GLP 1 AND SGLT2 LANDSCAPE- APPROVALS, EVIDENCE, AND MARKET POSITIONING INSIGHTS

Dissertation Submitted to

The IIHMR University, Jaipur

for the partial fulfillment for the award of the degree of

Master of Business Administration (MBA)

in

Healthcare Analytics

by

Muskan Singh

Under the Supervision and Guidance of

Dr. Kumar Parimal Shrestha

2026

IIHMR UNIVERSITY

CERTIFICATE

This is to certify that dissertation titled **GLP-1 and SGLT2 Landscape – Approvals, Evidence, and Market Positioning Insights** is a record of the research work undertaken by **Muskan Singh** in partial fulfillment of the requirements for the award of the degree of **MBA Healthcare Analytics** from the IIHMR University, Jaipur under my guidance and supervision and her approach to the research study has been sincere, scientific, and analytical.

Kumar Parimal Shrestha
Faculty Guide
IIHMR University,Jaipur

Date:18/06/2026

DECLARATION BY STUDENT

I hereby declare that this dissertation titled **"GLP-1 and SGLT2 Landscape – Approvals, Evidence, and Market Positioning Insights"** is the Bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

Muskan Singh

Name: Muskan Singh
Date: 18/06/2026

ABSTRACT

Title: GLP-1 and SGLT2 Landscape – Approvals, Evidence, and Market Positioning Insights

Author Name: Muskan Singh

Advisor Name: Kumar Parimal Shrestha

Keywords:

GLP-1 Receptor Agonists, SGLT2 Inhibitors, Type 2 Diabetes Mellitus (T2DM), Health Technology Assessment (HTA), Cost-Effectiveness, Cardiovascular Outcomes, Market Access, Empagliflozin, Semaglutide, Tirzepatide

Background:

Type 2 diabetes mellitus (T2DM) represents a growing global health burden requiring effective pharmacological management strategies. In recent years, newer drug classes such as GLP-1 receptor agonists and SGLT2 inhibitors have transformed treatment by offering benefits beyond glycemic control, including cardiovascular and renal protection. However, increasing competition among therapies particularly semaglutide and tirzepatide has led to diverse clinical, economic, and reimbursement claims. Differences in regulatory approvals (FDA vs EMA), therapy indications (T2DM, obesity, cardiovascular risk), and evidence maturity further complicate payer decision-making and optimal positioning of these therapies.

Objective:

To critically evaluate the landscape of GLP-1 receptor agonists and SGLT2 inhibitors by analyzing regulatory approvals, clinical and economic evidence, and payer perceptions, with the aim of identifying key drivers influencing market access, reimbursement decisions, and treatment positioning in T2DM management

Methodology:

A descriptive and analytical study was conducted using secondary data derived from multiple sources, including regulatory approval datasets (FDA and EMA), targeted literature reviews (TLR), and global health technology assessment (HTA) reports. Data on drug characteristics, indications, approval timelines, comparative clinical outcomes, and cost-effectiveness evidence were synthesized. Additionally, qualitative insights from HTA appraisals and payer

critiques were examined to understand evidence gaps and decision-making trends across major healthcare systems.

Results/Findings:

The analysis revealed that GLP-1 receptor agonists, especially semaglutide and tirzepatide, demonstrate superior outcomes in glycemic control and weight reduction, supported by multiple clinical trials and expanding indications such as obesity management. In contrast, SGLT2 inhibitors, particularly empagliflozin, showed strong and consistent evidence for cardiovascular and renal outcomes, validated through long-term trials and real-world studies.

Cost-effectiveness findings across studies were inconclusive, with nearly equal evidence supporting both drug classes, largely influenced by variability in modelling assumptions and data inputs. HTA agencies frequently raised concerns regarding GLP-1 and dual agonist therapies, including reliance on surrogate endpoints (HbA1c and weight), lack of long-term outcomes, and uncertainties in economic models. As a result, many GLP-1 therapies received restricted or negative reimbursement decisions, while SGLT2 inhibitors demonstrated more consistent acceptance due to stronger real-world and outcome-based evidence.

Conclusions:

The study concludes that while GLP-1 receptor agonists and dual GIP/GLP-1 therapies offer promising clinical advantages, particularly in glycemic control and weight management, their market positioning is limited by evidence gaps in long-term clinical outcomes and economic uncertainty. In contrast, empagliflozin and other SGLT2 inhibitors remain strongly aligned with payer expectations due to robust cardiovascular and renal evidence supported by real-world data. Future success in market access will depend on generating high-quality longitudinal evidence, improving economic modelling transparency, and aligning clinical outcomes with payer-relevant endpoints.

ACKNOWLEDGMENT

I express my heartfelt gratitude to everyone who supported, guided, and encouraged me throughout the journey of completing my dissertation, undertaken as a part of my MBA in Pharmaceutical Management.

First and foremost, I would like to extend my sincere appreciation to the administration of **IQVIA** for granting me the opportunity to undergo my dissertation in their esteemed organization.

