CDSS Final Project-CDSS Framework

Title: Optimizing Disease-Induced Obesity Management with GLP-1 Receptor Agonists: The Role of Clinical Decision Support Systems

Presented by

Srilekha Kadiyala

INFO B-642 Clinical Decision Support Systems

Luddy School of Informatics, Computing, and Engineering, IUPUI

Department of BioHealth Informatics

Josette Jones, Ph.D., RN, FAMIA

May 2nd , 2024

Introduction:

In the realm of healthcare, the management of Disease-Induced Obesity (DIO), particularly when it is associated to metabolic disorders like that of type 2 diabetes, presents a significant challenge. The introduction of GLP-1 receptor agonists like Semaglutide and Tirzepatide has significantly advanced the treatment of these conditions [2,4,5]. These agents not only enhance glycaemic control but also facilitate substantial weight loss, addressing two critical aspects of metabolic health. Despite their effectiveness, the variability in patient responses and the potential for severe side effects such as gastrointestinal complications and cardiovascular risks necessitate a refined, personalized approach to treatment [5,11].

This paper discusses the role of Clinical Decision Support Systems in enhancing the management of DIO. CDSS are designed to integrate and analyse vast arrays of clinical data from genetic markers to patient-reported outcomes to inform and tailor treatment strategies. By leveraging real-time data and sophisticated analytic tools, CDSS can dynamically adjust treatment plans, ensuring that they align closely with the evolving clinical needs of each patient. The deployment of these systems involves multiple stakeholders, including healthcare providers, patients, and policymakers, who must collaborate to ensure the systems are used effectively and ethically [15,18,19,20]. Through the deployment of these systems, this paper aims to showcase how personalized medicine can be effectively implemented to improve treatment outcomes, reduce adverse effects, and optimize the overall healthcare experience for patients with DIO and related metabolic disorders. By engaging these stakeholders in the design, implementation, and ongoing refinement of CDSS, the paper will explore ways to enhance the usability and effectiveness of these systems, ensuring they meet the complex needs of diverse patient populations [24,27].

Problem Statement: Clinical risk factors and etiology-based prognosis in the treatment of Disease-Induced Obesity: Assessing Semaglutide and Tirzepatide role through Clinical Decision Support Systems

The management of Disease-Induced Obesity (DIO) presents a complex challenge in clinical practice, especially when it is associated to metabolic disorders like that of type 2 diabetes. The administration of advanced therapeutic agents like Semaglutide and Tirzepatide has shown efficacy in not only controlling blood glucose levels but also in significantly reducing body weight, which is crucial for patients suffering from DIO [1, 2]. However, the variability in patient responses and the presence of side effects such as gastrointestinal issues and potential cardiovascular risks highlight the necessity for a more optimized approach to treatment [3]. This variability necessitates the development of sophisticated Clinical Decision Rules within Clinical Decision Support Systems to optimize treatment outcomes [11].

Extensive studies, including those summarized in the systematic review have demonstrated the benefits of Semaglutide in reducing glycaemic levels and body weight, which are pivotal in managing DIO. The review elaborates on its superior performance compared to other antidiabetic agents, making it a potential cornerstone in DIO management strategies. However, the increased risk of gastrointestinal adverse events and unclear long-term effects on diabetic retinopathy and pancreatitis call for cautious clinical judgment and personalized treatment plans [4].

To address these complexities, there is a clear imperative to refine and expand the CDRs within CDSS to harness detailed clinical insights and emerging research data. I have developed decision rules that adapt well to the evolving landscape of medical research and patient-reported outcomes to optimize treatment paradigms. For instance, integrating real-time data on patient

responses to Semaglutide and Tirzepatide can guide adjustments in dosing and monitor potential side effects, thereby enhancing the precision of obesity management strategies(5, 6).

This final paper will discuss the development and implementation of such CDSS, focusing on the integration of comprehensive clinical data, from genetic markers to treatment responses, to refine and enhance the efficacy of Semaglutide and Tirzepatide in managing Disease-Induced Obesity. It will explore how CDSS can be optimized to predict individual risks and tailor interventions, accordingly, thus addressing the critical need for personalized treatment plans in clinical practice.

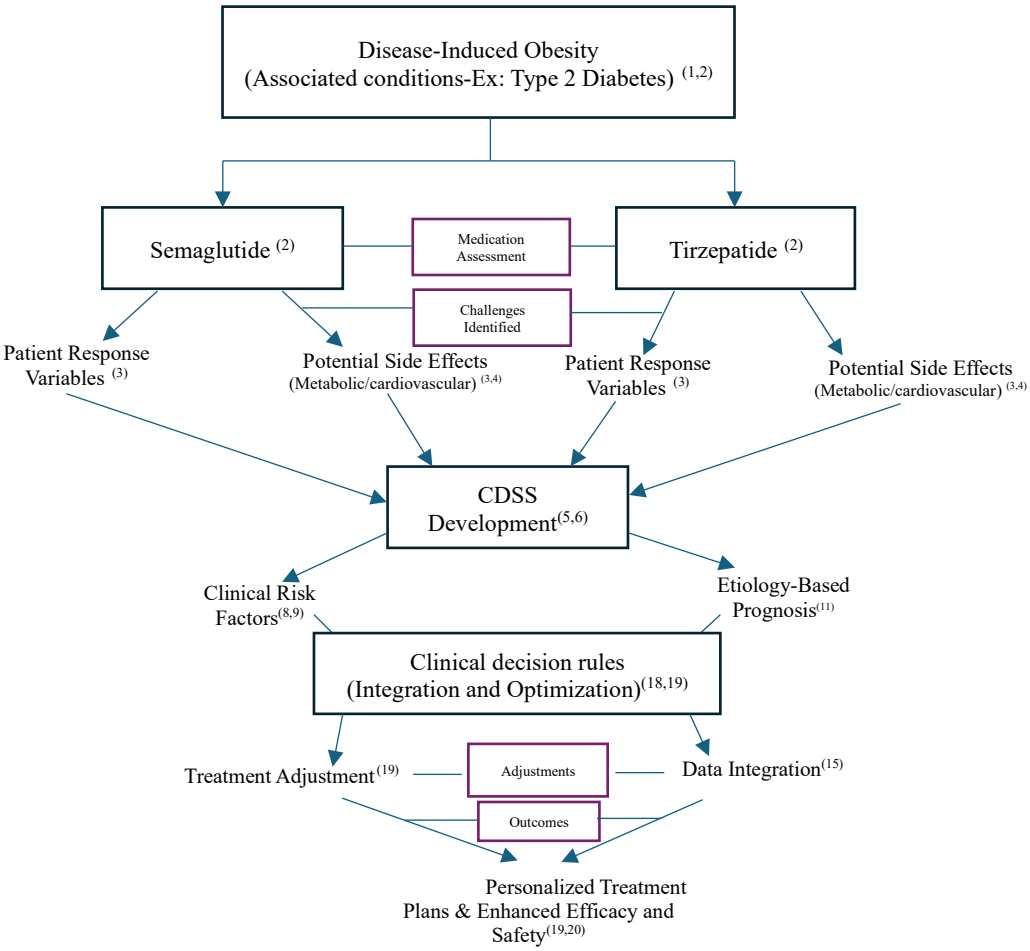


Figure 1. Overall Flow of Improving Clinical Decision Support System for Assessment of Disease-Induced Obesity

Literature Review:

Comprehensive findings from the literature:

The integration of glucagon-like peptide-1 (GLP-1) receptor agonists such as Semaglutide and Tirzepatide has significantly transformed the management of type 2 diabetes (T2D) and any other disease-induced obesity (DIO). These treatments address two fundamental aspects of metabolic disorders: glycaemic control and weight management. Studies have consistently shown that both Semaglutide and Tirzepatide elevate glycaemic control and facilitate weight loss in patients who have type 2 diabetes. However, comparative studies provide a mixed picture. While three of the studies indicate that Tirzepatide has superior efficacy in both glycaemic control and weight management, others highlight that Semaglutide maintains effective control with a well-established safety profile. These findings collectively suggest that while Tirzepatide might be preferred for patients with complex metabolic profiles, Semaglutide remains a reliable option for broader patient populations [7,8,9,10,11,12,13].

Moreover, the associated risks of hypoglycaemia associated with Semaglutide (ICD-10: E11.8) underscores the need for careful monitoring and personalized dose adjustments. Similarly, the dual mechanism of Tirzepatide, although beneficial in weight reduction, requires ongoing evaluation for potential cardiovascular impacts. These aspects highlight the importance of personalized treatment strategies to optimize outcomes and minimize adverse effects [2,13].

