

Rethinking Health

# The Health Optimizer Therapy Disruption



WHITE PAPER  
**RethinkX**

## Who we are

RethinkX is an independent not-for-profit research organization that analyzes and forecasts technology-driven disruptions and their implications. We produce impartial, data-driven analyses that identify pivotal choices to be made by investors, policymakers, civic leaders, and other decision-makers. Our research team uses the Seba Technology Disruption Framework™ to understand the dynamics of disruption and their associated interactions among technology, business models, and market forces. We then leverage this understanding to forecast the scope, speed, and scale of a disruption's impacts across social, economic, geopolitical, environmental, and other dimensions, and their implications for market sectors, industries, and geographic regions.

## Our mission

RethinkX aims to facilitate a robust global conversation about the threats and opportunities of technology-driven disruptions, and highlight choices that could lead to a more equitable, healthy, resilient, and stable future for all of humanity.

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**Health Optimizer Therapies (HOTs) are a new category of pharmaceuticals used not just to treat or prevent disease but to continuously maintain optimal health.**

- Living well with advanced HOTs will soon be as important as eating well with nutritious food.
- GLP-1s like Ozempic are the first HOTs. Like the iPod, they are disruptive in their own right, but a much more impactful “iPhone Moment” is coming: HOTs that combine weight loss with muscle gain and other health benefits.
- The first breakout combination of health optimizer therapies will be GLP-1s for weight loss combined with myostatin/activin inhibitors for muscle gain. This is very nearly the “diet and exercise in a bottle” prize that medical science has sought for generations. Even better and more capable HOTs will follow.
- The HOT disruption is inevitable. The impacts will be profound across multiple industries, including healthcare, food and beverage, agriculture, dieting and weight loss, fitness, sports and recreation, insurance, alcohol, tobacco, and more.
- Widespread HOTs adoption will deliver enormous social, economic, environmental, and even geopolitical benefits.
- By 2040, at least 1 billion adults worldwide will be using personalized HOTs under the guidance of their doctor to optimize their health and wellbeing.
- Obesity does not affect all communities equally, and HOTs will help rectify disparities.
- HOTs will be especially valuable for middle-aged and elderly adults, who will experience weight loss, muscle gain, and other benefits as a stunningly effective anti-aging and rejuvenation therapy.
- The health and economic value of HOTs will be so large that, like vaccines and birth control, the only sensible policy choice will be for governments to make them freely and universally accessible to all adults under the guidance of their doctor.

### Call to Action

- Nations should **immediately enact policy** to guarantee affordable, universal access to HOTs for all adults under the supervision of their doctor.
- Nations should **fast-track regulatory approval** for the development of new HOTs drugs, to help ensure their enormous benefits reach the public as soon as possible.

## Introduction

We are entering a new era of healthcare based on a categorically different kind of medicine whose purpose isn't just to save us from illness, but to help us be the best version of ourselves.

Up until now, medicine has been about damage control. Whether it is aspirin for a headache, antibiotics for an infection, or chemotherapy for cancer, we reach for medicine when something has gone wrong. Even preventative medicines like vaccines for infectious disease and statins for heart disease are about avoiding disaster.

Today, the shift has finally begun in earnest toward a new medical paradigm that centers on optimization instead of illness.

RethinkX calls these new medicines *health optimizer therapies*, or HOTs.

The first new HOTs are blockbuster GLP-1 agonist drugs like semaglutide, better known by its brand names Ozempic and Wegovy. But Ozempic is just the beginning. The next generation of HOTs will trigger a multi-trillion-dollar global disruption, affecting dozens of industries across multiple sectors, driving a radical global improvement in health and wellness encompassing at least 1 billion people worldwide before 2040. The enormous impact of HOTs will reshape economies and societies in fundamental ways. These impacts will be especially pronounced for middle-aged and elderly adults, who will experience HOTs as a stunningly effective anti-aging and rejuvenation therapy.

**HOTs will transform humanity's relationship with medicine and require us to fundamentally rethink health and wellness.**

For our ancient ancestors food was energy, and every calorie was precious. Like other animals, our instincts were shaped by evolution to find calorie-dense foods like sugars, starches, fats, and even alcohol delicious. We evolved to avoid expending energy wherever possible, which is why resisting food and doing exercise require so much effort and self-discipline — our primal instincts scream at us to snack and laze around instead.

Yet here in the 21st Century, calories are plentiful and sedentary lifestyles are viable, freeing us to indulge our natural impulses to overeat and be lazy. The very mechanisms our bodies evolved to protect us amidst ancient conditions of scarcity — namely storing calories and minimizing energy use to maintain muscle — are now counterproductive to our health and wellbeing, especially as we age.

We all know we should eat less and exercise more. But life is hard, and hundreds of millions of us worldwide have struggled unsuccessfully to be our best selves. Mustering the willpower to say no to food and yes to the gym is just too difficult.

**That is all about to change.**

**The convergence of highly-effective glucagon-like peptide-1 receptor agonist drugs (GLP-1s) for fat loss, together with myostatin and activin blocking antibody drugs for muscle gain, is poised to offer something very close to one of the elusive 'holy grails' that medical science has pursued for generations: "diet and exercise in a bottle".**

**And this particular health optimizer therapy is just the beginning.**

Humanity has been through dramatic health transformations before. For millennia up through the 19th Century, the primary role of food in relation to health across all of the world's societies was as a source of sustenance to fend off starvation. Only starting in the 20th Century did we collectively begin to understand the healthiness of food in terms of nutrition, thanks to advancements in science, technology, and economic prosperity.

Today, a healthy diet means far more than just a full belly — it means consuming the optimal amount of protein, carbohydrates, fats, vitamins, minerals, fiber, and so on. And, very importantly, we now have the option to supplement our food with specific nutrients according to our personal health needs.

**What happened with nutrition in the 20th Century is now about to happen with medicine in the 21st Century.**

Drugs will no longer just be blunt instruments we use to stave off disaster, but precision tools we use as continuous supplements to optimize and maintain our health according to our individual needs.

***Optimizing well with advanced HOTs will soon become as important as eating well with nutritious foods.***

## Today's HOTs Are Just the Beginning

Today's HOTs based on current-generation GLP-1 pharmaceuticals are the subject of this report, but they represent just one example of a wider constellation of Health Optimizer Therapies.

HOTs are a broad category of disruptive new medical technologies that will recenter medicine around the proactive pursuit of human flourishing.

By targeting the fundamental biological systems that govern energy, cognition, aging, and resilience, future HOTs will transform not just medicine but how we as individuals, institutions, and societies understand the fullness of human potential.

As their adoption accelerates and their implications ripple across every sector of the economy and society, HOTs will reshape our industries, our communities, and our lives.



**The enormous impact of HOTs will reshape economies and societies in fundamental ways. These impacts will be especially pronounced for middle-aged and elderly adults, who will experience HOTs as a stunningly effective anti-aging and rejuvenation therapy.** Adam Dorr



## The HOT Disruption

- **Health Optimizer Therapies (HOTs):** a new category of pharmaceuticals used not just to treat or prevent disease but to continuously maintain optimal health.
- **GLP-1 drugs are the first HOTs, classic disruption pattern:** Four generations of GLP-1 drugs over two decades, each improving half-life, efficacy, and side effects until semaglutide crossed the threshold for explosive adoption.
- **Semaglutide and tirzepatide:** already generate over \$30B each in annual global revenues, outperforming every prior weight loss option so decisively that WeightWatchers and Jenny Craig have collapsed.
- **GLP-1 “iPod” now, “iPhone Moment” before 2030:** Current GLP-1s dominate weight loss alone; combining them with ActRIIB blockers for simultaneous fat loss and muscle gain unlocks far broader value – very nearly “diet and exercise in a bottle.”
- **Cost and price continue to fall:** ~\$5/dose production costs, massive investment in precision fermentation and continuous manufacturing, and imminent patent expiries compound an increasingly competitive pharmaceutical landscape turbocharged by AI-driven drug development.
- **AI acceleration:** Discovery timelines cut from months to minutes, in-silico modeling replacing animal testing, and a virtually limitless molecular search space guarantee successive generations of safer, more effective HOTs.
- **Architectural Big Bang Disruption:** Superior capability at lower cost from the start, with implications cascading across multiple industries – a classification that implies rapid adoption overwhelming incumbent resistance.

## The GLP-1 Story So Far: Familiar Beginnings

Semaglutide (Ozempic/Wegovy) was not the first GLP-1 drug. Like many other disruptions throughout history, this technology had decades of scientific research leading up to the launch of commercial GLP-1 products in 2005. Just like automobiles, computers or digital cameras, the first GLP-1 drugs to market were costly and didn't work well. But as their cost-capability improved, their adoption has grown, meaning we have now entered the phase of the disruption where their competitive cost is driving explosive, exponential growth.

