Maybe Don't "Just Ask"

"We just asked." If you live in Canada, you've probably seen this tagline on a billboard along with the orange branding of Ozempic. But what is Ozempic? Why are these ads so vague? And, more importantly, why is marketing material for a prescription pharmaceutical popping up everywhere, from TV advertisements to posters at the Montreal airport to billboards at Toronto Blue Jays games?

Ozempic is one of three brand names for semaglutide, a glucagon-like peptide-1 receptor agonist, or GLP-1 agonist, developed by the Danish pharmaceutical company Novo Nordisk in 2012. The drug was approved for use in the United States in 2017 and in Canada in 2018. Importantly, this first approval was only for the treatment of type 2 diabetes mellitus [1]. So, how does semaglutide help diabetic patients? Like its drug class name suggests, semaglutide is a peptide (i.e., protein) drug that is designed to mimic the actions of glucagon-like peptide 1 (GLP-1), a hormone endogenously made by cells of the gastrointestinal tract and pancreas to reduce blood sugar by promoting the release of insulin by pancreatic cells in a glucose-dependant manner. In lay language, this means that GLP-1 and GLP-1-like molecules, such as semaglutide, increase our body's ability to secrete insulin into the bloodstream, which, crucially, acts to decrease blood sugar. GLP-1's, and therefore semaglutide, have many other physiological functions, such as inhibiting the release of the glucagon, slowing gastric emptying, increasing pancreatic beta cells' (the cells that secrete insulin) size and proliferation and generally decreasing one's appetite [2]. All these functions combat hyperglycemia, the main symptom and danger in type 2 diabetes. For this reason, Novo Nordisk's oral formulation of semaglutide, Rybelsus, is now a first-line treatment for type 2 diabetes [3].

Revolutionizing diabetes care is great, but that is unfortunately not what makes a drug newsworthy outside of endocrinology and metabolism journals. In 2021, following a large clinical trial looking specifically at the effects of semaglutide on weight loss in persons with and without diabetes, the FDA (and subsequently Health Canada) approved Wegovy. Results from this STEP trial were comparable to bariatric surgery, the most invasive therapy and final treatment option for obesity. This was unheard of for a drug [4]. While Wegovy has the same active ingredient, semaglutide, as Ozempic, semaglutide doses are higher in Wegovy injections (2.4 vs 1 mg). The indication also differs: while Ozempic remains a drug used to treat hyperglycemia in diabetics, Wegovy is primarily indicated for weight loss in obese and overweight individuals [5]. So, we have a new miracle drug to treat type 2 diabetes and obesity, two of the fastest-growing health problems in the world. This is all good news, right? Unfortunately, not quite.

It is no secret that pharmaceuticals can be a very lucrative business. The ethics of this are an entire field of study which is far too vast to cover in this essay. The capitalist drive, and immense time and financial investment required for drug development unfortunately means that shady marketing and publicity tactics are sometimes used to promote medications, *à la* OxyContin and Purdue Pharma. Whether this is taking place for semaglutide is up for debate. If it is, it is certainly not on the scale and severity of Purdue Pharma, which started the worldwide opioid epidemic that had killed over half a million people as of 2021 [6]. What is not up for debate, though, is the fact that I have seen more advertisements for a prescription drug in the past few months in Montreal than I ever have.

Semaglutide is positively life-changing for patients having type 2 diabetes and obese individuals, so marketing it to a greater audience should, in theory, not be an issue. In fact, you could argue that this aggressive marketing strategy is a net positive since these diseases have effectively become worldwide public health crises [7]. The problem is that Health Canada does not allow pharmaceutical companies to put out detailed advertisements about their products. Instead, they only allow the drug's name to figure on publicity material, which is why we see billboards with taglines such as "We just asked.", and not "Ozempic: life-changing antidiabetic drug" [8]. These non-specific "reminder" ads have as a side effect that patients who do not have the relevant diseases walk into their physician's office and ask about the drug. This, along with celebrities such as Elon Musk going on the record about taking Ozempic injections to lose weight and the role that weight and self-image have in people's decision making nowadays, add to the issue. The slogan "We just asked." makes it seem like you can get semaglutide injections as easily as ibuprofen. While it is still very much doctors' responsibility to do their due diligence, aggressive drug marketing of this type puts pressure on them to prescribe unneeded drugs [9]. Losing weight for cosmetic reasons is not a Health Canada- or FDA-approved indication for semaglutide, yet interest in the drug is growing exponentially amongst the general population [10]. One could argue that obesity and diabetes are also growing at an alarming rate, but the fact remains that we do not see influencers making Tik Tok's about metformin, or highway billboards advertising gliflozins, whereas semaglutide figures prominently on both. This is problematic for multiple reasons.

First, drugs are extensively studied in a specific disease population before being put on the market. This includes, of course, safety studies. In the case of semaglutide, this was done in people with type 2 diabetes and/or an overweight or obese BMI [4]. This means that researchers studied its safety in that population, and we therefore can't be sure that there aren't serious side effects for people who were not represented in these safety trials. This is an issue for all off-label drug prescriptions. Before a drug is approved, clinical researchers perform meticulous risk-benefit analyses to determine if its benefits outweigh its side effects. For example, nausea, vomiting, and fatigue are side effects of certain chemotherapeutics, but are outweighed by the elimination of malignant cells. However, if the patient does not have cancer, this risk-benefit scale suddenly tips toward the risks. The same thinking should be applied to semaglutide: should we expose someone to the admittedly low risk of pancreatitis for cosmetic weight loss that will not drastically improve their health? [11]

Second, just like anything that is manufactured, there are limits to how much semaglutide can be made. Recent surges in demand for the drug because of its weight loss capability have made it incredibly difficult for patients who rely on it for glycemic control to obtain it. Several of these patients now must go to multiple pharmacies to get their prescriptions filled, or, even worse, have had to be taken off the drug completely and switched to something that is perhaps less effective [12]. Imagine if you were told the drug you are taking to avoid potentially fatal health crises is unavailable because people who do not need it are obtaining prescriptions for it. Not to mention that off-label prescriptions are often not covered by insurance companies. Peptide drugs like Ozempic injections cost thousands of dollars per month, which raises another glaring issue: are wealthy people who do not need this drug and can afford the immense off-label cost driving the shortage?

Although the responsibility to put in place rules to avoid situations like Ozempic and OxyContin falls solely on pharmaceutical companies, regulatory agencies and physicians who write prescriptions, I hope this piece will make you reflect on drug advertising and reconsider "asking your doctor".

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