As the therapeutic use of GLP-1 receptor agonists expands, ongoing research is crucial to explore their long-term impacts, especially concerning cardiovascular health and potential neurocognitive benefits. Emerging data suggest these agents might have broader effects beyond their primary metabolic targets, which could redefine treatment paradigms in metabolic diseases. Recent comparative studies, such as those contrasting Tirzepatide and Semaglutide, reveal Tirzepatide's superior efficacy in significantly reducing HbA1c and body weight, highlighting its

potential for more complex metabolic profiles. This underscores the importance of sustained treatment to maintain these improvements, as discontinuation leads to significant weight regain and the reversal of cardiometabolic benefits. Concurrently, studies suggest that Type 2 diabetes often remains under-diagnosed, with many patients exhibiting microvascular complications at diagnosis. The variability in screening recommendations and the diagnostic efficacy of tests such as FPG, RPG, and A1C underscore the necessity for accurate diagnostic tools. The A1C test, recommended by the ADA, is crucial for early intervention, even when baseline levels are not overtly abnormal. The integration of Clinical Decision Support Systems (CDSS) has been pivotal in tailoring treatments to individual patient profiles, enhancing treatment efficacy by dynamically adjusting dosages based on real-time data and patient-specific factors. However, there remains a call for more comprehensive data integration to improve the predictive capabilities of these systems. (14,15,16,17,18).

While the majority of studies advocate for the expansion of CDSS in clinical settings, some caution about the challenges in integrating and analysing diverse data sources effectively. Moving forward, enhancing the data architecture within healthcare systems could address these challenges and leverage the full potential of GLP-1 receptor agonists in metabolic disease management. The proposed distributed CDSS architecture, as described in recent literature, emphasizes the utilization of localized EHRs along with continuous updates to knowledge bases through data mining. This approach ensures that CDSS remains effective over time by integrating the most current medical knowledge, thereby improving decision-making support for healthcare professionals and ensuring patient safety through updated and accurate clinical guidelines. (10,19,20,21).

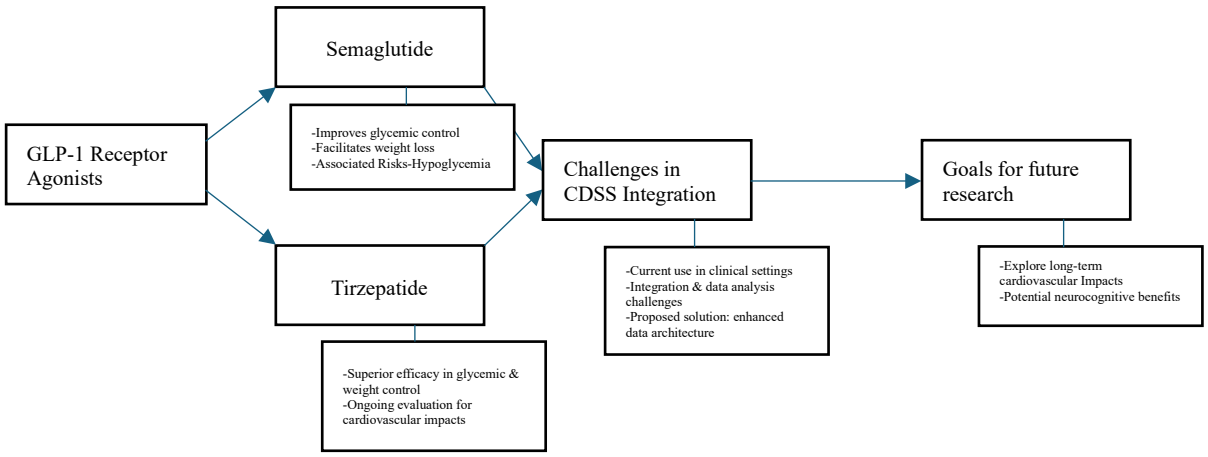


Figure 2: Comprehensive Literature Findings

CDSS Objective Statement

Research Question:

What role can a Clinical Decision Support System (CDSS) play in refining the treatment of Disease-Induced Obesity like type 2 diabetes or any other metabolic conditions with GLP-1 receptor agonists such as Semaglutide and Tirzepatide?

Rationale for CDSS Integration:

The management of disease-induced obesity (DIO) and type 2 diabetes involves navigating the intricate interplay of specific markers, lifestyle, and environmental factors unique to each patient. Given the dynamic nature of these conditions, treatment strategies must continuously adapt to maintain effective control of blood glucose levels and body weight. Traditional approaches can falter under the sheer complexity and volume of data, which complicates timely and accurate decision-making. GLP-1 receptor agonists like Semaglutide and Tirzepatide offer significant benefits for managing these metabolic disorders, but their effective use demands precision to maximize therapeutic outcomes and minimize risks, such as metabolic issues and potential cardiovascular impacts. CDSS can overcome these challenges by harnessing

thoroughly analysed insights, facilitating personalized treatment plans, and allowing for dynamic adjustments based on the evolving condition of the patient. This system supports clinicians in implementing the nuanced, patient-specific approaches necessary for managing complex, chronic conditions like DIO and type 2 diabetes effectively [2,8,9,10,11,12,13,19].

Objectives of the CDSS:

Enhanced Personalization of Treatment:

Goal: Develop individualized treatment strategies by integrating comprehensive data from EHR, diagnostic testing, and continuous health monitoring. *Impact:* This customization enhances the ability to fine-tune treatment regimens, including dosing and scheduling of GLP-1 receptor agonists, tailored to individual metabolic responses and lifestyle factors, thus enhancing efficacy and reducing potential side effects [8,19].

Dynamic Response to Disease Progression:

Goal: Implement adaptive algorithms that provide attainable responses to changes in patient condition, such as fluctuations in blood glucose levels or weight. *Impact:* Maintains optimal disease management across different stages, adjusting to patient-specific needs as they evolve, ensuring sustained control over the disease [2,3,4,5].

Comprehensive Data Integration:

Goal: Utilize advanced analytics to process a wide array of data inputs, including lifestyle habits, previous treatment outcomes, and patient preferences, to inform clinical decisions. *Impact:* Achieves a holistic understanding of each patient, which supports more informed, effective, and tailored treatment strategies [10,15].

Early Risk Management:

Goal: Identify potential risks early, particularly those associated with the use of GLP-1 receptor agonists, to implement preventative measures. *Impact:* Enhances patient safety by

reducing the likelihood of adverse effects through pre-emptive action and informed risk assessment [2,13].

Support for Informed Clinical Decisions:

Goal: Provide healthcare practitioners with evidence-based recommendations, guidelines, and timely alerts at the point of care. *Impact:* Improves clinical outcomes by ensuring that treatment decisions are supported by the latest research and best practice standards [10,24].

Continuous Learning and System Improvement:

Goal: Continuously collect and analyse outcome data to refine and enhance the algorithms and protocols of the CDSS. *Impact:* Promotes ongoing improvement in treatment effectiveness and patient satisfaction, contributing to broader advancements in healthcare management for DIO and type 2 diabetes [19,20,21].

Methods

Gathering and Analysis of Relevant Information

Gathering Relevant Knowledge: Our first strategy was to perform a thorough study of the literature to solve the difficulties in maximizing the use of GLP-1 receptor agonists, specifically tirzepatide and semaglutide, in the treatment of type 2 diabetes and disease-induced obesity (DIO). I searched many databases, including PubMed, Ovid, and UpToDate, with a mix of keywords and Medical Subject Headings (MeSH) phrases relevant to GLP-1 receptor agonists, DIO, type 2 diabetes, personalized medicine, and clinical decision support systems (CDSS) [15].

The search approach was to include a diverse variety of relevant papers, such as observational studies, systematic reviews, meta-analyses, and randomized controlled trials (RCTs) [4, 15]. Tight inclusion and exclusion standards were used to guarantee that only the best available evidence was chosen. Studies that examined the effectiveness, safety, or individualized

use of semaglutide or tirzepatide in the treatment of DIO or type 2 diabetes, as well as the use of CDSS in optimizing treatment regimens, were included [12]. Excluded studies included limited sample numbers, short follow-up times, or weak statistical analyses.

Analysis of Acquired Knowledge:

A narrative technique was used to synthesize the findings from the included research, highlighting areas of uncertainty, inconsistencies, and consistency in the present body of knowledge. The significance of customized treatment approaches was noted, as was the possibility of combining data from different sources (such as EHRs, patient-reported outcomes, and wearable technology) to support clinical decision-making [18, 19]. Additionally, the development of personalized treatment strategies can benefit from the application of cutting-edge analytical techniques like machine learning and predictive modelling [15, 19].

Gaps in the literature were also noted, such as a lack of long-term safety and effectiveness evidence for tirzepatide and semaglutide and the requirement for more study on the application of customized treatment plans in actual clinical settings [22].