These invaluable experiences have significantly contributed to my professional and personal development.

A special note of thanks to my mentors **Sheily Kamra and Anshu Rajput** for their continuous support, insightful guidance, and for providing me with golden opportunities to learn in a real-time industry setting. Their encouragement and mentorship played a vital role in shaping my understanding of the pharmaceutical sector.

I express my deepest gratitude to **Kumar Parimal Shrestha Sir**, my Faculty Mentor, for his invaluable support, expert advice, and continuous encouragement throughout the course of my dissertation.

His guidance has been instrumental in both my academic and professional growth. My sincere thanks to **Mr. Anshul Goyal** and the Placement Committee Team for their efforts in coordinating the dissertation process and providing us with all possible assistance.

Throughout the dissertation, I have learned and experienced a great deal that has enriched my knowledge and will serve as a strong foundation in my professional career.

I am committed to applying the insights and skills acquired through this journey in the most meaningful and impactful manner.

Thank you all for being an integral part of my learning journey

Yours Sincerely,
Muskan Singh

TABLE OF CONTENT

Chapter 1: Introduction

Type 2 Diabetes Mellitus (T2DM) has emerged as one of the most significant global health challenges of the 21st century, affecting millions of individuals and placing a substantial burden on healthcare systems worldwide. The increasing prevalence of T2DM is driven by factors such as sedentary lifestyles, unhealthy dietary patterns, obesity, and aging populations. Over time, the disease leads to serious complications, including cardiovascular disease, kidney failure, neuropathy, and stroke, making its effective management a critical priority in modern healthcare.

Traditionally, the pharmacological management of T2DM primarily focused on controlling blood glucose levels using older agents such as metformin, sulfonylureas, and insulin. However, advances in medical research have shifted the treatment paradigm toward therapies that not only manage glycemic levels but also provide broader clinical benefits. In this context, newer drug classes such as GLP-1 receptor agonists and SGLT2 inhibitors have gained prominence due to their ability to improve patient outcomes beyond glucose control.

Globally, 589 million adults (20–79 years) were living with diabetes in 2024, and this number is expected to increase to 853 million by 2050, highlighting the urgent need for advanced treatment strategies. Diabetes-related healthcare expenditure has already crossed USD 1 trillion globally, reflecting the economic burden of poor disease management. Among newer therapies, GLP-1 receptor agonists have shown rapid adoption, with usage increasing by over 150% globally (2018–2022) and accounting for 26.5% of treated diabetic patients in the U.S. by 2024. The global GLP-1 market alone was valued at approximately USD 66 billion in 2025 and is projected to reach USD 185 billion by 2033, indicating strong commercial expansion.

GLP-1 receptor agonists function by mimicking the action of endogenous incretin hormones, thereby stimulating insulin secretion, reducing glucagon release, slowing gastric emptying, and promoting satiety. This unique mechanism contributes to improved glycemic control as well as significant weight reduction, which is particularly beneficial for overweight or obese patients with T2DM. Over time, the GLP-1 class has evolved from early injectable therapies like exenatide to advanced formulations such as once-weekly semaglutide and even oral versions, enhancing patient convenience and adherence

On the other hand, SGLT2 inhibitors operate through an insulin-independent mechanism by promoting the excretion of excess glucose via the kidneys. This not only reduces blood glucose levels but also delivers additional cardiovascular and renal protection. Drugs such as empagliflozin (Jardiance) have demonstrated strong evidence in reducing the risk of heart failure, cardiovascular mortality, and progression of chronic kidney disease. These benefits have been validated through large-scale clinical trials and real-world studies, making SGLT2 inhibitors an essential component in the management of high-risk T2DM patients.

The growing adoption of these therapies has also led to increased competition among pharmaceutical companies, particularly with the emergence of advanced GLP-1 and dual GIP/GLP-1 therapies such as semaglutide and tirzepatide. These drugs have positioned themselves strongly based on their superior glycemic control and weight loss benefits. However, they also present challenges in terms of cost, long-term clinical evidence, and variability in treatment outcomes.

In parallel with clinical evaluation, regulatory and reimbursement frameworks play a crucial role in determining the success and accessibility of these therapies. Regulatory bodies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) are responsible for approving drugs based on safety, efficacy, and quality standards. The approval timelines, indications, and labeling differ between these agencies, influencing global market access and adoption. For instance, several GLP-1 and SGLT2 drugs have received approvals for additional indications such as cardiovascular risk reduction and weight management, reflecting an expansion in their therapeutic scope.

Beyond regulatory approval, Health Technology Assessment (HTA) agencies such as NICE (UK), CADTH (Canada), and G-BA (Germany) evaluate the clinical and economic value of therapies to determine reimbursement eligibility. These agencies focus on factors such as cost-effectiveness, long-term clinical outcomes, and overall healthcare impact. Evidence from multiple HTA reports indicates that while GLP-1 receptor agonists offer strong short-term benefits, their reliance on surrogate endpoints such as HbA1c levels and weight reduction often raises concerns regarding long-term effectiveness and real-world applicability.

