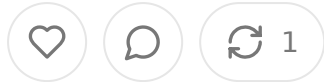


The GLP-1 Gold Rush: Where Smart Money Meets Weight Loss Medicine

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Abstract

This essay examines the rapidly evolving GLP-1 receptor agonist market through the lens of entrepreneurial and investment opportunity. Drawing on comprehensive research from Milliman and industry sources, I analyze the convergence of clinical efficacy, market demand, regulatory complexity, and behavioral health challenges that define this therapeutic category. The analysis reveals specific opportunity areas including adherence technology solutions, care management platforms, supply chain optimization, and value-based contracting infrastructure. Key findings include estimates of 26 percent waste in current GLP-1 spending due to discontinuation, projected utilization plateaus between 6 and 20 percent of commercial population from 2028-2030, and fundamental gaps in patient support infrastructure. For entrepreneurs and investors, the GLP-1 market represents not merely a pharmaceutical story but a systems-level transformation requiring innovation across multiple domains. The essay concludes with actionable strategic frameworks for market entry and competitive positioning.

Key Opportunity Areas:

- Adherence and persistence technology platforms
- Integrated care management solutions

- Pharmacy supply chain optimization tools
- Patient engagement and education systems
- Analytics and predictive modeling capabilities
- Value-based contracting infrastructure
- Social determinants of health integration
- Compounding pharmacy oversight and quality assurance

Market Context:

- Current GLP-1 spending approaching 4.6 percent of gross Medicaid costs
- Commercial utilization increased 57 percent Q1-Q4 2022
- Estimated 68 percent of patients discontinue therapy within 12 months
- Annual wholesale costs ranging from 12,200 to 17,600 dollars per patient
- Approximately 42 percent of U.S. population classified as obese

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Introduction and Market Context

Something remarkable is happening in American healthcare, though you would be forgiven for missing it amid the usual noise about artificial intelligence and digital health. The GLP-1 receptor agonist market represents one of those rare moments where genuine clinical efficacy, massive addressable market size, and structural system failures converge to create extraordinary opportunity. But this opportunity looks nothing like the typical health tech pitch deck fantasy. It requires understanding not just the science or the market dynamics but the intricate interplay between coverage policy, patient behavior, pharmacy benefit management, and care delivery models.

The numbers tell part of the story. Approximately 42 percent of the U.S. population meets clinical criteria for obesity. GLP-1 medications demonstrated weight loss efficacy ranging from 6.7 to 22.5 percent of body weight in clinical trials, dramatically outperforming previous pharmacologic interventions. Annual wholesale acquisition costs range from 12,200 to 17,600 dollars per patient for weight loss indications. Commercial market utilization increased 57 percent from the first to fourth quarter of 2022 alone. Medicaid spending on GLP-1s reached approximately 4.1 billion dollars in 2022, representing 4.6 percent of gross Medicaid pharmaceutical expenditure.

But these figures, impressive as they may be, obscure the more interesting dynamics. This market is simultaneously exploding and fundamentally broken. Demand vastly exceeds supply, creating shortages that have spawned a gray market in compounded versions. Coverage policies vary wildly across payers, with Medicare explicitly prohibited from covering weight loss indications while some commercial payers implement aggressive prior authorization requirements. Most critically, publishers

real-world evidence suggests that 68 percent of patients discontinue therapy within months, creating an estimated 26 percent waste rate in total spending.

For the analytically minded entrepreneur or investor, this combination of explosive growth and structural dysfunction should trigger recognition. These are exactly conditions that enable new entrants to capture value by solving real problems rather than creating marginal improvements to existing solutions. The question is not whether opportunities exist but rather which specific problems are most tractable and valuable to solve.

The Clinical and Economic Landscape

To understand where entrepreneurial opportunity lies, we need to establish the clinical and economic baseline with precision. GLP-1 receptor agonists work by mimicking naturally occurring incretin hormones, slowing gastric emptying and modulating appetite signaling in the brain. The first drug in this class, exenatide, received FDA approval for type 2 diabetes in 2005. Liraglutide followed in 2010 for type 2 diabetes and in 2014 for chronic weight management under the brand name Saxenda. Semaglutide, approved for diabetes as Ozempic in 2017 and for weight management as Wegovy in 2021, demonstrated substantially greater efficacy with average weight loss of 15 to 16 percent at maximum doses. The newest entrant, tirzepatide, is a dual GIP and GLP-1 receptor agonist showing weight loss up to 22.5 percent in clinical trials.