Literature and Clinical Guidelines-Comparative Analysis:

A comparative analysis of the literature and clinical guidelines was carried out to make sure that the Clinical Decision Support System (CDSS) for optimizing the use of GLP-1 receptor agonists in the treatment of Disease-Induced Obesity (DIO) and type 2 diabetes is based on the best available evidence and is in line with current clinical practice.

The recommendations from prestigious clinical practice guidelines, such as those published by the American Diabetes Association (ADA) [25] and the European Association for the Study of Diabetes (EASD) [26], were compared with the findings from the literature review, which included important studies on the efficacy, safety, and personalized use of tirzepatide and

semaglutide [1,5, 11, 13, 14, 19,24,25]. In order to make sure that the suggested CDSS is both clinically relevant and evidence-based, our comparison study sought to pinpoint areas of agreement and disagreement between the available data and clinical practice recommendations.

A solid foundation has been created for the development of a CDSS that optimises the use of GLP-1 receptor agonists in the management of DIO and type 2 diabetes by conducting a thorough literature review, analysing the acquired knowledge, and comparing the findings with current clinical practice guidelines. This method guarantees that the CDSS is based on the most up-to-date research and is consistent with clinical practice. It also points out areas that may require more study and improvement in order to enhance patient outcomes and customize treatment plans.

Creation and Implementation of Clinical Decision Rule (CDR) in OpenEMR

A. Process of Integration

Execution in OpenEMR:

Initial Implementation: The CDRs were established and configured within the OpenEMR framework, with inclusion and exclusion criteria based on clinical evidence and best practices to ensure accurate patient targeting and effective management. Two distinct plans were formulated: one addressing clinical considerations for Semaglutide and Tirzepatide, and another for prognosis based on etiology.

Challenges and Adjustments: Initial implementation faced system constraints, including rule duplication and technical glitches affecting integration depth. This led to refinements, concentrating on key elements to streamline the CDRs within OpenEMR's capabilities.

Peer Review and Missing Concepts:

While our subtopic was clinical risk factor considerations and etiology based prognosis: I had covered best about obesity, weight management, however, I needed to mention more about the risks such as glycaemic control, lifestyle factors etc.

Peer Feedback: Group 8's feedback highlighted the need for more specificity in CDR titles, content alignment, and actionable steps detailing. Their insights also emphasized comprehensive monitoring strategies to match patient profiles.

Literature Integration: Recent studies, including those by Kurtzhals et al. (2023) and Tsilingiris and Kokkinos (2024), underscored the importance of Semaglutide and Tirzepatide's efficacy in metabolic management, guiding refinements in the CDR plan [1,2].

Addressing Missing Concepts: The team identified gaps, such as long-term effects and monitoring of glycemic control, which were incorporated into the CDRs to improve their functionality and relevance to patient outcomes.

Final Refinements and Implementation:

Cohesive CDR Plan: The CDRs were refined to include detailed actions, clear alignment with titles, robust monitoring protocols, utilizing real-time data analytics and patient-specific information. This ensured an adaptive, comprehensive approach to DIO management.

Testing and Validation: Simulations were conducted, entering specific criteria to verify if the CDRs triggered appropriately, ensuring their effectiveness within the OpenEMR system.

In our group project, I focused on developing Clinical Decision Rules (CDRs) for Type 2 Diabetes management using Semaglutide and Tirzepatide, as detailed in the document provided. Here are the key aspects and some specific criteria from the CDRs:

1. Discontinuation of Semaglutide for Type 2 Diabetes:

- Inclusion Criteria: Patients already consuming Semaglutide.

- Actions: Educate on weight management.
- Relevance: This rule is vital in managing Disease-Induced Obesity (DIO) as it guides care when discontinuing Semaglutide, a crucial aspect of DIO management.

2. Semaglutide and Tirzepatide for Anti-Obesity Treatment:

- Inclusion Criteria: Overweight (BMI 27-30 kg/m^2), Obese (BMI $\geq 30 kg/m^2$).
- Actions: Biannual BMI assessment; Personalize treatment plan.
- Relevance: Uses pharmacotherapy to manage DIO effectively, addressing both weight management and metabolic control in Type 2 Diabetes.

3. GLP-1 RA Therapy for Type 2 Diabetes:

- Inclusion Criteria: Required blood glucose monitoring.
- Actions: Monthly blood glucose checks; Treat with GLP-1 RA.
- Relevance: Integrates glucose control into DIO management, enhancing the therapeutic approach for Type 2 Diabetes by using GLP-1 receptor agonists.

4. Tirzepatide & Semaglutide in Type 2 Diabetes Management:

- Inclusion Criteria: HbA1c $\leq 8\%$.
- Actions: Triannual blood glucose level assessment.
- Relevance: Provides a dual approach managing blood glucose and weight, which is crucial for DIO care, particularly in patients with Type 2 Diabetes.

These rules are designed to optimize the treatment of Type 2 Diabetes and manage DIO effectively, using data-driven insights to tailor treatments according to individual patient profiles

and conditions, enhancing both efficacy and safety in clinical practice.

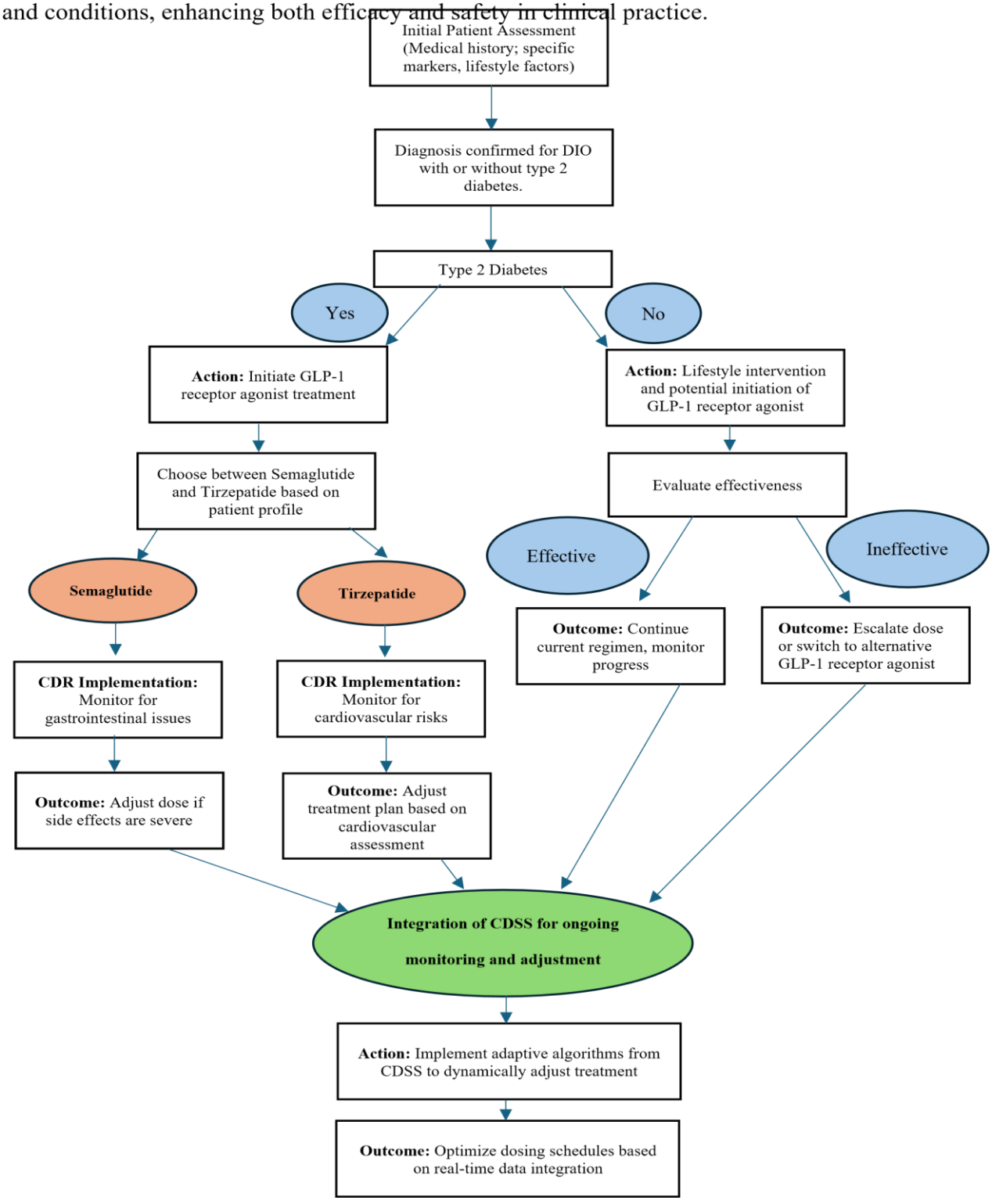


Figure 3: Decision flow for developing an assessment plan for disease-induced obesity

CDSS Prototype – Plans

I developed two comprehensive plans addressing crucial clinical considerations and risk factors associated with Semaglutide and Tirzepatide, as well as prognosis based on etiology. The plans, named "Semaglutide and Tirzepatide – Clinical Considerations/Risk Factors" and "Semaglutide and Tirzepatide - Prognosis based on etiology," respectively, aim to provide tailored guidance for healthcare professionals managing patients receiving these medications.