Conversely, SGLT2 inhibitors have demonstrated more consistent acceptance among HTA agencies due to their robust cardiovascular and renal outcomes supported by long-term trials and real-world evidence. This has resulted in relatively stronger reimbursement support and market positioning for drugs like empagliflozin.

Another important dimension in evaluating these therapies is their economic value. Cost-effectiveness studies comparing GLP-1 and SGLT2 therapies have shown mixed results, largely due to variations in modeling approaches, assumptions, and data inputs. Many economic models rely on surrogate measures and predictive risk equations, which may not fully capture real-world outcomes. Consequently, the lack of standardized methodologies has made it difficult to establish a clear superiority of one class over the other.

Given this complex landscape, it becomes essential to conduct a comprehensive analysis that integrates clinical evidence, regulatory frameworks, economic evaluations, and payer perspectives. Understanding these factors is critical not only for clinicians and healthcare providers but also for pharmaceutical companies aiming to position their products effectively in competitive markets.

This study, therefore, focuses on providing a holistic understanding of the GLP-1 and SGLT2 therapy landscape by examining their approvals, clinical and economic evidence, and market positioning strategies. By identifying the key drivers influencing adoption and reimbursement decisions, the research aims to contribute valuable insights for improving decision-making in healthcare policy and pharmaceutical strategy.

Chapter 2: Literature Review

2.1 Overview of GLP-1 and SGLT2 Therapies in T2DM Management

The management of Type 2 Diabetes Mellitus (T2DM) has undergone a significant transformation with the introduction of newer pharmacological classes, particularly GLP-1 receptor agonists and SGLT2 inhibitors. These therapies complement traditional treatment approaches by targeting multiple physiological pathways beyond glycemic control. While GLP-1 receptor agonists enhance insulin secretion, reduce glucagon release, and promote satiety, SGLT2 inhibitors reduce blood glucose levels through increased urinary glucose excretion.

Over time, the therapeutic landscape has expanded from early injectable GLP-1 agents such as exenatide to advanced once-weekly and oral formulations like semaglutide, as well as dual GIP/GLP-1 therapies such as tirzepatide. This evolution reflects a strong focus on improving patient adherence, efficacy, and convenience.

SGLT2 inhibitors, including empagliflozin, have gained prominence due to their well-documented cardiovascular and renal benefits, making them integral to treatment guidelines, especially for patients with high cardio-renal risk.

2.2 Significance of Clinical Outcomes in Therapy Evaluation

Clinical outcomes play a central role in determining the effectiveness of diabetes therapies. Traditionally, glycemic control measured by HbA1c levels served as the primary endpoint in clinical trials. However, modern healthcare frameworks emphasize broader outcomes such as cardiovascular events, mortality, and renal function.

GLP-1 receptor agonists have demonstrated strong efficacy in reducing HbA1c levels and promoting weight loss, making them attractive options for patients with obesity or poor glycemic control. However, many of these outcomes are based on surrogate markers, which may not fully capture long-term clinical benefits. Clinical evidence shows that empagliflozin reduces **cardiovascular mortality by 38%** and **heart failure hospitalization by 35%,** establishing its long-term clinical benefit. GLP-1 therapies demonstrate **greater HbA1c**

reduction (~1–1.5%) and weight loss (~5–10%), making them effective for metabolic control.

In contrast, SGLT2 inhibitors have shown consistent evidence in reducing cardiovascular mortality, heart failure hospitalization, and progression of chronic kidney disease, supported by both clinical trials and real-world evidence.

2.3 Economic Evaluation and Cost-Effectiveness Evidence

Cost-effectiveness analysis is a critical factor influencing the adoption and reimbursement of diabetes therapies. Economic models such as the CORE Diabetes Model and other simulation tools are commonly used to estimate long-term outcomes and costs.

Existing literature demonstrates mixed findings regarding the cost-effectiveness of GLP-1 receptor agonists and SGLT2 inhibitors. Some studies favor GLP-1 therapies due to their higher efficacy in glycemic control and weight reduction, while others highlight the long-term benefits of SGLT2 inhibitors in reducing hospitalization and complications.

However, significant variability exists across studies due to differences in model assumptions, time horizons, comparators, and funding sources. Many economic evaluations rely on surrogate outcomes and outdated risk equations, leading to uncertainty in results and limiting their applicability in real-world settings.

Studies show that nearly **12 economic evaluations** comparing GLP-1 and SGLT2 therapies resulted in mixed conclusions:

- 5 studies: SGLT2 more cost-effective
- 5 studies: GLP-1 more cost-effective
- 2 studies: No difference (IQVIA data)

2.4 Health Technology Assessment (HTA) Perspectives and Challenges

Health Technology Assessment (HTA) agencies play a crucial role in evaluating the value of new therapies and determining reimbursement decisions. Agencies such as NICE (UK), CADTH (Canada), G-BA (Germany), and PBAC (Australia) assess both clinical and economic

evidence to ensure optimal resource allocation. Several HTA bodies (UK, Canada, Germany) have imposed **restricted reimbursement policies on GLP-1 therapies** due to uncertainty in long-term outcomes.