The clinical profile matters because it drives both the opportunity and the constraints. These medications require dose escalation periods ranging from four weeks to 20 weeks depending on the specific drug and target dose. This extended titration period is necessary to minimize gastrointestinal side effects including nausea, vomiting, diarrhea, and constipation, which occur in 21 to 44 percent of patients depending on the specific adverse event and drug. More serious but rare side effects include acute pancreatitis, thyroid tumors, acute kidney injury, and acute gallbladder disease. The medications are administered as subcutaneous injections either daily or weekly, though oral formulations are in development.

Peak weight loss typically occurs at 12 to 18 months, and weight loss is maintained only while patients remain on therapy. Data from the STEP 1 trial extension show that patients regained two-thirds of their lost weight within a year of discontinuation. This pharmacologic profile has profound implications: effective treatment requires long-term, likely indefinite, administration of an expensive medication with significant side effects and complex dosing requirements.

From an economic perspective, the wholesale acquisition cost for these medications ranges from 12,200 dollars for older agents like Saxenda to 17,600 dollars for newer formulations. After rebates, net costs to payers are estimated around 10,100 dollars annually for preferred agents. At a population level, these costs compound rapidly for a commercial payer with 100,000 enrollees, assuming 40.9 percent obesity prevalence and 10 percent treatment uptake, would face total medication costs approaching 10 million dollars annually, with an estimated 4.7 million dollars representing waste from early discontinuation.

The utilization trends reveal the market trajectory. Between 2019 and 2022, Medicare prescription volume per 1,000 enrollees increased 278 percent for Trulicity and 187 percent for Ozempic, both indicated for diabetes. Saxenda, indicated for weight management, saw 543 percent growth over the same period. Commercial market showed even more dramatic recent acceleration, with quarterly utilization increasing 57 percent from Q1 to Q4 2022. Medicare Part D has also seen significant growth despite covering these medications only for diabetes indications, suggesting either increasing use as first-line diabetes therapy or potential off-label prescribing.

This clinical and economic landscape creates specific opportunity spaces. The medications work but require perfect execution across multiple dimensions: appropriate patient selection, effective side effect management, sustained behavior modification, long-term adherence, and ongoing clinical monitoring. Each of these represents a potential failure point and therefore a potential value creation opportunity for entrepreneurs who can engineer solutions.

The Adherence Crisis: A 4.7 Million Dollar Problem

The most immediately actionable opportunity in the GLP-1 market centers on adherence and persistence. Real-world analysis from two major pharmacy benefit managers examined patients newly initiated on GLP-1 agonists for obesity or prediabetes. At one year, only 32 percent remained persistent on therapy. Among those who continued, only 27 percent achieved adherence defined as proportion of days covered exceeding 80 percent. In simpler terms, more than two-thirds of patients start these medications do not maintain therapy for a year, and among those who continue, nearly three-quarters fail to take the medication consistently.

The financial implications are staggering. Using Milliman's modeling framework on a typical commercial population of 100,000 enrollees with 40.9 percent obesity prevalence and 10 percent treatment uptake, total annual medication costs would reach approximately 17.9 million dollars. Of this amount, an estimated 4.7 million dollars represents waste from patients who discontinue therapy before achieving meaningful clinical benefit. This 26 percent waste rate derives from patients who incur costs during dose escalation and early treatment but discontinue before the 12-month mark when sustained weight loss and metabolic benefits typically manifest.

The causes of poor adherence are multifactorial. Gastrointestinal side effects, which are usually temporary and manageable, can be severe enough to prompt discontinuation. Injectable administration creates barriers for needle-averse patients. High out-of-pocket costs, especially in plans with significant cost-sharing or prior to meeting deductibles, make sustained therapy economically challenging. Prior authorization requirements, even when ultimately approved, create friction that may discourage continuation. Perhaps most importantly, these medications are prescribed in the absence of comprehensive support systems for diet, exercise, behavioral modification, and ongoing clinical management.

For entrepreneurs, this adherence crisis represents a clear value proposition: solutions that materially improve persistence and adherence create immediate, quantifiable value for payers while improving patient outcomes. The math is straightforward.

payer spending 17.9 million dollars annually with 26 percent waste has 4.7 million dollars of addressable spend. A solution that reduces discontinuation by even 25 percent would save 1.2 million dollars annually for a 100,000-member plan, creating obvious willingness to pay for effective interventions.