The first plan focuses on identifying and managing clinical considerations and risk factors that may arise during treatment with Semaglutide and Tirzepatide. It includes rules created by team members to address specific adverse events, drug interactions, and patient monitoring strategies to ensure safe and effective use of these medications. The second plan is designed to assess prognosis based on the underlying etiology of the patient's condition, considering factors such as cardiovascular risk, insulin resistance, and obesity. It provides guidance for optimizing treatment plans and adjusting medication regimens to improve longterm outcomes for patients. Both plans are implemented within OpenEMR , where they are currently active and accessible to healthcare providers. These plans serve as valuable tools for clinicians, offering evidence-based recommendations and decision support to enhance the quality of care provided to patients receiving Semaglutide and Tirzepatide therapy.

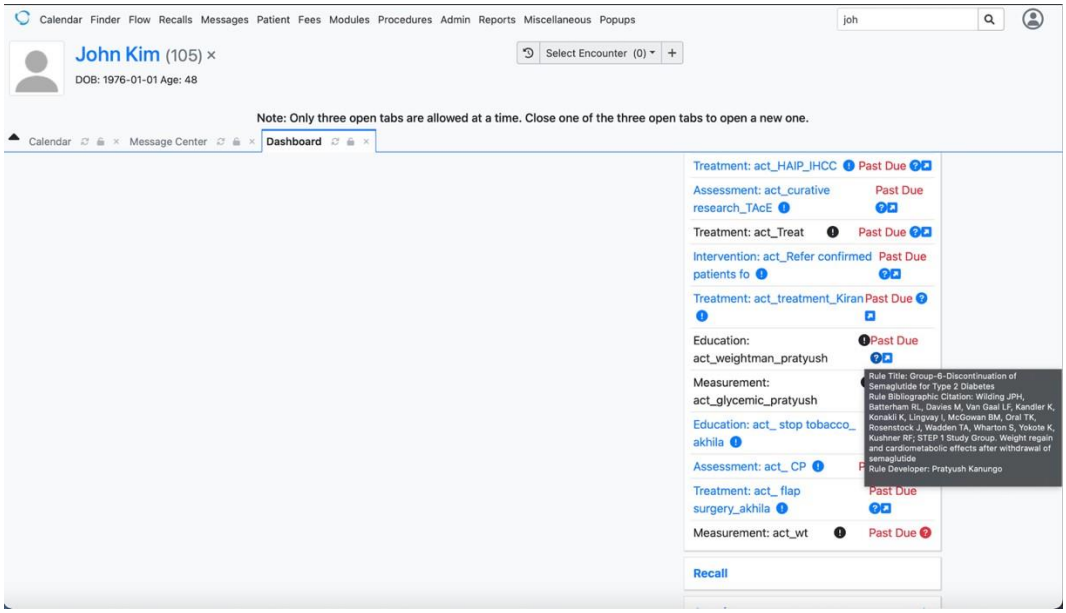


Figure 4: CDR Alert pop up for a patient meeting our inclusion criteria.

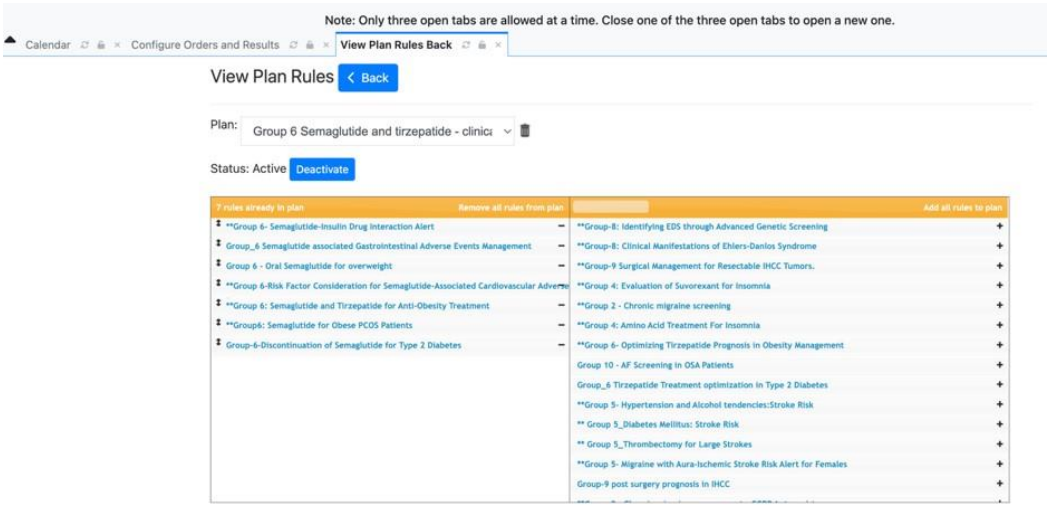


Figure 5: CDSS Plan- Semaglutide and Tirzepatide – Clinical Considerations/Risk Factors

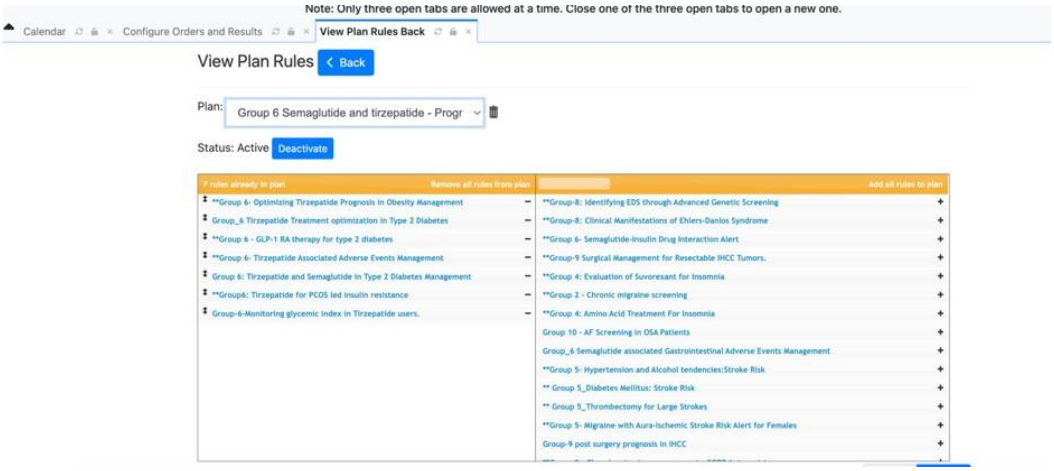


Figure 6: CDSS Plan- Semaglutide and Tirzepatide- Prognosis based on etiology

ATLAS Cohort Selection and Creation:

Introduction:

In the initial phases of our project, I found no existing cohorts that matched our topic. To address this, I created two distinct cohorts, one to assess the prognosis and long-term effectiveness of semaglutide and tirzepatide, and another to explore the clinical risks that are associated with them. I then combined these into a single, comprehensive cohort after realizing the benefits of an integrated approach.

The revised cohort on the management of disease-induced obesity (DIO) with semaglutide and tirzepatide provides a systematic approach to assess the prognosis and possible risks factors of these GLP-1 receptor agonists. It is primarily designed for individuals with metabolic disorders associated with obesity, such as type 2 diabetes. It specifically targets those who have not taken any GLP-1 or GIP agonists in the previous six months and have not reacted well with standard treatments like metformin or insulin. The cohort's design, featuring thorough follow-up assessments, is crucial for understanding the optimal use of these medications in clinical settings. This comprehensive study will help in the development of specialized medical

interventions for DIO with the goal of enhancing patient outcomes and controlling clinical risk factors.

Ultimately, this cohort aims to collect essential data on the safety and effectiveness of Semaglutide and Tirzepatide, thereby improving our understanding of how to best use these medicines. It is expected that the results will contribute to the make use of customized medicine in the treatment of diabetes induced obesity (DIO), especially for individuals with significant metabolic disorders. This will have a major impact on broader strategies for managing diabetes and obesity.

Cohort Entry Events:

To select eligible participants for our study, I created specific entry events:

Condition Occurrence: Participants must be adults who are of age 18 or are older with a diagnosis of obesity directly linked to metabolic disorders such as type 2 diabetes.

