of patients seeking treatment and lowering the cost of care. This, in turn, will allow payers and governments to provide more equitable healthcare provision to populations worldwide.





## Conclusion

**In conclusion, the age of GLP-1s is upon us. This new class of drugs is poised to revolutionize healthcare, going far beyond its initial promise of treating type 2 diabetes and obesity. Pharmaceutical companies must prioritize investment in GLP-1 research and development, as the potential to transform the treatment of a multitude of diseases, from heart failure and chronic kidney disease to Alzheimer's and cancer, is simply too great to ignore. The future of medicine is here, and it is led by the GLP-1s.**

## Ipsos Research Solutions

Ipsos' Obesity and Metabolic Centre of Expertise conducts both qualitative and quantitative custom research, ethnographic studies, social intelligence, market access and strategic advisory services to answer business questions across the obesity and metabolic product lifecycles.

Multi-client studies run by Ipsos include:

- Ipsos Global Obesity & Cardiometabolic Disease Therapy Monitor
- Ipsos Global Consumer Obesity Monitor
- Ipsos MASH Therapy Monitor
- Ipsos GLP-1 Market Sizing Monitor

Please get in touch if you would like further information about these studies, or others we are developing in this area:

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