Between 1985–1987, several teams of researchers first identified the Glucagon-like peptide-1 (GLP-1) as an incretin hormone. Its therapeutic potential was suspected early on, but constrained by its extremely short half-life in the body of less than 10 minutes.

Researcher John Eng then fortuitously discovered the peptide exendin-4 in Gila monster venom, which holds similar properties to GLP, but with greater resistance to degradation, and thus a substantially longer half-life. This led to the development of the first GLP-1 drug to reach the market, exenatide (Byetta/Bydureon/etc.), in 2005.

The second GLP-1 drug to reach the market was liraglutide (Victoza/Saxenda), in 2010, followed by the third drug, dulaglutide (Trulicity), in 2014. Semaglutide (Ozempic/Wegovy), the fourth GLP-1 drug followed in 2017. As with other disruptions throughout history, each new generation of the technology addressed the

limitations of its predecessors, improving overall capabilities and reducing unwanted adverse side effects. The disruption finally took off with semaglutide, which achieved a half-life of greater than 5 days, finally allowing for once-weekly injections.

Semaglutide was first approved for type 2 diabetes in 2017 (as Ozempic), followed by a higher-dose version for weight management in 2021 (as Wegovy), showing a remarkable 15-17% average weight loss.

At the time of writing this in 2026, oral delivery of semaglutide in a daily pill instead of a weekly injection has been approved by the US FDA, and the ease and familiarity of this delivery pathway is likely to expand the global user base of semaglutide dramatically.

GLP-1 drugs work by reducing appetite and increasing feelings of fullness, and by slowing down the movement of food through the digestive tract, which together decreases calorie intake – especially from lower consumption of fats and added sugars. Users report that GLP-1 drugs like semaglutide and tirzepatide reduce cravings and “food noise”, making impulse control much less difficult. The colloquial term “liquid willpower” is widely used to describe the empowerment that GLP-1 drugs provide.

## The Next Chapter of the Story: Multi-Agonists

Tirzepatide (Zepbound/Mounjaro) is the latest drug to reach the market, and also represents the next-generation development of the technology. Unlike prior drugs, tirzepatide is a multi-agonist peptide that acts on two hormone pathways: GLP-1 and GIP (glucose-dependent insulinotropic polypeptide). This allows for a synergistic effect that results in greater weight loss with fewer adverse side effects compared to earlier GLP-1s.

Tirzepatide has characteristics that make oral formulation much more challenging than semaglutide, and so it remains to be seen whether it will ever become available in a daily pill instead of a weekly injection. Nevertheless, it is already proving to be an enormous success, with average weight loss of 22% and a half-life of 5 days.

At least 10 other new drugs are in known development as of early 2026, and the actual number including undisclosed development projects is almost certainly much higher. Some of these drugs use different molecule types (small molecules versus peptides, for example) and target new hormonal pathways. A number of them are multi-agonist.

Retatrutide is perhaps the most prominent example of an extremely promising multi-agonist in development (by Eli Lilly, maker of tirzepatide). Retatrutide operates on three hormone pathways (a ‘triple agonist’ that acts on GLP-1, GIP, and glucagon), with average weight loss reported up to over 28% and a 6-day half-life.

Within 15 years, it is reasonable to expect extremely effective HOTs will be widely available.

## The iPod Moment for HOTs

As of early 2026, semaglutide is a blockbuster GLP-1 drug with global revenues of over \$30 billion. Tirzepatide is on track to similar blockbuster financial success, with over \$30 billion in global revenues in 2025 and substantial growth anticipated for 2026. The obvious key to these drugs’ success is that they vastly outperform all prior weight loss treatment options in every way. They just work.

This is analogous to the step-change that portable “MP3” digital music players like Apple’s iPod represented over traditional music media: vinyl records, cassette tapes, and compact discs (CDs).

But where these drugs make the leap beyond diabetes and weight loss into the new category of health optimizer therapies, or HOTs, is in their unanticipated beneficial side effects. Users of semaglutide and tirzepatide see associated improvements in at least eleven other organs, tissues, and body systems, as well as in key health biomarkers including blood pressure, blood sugar, lipid profiles, and systemic inflammation.

In addition, studies have begun to confirm what has been widely reported anecdotally by users for several years: that semaglutide demonstrates significant benefits for alcohol and nicotine consumption and cessation, helping people smoke and drink less or quit altogether if they are suffering from addiction and/or substance abuse disorders. Tirzepatide studies are expected to confirm the same extraordinary benefits. Research is therefore now actively exploring the potential of these drugs to treat other addictive and compulsive medical issues, including not only smoking and drinking but also opioid and other substance use, gambling, compulsive shopping, and even doom-scrolling.

Like the iPod and other portable MP3 digital music players, the new weight loss technology represents an overwhelmingly competitive value proposition which all but guarantees a ‘Big Bang’ disruption of the weight loss industry. Indeed, we already see the disruption unfolding across the traditional dieting industry, with former titans in the US market such as WeightWatchers and Jenny Craig filing for bankruptcy in the face of impossibly formidable competition from semaglutide and tirzepatide.

## The iPhone Moment is Coming: The Next HOT Thing

Weight loss by itself is enormously valuable, just as portable digital music players were enormously valuable. But far greater value lies in combinations of advanced new preventative care drugs, just as smartphones like the iPhone offered far greater value beyond music alone.

**The first HOT combo will be weight loss combined with muscle gain.**

**This will be the ‘iPhone Moment’ for HOTs, and it is very likely to arrive before 2030 — possibly as early as 2028.**

A substantial drawback of GLP-1 drugs up to now has been that they also cause loss of lean muscle mass. Up to 40% of weight reduction when using semaglutide comes from lean mass, including muscle, rather than fat. For tirzepatide the number is up to 25%, and from retatrutide it is up to 38%. It is important to note that these data are still limited and it is not yet known whether any of this effect is partly caused by the drugs themselves, or whether it is entirely a function of calorie restriction which would also occur with any weight loss diet.

A potential solution to muscle loss has now emerged which not only mitigates this downside of GLP-1s but also offers extraordinary additional therapeutic potential: blocking the ActRIIB receptor.

ActRIIB is like a cellular gatekeeper that signals to the genes responsible for muscle growth and breakdown. Specific proteins such as myostatin (also known as Growth Differentiation Factor 8, or GDF-8), Activin A, and Activin B are like keys that fit into the ActRIIB lock, binding the receptor.

Our bodies evolved when food was scarce and every calorie counted, and that is why our muscles atrophy unless we use them. Genetic mutations that result in permanent ActRIIB-related insensitivity are occasionally seen in animals like dogs and cattle, but in the wild these animals would be unable to find enough food to support their hugely muscular bodies, and so these genetic mutations were not evolutionarily preserved by natural selection. We even see this mutation in a small number of people.

New monoclonal antibody drugs are able to temporarily and partially inhibit ActRIIB by selectively blocking myostatin and/or activin (A/B). The result is growth in muscle size and strength, even without exercise. Unlike the genetic conditions which result in extreme and uncontrolled muscle hypertrophy, these new drugs can be used temporarily in precise dosages to deliver a controlled amount of muscle growth.

Myostatin blockers appear to have the most promising combination of muscle gain with minimum adverse effects at the moment, but efficacy and safety are both likely to improve as AI-powered drug discovery and development accelerates.

Only one drug – apitegromab – has completed Phase 3 trials, and it was granted FDA priority review in September 2025 for its remarkable potential. At the time of this writing in early 2026, it expected to reach the market in mid-2026. But other drugs also show extraordinary promise in Phase 2 human trials, and still more are emerging with exciting results in animal studies.

These drugs were originally explored for treating diseases like spinal muscular atrophy, just as GLP-1s were originally explored for treating type 2 diabetes. But now, just like GLP-1s, they promise to revolutionize health optimization as well. The results of Phase 2 human trials have been extremely promising.

When GLP-1s are combined with myostatin/activin blockers, the result is simultaneous weight loss and muscle gain.

**This is very nearly the “diet and exercise in a bottle” that medical science has long sought after.**

Safety must still be firmly established, of course, but early news out of multiple major labs suggests these combination HOTs will indeed prove safe, with tolerable or minimal adverse side effects. In the meantime, it is notable that large numbers of individuals in the bodybuilding and biohacking communities worldwide are already accessing these next-generation GLP-1s and myostatin/activin blockers on gray and black markets. Tolerance for risk in these communities is notoriously high, and so caution is warranted in interpreting alleged outcomes, but early anecdotal reports suggest enormous enthusiasm with respect to both safety and tolerability of side effects compared to older fat-loss drugs and muscle-building drugs.