Continuous Observation: A minimum of 90 days of observation both before and after the event index date is required to capture detailed baseline and post-treatment data.

Limiting Initial Events: Only the earliest relevant medical event per person is considered to ensure data accuracy and focus on initial treatment responses.

Inclusion Criteria:

1. **Disease-Induced Obesity Diagnosis:** Individuals require a clinical diagnosis of obesity that is caused directly by metabolic disorders such as type 2 diabetes, with a focus on those for whom obesity is associated with metabolic problems.
2. Age Requirement: Participants must be individuals aged 18 or older to ensure that the cohort represents the demographic most affected by DIO and treated with these medications.

3. Body Mass Index Parameter: A BMI of 30 kg/m² or higher is necessary to classify participants as obese, identifying those who might benefit from weight management treatments.
4. Glycaemic Control Status: Individuals must have a HbA1c level of 7.0% or higher, with an emphasis on those who struggle with significant glycaemic control challenges.
5. Treatment Response History: Individuals should have an inadequate response to standard diabetes treatments like metformin or insulin and no GLP-1 or GIP agonist use in the last six months to avoid prior treatment biases.
6. Pre-screening Requirement: A recent cardiovascular checkup (within six months) must verify that there are no significant cardiovascular problems to assure participant safety during the treatment.
7. Availability for Regular Follow-up Assessments: Participants must be willing and able to attend regular follow-up sessions as needed by the study protocol. This ensures constant data collection and monitoring of health outcomes.

Cohort Exit Criteria:

1. Fixed Duration Persistence: Each participant's data is collected for a fixed duration, ending 30 days after the initial or ending event date. This method simplifies the observation period across the cohort.
2. Specific exit conditions:

   Drug-related side effects: If serious adverse effects from the drugs are seen, participants will be removed from the cohort in order to prioritize their safety.

   Achievement of Treatment Goals: Participants who achieve a HbA1c level of less than 7% will be considered for exit criteria, indicating successful glycaemic control and meeting one of the study's objectives.

Cohort Eras:

Collapse Gap Size: Set to 90 days to integrate data from events within this interval for continuous observation.

Left Censoring: Data collection begins on May 1, 2024, focusing on recent and relevant treatment data.

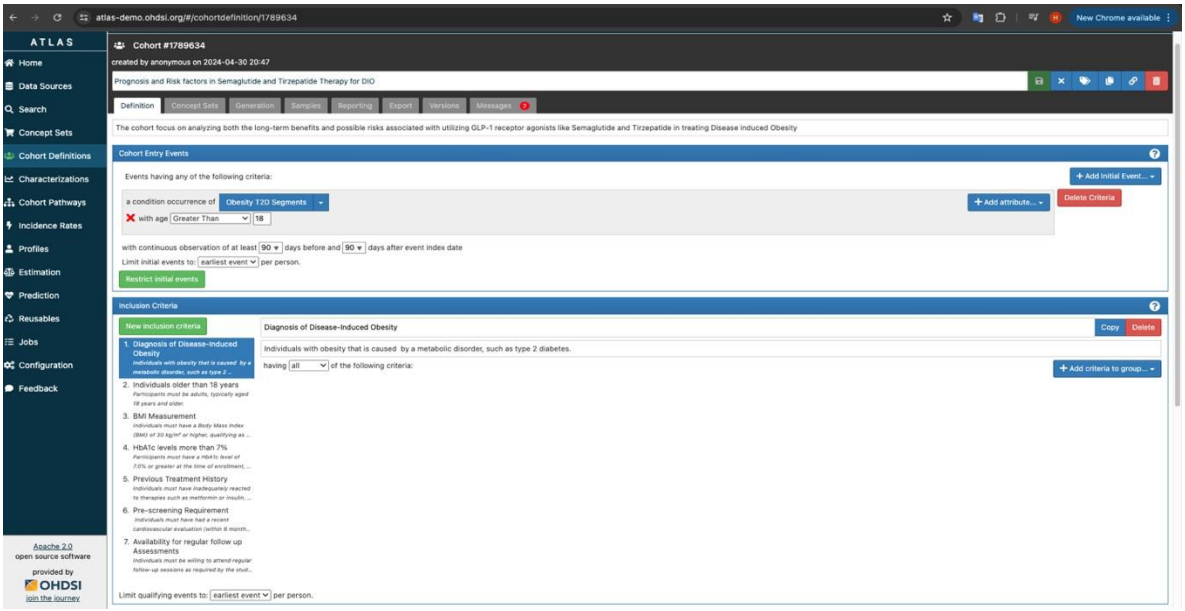
Right Censoring: Data collection ends on August 1, 2024, assuring uniform analysis for all participants.

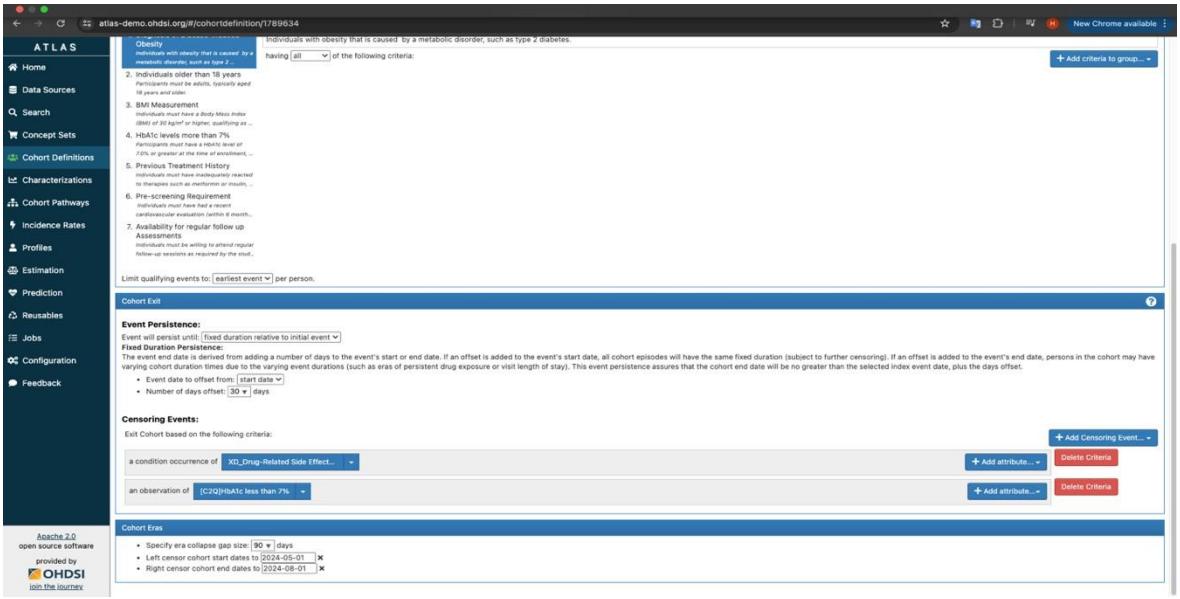
Steps for Creating a Cohort:

To set up and manage the cohort effectively following steps need to be considered:

- To find potential participants, explore appropriate databases that provide comprehensive medical records.
- Potential participants are screened according to clinical and demographic criteria to make sure they fulfil the standards for cohort entry events.
- Confirm that all participants meet the study's health and medical history requirements as specified in the inclusion criteria.
- Set up clear guidelines for participant exit event to protect the integrity of the study's findings.
- Set up the cohort eras by specifying the data collection periods and setting the data handling rules to manage data grouping over time.

Screenshots of revised cohort:





CDSS Verification Proposal

In developing a Clinical Decision Support System (CDSS) for Semaglutide and Tirzepatide therapy within the OpenEMR platform, our validation approach draws from recent literature insights and the CDSS prototype document. The primary objectives encompass functionality testing, accuracy assessment, and user satisfaction evaluation. These objectives

align with recent studies emphasizing the need to minimize false positive alerts and enhance user satisfaction through improved alert management systems [27].

The methodology entails implementing the CDSS prototype in a controlled OpenEMR environment and conducting thorough testing to ensure seamless integration and accurate decision-making. Clinical scenarios derived from up-to-date research will validate the CDSS responses, while a mechanism to gather feedback from end-users will facilitate iterative improvements in CDSS algorithms and user interface. Emphasis will be placed on reducing alert fatigue and enhancing clinical relevance through precise patient data integration and refined alert algorithms, in line with recent literature findings [27].

Key performance indicators, including system response time, clinical recommendation accuracy, user satisfaction scores, and reduction in false positive rates, will be utilized to assess the CDSS impact on clinical outcomes and user engagement. Through continuous feedback from healthcare professionals and iterative testing cycles, the validation process aims to ensure that the CDSS prototype not only integrates effectively within OpenEMR but also significantly contributes to improved clinical decision-making, aligning with the dynamic demands of modern healthcare environments.