But what would an effective solution actually look like? The research points to several critical components. First, intensive patient education before and during dose escalation. Patients need to understand expected side effects, strategies for managing nausea and gastrointestinal symptoms, the rationale for slow dose titration, and realistic expectations for weight loss trajectory. Second, ongoing clinical support from trained staff who can troubleshoot problems as they arise, adjust dosing when appropriate, and provide encouragement during difficult phases of treatment. Third, integration with comprehensive lifestyle modification programs including nutrition counseling, exercise prescription, and behavioral therapy. Fourth, technological infrastructure that enables monitoring, engagement, and intervention at scale rather than requiring purely human-intensive case management.

Several entrepreneurial approaches could address these needs. A digital therapy platform specifically designed for GLP-1 patients could deliver structured education, symptom tracking, side effect management protocols, and integration with telemedicine for clinical decision support. A specialized pharmacy program could combine medication dispensing with wraparound clinical services, potentially embedded within the pharmacy benefit itself. A care management company could deploy trained coaches who work with patients from initiation through long-term maintenance, using predictive analytics to identify high-risk patients before they discontinue. A technology-enabled weight management clinic could offer in-person or virtual visits with physicians, nurses, dietitians, and behavioral health specialists in an integrated care model.

The key insight is that the adherence problem is fundamentally a care delivery and patient support problem rather than a pharmaceutical problem. The medication will work, but only when taken correctly and consistently by appropriate patients with adequate support. This creates opportunity for entrepreneurs who can build the infrastructure, systems, and services that enable sustained therapy. The value

proposition is clear, the willingness to pay exists, and the target customer—paye self-insured employers—has both the resources and the motivation to contract f solutions that materially reduce waste.

Coverage Complexity Across Market Segments

Understanding the coverage landscape is essential because it defines both the addressable market and the strategic positioning required for different solutions. Coverage policies vary dramatically across commercial, Medicare, Medicaid, and exchange markets, creating a complex and fragmented environment that itself generates opportunity.

Commercial payers represent the most accessible market. Of the 17 largest U.S. insurers, 11 have published coverage policies for GLP-1s for weight management; nine of those 11 impose restrictions beyond FDA labeling requirements. Common restrictions include requiring documented participation in lifestyle modification programs, imposing stricter BMI thresholds than the FDA label, mandating step therapy through older weight loss medications, and requiring periodic reassessn to demonstrate continued weight loss. Prior authorization is nearly universal, with reported rates of utilization management among employer groups ranging from 80 percent. Self-insured employer coverage ranges from 33 to 63 percent according to pharmacy benefit manager surveys, with significant variation based on employer industry, and benefits philosophy.

The Medicare market presents more complex challenges. Federal law explicitly excludes weight loss medications from Medicare Part B and Part D coverage, a provision dating to the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. However, GLP-1s indicated for diabetes—Ozempic, Victoza, Mounjaro, and others—must be covered under Part D protected class provisions. This creates a situation where the identical active ingredient is covered when prescribed for diabetes but not when prescribed for weight management. Predictably, this has led to growth in diabetes-indicated GLP-1 utilization within Medicare, raising questions about

appropriate diagnosis verification and potential off-label use. Some Medicare Advantage plans have implemented prior authorization requiring diabetes diagnosis confirmation, but the underlying policy framework remains constrained by the statutory exclusion.

Several potential pathways could expand Medicare coverage. Congressional legislation, such as the Treat and Reduce Obesity Act which has been proposed in multiple sessions, would explicitly authorize coverage. An administrative interpretation by CMS redefining these medications as treatments for chronic disease rather than weight loss agents could enable coverage without legislative action. A real-world innovation center demonstration project could test coverage and outcomes in a defined population. Most intriguingly, expanded indications beyond weight loss create coverage obligations. For example, semaglutide has recently been shown to reduce major adverse cardiovascular events by 20 percent in adults with overweight/obesity and established cardiovascular disease. If this indication gains FDA approval and CMS determines it constitutes a covered use distinct from weight loss, coverage could be required even for patients whose primary indication is weight management.

The Medicaid market shows wide state-level variation. Medicaid programs may exclude weight loss medications but must cover drugs indicated for diabetes. State programs that do cover GLP-1s for weight management typically impose extensive prior authorization requirements including BMI thresholds, comorbidity requirements, participation in lifestyle modification programs, and periodic reassessment for continued coverage. A survey of state Medicaid programs found fewer than 15 states explicitly cover GLP-1s for weight management as of 2023, though this number appears to be increasing. Several states including Mississippi, Virginia, and Michigan have implemented detailed coverage criteria including reauthorization requirements tied to documented weight loss.