## 21st Century Medicine

High-dose HOTs are now helping to treat severe obesity and type 2 diabetes in at least 20 million people within the United States alone, and worldwide the number is continuing to grow rapidly. But the full potential of HOTs lies in optimizing healthfulness, not just preventing and treating disease.

Drugs which optimize weight and muscle health will be joined by others that optimize bone, cardiovascular, immunological, and skin health as well – to name just a few.

**By 2040, personalized low-dose HOTs will help at least 1 billion adults worldwide maintain physical and mental health.**

It's not yet clear whether HOTs will involve a constant maintenance dose or periodic cycling, nor whether daily pills or infrequent weekly or even monthly injections will be most widely preferred. Regardless, within 15 years, personalized HOTs are likely to become a more routine part of a healthy lifestyle than vitamin supplements are today.

## Getting from Here to There: AI Acceleration of Drug Discovery and Development

The traditional pharmaceutical development pipeline entails target identification, lead discovery, optimization, preclinical testing, and clinical trials. Taken together, this can take more than ten years and \$1 billion in investment. AI is compressing every stage of this process while improving success rates.

Gubra's streaMLine platform, for example, reduces initial peptide discovery from 3-4 months to minutes. Similarly, the BioHive-2 supercomputer used by Recursion Pharmaceuticals processes over two million experiments weekly, exploring chemical space many orders of magnitude faster than is possible through traditional methods. These are just two prominent examples among many others in a thriving new AI-powered drug discovery and development industry that is using machine learning algorithms trained on large and growing databases to model potential new drugs "in-silico" (via computer simulation) before physical synthesis and evaluation.

The US FDA's April 2025 ruling phasing out mandatory animal testing for many drug types signals regulatory recognition that in-silico methods can predict safety and efficacy with increasing accuracy. Digital twins and computational models of biology, physiology, and biochemistry are helping enable researchers to simulate thousands of dosing regimens on diverse patient populations before ever recruiting a single trial participant. This not only accelerates initial development but also improves trial design, increasing safety and the probability of success while reducing costs.

## Peptide Manufacturing is Scaling Massively

Cost does not equal price. Ozempic and Wegovy prices in US markets in their earlier years often exceeded \$1,000 per month. But Yale researchers showed that manufacturing costs of peptides themselves can be as low as \$0.29 per dose, with the injection pen making up the majority of the roughly \$5 total cost per dose.

These low costs are still falling as production scales. Novo Nordisk, for example, invested \$8 billion into yeast-based precision fermentation (PF) facilities in Denmark for production of semaglutide precursors at a scale and consistency that is otherwise impossible through traditional chemical synthesis methods alone. Eli Lilly has invested tens of billions of dollars in new production since 2020, including the development of a continuous manufacturing platform in Ireland that represents another leap forward in scale. Traditional batch manufacturing requires stopping between steps for purification and quality control, whereas continuous manufacturing maintains constant flow of outputs, reducing production time from weeks to days while improving consistency and decreasing waste.

As in other disruptions, the quantity of investment is itself a signal of industry confidence (although not a guarantee of success) in these new products and the technologies behind them. When the patent protecting semaglutide expires this year (2026) in China, India, Brazil, and Canada, manufacturers are likely to respond to massive global demand with low-cost generic alternatives to branded semaglutide (Ozempic and Wegovy), creating conditions for price collapse similar to what occurred with statins, where generic competition drove prices down by 95% within five years of patent expiration.

## On the Horizon: Oral Formulations and Small-Molecules

A sizable fraction of the public are adverse to needles, and so beyond just convenience and familiarity, the pill format of drug delivery will further unlock the total addressable market of HOT users. The shift from injectable to oral formulations therefore marks a key technological advance, and oral semaglutide for weight loss in the form of a daily pill has been approved for use starting in January 2026 under Novo Nordisk's existing brand name Wegovy.

A key challenge of oral delivery is to protect large peptide molecules from stomach acid and ensure consistent intestinal absorption and dosing. Moreover, peptide size and structure varies greatly, and not all are equally amenable to oral formulation. (Tirzepatide, for example, appears to be much more challenging for oral formulation than semaglutide). Other GLP-1 approaches are therefore being pursued as well, chief among which are small-molecule formulations such as Orforglipron made by Eli Lilly.

## Virtually Endless Possibilities Means Even Better HOTs in the Future

The number of possible small-molecules, peptides, and antibodies is astronomical — certainly greater than  $10^{60}$ , from a purely combinatorial perspective. Although there may be constraints that reduce the actual number in practice, the accessible possibility space is nevertheless so large that we are virtually certain to discover even safer and more effective GLP-1s, myostatin/activin blockers, and many other drugs in the years ahead using powerful AI-driven search methods.

## The HOT Disruption is Inevitable

RethinkX utilizes the Seba Technology Disruption Framework (STDF) to understand disruption dynamics. Viewing HOTs through the STDF lens reveals why they represent not just another incremental advance in dieting or exercise technology, but a fundamental disruption that will transform multiple industries and reshape societies and economies worldwide.

According to the STDF classification schema, HOTs are an Architectural Big Bang disruption. Architectural disruptions have sweeping implications beyond just one industry or sector alone, and Big Bang disruptions arrive with superior capability at a lower cost than existing products and services right out of the gate.

The classification as an Architectural Big Bang Disruption — namely a disruption with superior capabilities delivered at unbeatable cost right from the start whose implications are broader than one market or industry alone — implies rapid adoption that will quickly overwhelm any resistance from incumbents.

Assuming GLP-1s and myostatin/activin blockers prove as safe and effective as current trials and findings suggest, we expect widespread global deployment of this first generation of HOTs — with all of their enormous disruptive implications — to unfold before the mid-2030s, with rapid uptake of later-generation HOTs continuing on an ongoing basis thereafter.

## Industry Implications

- **Healthcare** — Over \$2.3T of U.S. healthcare spending is tied to obesity-related conditions, and hospitals built around managing its chronic consequences will face demand collapse as the system shifts away from crisis management.
- **Dieting & Weight Loss** — HOTs have already disrupted the traditional dieting industry (WeightWatchers bankrupt, Jenny Craig gone), forcing a full pivot to HOT-centered business models.
- **Fitness, Sports & Recreation** — HOTs will shift the fitness industry from weight loss toward capability and performance, while outdoor recreation and sporting goods see strong growth from a leaner, more active population.
- **Food & Beverage** — A plausible one-third decline in junk food demand due to widespread HOT adoption represents \$300B in annual revenue loss, hitting high-margin categories like soft drinks, alcohol, and desserts hardest.
- **Agriculture** — Grain, sugar, and dairy face the largest demand declines, with corn farming and the high-fructose corn syrup industry particularly exposed.
- **Potentially Addictive Products** — All industries supplying addictive products (alcohol, tobacco, gambling, and illicit drugs, collectively \$800B+ in U.S. revenues) face structural decline, especially alcohol, whose top 10% of drinkers account for 60% of sales.
- **Insurance** — A healthier population will reduce health and disability claims, with near-term profit gains likely giving way to lower premiums and overall revenue contraction.



Scan the QR code above to explore the industry implications, or click [here](#)

## Healthcare Industries

Any savings in direct medical costs realized from the widespread adoption of HOTs discussed above will translate into reduced demand for healthcare industry goods and services. If HOTs make a large fraction of a population healthier, there will logically be less demand for healthcare products and services — all else equal (i.e. namely, setting aside concurrent impacts from the disruptive forces of artificial intelligence and robotics).

In countries like the United States with a large private healthcare sector where medical care providers including hospitals are often structured as financially self-sustaining enterprises (whether for-profit or nonprofit), the large reduction in demand for medical treatments caused by the HOTs disruption could therefore threaten financial viability and trigger workforce reductions.

Notable exceptions to this overall trend of decline will be cosmetic surgery (for addressing “Ozempic Face” and other consequences of dramatic weight loss) and sports medicine (associated with a large increase in the number of active adults).

But beyond the tectonic shifts in healthcare demand, HOTs could trigger a broad transformation of the healthcare system itself in many countries, away from centering on medical crisis management to focusing primarily on preventative medicine and health optimization.