CDSS Validation Proposal

Our CDSS targets improving therapeutic outcomes for patients with Disease-Induced Obesity (DIO) through personalized treatment plans utilizing Semaglutide and Tirzepatide. Given the complexity of DIO and its comorbidities like Type 2 Diabetes, a personalized CDSS approach holds promise in streamlining treatment protocols and enhancing patient management.

To assess the CDSS's effectiveness, usability, and technical performance, I propose a multifaceted validation approach. Firstly, a prospective cohort study with historical controls will compare clinical outcomes of patients undergoing Semaglutide and Tirzepatide therapy with and

without CDSS support over 6 months. Statistical models will analyse the CDSS's impact on weight reduction and HbA1c levels, adjusting for baseline differences [27]. Secondly, a mixedmethods study involving quantitative surveys and qualitative interviews will gauge user satisfaction and usability among healthcare providers utilizing the CDSS. Thematic analysis and descriptive statistics will offer insights into usability and satisfaction levels [27]. By focusing on these areas, our validation aims to rigorously assess the CDSS prototype's effectiveness, efficiency, and user satisfaction in managing Semaglutide and Tirzepatide therapy for patients with DIO, ensuring its practical relevance in real-world clinical settings.

Evaluative Reflection:

Limitation

Study Scope: The project's study focuses only on features of type 2 diabetes therapy with tirzepatide and semaglutide, leaving out thorough evaluations of elements like long-term consequences, practical effectiveness, and patient support techniques. This might have an influence on the creation of Clinical Decision Rules (CDRs) and the Clinical Decision Support Systems (CDSS) general efficacy in directing treatment choices.

Patient Diversity: The project does not give enough thought to the variety of patient groups and their requirements, preferences, and difficulties. This error might possibly compromise treatment results by leading to the creation of CDRs that do not adequately reflect or serve all patients with type 2 diabetes [5].

Integration of Real-world Evidence: When developing CDRs and CDSSs, there is a need to include patient-reported outcomes and real-world evidence more thoroughly. This omission might compromise the results and suggestions' validity and generalizability, making it more difficult for them to be used in actual clinical settings [22].

Future needs and directions

Improving CDSS with Advanced Analytics: In order to improve CDRs and CDSS even further, future research should consider the possibility of utilizing sophisticated analytical methods like machine learning and predictive modelling [15, 19]. Through the utilization of these methodologies, CDSS may enhance its adaptability and responsiveness to the unique requirements of each patient, hence facilitating the provision of really customized care [17]. To stimulate innovation and raise CDSS's efficacy in treating type 2 diabetes, interaction with specialists in these domains will be crucial [19].

Executing Long-Term Studies: Future research should give priority to undertaking long-term studies in order to overcome the limitations in knowing the long-term effects of tirzepatide and semaglutide [21, 22]. In addition to offering important new insights into the management of type 2 diabetes, these studies should evaluate the long-term sustainability, safety, and effectiveness of treatment results [1, 2].

Collaboration with Stakeholders: The effective development and use of CDRs and CDSS will depend on fostering partnerships between researchers, healthcare professionals, patients, and technology specialists [24]. Involving stakeholders early on in the study process will guarantee that the final tools are accessible, applicable to clinical settings, and suit the requirements and preferences of all parties. Collaboration among stakeholders, such as researchers, medical professionals, patients, and technology specialists, guarantees clinical decision rules and support systems are applicable, accessible, and continuously improved[20].

Critical implications for practice or science

Individualized Treatment Approach: By considering each patient's unique risk factors and prognosis for both semaglutide and tirzepatide, CDSS integration makes individualized treatment approaches possible. This optimizes therapeutic outcomes by enabling medical professionals to customize treatment strategies to meet the unique demands of each patient [19].

Improved Patient involvement: By offering explicit justifications and evidence-based suggestions for Semaglutide and Tirzepatide treatment choices, the use of CDSS improves patient involvement. This promotes cooperation between medical professionals and patients, which enhances treatment compliance and improves health results [(27)].

Effective Resource usage: By optimizing clinical processes and minimizing needless interventions for semaglutide and tirzepatide, CDSS deployment enhances resource usage. Through fast and precise treatment suggestions, CDSS enhances overall healthcare delivery by enabling healthcare practitioners to deploy resources more effectively [(10)].

References

1. Kurtzhals, P., Kreiner, F. F., & Bindra, R. S. (2023). The role of weight control in the management of type 2 diabetes mellitus: Perspectives on semaglutide. Diabetes Research and Clinical Practice, 203, 110881. https://doi.org/10.1016/j.diabres.2023.110881
2. D. Tsilingiris and A. Kokkinos, “Advances in obesity pharmacotherapy; learning from metabolic surgery and beyond,” *Metabolism, Clinical and Experimental*, vol. 151, p. 155741, Feb. 2024, doi: 10.1016/j.metabol.2023.155741.
3. T. D. Müller, M. Blüher, M. H. Tschöp, and R. D. DiMarchi, “Anti-obesity drug discovery: advances and challenges,” *Nature Reviews. Drug Discover/Nature Reviews. Drug Discovery*, vol. 21, no. 3, pp. 201–223, Nov. 2021, doi: 10.1038/s41573-021-00337-8.
4. Andreadis, P., Karagiannis, T., Malandris, K., Avgerinos, I., Liakos, A., Manolopoulos, A., Bekiari, E., Matthews, D. R., & Tsapas, A. (2018). Semaglutide for type 2 diabetes mellitus: A systematic review and meta-analysis. Diabetes, Obesity and Metabolism, 20(9), 2255

5. Chao, A. M., Tronieri, J. S., Amaro, A., & Wadden, T. A. (2022). Clinical Insight on Semaglutide for Chronic Weight Management in Adults: Patient Selection and Special Considerations. *Drug design, development and therapy, 16,* 4449–4461. https://doi.org/10.2147/DDDT.S365416
6. Nauck, M. A., & D'Alessio, D. A. (2022). Tirzepatide, a dual GIP/GLP-1 receptor coagonist for the treatment of type 2 diabetes with unmatched effectiveness regrading glycaemic control and body weight reduction. *Cardiovascular diabetology, 21*(1), 169. https://doi.org/10.1186/s12933-022-01604-7
7. Rodbard, H. W., Lingvay, I., Reed, J., de la Rosa, R., Rose, L., Sugimoto, D., Araki, E., Chu, P.-L., Wijayasinghe, N., & Norwood, P. (2018). Semaglutide added to Basal Insulin in Type 2 Diabetes (SUSTAIN 5): A randomized, controlled trial. The Journal of Clinical Endocrinology & Metabolism, 103(6), 2291-2301. https://doi.org/10.1210/jc.2018-00070
8. Inman, T. R., Plyushko, E., Austin, N. P., & Johnson, J. L. (2018). The role of basal insulin and GLP-1 receptor agonist combination products in the management of type 2 diabetes. Therapeutic Advances in Endocrinology and Metabolism, 9(5), 151-155. https://doi.org/10.1177/2042018818763698
9. Carmina, E., & Longo, R. A. (2023). Semaglutide treatment of excessive body weight in obese PCOS patients unresponsive to lifestyle programs. Journal of Clinical Medicine, 12(18), 5921. https://doi.org/10.3390/jcm12185921
10. Sutton, R.T., Pincock, D., Baumgart, D.C. et al. An overview of clinical decision support systems: benefits, risks, and strategies for success. npj Digit. Med. 3, 17 (2020). https://doi.org/10.1038/s41746-020-0221-y

11. Lin, F., Yu, B., Ling, B., Lv, G., Shang, H., Zhao, X., Jie, X., Chen, J., & Li, Y. (2023). Weight loss efficiency and safety of tirzepatide: A Systematic review. PloS one, 18(5), e0285197. https://doi.org/10.1371/journal.pone.0285197

12. Frías, J. P., Davies, M. J., Rosenstock, J., Pérez Manghi, F. C., Fernández Landó, L., Bergman, B. K., Liu, B., Cui, X., & Brown, K. (2021). Tirzepatide versus Semaglutide once weekly in patients with Type 2 Diabetes. N Engl J Med, 385(6), 503-515. https://doi.org/10.1056/NEJMoa2107519

13. Jastreboff, A. M., Aronne, L. J., Ahmad, N. N., Wharton, S., Connery, L., Alves, B., Kiyosue, A., Zhang, S., Liu, B., Bunck, M. C., & Stefanski, A. (2022). Tirzepatide once weekly for the treatment of Obesity. N Engl J Med, 387(3), 205-216. https://doi.org/10.1056/NEJMoa2206038