Literature indicates that HTA bodies often raise concerns regarding GLP-1 and dual GIP/GLP-1 therapies due to reliance on surrogate endpoints, lack of long-term outcomes, and uncertainty in economic modeling. As a result, many of these therapies receive restricted or conditional approvals.

For example, semaglutide and tirzepatide have shown promising results in weight reduction and glycemic control, yet HTA agencies frequently limit their use due to insufficient evidence on long-term cardiovascular and mortality outcomes.

In contrast, SGLT2 inhibitors such as empagliflozin are more favorably evaluated by HTA bodies because of robust clinical trial data and real-world evidence supporting cardiovascular and renal benefits.

2.5 Role of Regulatory Approvals in Market Access

Regulatory approval is a fundamental step in the lifecycle of pharmaceutical products, determining their availability in the market. The U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) provide approvals based on safety, efficacy, and quality data.

A comparative analysis shows that both agencies approve a wide range of GLP-1 and SGLT2 therapies, with slight differences in approval timelines, indications, and dosing guidelines. For instance, several GLP-1 therapies have been expanded to include indications for chronic weight management and cardiovascular risk reduction, demonstrating their growing therapeutic relevance.

The increasing number of approvals reflects the rapid innovation in diabetes treatment; however, regulatory approval alone does not guarantee market success, as reimbursement decisions depend on additional economic and clinical considerations.

2.6 Market Positioning and Competitive Dynamics

The diabetes therapy market is highly competitive, with pharmaceutical companies positioning their products based on clinical efficacy, economic value, and patient outcomes. GLP-1 receptor agonists such as semaglutide and tirzepatide are often positioned as superior therapies due to their strong impact on glycemic control and weight loss.

These therapies leverage claims related to improved clinical outcomes and cost-effectiveness to gain market share. However, literature suggests that such claims are frequently challenged by HTA bodies due to methodological limitations and insufficient long-term data.

On the other hand, SGLT2 inhibitors such as empagliflozin maintain a strong market position due to their established clinical benefits, particularly in reducing cardiovascular and renal risks. Real-world evidence and long-term outcome data further strengthen their credibility among payers and healthcare providers.

2.7 Research Gaps and Need for the Current Study

Despite extensive research on GLP-1 and SGLT2 therapies, several gaps remain in the existing literature. Most studies focus on isolated aspects such as clinical efficacy or economic evaluation, with limited integration of regulatory, HTA, and real-world evidence.

Additionally, many economic models are based on assumptions and surrogate endpoints, leading to inconsistencies in cost-effectiveness findings. There is also a lack of comprehensive analysis that combines clinical, economic, and payer perspectives to provide a unified understanding of therapy positioning.

The present study addresses these gaps by offering a holistic evaluation of GLP-1 and SGLT2 therapies, integrating regulatory approvals, clinical outcomes, economic evidence, and HTA insights. This approach aims to provide actionable recommendations for improving market access strategies and enhancing evidence-based decision-making in T2DM management.

CHAPTER 3: METHODOLOGY

3.1 Study Design

This study adopts a descriptive and analytical research design, primarily based on a synthesis of secondary data. The research integrates information from regulatory datasets, targeted literature reviews (TLR), and Health Technology Assessment (HTA) reports to evaluate the comparative landscape of GLP-1 receptor agonists and SGLT2 inhibitors in Type 2 Diabetes Mellitus (T2DM).

The study focuses on identifying patterns in clinical outcomes, cost-effectiveness, regulatory approvals, and payer decisions. A comparative and interpretative approach is used to analyze differences between these therapy classes and to assess their market positioning dynamics.

3.2 Study Setting

The study is conducted in the context of the global pharmaceutical and healthcare market, with a focus on major regulatory and reimbursement environments. This includes regions where key regulatory bodies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) govern drug approvals, as well as countries with established HTA frameworks like the UK, Canada, Germany, France, and Australia.

These settings are selected because they represent developed healthcare systems where clinical evidence, economic evaluation, and payer decision-making significantly influence drug adoption and market access.

3.3 Data Source

The study is based on secondary data sources, including:

• Regulatory approval datasets listing GLP-1 and SGLT2 molecules, their indications, dosing, and timelines (FDA and EMA)

• IQVIA Targeted Literature Review (TLR) reports analyzing economic models and clinical evidence

• HTA extraction reports and payer decision summaries across multiple countries

• Pharmaceutical and market access presentations providing insights into competitor claims and positioning strategies

Data were compiled, reviewed, and structured into comparative frameworks using Microsoft Excel for further analysis.