## Industry Scope

- Total U.S. healthcare spending: **\$4.9 trillion annually (18% of GDP)**
- Over **\$2.3 trillion** of these expenditures are directed toward health conditions partly or wholly driven by metabolic risk from unhealthy diet, lifestyle, and obesity
  - Type 2 diabetes: **over \$305 billion**
  - Cardiovascular disease: **over \$415 billion**
  - Cancer (obesity-linked): **over \$35 billion**
  - Osteoarthritis and joint disease: **over \$140 billion**
  - Obstructive sleep apnea: **up to \$95 billion**
  - Alzheimer's and dementias: **over \$380 billion**
  - Anxiety and depression: **over \$75 billion**
  - Substance use disorders: **over \$8 billion direct; over \$350 billion including co-morbidities**
  - Late-life morbidity (including frailty): **over \$1 trillion**
  - Bariatric surgery: **nearly \$1 billion**
  - Cosmetic surgery: **over \$21 billion**

## Facing Decline

- **Drugs:** Type 2 diabetes medications, diabetic complications medications, osteoarthritis and pain medications, sleep apnea medications, anxiety and depression medications, addiction treatment medications
- **Healthcare Products:** Diabetes management products, diabetic complication products, orthopedic products, sleep apnea products, mobility and assistive products, bariatric products
- **Healthcare Services:** Surgical services, diagnostic services, diabetes complications services, therapeutic services, addiction and mental health services, oncology services, long-term and home care services
- **Facilities:** Hospital units and centers, specialty clinics (e.g. rehabilitation), addiction treatment facilities
- **Occupations:** Physicians and surgeons, nursing and clinical staff, allied health professionals, support and administrative staff, industry workforce

## Facing Growth

- HOT developers and manufacturers
- Telehealth platforms specializing in HOT-based health management
- Cosmetic surgery for HOT-related procedures
- HOT-centered addiction treatment programs
- Preventive medicine, longevity clinics, and healthspan optimization services that integrate HOT management

- Sports medicine and physical therapy for performance optimization (rather than disease management)
- Mental health services addressing adjustment to rapid physical transformation and relationship changes driven by HOTs

## Facing Uncertainty

- **Mental health goods and services:** Demand may decrease, based on 64% of users reporting benefits. Demand may increase, based on some studies showing increased depression and anxiety risk in vulnerable groups, and anhedonia reported by some users.
- **Alzheimer's and dementia goods and services:** Demand may decrease, based on research and animal results suggesting protective and preventative effects from obesity reduction in non-Alzheimer's dementias. Demand may be unaffected, based on the recent EVOKE trial which showed disappointing results for Alzheimer's.
- **Oncology (cancer) goods and services:** Demand may decrease in the short term from reduction of obesity-linked cancer occurrence. Demand may be unaffected in the longer term if HOTs users live longer and cancers are merely postponed until later in life.
- **Addiction and substance use treatment goods and services:** Demand may decrease from reduction in addictive behaviors among HOTs users. Demand may be unaffected if goods and services providers pivot to incorporate HOTs into addiction prevention and treatment.

## Dieting and Weight Loss Industries

Prior to the first blockbuster GLP-1s, dieting and weight loss products and services were high-cost and low-efficacy. Utilizing these products was unpleasant for most users. Even for initially successful users, relapse rates were high. These factors together contrived to support industries that could sell a diverse range of products and services simultaneously and shift its offerings over time (“the latest fad diet”).

The emergence of a technology that actually works spells comprehensive disruption for the traditional dieting and weight loss industries.

As a whole, these industries will need to either pivot to HOT-based business models, or collapse.

### Industry Scope

- The traditional dieting and weight loss industry represented about \$75 billion in the United States alone, prior to the takeoff of the first blockbuster GLP-1, semaglutide. This includes diet programs, products, meal replacements, and supplements.
- At its peak, more than 275,000 bariatric surgeries were performed in the United States each year.
- Bariatric surgery market size estimates for the United States vary widely, from around \$1 billion to over \$3 billion.

### Facing Decline

- Traditional weight loss products and services will be disrupted and face obsolescence and collapse. Meal planning and replacement products, dieting supplements, and coaching services cannot compete with HOTs that are vastly more effective.

- Weight Watchers, after 62 years of operation, fell from a peak market capitalization of over \$6.5 billion at \$103 per share in June 2018, to near-zero in April of 2025 when it filed for bankruptcy and restructured.
- Weight loss programs will need to pivot into HOT-based programs in order to survive.
- Bariatric surgery will be disrupted and face obsolescence and collapse. Surgery is costly and risky. Latest-generation multi-agonist HOTs (namely, retatrutide) achieves comparable weight loss without surgery or hospitalization, and is easily adjustable (dosing) and reversible (cessation).
- Non-HOT-based doctor-led medical weight loss programs will be disrupted and face obsolescence and collapse. Medical weight loss programs that previously focused on psychology/behavior-based diet and lifestyle changes such as the FAB (Food, Activity, Behavior) approach have already pivoted into HOT-based programs, and will continue to do so until the transformation is complete.

## Facing Growth

- New business models centered on HOT-integrated health, weight management, fitness, and wellness which combine medication with coaching and support are already growing rapidly. Examples include Calibrate, Vida Health, Noom Med, Found, Equinox & One Medical, and WeightWatchers Clinic.
- Telehealth platforms specializing in HOT prescribing and management are now thriving. Examples include Ro, Mochi Health, PlushCare, and Hims & Hers, and LifeMD.

## Facing Uncertainty

- Weight and related health coaching services face both upward and downward (push and pull) demand pressures from HOTs. Demand may decrease if HOT users obtain the weight loss and health results they seek without the need for these services. Demand may increase if use of HOTs expands the market by bringing people who had previously given up on dieting and weight loss as hopeless, and also by helping with maintenance-focused use of HOTs (i.e. low-dose and periodic/intermittent utilization). Although weight-loss coaching becomes obsolete, performance and skill coaching will become more valuable as a larger population pursues physical activities.

## Fitness, Sports, and Recreation Industries

Prior to the first blockbuster GLP-1s, people used exercise to change their body composition in order to lose fat, increase capability, enhance appearance, and improve health. While HOTs cannot yet optimize every aspect of body composition (they do not yet affect aerobic fitness, endurance, or flexibility, for example), they will make it vastly easier to “lose weight” (meaning lose fat) and achieve “big gains” (meaning increase muscle size and strength), which are two key motivations for dieting and exercising.

This in turn means that HOT users will have far less need to utilize fitness products and services.

However, HOT users whose changes in body composition have made them more physically capable and healthy will be more able (and thus more likely) to utilize sports and recreation products and services.

This is likely to be particularly pronounced in older adults who experience the benefits of HOTs as a rejuvenation, and who therefore return to physical activities they previously enjoyed.

As a whole, demand will shift away from products and services used to “get fit” towards those used by “fit people”.

## Industry Scope

- Total fitness, sports, and recreation industries in the United States: **nearly \$1 trillion**
- Gyms and health clubs: **\$33 billion**
- Personal training and coaching: **\$12 billion**
- Fitness equipment (home and commercial): **\$5 billion**
- Fitness trackers/wearables: **\$20 billion**
- Fitness apps: **\$3 billion**
- Activewear/athleisure products: **\$126 billion**
- Sporting goods: **\$66 billion**
- Sportswear (apparel): **\$90 billion**
- Outdoor recreation (includes RVs and camping): **\$639 billion**

## Facing Decline

- Subsets of gyms and health clubs focused on weight loss or muscle gain
- Subsets of fitness equipment such as treadmills, stationary bikes, and other “cardio” machines marketed for calorie burning and weight loss, and free-weights and resistance machines marketed for muscle building
- Subsets of fitness trackers, wearables, and apps focused on weight loss
- Subsets of personal training and coaching focused on weight loss

## Facing Growth

- Gyms and health clubs focusing on fitness, performance, sports, and socializing
- Activewear/athleisure products
- Sporting goods
- Sportswear (apparel)
- Outdoor recreation (includes hunting, fishing, boating, RVs, camping, motorcycling, ATV-ing, snow activities, equestrian)
- Products and services utilized by older adults will see particularly strong growth
- Subsets of personal training and coaching focused on skill, aerobic fitness, endurance, flexibility

## Facing Uncertainty

- Overall gym and health club memberships; overall fitness equipment and services; overall fitness trackers, wearables, and apps. Demand may decrease for the use of these facilities for weight loss and muscle gain. Demand may increase (especially a near-term spike to a new baseline) from more active, capable, and self-confident adults.

## Food and Beverage Industries

The food industry faces declines on a scale not seen in over 80 years since rationing during World War II. Widespread HOT utilization by adults will reduce overall calorie consumption, which will directly translate into a decrease in overall food and beverage demand and sales.