The ACA exchange market adds another layer of complexity. Weight loss medications are not considered essential health benefits under the ACA and therefore are not required coverage. Plans may choose to cover these medications but are not obligated to do so. This creates heterogeneity in coverage across exchange plans even within the same rating area.

For entrepreneurs, this coverage complexity creates several strategic implications. First, solutions must be designed with sufficient flexibility to accommodate varying coverage policies, prior authorization requirements, and utilization management approaches across different payer types. Second, there is opportunity in helping payers implement and manage coverage policies effectively, particularly around diagnosis verification, appropriate use criteria, and outcomes monitoring. Third, the policy landscape is dynamic, with potential for significant expansion particularly in Medicare, creating both opportunity and risk depending on how market entry strategies align with policy evolution.

Perhaps most importantly, the coverage complexity underscores that effective solutions must create value across multiple stakeholder perspectives. A technology platform that only benefits patients will struggle if it increases costs for payers. Conversely, utilization management tools that reduce spending by restricting access will face patient and provider resistance. The winning strategies will create aligned incentives where improved patient outcomes, enhanced adherence, and reduced costs collectively benefit patients, providers, and payers simultaneously.

Strategic Opportunity Framework for Entrepreneurs

Having established the clinical, economic, and policy context, we can now construct a systematic framework for evaluating entrepreneurial opportunities in the GLP-1 market. The framework organizes opportunities across several dimensions: problem severity, solution tractability, value capture potential, and strategic defensibility.

Problem severity is highest in areas where current failures create the most significant costs or clinical harms. The adherence crisis clearly meets this threshold, with 2 percent estimated waste representing billions of dollars annually at scale. Inadequate patient education and support leading to poor side effect management and early discontinuation represents high-severity problems. Diagnosis verification and appropriate use represents moderate severity, with real concerns about off-label but less clear quantification of the magnitude. Supply chain complexity and pricing

optimization represents high severity for payers though the problem may be more difficult for new entrants to address directly.

Solution tractability refers to whether the problem is amenable to solution given available technology, care delivery models, and market structures. Patient education, engagement, and support is highly tractable using digital therapeutics, telemedicine, and care management approaches that have been validated in other therapeutic areas. Diagnosis verification and utilization management is tractable through integration with pharmacy benefit management systems and electronic health record data. Predictive analytics for identifying high-risk patients likely to discontinue is tractable given existing data science techniques. Supply chain and pricing optimization is tractable for entrepreneurial ventures given the concentration and market power of incumbent pharmacy benefit managers and wholesalers.

Value capture potential depends on whether customers have both willingness and ability to pay for solutions. Payers and self-insured employers facing tens of billions in annual GLP-1 spending have clear willingness to pay for solutions that reduce waste. The math strongly favors contracting for solutions that cost less than the savings generated. Provider organizations, particularly those in value-based arrangements, have similar economics. Direct-to-consumer solutions face weaker value capture dynamics given high out-of-pocket costs for the medications themselves. Pharmaceutical manufacturers have willingness to pay for solutions that increase appropriate utilization and adherence, though entrepreneurs must navigate the complex regulatory environment around manufacturer support for third-party services.

Strategic defensibility encompasses competitive moats, network effects, regulatory barriers, and ability to scale. Technology platforms with high switching costs, particularly those embedded in clinical workflows, benefit from strong retention. Care management models that require significant clinical expertise and training create barriers to fast follower competition. Solutions that aggregate data across multiple payers or provider organizations can create network effects. Regulatory approval pathways, such as FDA clearance for digital therapeutics or quality

certification for specialized care programs, create defensibility through time and capital requirements.

Applying this framework reveals several high-priority opportunity areas. Digital patient engagement platforms that combine education, symptom tracking, side effect management protocols, and connection to clinical support represent high severity, high tractability, strong value capture, and moderate defensibility. Specialized care management programs deploying trained coaches for GLP-1 patients offer similar characteristics with potentially stronger defensibility through clinical expertise development. Predictive analytics tools that identify high-risk patients for targeted intervention combine tractability with value capture but face defensibility challenges unless integrated into broader platforms. Diagnosis verification and appropriate tools address a real but lower-severity problem with good tractability and value capture to payers implementing coverage programs.

Several opportunity areas appear less attractive under this framework. Direct pharmaceutical supply, even through compounding or international sourcing, faces significant regulatory risk, quality concerns, and reputational hazards that outweigh potential margins. Direct-to-consumer weight loss programs, while potentially addressing patient needs, face difficult value capture dynamics and intense competition in an increasingly crowded market. Infrastructure for value-based contracting, while strategically important, may be premature given the limited adoption of such arrangements to date. Technology solutions focused purely on injection technique or medication administration represent low-severity problems with limited value capture potential.