3.4 Variables Measured

The variables used in this study included:

Variable	Definition
Drug Class	GLP-1 receptor agonists or SGLT2 inhibitors
Molecule Characteristics	Formulation, dosage, frequency, and indication
Clinical Outcomes	HbA1c reduction, weight loss, cardiovascular and renal benefits
Regulatory Approval	Approval year, agency (FDA/EMA), and indication scope
Cost-Effectiveness	Incremental cost-effectiveness ratios (ICERs) and model outcomes
HTA Decision	Approval status, restrictions, or rejection by HTA bodies
Evidence Type	Clinical trial data vs real-world evidence (RWE)
Market Positioning Claims	Claims related to efficacy, cost, and patient outcomes

3.5 Data Analysis Tools

The analysis was conducted using a combination of qualitative and quantitative approaches:

• Microsoft Excel: Used for data organization, categorization, and comparative tabulation

• Descriptive Analysis: Used to summarize trends in drug approvals, clinical outcomes, and HTA decisions

• Comparative Analysis: Conducted between GLP-1 and SGLT2 therapies across multiple parameters (clinical, economic, and regulatory)

• Qualitative Review: Interpretation of HTA reports and literature findings to identify patterns, limitations, and payer concerns

Graphical and tabular representations were used to highlight differences in approvals, clinical effectiveness, and reimbursement outcomes.

3.6 Ethical Considerations

This study is based entirely on secondary data from publicly available and authorized sources, including regulatory datasets and published reports. No patient-level data or confidential information was used.

Therefore:
• No human subjects were involved
• No personal health data was accessed
• Formal ethical clearance was not required

Proper citation and acknowledgment of all data sources were ensured to maintain academic integrity.

3.7 Limitations of the Methodology

• The study relies primarily on secondary data, limiting control over data quality and completeness

• Variability in economic models and assumptions across studies may affect comparability

• Limited availability of long-term real-world data for newer therapies such as tirzepatide

• Differences in HTA frameworks across countries may introduce variability in interpretation

• The study does not include primary data collection or stakeholder interviews

3.8 Reliability and Validity

The reliability of the study is supported by the use of multiple credible data sources, including IQVIA reports, regulatory datasets, and HTA publications. Cross-verification of findings across different sources enhances consistency and accuracy.

Validity is ensured through:

- Inclusion of globally recognized regulatory and HTA frameworks
- Comparative analysis across multiple countries and datasets
- Integration of both clinical trial evidence and real-world data

This comprehensive approach enhances the robustness of the findings and ensures meaningful insights into healthcare and pharmaceutical decision-making.

CHAPTER 4: RESULTS AND DISCUSSION

4.1 Overview of Key Findings

The analysis of the GLP-1 receptor agonists and SGLT2 inhibitors landscape reveals significant differences in clinical effectiveness, economic outcomes, and market positioning. The study integrates evidence from regulatory approvals, HTA decisions, and global market data to examine how these therapies are perceived and adopted.

Globally, the burden of T2DM continues to rise, with approximately 589 million adults living with diabetes in 2024, representing nearly 1 in 9 adults worldwide. This increasing prevalence is a key driver behind the rapid growth and adoption of advanced therapies such as GLP-1 and SGLT2 drugs.

4.2 Clinical Outcomes Comparison

GLP-1 Therapies (Semaglutide, Tirzepatide)

The results indicate that GLP-1 receptor agonists demonstrate superior reductions in HbA1c levels and body weight. Market data suggests that semaglutide-based products dominate the segment, accounting for more than 50% of the global GLP-1 market share in 2025.

Additionally, GLP-1 drugs have shown rapid adoption, with usage increasing by over 150% between 2018 and 2022, and nearly 26.5% of diabetic patients in the U.S. using GLP-1 injectables by 2024.

These findings confirm that GLP-1 therapies are highly effective in improving glycemic outcomes and supporting weight management, making them particularly attractive for obese T2DM patients.

SGLT2 Inhibitors (Empagliflozin)

In contrast, SGLT2 inhibitors show stronger long-term cardiovascular and renal benefits. The EMPA-REG OUTCOME trial demonstrated that empagliflozin reduced:

- Cardiovascular death by 38%
- Hospitalization for heart failure by 35%
- All-cause mortality by 32%

Further real-world evidence indicates improved outcomes in heart failure patients, with lower risk of hospitalization and mortality compared to other therapies.

This highlights that while GLP-1 therapies excel in surrogate endpoints, SGLT2 inhibitors provide clinically meaningful long-term outcomes, particularly in high-risk populations.

4.3 Economic and Cost-Effectiveness Findings

The study identified that cost-effectiveness results remain highly variable across different economic models. This variability arises due to:

- Differences in time horizons
- Use of surrogate endpoints
- Variations in comparator therapies

From a market perspective, the GLP-1 segment is experiencing rapid growth, with the global market valued at approximately USD 66 billion in 2025 and projected to reach USD 185 billion by 2033, growing at a CAGR of 12–13%.

This growth is driven by increasing demand for weight-loss therapies and expanding indications beyond diabetes. However, despite high market value, the high cost of GLP-1 drugs continues to be a barrier for widespread reimbursement.

On the other hand, SGLT2 inhibitors, though less expensive in many markets, deliver long-term cost savings by reducing hospitalizations and complications, thereby improving their economic value from a payer perspective.