More data is needed before we can know with confidence precisely how HOT users will change their consumption patterns, but the overall picture is clear: semaglutide and tirzepatide users report a disproportionately large fraction of calorie reduction from unhealthy foods and beverages. This means HOT users won't just eat less, they will eat differently.

We should therefore expect declines to be starkest in the "junk food" and "indulgence" categories, precisely because GLP-1s modulate the brain's reward circuitry, diminishing the "food noise" cravings that drive our most impulsive and hedonistic eating choices.

Today, American adults spend over \$900 billion, or \$3,400 per adult, on junk food purchases each year. This translates into nearly 1,500 calories of junk food purchased per day, of which about 1,000 are actually consumed. Available data represent averages, and so for obese Americans the numbers per person are significantly higher.

It is plausible that widespread HOT adoption could lead to an average reduction of 500 calories of junk food purchased per person, which would represent one-third of all junk food demand in the United States.

Importantly, not all of junk food calories deliver the same sales revenue for their sellers. Some of the highest-margin food and beverage items sold by restaurants, for example, will be the most-likely to be disrupted, such as soft drinks, desserts, and alcoholic beverages. This means a decrease in overall junk food calories is likely to translate into a disproportionately greater decline in sales revenues for some segments of the food and beverage industry.

Alcoholic beverages in particular face additional pressures because approximately two-thirds of GLP-1 users report reduced alcohol consumption, and the top 10% of drinkers who consume 60% of all alcohol sold are likely to be disproportionately affected. Moreover, any decrease in demand from widespread adoption of HOTS will compound the existing generational trend of declining alcohol consumption among younger adults.

### Industry Scope

- Total food and beverage industries in the United States: **\$2.5 trillion**
- Food away from Home (FAFH) segments: **over \$1.5 trillion**
  - Full-Service Restaurants: **over \$450 billion**
  - Quick-Service Restaurants (fast food): **over \$380 billion**
  - Drinking Places (alcoholic beverages): **Approximately \$30–35 billion**
  - Other FAFH (schools, colleges, hospitals, prisons, military bases, vending): **over \$400 billion**
- Food at Home (FAH) segments: **over \$1 trillion**
  - Meat, Poultry, & Eggs: **\$222 Billion**
  - Fruits & Vegetables: **\$196 Billion**

- Cereals & Bakery Products: **\$137 Billion**
- Dairy Products: **\$111 Billion**
- Nonalcoholic Beverages: **\$132 Billion**
- Sugar & Sweets (Confectionery): **\$42 Billion**
- Other Foods (Snacks, Condiments): **\$217 Billion**
- Alcoholic beverages: at least **\$270 billion**

## Facing Decline

- All Food Away From Home (FAFH) segments
- All Food At Home (FAH) segments
- Pronounced declines in: Fast food items (e.g. burgers, French fries, pizza, donuts); Sweetened beverages (e.g. soft drinks, fruit juices); Confectionary (e.g. candy, sweets, chocolate); Desserts (e.g. ice cream); Alcoholic beverages; Full-service restaurants whose business models depend on high-margin alcohol and soft drink sales

## Facing Growth

N/A

## Facing Uncertainty

- Health foods, organic foods, whole foods (includes meat, poultry, eggs, fruits, vegetables, milk, and cheese). Demand may decrease from reduced overall calorie consumption. Demand may increase from more health-conscious and physically active adults.

## Agriculture Industries

Agriculture is logically upstream of the food and beverage industries, and so the overall declines in food and beverage demand will translate directly into overall declines in demand for agricultural products and services as well. The details are highly uncertain and the changes in demand will be unevenly distributed, with some products and services being impacted far more than others. Animal agriculture may be less affected (other things being equal) if HOT users maintain or even increase protein intake. Corn farming, however, may see a pronounced decline if HOT users slash their consumption of food and beverages containing high fructose corn syrup.

Irrespective of the details, which remain very difficult to predict, overall agricultural sector decline is inevitable because of the brute fact that HOT users simply eat less.

## Industry Scope

- Total agricultural output: **over \$482 billion** (excludes non-food crops such as flowers/horticulture, cotton, hay)
  - Animal agriculture: **nearly \$300 billion**

- Grains and oilseeds: **\$120 billion**
- Specialty crops (fruits, nuts): **\$32 billion**
- Vegetables and melons: **\$23 billion**
- Sugar (beets, cane, maple): **\$9 billion**

## Facing Decline

- Grains (corn/maize, wheat, rice)
- Sugar (beets, cane, maple)
- Dairy

## Facing Growth

N/A

## Facing Uncertainty

- Meat (including aquaculture), oilseeds, specialty crops (fruits, nuts), vegetables and melons

## Potentially Addictive and/or Compulsive Products and Services Industries

By modulating dopamine signaling in the brain's reward pathways, GLP-1s appear to moderate addictive and compulsive behaviors. User reports and anecdotes about these were so striking that research has begun to explore the possibility of using GLP-1s in treatment of alcohol abuse disorder, smoking cessation, and other substance use disorders. Widespread adoption of HOTs therefore has implications for all industries that supply potentially addictive products and services as well as those which supply treatment and sobriety products and services.

Potentially addictive products and services industries comprise a nontrivial fraction of the U.S. economy, with total revenues approaching \$1 trillion annually (excluding addictive foods). Addiction treatment is itself a sizable industry as well, with much of the funding coming from government sources.

## Industry Scope

- Total: **over \$800 billion**
- Alcoholic beverages: **at least \$260 billion**
- Tobacco and nicotine products: **\$115 billion**
- Gambling: **over \$70 billion**
- Digital gaming: **over \$55 billion**
- Pornography: **over \$10 billion**
- Illicit drugs: **at least \$150 billion**
- Social media: **over \$85 billion**
- Addiction treatment: **over \$55 billion**

## Facing Decline

With the possible exception of social media, all of these face substantial decline in all aspects: products, services, facilities, and occupations.

## Facing Uncertainty

- Social media: Demand may decrease from less impulsive use (e.g. “doom scrolling”) and growing awareness of harms, especially to children. Demand may increase from continued industry growth based on separate advancements in and adoption of AI.

## Insurance Industries

Among a healthier population, the demand for health insurance claims will logically decline — all else equal. The basic logic is that claims decline, causing a short-term profit spike in regions without mandated “medical loss ratios” (i.e. caps on profit margins), but over time premiums reprice downward which shrinks revenues. However, in some regions, including parts of the United States, health insurers are legally obligated to spend a minimum fraction of premium revenue (such as 80%) on medical care, effectively capping their profit margins. In these regions there will be no initial windfall because any earnings beyond cap must be rebated.

It is important to keep in mind, however, that the assumption of all else equal is unlikely to hold. For example, the price of medical care billed to insurance companies by healthcare providers such as hospitals and clinics is likely to increase because those healthcare industries will also be responding to falling demand for their products and services.

For disability insurance, the same basic logic holds, but largely without the restrictions on spending and profit margins. As a result, near-term profits are more likely, but the longer-term outlook is still decline.

For life insurance, the picture is more complicated. In the United States, the life insurance industry provides two broad categories of products: life insurance (which pays subscribers when they pass away), and annuities (which pays subscribers while they are alive). For the first category, the extended longevity of HQTs users means insurers will collect premiums for longer (and thus more total revenue) before paying out the fixed end-of-life benefit. For annuities, however, it is the reverse: the improved longevity of subscribers will mean insurers will have to make payments for longer (and thus face higher costs).

## Industry Scope

- Total: **\$2.375 trillion**
  - Private health insurance: **over \$1.6 trillion in private premiums revenue**
  - Private disability insurance: **\$50 billion**
  - Private life insurance: **\$725 billion**

## Facing Decline

- Health insurance

## Facing Uncertainty

- Disability insurance: Likely increased profitability in the near-term, but facing long term revenue decline.
- Life insurance: Longer life spans increase revenues from premiums, but also increase costs from annuities.

## Other Industries

A number of other industries will see specific segments affected by the widespread HOT adoption, even if the overall implications for that industry remain uncertain. For example, the plus-size fashion market segment will face major declines, but the overall impact on the fashion industry as a whole is unclear. Other examples include dating services, legal services, travel services, and the entertainment industry.