14. Mary E. Cox, David Edelman; Tests for Screening and Diagnosis of Type 2 Diabetes. Clin Diabetes 1 January 2009; 27 (4): 132–138. https://doi.org/10.2337/diaclin.27.4.132

15. Bellazzi, R., & Zupan, B. (2008). Predictive data mining in clinical medicine: current issues and guidelines. International journal of medical informatics, 77(2), 81–97. https://doi.org/10.1016/j.ijmedinf.2006.11.006

16. Jornayvaz, F. R., & Shulman, G. I. (2012). Diacylglycerol activation of protein kinase Cε and hepatic insulin resistance. Cell metabolism, 15(5), 574–584. https://doi.org/10.1016/j.cmet.2012.03.005

17. Vadher, K., Patel, H., Mody, R., Levine, J. A., Hoog, M., Cheng, A., Pantalone, K. M., & Sapin, H. (2022). Efficacy of tirzepatide 5, 10 and 15 mg versus semaglutide 2 mg in patients with type 2 diabetes: An adjusted indirect treatment comparison. Diabetes, Obesity and Metabolism, 24(9), 1861–1868. https://doi.org/10.1111/dom.14775

18. Wilding, J., Batterham, R. L., Davies, M. J., Van Gaal, L. F., Kandler, K., Konakli, K., Lingvay, I., McGowan, B., Oral, T. K., Rosenstock, J., Wadden, T. A., Wharton, S., Yokote, K., & Kushner, R. F. (2022b). Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. *Diabetes, Obesity & Metabolism/Diabetes, Obesity and Metabolism*, *24*(8), 1553–1564. https://doi.org/10.1111/dom.14725

19. Chen Z, Liang N, Zhang H, Li H, Yang Y, Zong X, Chen Y, Wang Y, Shi N. Harnessing the power of clinical decision support systems: challenges and opportunities. Open Heart. 2023 Nov 28;10(2):e002432. doi: 10.1136/openhrt-2023-002432. PMID: 38016787; PMCID: PMC10685930.

20. Middleton, Blackford & Sittig, Dean & Wright, A.. (2016). Clinical Decision Support: a 25 Year Retrospective and a 25 Year Vision. IMIA Yearbook. 25. S103S116. 10.15265/IYS-2016-s034.

21. El–Sappagh, S., & El-Masri, S. (2014). A distributed clinical decision support system architecture. Journal of King Saud University. Computer and Information Sciences/Mağalaẗ Ğam'aẗ Al-malīk Saud : Ùlm Al-ḥasib Wa Al-ma'lumat, 26(1), 69–78. https://doi.org/10.1016/j.jksuci.2013.03.005

22. Popoviciu, M. S., Păduraru, L., Yahya, G., Metwally, K., & Cavalu, S. (2023). Emerging Role of GLP-1 Agonists in Obesity: A Comprehensive Review of Randomised Controlled Trials. International journal of molecular sciences, 24(13), 10449. https://doi.org/10.3390/ijms241310449

23. Filippatos TD, Panagiotopoulou TV, Elisaf MS. Adverse Effects of GLP-1 Receptor Agonists. Rev Diabet Stud. 2014 Fall-Winter;11(3-4):202-30. doi: 10.1900/RDS.2014.11.202. Epub 2015 Feb 10. PMID: 26177483; PMCID: PMC5397288.

24. Gorgojo-Martínez JJ, Mezquita-Raya P, Carretero-Gómez J, Castro A, Cuenca AMC,

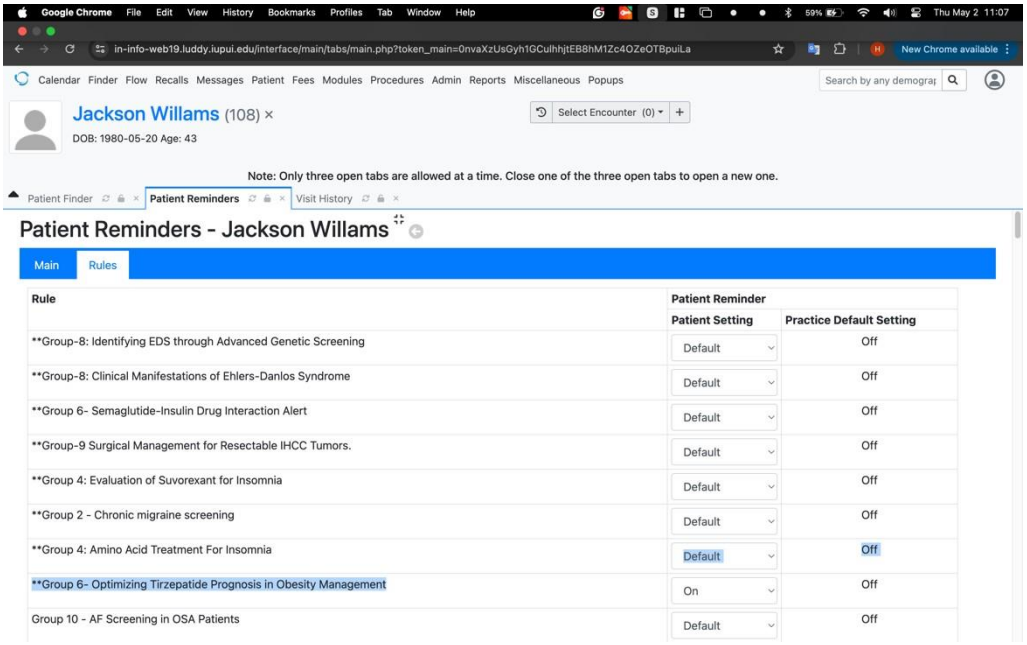
De Torres-Sánchez A, et al. Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus. Journal of Clinical Medicine [Internet]. 2022 Dec 24;12(1):145. Available from: https://www.mdpi.com/2077-0383/12/1/145 25.

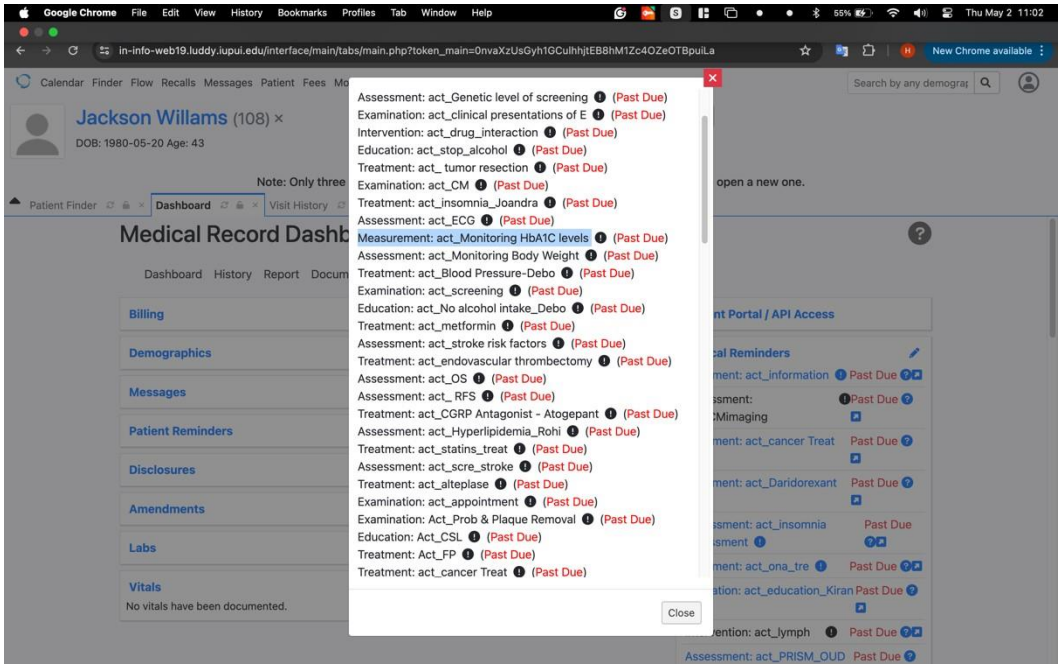
Oral Semaglutide Reduces Occurrence of Major Cardiac Events in People with Type 2 Diabetes With High Cardiovascular Risk | *ADA*. (n.d.). https://diabetes.org/newsroom/oral-semaglutide-reduces