4.4 HTA and Payer Decision Trends

Health Technology Assessment (HTA) agencies play a critical role in determining the adoption of these therapies. The findings suggest that HTA bodies are more cautious toward GLP-1 and dual agonist therapies due to:

- Heavy reliance on surrogate endpoints (HbA1c, weight loss)
- Limited long-term cardiovascular outcome data
- Uncertainty in economic modeling assumptions

For example, NICE (UK) approved semaglutide for reducing cardiovascular risk only after strong outcome-based evidence became available through recent trials, highlighting the importance of robust data for reimbursement decisions. [nice.org.uk]

In contrast, SGLT2 inhibitors like empagliflozin have been consistently favored due to their strong evidence base in cardiovascular and renal outcomes, making them more aligned with payer expectations.

4.5 Market Positioning and Competitive Dynamics

The results demonstrate that GLP-1 therapies dominate in commercial growth, while SGLT2 inhibitors lead in clinical and payer alignment.

- GLP-1 market size: ~USD 53 billion in 2024, projected to reach USD 157 billion by 2030
- Semaglutide alone generated over USD 40 billion revenue in 2024, making it one of the top-selling drugs globally.

This indicates strong commercial success driven by demand for weight loss and metabolic benefits.

However, competitor claims around superiority (particularly for semaglutide and tirzepatide) are often challenged by HTA bodies due to lack of long-term evidence.

SGLT2 inhibitors, particularly empagliflozin (Jardiance), maintain a strong value proposition based on:

- Real-world evidence (RWE)
- Proven cardiovascular mortality reduction
- Broader clinical indications (heart failure, CKD)

4.6 Discussion

The findings highlight a critical divergence between clinical efficacy, real-world outcomes, and payer acceptance.

While GLP-1 therapies provide strong short-term benefits (HbA1c reduction and weight loss), their long-term clinical value remains uncertain in many cases. This creates challenges in reimbursement and payer acceptance, despite strong commercial demand.

In contrast, SGLT2 inhibitors demonstrate consistent and high-quality outcome data, making them more favorable from a healthcare system perspective. Their ability to reduce hospitalizations and mortality aligns closely with payer priorities, particularly in cost-constrained environments.

Another important observation is that economic models lack standardization, leading to inconsistent conclusions regarding cost-effectiveness. This suggests the need for more transparent and real-world–aligned economic evaluations.

Overall, the study concludes that the future of T2DM therapy will depend on:

- Generation of long-term outcome data for newer therapies
- Integration of real-world evidence into decision-making
- Alignment of clinical benefits with payer expectations

CHAPTER 5: RECOMMENDATIONS AND CONCLUSION

5.1 Conclusion

The management of Type 2 Diabetes Mellitus (T2DM) has evolved significantly with the emergence of advanced therapeutic classes such as GLP-1 receptor agonists and SGLT2 inhibitors. This study aimed to evaluate the comparative landscape of these therapies in terms of regulatory approvals, clinical outcomes, economic evidence, and payer perspectives.

The findings demonstrate that while both therapy classes have transformed diabetes care, they differ substantially in their clinical value proposition and market positioning. GLP-1 receptor agonists, particularly semaglutide and tirzepatide, have shown superior efficacy in reducing HbA1c levels and promoting weight loss, which has led to rapid market growth. The global GLP-1 market was valued at approximately USD 66 billion in 2025 and is projected to exceed USD 185 billion by 2033, reflecting strong commercial demand.

However, despite their strong clinical efficacy, GLP-1 therapies face challenges related to high cost, reliance on surrogate endpoints, and uncertainty in long-term outcomes, which often limit their acceptance by HTA bodies and payers.

In contrast, SGLT2 inhibitors such as empagliflozin demonstrate robust and consistent evidence in improving cardiovascular and renal outcomes. Clinical trial data indicate that empagliflozin reduces cardiovascular death by 38%, hospitalization for heart failure by 35%, and overall mortality by 32%, establishing its strong real-world value.

From a payer and healthcare system perspective, SGLT2 inhibitors are more aligned with long-term value-based care, as they reduce hospitalizations and disease complications. This makes them more favorable in HTA evaluations compared to GLP-1 therapies, which are often restricted due to limited long-term evidence and economic uncertainties.

Another important finding is the lack of standardization in cost-effectiveness models, leading to inconsistent conclusions across studies. Many analyses are based on short-term clinical data and predictive modeling assumptions, which do not fully capture real-world outcomes.

Overall, the study concludes that while GLP-1 therapies dominate in terms of innovation and market expansion, SGLT2 inhibitors maintain a stronger position in clinical validation, real-world evidence, and payer acceptance. The future of T2DM management will depend on the

ability of newer therapies to generate long-term evidence and demonstrate sustained value across clinical and economic dimensions.

5.2 Recommendations

Based on the findings and analysis, the following recommendations are proposed to improve clinical adoption, market access, and overall value realization of T2DM therapies:

A. Clinical and Evidence-Based Recommendations

1. **Focus on Long-Term Outcome Studies**
   Pharmaceutical companies should invest in long-term clinical trials and real-world evidence (RWE) generation to demonstrate sustained cardiovascular, renal, and mortality benefits. This will strengthen the evidence base, particularly for GLP-1 and dual agonist therapies.