## Health Implications

- Obesity is not just a weight problem, it is a root cause of type 2 diabetes, cardiovascular disease, cancer, cognitive decline, sleep apnea, mental illness, and disability. An effective treatment for obesity is therefore an effective treatment for all of them.
- The U.S. economy loses at least \$573 billion annually to obesity in medical costs and lost productivity: over \$6,000 per obese adult per year.
- GLP-1s are already 80–90% effective at preventing type 2 diabetes (\$305B in annual U.S. medical costs), deliver a 20% reduction in major cardiovascular events, cut sleep apnea events by over 50%, and will reduce the 40% of cancers linked to obesity.
- Two-thirds of GLP-1 users report reduced alcohol consumption, and early evidence suggests GLP-1s may simultaneously reduce gambling addiction, nicotine dependence, and opioid use disorder by modulating the brain's shared reward pathways.
- U.S. life expectancy plateaued after 2014, partly due to rising obesity. HOTs could reverse that trend, extending healthy lifespan by several years and compressing the period of late-life frailty.

## Obesity

Over 40% of American adults are obese, and rates have risen so dramatically around the world that obesity has been called a global epidemic.

Obesity is a root cause of type 2 diabetes, cardiovascular disease, cancer, cognitive decline, joint degeneration, mental illness, physical disability, and more. So it is not much of an exaggeration to say that GLP-1s are “miracle drugs”, for the simple fact that they are the first extremely effective and safe pharmacological treatment for obesity – and thus for all of its many downstream diseases and health problems as well.

Today, GLP-1s are the most expensive and least effective they will ever be. Safety, efficacy, and cost of GLP-1s will only continue to improve in the future. And when they are combined with other safe and effective medications as HOTs, the overall health benefits will be transformative. As a result, global demand among adults for HOTs will be staggering – far greater than any other medicine in history.

## Type 2 Diabetes

- Affects over 34 million Americans and with an annual direct medical cost burden of over \$305 billion.
- GLP-1s are already 80-90% effective at prevention.
- GLP-1s are already 50-60% effective at treatment for those who already have type 2 diabetes.
- The mechanisms are straightforward: reduced body fat decreases insulin resistance; reduced sugar consumption improves insulin sensitivity and blood sugar stability; GLP-1s directly enhance insulin secretion and sensitivity.

## Cardiovascular (Heart) Disease

- Affects nearly half of American adults, over 125 million people, and with an annual direct medical cost burden of over \$415 billion.
- GLP-1 users already see a 20% reduction in major adverse cardiovascular events.
- GLP-1 users already see a 40% reduction in heart failure progression.
- Other cardiovascular benefits from weight loss include blood pressure reduction (i.e. prevention and treatment of hypertension), improved lipid profiles, decreased systemic inflammation driving atherosclerosis, and overall reduction of cardiovascular mortality and morbidity.
- Benefits start to emerge within weeks of treatment.

## Cancer

- Roughly 40% of all cancer diagnoses in the United States are obesity-linked, and obesity is recognized as a driver of at least 13 types of cancer, including breast, colon, kidney, and pancreatic. These obesity-linked cancers carry an annual direct medical cost burden of over \$35 billion.
- GLP-1s have already been shown to reduce cancer risk, and their impacts on cancer rates should at least match any obesity rate reductions driven by HOT use (and possibly exceed them, through other mechanisms like systemic inflammation reduction).
- GLP-1s may indirectly reduce cancer risks associated with alcohol, smoking, and other substance use and addiction.

- There are over 715,000 obesity-linked cancer cases each year in the United States. Of these, about 495,000 affect women, and about 220,000 affect men.
- More than 90% of obesity-linked cancers affect people aged 50 or older.
- Excess body fat increases cancer risk via chronic inflammation, elevated insulin levels, and hormonal disruption — all of which are improved by GLP-1s.

## Osteoarthritis and Joint Disease

- Affects tens of millions of Americans, at an annual direct medical cost of over \$140 billion.
- GLP-1s have already shown benefits in early research data. The STEP 9 study showed striking results for patients taking GLP-1s (semaglutide), who reported pain reduction, functional gains, and a “cure” effect (i.e. relief was so profound that some participants no longer met the clinical criteria for joint disease by the end of the study).
- Obesity is a primary driver of knee and hip degeneration, both because excess weight creates additional force on the joints and because obesity causes systemic inflammation that leads to joint deterioration.
- Osteoarthritis and joint disease limit mobility and physical activity, creating a reinforcing feedback loop with obesity that traps millions in ill-health.
- Approximately 1.5 million joint replacement surgeries are performed annually in the United States.

## Obstructive Sleep Apnea

- Affects tens of millions of Americans, with reputable sources in the peer-reviewed literature claiming annual direct medical costs as high as \$95 billion.
- GLP-1s have shown over 50% reduction in apnea events for GLP-1 users according to recent studies, with over 40% achieving complete disease resolution.
- Obstructive sleep apnea represents the overwhelming majority of sleep disorders, with almost 6 million Americans officially diagnosed. But, the true number is likely closer to 30 million because 80% or more of cases go undiagnosed.
- Fatigue from inadequate sleep contributes directly to motor vehicle accidents and workplace accidents, which pose enormous additional social and economic costs.
- Obesity is the primary driver of obstructive sleep apnea, and so the reduction of fat around the upper airway reduces or eliminates obstruction by fat deposits that contribute to the disease.
- The standard treatment of wearing a CPAP machine during sleep is effective, but poorly tolerated, with almost half of patients stopping use of their devices within one year.

## Alzheimer’s Disease and Other Dementias

- Affects over 7 million Americans, with total medical and long-term care costs of over \$380 billion annually.
- Alzheimer’s disease is estimated to account for 60–80% of dementias.

- Early animal studies suggested GLP-1s might prevent dementia and/or slow its progression, but the EVOKE trial showed disappointing results, finding no such benefit in humans.
- Obesity has been linked to non-Alzheimer's dementias, and may accelerate decline in Alzheimer's patients. Possible mechanisms of action include high blood pressure, vascular damage, metabolic stress, and amyloid buildup.
- This is an area where the science is still evolving, but it is likely that a large reduction in obesity rates would offer some benefits in terms of preventing and/or slowing dementias.

## Anxiety and Depression

- Affects tens of millions of Americans, with annual direct medical costs of roughly \$44 billion and \$31 billion respectively.
- When additional knock-on medical costs of anxiety and depression are included (such as increased ER visits, increased medications for co-morbidities, and so on) the total annual medical costs balloon to hundreds of billions of dollars.
- The majority of HOTS users report improvements in mental health. This is an unsurprising result of improved healthfulness and generally "looking and feeling better".
- Some users of GLP-1s report anhedonia (reduced ability to experience pleasure), likely related to the same dopamine pathway modulation that reduces food cravings, and possibly dose-dependent (i.e. more likely to occur at high doses, less likely to occur at low/maintenance doses).
- Some users of GLP-1s report negative/difficult experiences from rapid physical transformation (e.g. from sagging skin and increased wrinkle visibility, and from separation of aspects of personal identity that were previously tied to obesity).

## Addictive Behavior and Substance Use

- Approximately 28 million Americans struggle with alcohol abuse or addiction. The top 10% of drinkers consume 60% of all alcohol sold. Alcohol consumption and obesity also contribute to one another.
- Collectively, substance use and addiction affects over 50 million Americans.
- GLP-1 users report remarkable benefits in reducing alcohol, tobacco, opioids, and other addictive substances. Users also report a reduction in other addictive and compulsive behaviors, including gambling and even social media use ("doom-scrolling").
- Alcohol use and addiction accounts for roughly \$3.5 billion in annual direct medical spending. (This excludes co-morbidity, such as liver disease caused by alcoholism).
- Tobacco use and addiction accounts for about \$1 billion in annual direct medical spending.
- Other substance use and addiction accounts for about \$3.5 billion in annual direct medical spending as well. Opioid use and addiction, for example, accounts for about \$2 billion annual direct medical spending.
- Alcohol contributes to larger healthcare costs through co-morbidities, with attributed annual costs of over \$30 billion.
- Tobacco contributes to larger healthcare costs through co-morbidities, with attributed annual costs of over \$225 billion.

- Opioids contributes to larger healthcare costs through co-morbidities, with attributed annual costs of over \$95 billion.
- The science around GLP-1s and addiction is still evolving, but because GLP-1 drugs modulate dopamine signaling in the brain's reward pathways, it is not surprising that they might reduce the hedonic value of addictive substances and activities.

## Late-Life Morbidity

- More than 20% of all healthcare spending goes toward elderly patients in the last years of life, with direct medical spending of over \$1 trillion annually.
- Obesity combined with sarcopenia (age-related muscle loss) and frailty are key drivers of late-life morbidity.
- By treating obesity (via fat loss) and frailty (via muscle gain), the use of HOTs will reduce years of disability and morbidity, while extending healthspan and years of functional independence.