The framework also highlights the importance of timing and sequencing. Early-stage opportunities exist in areas where the market is clearly broken and customers are actively seeking solutions—patient adherence and engagement being the canonical example. As the market matures and initial solutions are deployed, second-order opportunities emerge in analytics, optimization, and integration of multiple point solutions into comprehensive platforms. Later-stage opportunities will likely center on value-based arrangements, total cost of care management, and integration with broader metabolic health and obesity treatment ecosystems.

Technology Infrastructure Gaps

The current technology infrastructure supporting GLP-1 therapy has significant gaps that create entrepreneurial opportunity. Most patients receive prescriptions through traditional channels: a physician visit, prescription sent to pharmacy, medication dispensed, minimal follow-up beyond routine appointments. This model was never designed for medications requiring extended dose titration, intensive side effect management, behavioral modification, and long-term adherence monitoring.

Electronic health records capture prescribing data but rarely include structured information about patient education, side effect counseling, adherence patterns, or outcomes beyond weight measurements at office visits. Pharmacy systems track dispensing and refills but lack integration with clinical data that would enable proactive intervention when patients miss refills or show patterns suggesting discontinuation risk. Patient portals provide access to information but are passive tools rather than active engagement platforms. Remote patient monitoring capabilities exist in some settings but are not systematically deployed for GLP-1 therapy management.

Several specific technology gaps create opportunity. First, there is no widely adopted platform for systematic patient education about GLP-1 therapy. Patients rely on information from prescribers during brief office visits, pharmaceutical manufacturer websites and patient education materials, and increasingly unreliable information from social media and internet searches. A comprehensive, evidence-based, engaging digital education platform covering everything from injection technique to nutritional guidance to realistic expectation-setting would address this gap.

Second, there is inadequate infrastructure for systematic symptom tracking and side effect management. Patients experiencing nausea, vomiting, or other adverse effects typically wait until their next scheduled appointment or call their provider's office leading to delays in management and potentially prompting discontinuation. A mobile application enabling real-time symptom reporting, algorithm-driven recommendations for symptom management, and escalation to clinical staff when needed would improve the patient experience and reduce discontinuation.

Third, there is limited use of predictive analytics to identify patients at high risk of discontinuation before it occurs. Patterns in refill behavior, symptom reports, engagement with educational content, and clinical markers could potentially predict discontinuation risk, enabling proactive outreach and intervention. This requires integration of data from multiple sources—pharmacy claims, electronic health records, patient-reported information—and application of machine learning techniques to identify high-risk patterns.

Fourth, the infrastructure for connecting patients with comprehensive lifestyle modification support is generally ad hoc. Referrals to dietitians, exercise physiologists, or behavioral health specialists happen inconsistently if at all. Digital therapeutics for weight management exist but are rarely integrated with medical management. A platform that systematically connects GLP-1 patients with evidence-based lifestyle modification programs would address this gap.

Fifth, there are opportunities in clinical decision support tools for providers managing GLP-1 therapy. Questions about dose titration speed, management of effects, criteria for discontinuation, and assessment of treatment response occur frequently. Provider-facing tools that codify best practices and provide decision support at the point of care could improve treatment quality and outcomes.

The technology infrastructure opportunities are not purely about building applications or platforms. They require careful attention to clinical workflow integration, payer contracting models, regulatory considerations, and change management. A sophisticated symptom tracking application that does not integrate with provider workflows will not be used consistently. A predictive analytics tool that generates alerts but does not enable efficient intervention will create alarm fatigue. A patient education platform that is not incorporated into the prescribing and dispensing process will reach only a small fraction of patients.

Successful technology solutions will need to be embedded in the care delivery and payment infrastructure rather than operating as standalone consumer-facing tools. This suggests partnership models with health systems, payer-sponsored implementations, integration with pharmacy benefit managers, or direct contrac

with self-insured employers. The most valuable technology platforms will likely be those that aggregate across multiple data sources, integrate with existing clinical and administrative systems, and enable action rather than just generating information.

The Care Management Imperative

Technology infrastructure is necessary but not sufficient. The evidence strongly suggests that effective GLP-1 therapy requires intensive human support, at least during initiation and dose escalation. This creates an opportunity in care management models specifically designed for GLP-1 patients.