2. **Shift from Surrogate to Clinical Endpoints**
   Greater emphasis should be placed on clinically meaningful outcomes such as mortality, cardiovascular events, and quality of life, rather than relying solely on surrogate markers like HbA1c and weight loss.

3. **Expand Real-World Evidence Generation**
   Integration of real-world data through observational studies and registries can enhance trust among payers and healthcare providers by validating trial results in practical settings.

B. Economic and Market Access Recommendations

1. **Standardization of Cost-Effectiveness Models**
   There is a need to develop more transparent and standardized economic models that incorporate real-world data and reflect current clinical practice. This will reduce variability and improve decision-making consistency.

2. **Value-Based Pricing Strategies**
   Pharmaceutical companies should adopt pricing strategies aligned with demonstrated

clinical outcomes, especially for high-cost therapies like GLP-1 drugs, to improve affordability and reimbursement acceptance.

3. **Early Engagement with HTA Agencies**
   Engaging with HTA bodies during the early stages of drug development can help align clinical trial design with payer expectations, improving the likelihood of favorable reimbursement decisions.

C. Regulatory and Policy-Level Recommendations

1. **Harmonization of Regulatory and HTA Requirements**
   Improved alignment between regulatory approvals (FDA/EMA) and payer requirements can reduce delays in market access and ensure faster patient access to innovative therapies.

2. **Encourage Broader Indication Approvals**
   Expanding the approved indications for therapies—such as cardiovascular disease, obesity, and chronic kidney disease—can enhance their overall value proposition and utilization.

3. **Promote Evidence-Based Policy Frameworks**
   Policymakers should prioritize therapies with strong long-term evidence and real-world benefits, ensuring efficient allocation of healthcare resources.

D. Strategic Recommendations for Pharmaceutical Positioning

1. **Strengthen Real-World Value Communication**
   Companies should highlight real-world outcomes and long-term benefits, particularly for SGLT2 inhibitors, to strengthen payer confidence.

2. **Balanced Positioning Strategy**
   GLP-1 therapies should be positioned not only for glycemic control and weight loss but also supported with long-term clinical evidence to address payer concerns.

3. **Integrated Clinical-Economic Approach**
   Combining clinical outcomes with economic value in communication strategies will help in better stakeholder engagement and improved market positioning.

5.3 Future Scope of the Study

Further research can explore the following areas:

• Comparative analysis of patient adherence and treatment persistence across therapy classes

• Evaluation of real-world effectiveness in diverse patient populations

• Integration of artificial intelligence and predictive analytics in treatment selection

• Cross-country comparison of HTA decision frameworks and reimbursement policies

• Long-term economic impact of emerging therapies such as dual GIP/GLP-1 agonists

5.4 Final Remarks

The findings of this study highlight that the evaluation of diabetes therapies extends beyond clinical efficacy to encompass economic considerations, regulatory frameworks, and payer perspectives. With the global diabetes population expected to rise to 853 million by 2050, the demand for effective and sustainable treatment solutions will continue to grow.

Improving treatment outcomes requires a holistic and evidence-based approach, where clinical innovation is supported by long-term data, economic value, and policy alignment.

Ultimately, the goal of advancing T2DM management is not only to improve market performance but to enhance patient outcomes, reduce disease burden, and ensure sustainable healthcare delivery worldwide.

CHAPTER 6: REFERENCES

International Diabetes Federation. *IDF Diabetes Atlas – Global Diabetes Data & Statistics* [Internet]. Brussels: IDF; 2025 [cited 2026 May 30]. Available from: https://diabetesatlas.org/ [grandviewr...search.com]

- Grand View Research. *GLP-1 Receptor Agonist Market Size & Industry Report* [Internet]. 2025 [cited 2026 May 30]. Available from: https://www.grandviewresearch.com/industry-analysis/glp-1-receptor-agonist-market [pmc.ncbi.nlm.nih.gov]
- OneTwenty. *Semaglutide and GLP-1 Statistics Report* [Internet]. 2026 [cited 2026 May 30]. Available from: https://onetwenty.com/blog/semaglutide-statistics [ajconline.org]
- Emergen Research. *Global Semaglutide Market Size, Share & Trends Report* [Internet]. 2025 [cited 2026 May 30]. Available from: https://www.emergenresearch.com/industry-report/semaglutide-market [frontiersin.org]
- Zinman B, Wanner C, Lachin JM, et al. *Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes* [Internet]. N Engl J Med; 2015 [cited 2026 May 30]. Available from: https://www.nejm.org/doi/pdf/10.1056/NEJMoa1504720 [PPT1 | PowerPoint]
- Modzelewski KL, Pipilas A, Bosch NA, et al. *Comparative Outcomes of Empagliflozin vs Dapagliflozin in Heart Failure Patients* [Internet]. JAMA Network Open; 2024 [cited 2026 May 30].
  Available from: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2818219 [GLP 1 Molecules | Word]
- National Institute for Health and Care Excellence (NICE). *Semaglutide for Reducing Risk of Major Cardiovascular Events* [Internet]. London: NICE; 2026 [cited 2026 May 30]. Available from: https://www.nice.org.uk/guidance/ta1152 [thelancet.com]
- IQVIA. *Jardiance T2DM Market Access Competitive Response – TLR & HTA Findings Report* [Internet]. 2024 [cited 2026 May 30]. Available from: Internal IQVIA Report
- IQVIA. *Jardiance T2DM Competitive Response – HTA Extraction Report* [Internet]. 2024 [cited 2026 May 30]. Available from: Internal IQVIA Report
- IQVIA. *T2D Treatment Landscape: Economic Models, HTA Decisions and Competitor Positioning* [Internet]. 2026 [cited 2026 May 30]. Available from: Internal IQVIA Presentation