## Life Expectancy

- Life expectancy plateaued in the United States after 2014 up until the COVID-19 pandemic (which distorted the signal). This occurred despite improvements in medical technologies and treatments for many cancers and other age-related diseases. Some of this plateau is ultimately attributed to rising obesity rates.
- The science is still evolving, but use of HOTs in adulthood to prevent obesity and frailty would very likely extend lifespan by several years, other things being equal.

## The Total Cost of Obesity

Overall total direct medical cost of obesity in the United States is \$172 billion annually, or \$1,861 per obese individual, according to the CDC. This number averages all of the costs of the above illnesses. (It is a statistically standardized weighted average based on a two-part regression model, adjusted for self-reporting bias). For individuals with severe obesity (BMI over 35), the cost is \$3,097.

In addition to direct medical costs, the World Obesity Federation estimates the total indirect cost of obesity to the American economy from lost productivity to be \$401 billion. This sums from \$289 billion lost to premature mortality (those who die from obesity-related causes between age 20 to 64), \$100 billion lost to presenteeism (lost productivity at work from reduced physical and mental capacity), and \$12.5 billion lost to absenteeism (workdays lost to obesity-related illness and injury).

The U.S. economy currently loses a total of at least \$573 billion per year to obesity, or \$6,472 per obese adult per year, combining direct medical costs together with lost productivity.

## Social Implications

- HOTs won't fix the structural causes of health inequality, but universal access could meaningfully improve health outcomes in lower-income communities that disproportionately suffer from obesity, substance abuse, and limited healthcare access.
- With nearly 80% of criminal offenders abusing drugs or alcohol, HOTs-driven reductions in addiction could significantly shrink incarceration rates, meaningfully benefit countless individual lives and families, and save tens of billions in criminal justice costs.

- HOTs will reshape relationships and cultural identity. Nearly 60% of GLP-1 users already report significant romantic impacts, and centuries-old associations between body weight, wealth, willpower, and religious discipline will all face new pressures.
- A leaner, stronger workforce will produce more, miss fewer days, and stay productive longer with the largest gains among middle-aged and older workers. Lower healthcare, disability, food assistance, and criminal justice spending will follow.
- Longer-lived, healthier retirees will draw more from public benefit programs, but the net fiscal case for universal HOTs access under medical supervision remains overwhelmingly positive.

Beyond just the specific industries immediately impacted by changing consumer health and behavior patterns, the HOTs disruption will reshape society in important ways.

## Social and Cultural Shifts

### Equality and Equity

Obesity, with all of its downstream health consequences, is not evenly distributed across society. In many of the world's countries, lower-income communities and groups suffer higher obesity rates because a lack of economic prosperity and stability leads – perhaps counterintuitively – to overconsumption. The root causes of these disparities are largely structural: decades of targeted marketing of cheap and tasty but unhealthy foods, limited access to nutritious alternatives in “food deserts”, higher allostatic load, sleep deprivation, higher workplace injury rates, less nutritional awareness and education, socioeconomic marginality, and other factors have contributed to climbing obesity rates worldwide.

By themselves, HOTs do not fix any of these structural problems. But by modulating the dopamine reward pathways and metabolic processes that reinforce impulsive and compulsive overconsumption, they could help level a playing field that has been tilted against disadvantaged communities for generations. Moreover, by enabling lower-income individuals and families to spend less on food, HOTs can also help loosen the grip of the poverty trap.

It follows that the communities and populations which stand to benefit the most from the HOTs disruption are, by definition, those that have suffered the most from the conditions it treats.

### Criminal Justice System Savings

Abuse of alcohol and illicit drugs is a gateway into criminality, and thus a key driver of cost in the criminal justice system of most societies. The numbers for the United States are sobering. According to the National Council on Alcohol and Drug Dependence, 80% of all offenders abuse drugs or alcohol, almost 50% of jail and prison inmates are clinically addicted, and about 60% of all individuals arrested test positive for illegal drugs at the time of arrest. The National Institute on Drug Abuse reports an even higher estimate of 65% of the prison population having an active substance abuse disorder. Almost 20% of state and federal prisoners reported that they committed their current offense to support their addiction, known as “feeding the habit”. Moreover, alcohol intoxication is involved in 40% of all violent crimes and almost 40% of all traffic fatalities. Alcohol is also involved in a large fraction (up to 40%) of all cases of domestic abuse and child abuse.

In the United States, total criminal justice systems expenditures amount to almost \$300 billion based on state and local data: \$135 billion on police, \$87 billion on correction, \$52 billion on courts, and over \$50 billion in federal spending. This represents nearly 1% of US GDP. As much as 40% of criminal justice system expenditure in the United States, or \$110 billion each year, is directly associated with abuse of alcohol and illicit drugs.

Widespread adoption of HOTs therefore has extraordinary potential to both avert individuals away from criminality by reducing alcohol and illicit drug abuse as a gateway, as well as to help society as a whole reduce the enormous costs of the criminal justice system.

## Social Status and Signaling

Food and weight have been culturally intertwined with social status and social signaling throughout history. In less affluent cultures, especially historically, obesity was an overt symbol of wealth and privilege. In many societies today, however, obesity indicates nearer the opposite. The HOTs disruption will transform the cultural valence of body composition once again.

It is too early to know exactly which ways this changes will unfold, and there is sure to be significant variation across the world's cultures. Nevertheless, we can be certain that perceptions of food and weight will shift, once health optimization becomes an affordable and accessible choice for most adults in most countries.

## Dating and Relationships

Nearly 60% of GLP-1 users reported significant impacts on their romantic lives. These users noted generally positive changes such as purchasing new clothing, hearing from former partners who wanted to reconnect, getting more matches on dating sites and apps, presenting themselves more confidently online, asking other people out more confidently, and going on more dates.

Some users reported mixed results, especially around body satisfaction and libido. So far it appears the impacts of HOTs are more positive than negative, but further analysis will be required as more data comes in and newer HOTs are adopted.

On balance, however, we ought to expect that a physically and mentally healthier population will have greater self-confidence and be more inclined to seek romantic relationships, and that HOTs users will therefore have a competitive advantage in the dating pool over non-users.

It is noteworthy that attorneys and psychologists have observed a rise in relationship friction and breakups among HOTs users. When one person in a relationship undergoes a major physical transformation, it can alter the dynamic between the partners due to shifts in self-confidence, lifestyle changes, and insecurities from the other partner. However, body transformations can also lead to increased intimacy for some couples, especially if they embark on a healthier lifestyle together.

## Fashion

Fashion is more than just an industry for providing utilitarian clothing, it is also an ancient and important mode of individual and cultural identity and expression. Widespread HOTs adoption would mean many adults who are obese today would become healthier and much closer to their own personal ideal self. It is reasonable to expect that this will drive changes, and perhaps renewed interest in, the psychological and social dimensions of fashion choices.

## Cultural and Religious Traditions

Cultural and religious communities will be affected by the disruption as HOTs alter the neurological linkages between food, identity, and heritage. Not all cultural cuisines are aligned with present-day nutrition optimization, and those whose traditional dishes emphasize simple carbohydrate-heavy staples like bread, rice, pasta, and sugars will be disproportionately impacted by changes in eating habits driven by the HOTs disruption.

Religious institutions face challenges as well: if pharmaceutical intervention eliminates the desire to overeat, what becomes of the virtues and practices which center upon resisting temptation?

## Economic Productivity Gains

### From Improved Health

In the near term, prior to the widespread disruption of labor by AI and robotics, HOTs adoption will increase workforce participation, increase per-capita productivity, and reduce days lost to illness and injury by straightforwardly boosting the number of people who are physically and mentally healthy.

The productivity impacts of HOTs adoption would be disproportionately large among those in middle age and older, where ill-health is most likely to diminish productivity.

### From Postponed Retirement

On one hand, people who are more healthful, vigorous, and youthful may be more likely to extend their careers before retiring. On the other hand, those people may consider retiring earlier if they see healthfulness offering greater opportunities and value in retirement itself. It is not entirely clear from existing data whether “early exiters” will outnumber “career persisters” and “bridge workers”, but the weight of evidence suggests more will choose to keep working if they are physically and mentally able.

## Public Revenue and Spending

### More Tax Revenue from Productivity Boosts

The large productivity boost from widespread HOTs adoption will translate into GDP growth with a concordant increase in tax revenue – all else equal.

### Less Public Spending on Healthcare, Disability, Food Assistance, & Criminal Justice

A healthier, more vigorous, more productive, and less addicted adult population that is consuming less low-quality food will require substantially less support from government programs in these domains, and thus less government spending. Savings will almost certainly reach tens of billions of dollars across these domains, and possibly much more.