The clinical rationale is straightforward. During the first three to six months of therapy, patients navigate injection technique learning, dose escalations every two to four weeks, management of gastrointestinal side effects that peak during escalation, adjustment to appetite suppression and eating pattern changes, and behavioral modification around diet and exercise. This is far more complex than taking an oral medication for hypertension or diabetes where dose is stable and side effects are minimal.

Care management for chronic conditions has well-established precedents in other therapeutic areas. Disease management programs for diabetes, heart failure, asthma, and other conditions have demonstrated improved outcomes and, in some cases, reduced total cost of care. Oncology nurse navigator programs have shown value in helping patients navigate complex treatment protocols. Transplant programs employ care coordinators who manage immunosuppressive therapy, monitor for rejection, and coordinate multidisciplinary care. The GLP-1 care management opportunity follows similar logic but with specific adaptations for the unique challenges of weight loss pharmacotherapy.

An effective GLP-1 care management program would include several components. During the pre-prescription phase, comprehensive patient education about the mechanisms of action, expected effects and side effects, behavioral modification requirements, and realistic outcomes. This education needs to be detailed enough that patients are making truly informed decisions about initiating therapy. During dose

initiation and escalation, close monitoring for side effects with coaching on management strategies, troubleshooting problems as they arise, and clinical escalation when needed. Throughout therapy, ongoing support for dietary changes, physical activity, behavioral modification, and management of psychosocial aspects of weight loss. At key decision points, such as reaching maximum dose or achieving weight goals, guidance on maintenance strategy and long-term planning.

The staffing model for such programs could vary. Registered nurses with training in obesity medicine and motivational interviewing could serve as primary care managers supported by physicians for clinical oversight and prescribing. Dietitians could provide specialized nutritional counseling. Exercise physiologists could design and monitor activity programs. Behavioral health specialists could address emotional eating, body image issues, and other psychological aspects. The key is having staff with sufficient time, training, and support systems to provide intensive, personalized care rather than perfunctory check-ins.

The business model for care management programs depends on customer segmentation and payment mechanisms. Payers and self-insured employers could contract for care management as a carved-out benefit, paying a per-member-per-month fee for enrolled patients. The value proposition is the reduction in wasted spending from early discontinuation plus potential longer-term medical cost savings from sustained weight loss. Provider organizations in value-based contracts could implement care management as a strategy for managing total cost of care.

Pharmaceutical manufacturers could sponsor patient support programs, though this raises regulatory considerations around manufacturer involvement in clinical care.

The unit economics of care management need careful analysis. If a care manager program costs 200 dollars per member per month and serves patients for an average of 12 months, total cost per patient is 2,400 dollars. For a payer spending 10,100 dollars annually on medication, care management adds approximately 24 percent to total costs. This is justifiable only if care management materially improves adherence and persistence. Using the 68 percent discontinuation baseline, if care management reduces discontinuation to 50 percent, the savings from avoided waste could exceed the cost of the program depending on the specific financial model.

Several companies are already operating in this space or adjacent markets. Digital health companies offering weight management programs are adding GLP-1 support services. Specialty pharmacies are developing enhanced services for GLP-1 patients. Telehealth platforms are creating GLP-1-focused practices. The market is nascent enough that business models, service delivery approaches, and competitive positioning remain fluid. Entrepreneurs entering now have opportunity to define practices and build defensible market positions before the space becomes crowded and commoditized.

The care management opportunity is particularly interesting because it represents a genuine service business rather than pure technology play. While technology platforms are important for enabling scale and efficiency, the core value derives from human expertise, coaching capability, and clinical judgment. This creates natural barriers to entry and defensibility that pure software solutions lack. It also creates challenges in scaling and maintaining quality as programs grow. Entrepreneurs building care management businesses need to think carefully about clinical training, quality assurance, workforce management, and incentive alignment to maintain effectiveness at scale.

Supply Chain and Pharmacy Benefit Design

The pharmaceutical supply chain and pharmacy benefit design for GLP-1s present both challenges and opportunities. Current market dynamics include manufacturing shortages, intense PBM competition for rebates, complex prior authorization requirements, variable patient cost-sharing, and emerging gray markets in compounded products. Understanding these dynamics is essential for identifying value creation opportunities.

The supply chain begins with pharmaceutical manufacturers who produce the drugs and set list prices. These list prices, expressed as wholesale acquisition costs, range from 12,200 to 17,600 dollars annually for GLP-1s indicated for weight management. Manufacturers negotiate rebates with pharmacy benefit managers in exchange for

favorable formulary placement. These rebates can be substantial, with published estimates suggesting net prices approximately 40 percent below list prices for preferred products. The rebates are paid retrospectively based on utilization, typically on a quarterly basis.