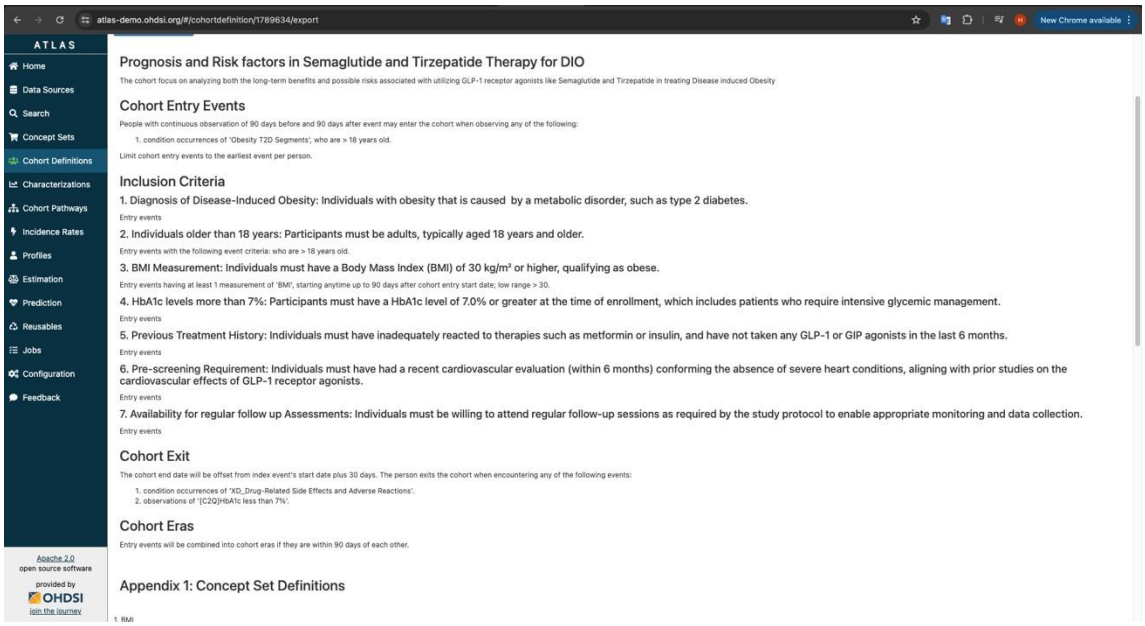
26. Guidelines | EASD. (n.d.). https://www.easd.org/guidelines.html

27. Van De Sijpe, G., Quintens, C., Walgraeve, K., Van Laer, E., Penny, J., De Vlieger, G., Schrijvers, R., De Munter, P., Foulon, V., Casteels, M., Van der Linden, L., & Spriet, I. (2022). Overall performance of a drug-drug interaction clinical decision support system: quantitative evaluation and end-user survey. *BMC medical informatics and decision making*, *22*(1), 48. https://doi.org/10.1186/s12911-022-01783-z.

Appendix:


Google Chrome File Edit View History Bookmarks Profiles Tab Window Help
Thu May 2 11:07
in-info-web19.luddy.iupui.edu/interface/main/tabs/main.php?token_main=0nvaXzUsGyh1GCulhhjtEB8hM1Zc4OZeOTBpuiLa
New Chrome available
Calendar Finder Flow Recalls Messages Patient Fees Modules Procedures Admin Reports Miscellaneous Popups
Search by any demograp
Jackson Willams (108) ×
DOB: 1980-05-20 Age: 43
Select Encounter (0)
Note: Only three open tabs are allowed at a time. Close one of the three open tabs to open a new one.
Patient Finder
Patient Reminders
Visit History
Patient Reminders - Jackson Willams
Main
Rules
Rule
Patient Reminder
Patient Setting
Practice Default Setting
**Group-8: Identifying EDS through Advanced Genetic Screening
Default
Off
**Group-8: Clinical Manifestations of Ehlers-Danlos Syndrome
Default
Off
**Group 6- Semaglutide-Insulin Drug Interaction Alert
Default
Off
**Group-9 Surgical Management for Resectable IHCC Tumors.
Default
Off
**Group 4: Evaluation of Suvorexant for Insomnia
Default
Off
**Group 2 - Chronic migraine screening
Default
Off
**Group 4: Amino Acid Treatment For Insomnia
Default
Off
**Group 6- Optimizing Tirzepatide Prognosis in Obesity Management
On
Off
Group 10 - AF Screening in OSA Patients
Default
Off


Google Chrome File Edit View History Bookmarks Profiles Tab Window Help
Thu May 2 11:02
in-info-web19.luddy.iupui.edu/interface/main/tabs/main.php?token_main=0nvaXzUsGyh1GCulhhjtEB8hM1Zc4OZeOTBpuiLa
New Chrome available
Jackson Willams (108) ×
DOB: 1980-05-20 Age: 43
Patient Finder
Dashboard
Visit History
Medical Record Dashb
Dashboard History Report
Billing
Demographics
Messages
Patient Reminders
Disclosures
Amendments
Labs
Vitals
No vitals have been documented.
Assessment: act_Genetic level of screening (Past Due)
Examination: act_clinical presentations of E (Past Due)
Intervention: act_drug_interaction (Past Due)
Education: act_stop_alcohol (Past Due)
Treatment: act_ tumor resection (Past Due)
Examination: act_CM (Past Due)
Treatment: act_insomnia_Joandra (Past Due)
Assessment: act_ECG (Past Due)
Measurement: act_Monitoring HbA1C levels (Past Due)
Assessment: act_Monitoring Body Weight (Past Due)
Treatment: act_Blood Pressure-Debo (Past Due)
Examination: act_screening (Past Due)
Education: act_No alcohol intake_Debo (Past Due)
Treatment: act_metformin (Past Due)
Assessment: act_stroke risk factors (Past Due)
Treatment: act_endovascular thrombectomy (Past Due)
Assessment: act_OS (Past Due)
Assessment: act_ RFS (Past Due)
Treatment: act_CGRP Antagonist - Atogepant (Past Due)
Assessment: act_Hyperlipidemia_Rohi (Past Due)
Treatment: act_statins_treat (Past Due)
Assessment: act_scre_stroke (Past Due)
Treatment: act_alteplase (Past Due)
Examination: act_appointment (Past Due)
Examination: Act_Prob & Plaque Removal (Past Due)
Education: Act_CSL (Past Due)
Treatment: Act_FP (Past Due)
Treatment: act_cancer Treat (Past Due)
Close
Portal / API Access
Reminders
Past Due
Assessment: act_PRISM_OUD Past Due


atlas-demo.ohdsi.org/#/cohortdefinition/1789634/export
New Chrome available
ATLAS
Home
Data Sources
Search
Concept Sets
Cohort Definitions
Characterizations
Cohort Pathways
Incidence Rates
Profiles
Estimation
Prediction
Reusables
Jobs
Configuration
Feedback
Apache 2.0
open source software
provided by
OHDSI
join the journey
Prognosis and Risk factors in Semaglutide and Tirzepatide Therapy for DIO
The cohort focus on analyzing both the long-term benefits and possible risks associated with utilizing GLP-1 receptor agonists like Semaglutide and Tirzepatide in treating Disease induced Obesity
Cohort Entry Events
People with continuous observation of 90 days before and 90 days after event may enter the cohort when observing any of the following:
1. condition occurrences of 'Obesity T2D Segments', who are > 18 years old.
Limit cohort entry events to the earliest event per person.
Inclusion Criteria
1. Diagnosis of Disease-Induced Obesity: Individuals with obesity that is caused by a metabolic disorder, such as type 2 diabetes.
Entry events
2. Individuals older than 18 years: Participants must be adults, typically aged 18 years and older.
Entry events with the following event criteria: who are > 18 years old.
3. BMI Measurement: Individuals must have a Body Mass Index (BMI) of 30 kg/m² or higher, qualifying as obese.
Entry events having at least 1 measurement of 'BMI', starting anytime up to 90 days after cohort entry start date; low range > 30.
4. HbA1c levels more than 7%: Participants must have a HbA1c level of 7.0% or greater at the time of enrollment, which includes patients who require intensive glycemic management.
Entry events
5. Previous Treatment History: Individuals must have inadequately reacted to therapies such as metformin or insulin, and have not taken any GLP-1 or GIP agonists in the last 6 months.
Entry events
6. Pre-screening Requirement: Individuals must have had a recent cardiovascular evaluation (within 6 months) conforming the absence of severe heart conditions, aligning with prior studies on the cardiovascular effects of GLP-1 receptor agonists.
Entry events
7. Availability for regular follow up Assessments: Individuals must be willing to attend regular follow-up sessions as required by the study protocol to enable appropriate monitoring and data collection.
Entry events
Cohort Exit
The cohort end date will be offset from index event's start date plus 30 days. The person exits the cohort when encountering any of the following events:
1. condition occurrences of 'XD_Drug-Related Side Effects and Adverse Reactions'.
2. observations of '[C2Q]HbA1c less than 7%'.
Cohort Eras
Entry events will be combined into cohort eras if they are within 90 days of each other.
Appendix 1: Concept Set Definitions
1. BMI