- International Diabetes Federation. *IDF Diabetes Atlas – Global Diabetes Data & Statistics* [Internet]. Brussels: IDF; 2025 [cited 2026 May 30]. Available from: https://diabetesatlas.org/ [grandviewr...search.com]
- Grand View Research. *GLP-1 Receptor Agonist Market Size & Industry Trends Analysis Report* [Internet]. US: Grand View Research; 2025 [cited 2026 May 30]. Available from: https://www.grandviewresearch.com/industry-analysis/glp-1-receptor-agonist-market [pmc.ncbi.nlm.nih.gov]

- OneTwenty. *Semaglutide and GLP-1 Statistics You Need to Know (2026)* [Internet]. 2026 [cited 2026 May 30]. Available from: https://onetwenty.com/blog/semaglutide-statistics [ajconline.org]
- Emergen Research. *Global Semaglutide Market Size, Share & Trends Report 2025–2035* [Internet]. 2025 [cited 2026 May 30]. Available from: https://www.emergenresearch.com/industry-report/semaglutide-market [frontiersin.org]
- Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. *Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes* [Internet]. N Engl J Med. 2015 [cited 2026 May 30]. Available from: https://www.nejm.org/doi/pdf/10.1056/NEJMoa1504720 [PPT1 | PowerPoint]
- Modzelewski KL, Pipilas A, Bosch NA, et al. *Comparative Outcomes of Empagliflozin vs Dapagliflozin in Patients with Heart Failure* [Internet]. JAMA Network Open. 2024 [cited 2026 May 30]. Available from: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2818219 [GLP 1 Molecules | Word]
- National Institute for Health and Care Excellence (NICE). *Semaglutide for reducing the risk of major adverse cardiovascular events (TA1152)* [Internet]. London: NICE; 2026 [cited 2026 May 30]. Available from: https://www.nice.org.uk/guidance/ta1152 [thelancet.com]

CHAPTER 7: ANNEXURES:

Annexure A: GLP-1 and SGLT2 Approved Molecules Overview

This annexure includes detailed tables of GLP-1 receptor agonists and SGLT2 inhibitors approved by regulatory authorities (FDA and EMA), covering:

- Molecule name
- Brand name
- Formulation (injectable/oral)
- Dosage and frequency
- Year of approval
- Approved indications

Annexure B: Comparative Clinical Outcomes Table

This annexure presents a comparative summary of key clinical outcomes for GLP-1 receptor agonists and SGLT2 inhibitors:

Parameter	GLP-1 Therapies	SGLT2 Inhibitors
HbA1c Reduction	High	Moderate
Weight Loss	High	Moderate
Cardiovascular Benefit	Limited/Variable	Strong (Proven)
Renal Protection	Emerging	Strong
Evidence Type	Mostly clinical trials	Clinical + real-world evidence

Annexure C: HTA Decision Summary Across Countries

This annexure includes a summary of HTA outcomes:

Country	Therapy	Decision	Key Reason
UK (NICE)	Semaglutide	Restricted	Cost & uncertainty
Germany (G-BA)	GLP-1	Limited benefit	Surrogate endpoints
Canada (CADTH)	GLP-1	Conditional	Cost-effectiveness concerns
Australia (PBAC)	Tirzepatide	Rejected	High budget impact

Annexure D: Economic Model Comparison

Details of economic models used in the study:

- CORE Diabetes Model
- Cardiff Model
- UKPDS Risk Equations
- IHE-DCM Model

This section highlights assumptions, limitations, and variability in outcomes across models.

Annexure E: Key Terminologies

- GLP-1 RA: Glucagon-Like Peptide-1 Receptor Agonist
- SGLT2: Sodium-Glucose Cotransporter-2
- HTA: Health Technology Assessment
- HbA1c: Glycated Hemoglobin
- ICER: Incremental Cost-Effectiveness Ratio

- RWE: Real-World Evidence

Annexure F: Data Sources Used

- IQVIA Reports (TLR, HTA Extraction, Market Access Analysis)
- Regulatory datasets (FDA & EMA approvals)
- Published economic and clinical studies
- Global diabetes and pharmaceutical market reports