Pharmacy benefit managers serve as intermediaries between manufacturers, payers, and pharmacies. They negotiate rebates with manufacturers, process claims adjudication, implement formulary designs and prior authorization requirements, contract with pharmacy networks, and provide clinical programs. The PBM business model depends on rebate retention, spread pricing, and administrative fees. For high-cost specialty medications like GLP-1s, rebates represent significant revenue, creating strong incentives for PBMs to secure exclusive or preferred formulary positions in exchange for higher rebate guarantees.

Payers, including commercial insurers, self-insured employers, Medicare plans, and Medicaid programs, contract with PBMs for pharmacy benefit management services. They typically receive a portion of manufacturer rebates, though the exact sharing arrangement varies by contract. Payers implement utilization management strategies including prior authorization, step therapy, and quantity limits to control spending. For GLP-1s, these strategies can be quite restrictive, reflecting the high cost and concerns about appropriate use.

Pharmacies dispense medications and receive reimbursement based on contracted rates with PBMs. For specialty medications, specialty pharmacies play an increasingly important role, offering enhanced services including patient education, adherence monitoring, and clinical support. Specialty pharmacy reimbursement typically includes both ingredient cost and dispensing fees, with potential for performance-based payments tied to adherence or outcomes.

Patients experience this system through cost-sharing requirements including copayments, coinsurance, and deductibles. For high-cost drugs like GLP-1s, out-of-pocket costs can be substantial. A patient with 20 percent coinsurance facing a 15,000 dollar annual drug cost would owe 3,000 dollars per year. Manufacturer copay assistance

programs can reduce or eliminate patient cost-sharing but create perverse incentives where patients face minimal out-of-pocket costs while payers bear the full price.

This complex supply chain creates several entrepreneurial opportunities. First, there is opportunity in formulary strategy consulting and analytics. Payers and PBMs use sophisticated modeling to evaluate tradeoffs between rebates, utilization, and total cost of care. Tools that enable scenario analysis of different formulary designs, prior authorization criteria, and rebate strategies would have clear value. This is particularly true for self-insured employers who may lack the internal expertise to evaluate PBM proposals and optimize pharmacy benefit design.

Second, there are opportunities in specialty pharmacy services specifically tailored for GLP-1s. While specialty pharmacies exist, few have developed comprehensive programs specifically for weight management pharmacotherapy. A specialty pharmacy that combines medication dispensing with the care management capabilities discussed previously could capture value both through pharmacy margins and through contractual arrangements with payers for clinical services.

Third, there may be opportunities in transparency and cost optimization tools that help patients navigate the complexity of manufacturer assistance programs, pharmacy shopping, and alternative sourcing. The proliferation of compounded semaglutin, despite quality and regulatory concerns, demonstrates demand for lower-cost alternatives. Legitimate approaches to cost reduction, such as helping patients understand manufacturer assistance program eligibility or identifying lowest-cost pharmacy options, could meet this need.

Fourth, as value-based contracting becomes more prevalent, there will be opportunities in the infrastructure to support such arrangements. Value-based contracts for pharmaceuticals require data integration, outcomes tracking, rebate reconciliation, and contract administration that current systems often handle poorly. Technology platforms and service providers that enable manufacturers and payers to implement and manage outcomes-based arrangements would facilitate this market evolution.

The compounding pharmacy phenomenon deserves specific attention. During GLP-1 shortages, compounding pharmacies have produced and marketed semaglutide and tirzepatide, often at significantly lower prices than branded versions. Patients have accessed these products through cash payment, with reported monthly costs as low as 300 dollars compared to over 1,000 dollars for branded versions. This creates an appeal for uninsured patients or those with high cost-sharing.

However, compounded GLP-1s raise significant concerns. These products are not FDA-approved and have not undergone the rigorous quality testing required for commercially manufactured drugs. There have been reports of contamination, incorrect dosing, and use of salt forms of active ingredients that differ from approved formulations. Several states have taken action to restrict compounding of GLP-1s. Manufacturers have filed lawsuits challenging compounding pharmacies for intellectual property violations and patient safety concerns. The FDA has issued warnings about compounded versions.

For entrepreneurs, the compounding market presents risks that likely outweigh potential rewards. The regulatory environment is unfavorable and potentially moving toward greater restriction. Quality concerns create liability exposure. Manufacturer opposition creates legal risk. Most importantly, the market may be transient—as manufacturer production increases and shortages resolve, the economic rationale for compounded versions weakens. Entrepreneurs interested in improving access and affordability would be better served by working within the legitimate pharmaceutical supply chain to reduce costs through rebates, assistance programs, and care model innovations rather than attempting to compete on price through regulatory arbitrage.