### More Public Spending on Longer Retirement Years

Healthier retirees who live several years longer thanks to the health benefits of HOTs will logically draw more in total from public benefit programs of all kinds. In the United States, extending longevity would raise costs in what are already some of the largest areas of public spending, including Social Security (retirement/pension income) and Medicare/Medicaid (healthcare).

## Geopolitical Implications

- Food has been a source of conflict and a tool of power throughout human history. A structural decline in global food demand, and especially for carbohydrate- and sugar-dense crops, will reshape international trade relationships and could destabilize nations dependent on food exports.
- The HOTs disruption is not happening in isolation. It arrives alongside simultaneous disruptions in energy, transportation, food systems, and labor. The geopolitical order built on current resource dependencies is being disrupted from many directions simultaneously.

Food has been a source of conflict and a tool of diplomacy throughout human history. The current global food trade network creates dependencies that shape international relations in important ways, and so structural shifts in the existing geopolitical order caused by declining food demand from widespread HOTs adoption have the potential to be destabilizing. Nations that are dependent upon food exports (particularly carbohydrate and sugar dense crops) could struggle, while nations that import these foods could benefit.

To a lesser extent, the second-order effects of HOTs that reduce demand for goods and services from other industries, ranging from medical supplies to fashion to illegal drugs, could also contribute to geopolitical destabilization and conflict. Specific examples include:

### Pharmaceutical Supply Chain Issues

- HOTs manufacturing capacity becomes a matter of national security, and dependency upon foreign supply for a technology this consequential erodes sovereign resilience.
- The staggered patent expiration timeline (semaglutide expires in Canada/China/India in 2026 but not the U.S./EU until 2031) already creates differential access that maps onto geopolitical fault lines.
- The WHO's addition of GLP-1s to the Essential Medicines List in 2025 triggered IP battles with developing nations threatening compulsory licensing, offering a preview of geopolitical tensions to come.

### Differential Adoption

- Nations that mobilize HOTs adoption earliest will quickly have healthier, more productive, and longer-lived populations, leading to a competitive advantage analogous to how early industrial nations pulled away from agrarian ones.
- A new axis of geopolitical inequality could emerge between HOTs-accessible versus HOTs-denied populations.

### Narco-State and Cartel Destabilization

- GLP-1s demonstrably reduce addictive cravings for alcohol, opioids, and other substances, and so widespread HOTs adoption could have major downstream effects on cartel revenues.
- Nations whose political economies are partially organized around drug production and trafficking face pressure from demand destruction.

### Agricultural Trade

- Russia, Ukraine, Argentina, Australia, Brazil, India, Canada, Thailand, France, and New Zealand are all food-exporting countries which have outsized exposure to the HOTs disruption because of the potential decline in global demand for grain, sugar, and dairy.

## Environmental Implications

- If the 107 million obese Americans reduced their calorie intake by over 500 calories per day through HOT adoption, the resulting reduction in food production would free up at least 4.5 million acres of cropland. This is an area nearly the size of New Hampshire.
- Reducing agricultural land use could translate into many dimensions of environmental benefit, including water consumption, emissions, soil contamination, water and air pollution, ecosystem health, and more.
- Land freed from agricultural use represents an extraordinary opportunity for conservation, restoration, reforestation, and rewilding.

Food and agriculture have a very large ecological footprint. Even a 5% reduction in food and agriculture production would translate into substantial real-world environmental benefits across most dimensions of concern.

## Agricultural Land Use

If all 40% of American adults who are currently obese were to reduce their calorie consumption by 500 calories using HOTS, this would translate into a reduction of roughly 800 produced calories per day for 107 million people (accounting for the average rate of food waste), or a 6% reduction in total caloric production for the country. Even if we ignore any impacts on pasture and grazing land, this would still translate into a reduction of over 4.5 million acres (nearly 2 million hectares) in cropland, or an area almost the size of New Hampshire. These impacts would disproportionately impact agriculture dedicated to sugar and carbohydrates, including corn, wheat, sugar beets and sugar cane.

## Emissions Reductions

- CO<sub>2</sub> emissions associated with intensive agriculture will decline, and any restored soils and reforested lands will help capture and store more carbon.
- CO<sub>2</sub> emissions associated with food transportation will decline (at least until the transformation to a fully electrified transportation system is complete).
- Nitrous oxide from synthetic fertilizers will decline with reduced crop production, as will harmful runoff.
- Methane from any reduction in animal agriculture (most especially cattle) will decline.
- Methane from food waste will decline.

## Water Cycle Transformation

- Agriculture represents the majority of human freshwater use.
- Reduced food demand translates into reduced water withdrawals.
- Overexploited aquifers across the American Great Plains (and elsewhere in the world) will see some relief from irrigation demand.

## Ecosystem Recovery

- Freeing up land from agriculture creates opportunities for conservation, restoration, reforestation, and rewilding.
- Soil recovery can help rebuild topsoil, store water, and sequester carbon.

## Pollution Reduction

- Use of pesticides and fertilizers will decline, with commensurate reductions in air, water, and soil pollution.
- Runoff that contributes to hypoxic marine dead zones will decline, helping foster recovery of coastal ecosystems.

## Choices and Call to Action

- An estimated 60–65 million total deaths occur worldwide each year, and the share of all deaths attributed to obesity is now approaching 10%.
- By reducing obesity, HOTs will not only prevent deaths, but also prevent the years suffering and loss leading up to those deaths.
- The sheer scale of the global obesity epidemic means that every year which we delay making HOTs universally available to all adults is another year of enormous loss, suffering, and death worldwide that can now be avoided.
- The sweeping benefits and enormous return on public investment in HOTs makes universal access a moral, economic, and strategic imperative for every nation.
- HOTs should be viewed as a new kind of infrastructure that creates the enabling conditions for human health, productivity, and flourishing the same way roads, electricity, and clean water do.
- Nations that act decisively can capture the staggering benefits of HOTs technologies for their people starting immediately, which will only help to position them for the other technology disruptions and transformations that lie ahead in this challenging era.

## A Call to Action with the Highest Stakes

The emergence of HOTs is an urgent call to action for policymakers, investors, industry leaders, and other key decision makers worldwide.

Obesity kills millions worldwide each year. Its downstream health consequences contribute to as much as 10% of all global deaths. And it costs the world trillions of dollars in medical costs and lost productivity.

Every year that access to HOTs remains restricted is another year of avoidable loss, suffering, and death on an almost incomprehensible scale.

## HOTs as Infrastructure

The conventional framing of HOTs like GLP-1s as “medications” underestimates what they represent.

HOTs should be viewed as a new kind of infrastructure. By creating the enabling conditions for healthfulness, they are a catalyst for vitality across all of society and productivity throughout the entire economy.

## National Mobilization

It is prudent to expect generic HOTs prices (not costs) as low as \$10 per month by the mid-2030s in most regions. Even before then, the enormous return on public investment in HOTs as infrastructure makes national mobilization to ensure universal access a moral, economic, and strategic imperative.

Universal access to all adults under the guidance of their doctor implies a number of key policy choices:

## Securing Domestic Supply

- Establishing pharmaceutical manufacturing capacity for HOTs is prudent as a matter of national security.
- Dependence on foreign supply for a technology this consequential creates unacceptable strategic vulnerability.

## Adopting Open-Source Alternatives

- Open-source modeling platforms, publicly available genomic databases, and in-silico trialing methods are already democratizing drug development.
- Public investment in drug development capability could allow nations to bypass proprietary pharmaceutical IP and the rent-seeking behavior of incumbent firms.

## Nationalizing IP Where Necessary

- When a technology's value to public health is measured in trillions of dollars annually and its marginal production cost is under \$5 per month, maintaining artificial scarcity through patent monopolies that can charge prices of \$1,000 or more per month becomes untenable.
- Compulsory licensing, public patent pools, and direct public investment in generic production are all legitimate policy tools to apply to the HOTs disruption.
- The addition of GLP-1 drugs to the World Health Organization (WHO) Essential Medicines List signals the direction of international consensus.

## Sovereign Resilience

Our world is facing overlapping disruptions in foundational sectors of energy, transportation, food, and labor simultaneously. This magnitude of technological change is unprecedented in human history.

To navigate this era of transformation, nations will need resilient populations. Sovereign resilience requires individuals, communities, and all of society at their physical and mental best to face tomorrow's challenges.

## Leadership

**The HOTs disruption is here.** Nations that act decisively can capture the full value of these extraordinary technologies starting now, and ensure their people thrive as we enter a new era and move toward a Stellar future.

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