Long-Range Forecasting and Market Maturation

Understanding the future trajectory of the GLP-1 market is essential for timing investment and positioning ventures. The Milliman research on long-range forecasting provides valuable insights into when and at what level utilization may stabilize.

The forecasting model uses a Markov chain approach, treating patients as moving between states: healthy, obese but not on drug, diabetic but not on drug, healthy on drug, obese and on drug, diabetic and on drug, and terminated coverage. Transition probabilities between states are calibrated using historical data, with adjustments for several factors including coverage expansion, increased popularity, drug shortages, and changes in prescribing patterns. The model projects forward to identify when the system reaches steady state equilibrium where the distribution of patients across states stabilizes.

The baseline forecast, using what Milliman terms the middle-low scenario, projects that 7.9 percent of a typical commercial population would be taking GLP-1s in a given month once utilization plateaus. This plateau is projected to occur between 2028 and 2030. The forecast range across different scenarios spans from 6.3 percent in the low scenario to 20.4 percent in the highest scenario. The spread reflects uncertainty about several key parameters including the take-up rate among patients without diabetes, medication persistence over time, the degree to which GLP-1s become first-line therapy for weight management versus remaining later-line options, and whether new indications such as cardiovascular risk reduction dramatically expand the eligible population.

Several insights emerge from this analysis. First, even in the middle scenarios, GLP-1 utilization in commercial populations is projected to be substantially higher than current levels, implying continued strong growth for several years. Second, the range of scenarios is wide, reflecting genuine uncertainty about how clinical practice, coverage policies, and patient behavior will evolve. Third, the plateau timing of 2028 to 2030 suggests a window of approximately five to seven years during which the market remains in high-growth mode rather than mature equilibrium.

For entrepreneurs and investors, these projections have strategic implications. Ventures launched in the next two to three years will be entering during a period of rapid market expansion, potentially benefiting from rising tide dynamics where overall growing utilization creates opportunity for multiple players. However, these ventures will also need to be positioned for market maturation in the latter part of the de-

when growth slows and competitive dynamics may shift from land grab to market share competition.

The projections also highlight the importance of understanding what drives the scenario range. The key variables are take-up rates among non-diabetic populations, medication persistence, and whether GLP-1s become dominant first-line therapy. Entrepreneurs whose business models depend on high overall utilization should assess which scenario is most likely and whether their model remains viable under less optimistic assumptions. Conversely, ventures focused on improving persistence and adherence may actually benefit more in scenarios where baseline adherence remains problematic, as the value proposition for their solutions is stronger.

The geographic and demographic distribution of GLP-1 utilization also matters in market strategy. The Milliman analysis is based on typical commercial populations but substantial variation exists across different markets. Obesity prevalence varies by geography, with higher rates in Southern and Midwestern states. Age distribution affects utilization, as obesity rates and willingness to pursue pharmacologic treatment vary by age cohort. Socioeconomic factors influence both obesity prevalence and access to treatment. Entrepreneurs need to consider whether their solutions are designed for broad national deployment or whether they should focus on specific high-prevalence, high-utilization markets where the unit economics are most favorable.

The model's assumption about full coverage of GLP-1s for weight loss by 2025 is notable. Currently, only a minority of commercial plans provide unrestricted coverage. The projection assumes substantial expansion in coverage over the next years, driven by some combination of competitive pressure, evidence of cost-effectiveness, regulatory requirements, or other factors. This assumption may or not prove accurate. If coverage remains more restricted than the model assumes, actual utilization could come in below even the low scenario. Conversely, if Medicare coverage is authorized through legislative or administrative action, utilization could exceed even the high scenario. Entrepreneurs need to monitor policy developments closely and maintain flexibility to adjust strategy as the coverage landscape evolves.

The long-range forecasting also reveals the magnitude of spending involved. At a middle-low scenario of 7.9 percent utilization and assuming net costs of 10,100 dollars annually per patient, a commercial population of one million members will generate approximately 798 million dollars in annual GLP-1 spending once utilization plateaus. For the entire U.S. commercial population of approximately 180 million covered lives, this implies total spending exceeding 140 billion dollars annually at steady state. Even accounting for future generic entry and price erosion, the market size will be enormous. This creates room for substantial value capture by entrepreneurs who can capture even small percentages of total spending through solutions that improve outcomes, reduce waste, or enhance efficiency.

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