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## Development of an AI-Powered Clinical Pathway Optimizer for Personalized Healthcare Treatment Planning

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#### **Abstract**

AI-Powered Clinical Pathway Optimization in Personalized Healthcare provides an overview of how AI can optimize clinical pathways and explore significant application areas in personalized healthcare focusing on health conditions that require the collaboration of multidisciplinary medical teams and the personalization of treatment goals. Personalized healthcare requires medical teams to define a clinical pathway personalized to the patients' specific characteristics and requests, particularly the treatment objectives. A clinical pathway is a multidisciplinary therapeutic plan developed for a specific health condition and sequence activities and goals. Personalized healthcare variability and goals may often not allow complete automation of clinical pathways, requiring clinical intervention and decision-making with consideration of patients' situations. However, decision support systems can significantly reduce the time and expertise needed by medical teams to explore possible alternatives. More innovative solutions are needed. Personalized healthcare is increasingly gaining acceptance. Personalized healthcare is commonly identified with precision medicine, which aims to identify and explore the different characteristics, preferences, genetic and biological characteristics, and environmental contexts of patients suffering from the same disease to treat patients individually. However, personalized healthcare is a broader concept. It concerns practically all health conditions. Personalized healthcare requires defining clinical pathways personalized for each patient, particularly regarding the treatment objectives. A clinical pathway is a multidisciplinary therapeutic plan developed for a patient or for a cohort of patients with the same diagnosis-related to health conditions - indicating the sequence of steps and the time intervals to achieve the expected outcome diagnoses. Indeed, clinical pathways not only concern a single discipline but involve the various health professionals' collaboration and coordination of c

Keywords: Clinical Decision Support Systems (CDSS), Personalized Medicine, Healthcare Predictive Analytics, Machine Learning in Healthcare, Clinical Pathway Optimization, Patient-Specific Treatment Planning, Electronic Health Records (EHR) Integration, Natural Language Processing (NLP) for Medical Data, Outcome-Based Treatment Modeling, Medical Knowledge Graphs, AI-Driven Treatment Recommendations, Precision Health Algorithms, Real-Time Clinical Data Analysis, Risk Stratification Models, Interoperable Health IT Systems.

#### 1. Introduction

In recent years, healthcare systems have undergone a major transformation driven by technological advancements and changes in stakeholder perspectives. Biomedical and digital technologies have enabled the generation of unprecedented amounts of healthcare data in forms ranging from high-dimensional patient records to highly granular digital trail data. In addition, patients play a more prominent role in generating and sharing data to help researchers and healthcare providers understand disease processes and treatment effects and inform treatment decisions. These trends are associated with the emergence of the personalized healthcare paradigm, which acknowledges the interindividual variability in the natural history, presentation and response to treatment of human diseases, and emphasizes the need to tailor and optimize care for each patient. This paradigm

recognizes that there is no one-size-fits-all approach in healthcare, and always seeks to account for interindividual variability to optimize the timing, technique and amount of delivery of any healthcare intervention, procedure or service to achieve favorable clinical and economic outcomes.

As a result of the above advancements and perspectives, patient management strategies are evolving from reactive treatment approaches that emphasize the use of interventions after disease onset following standard clinical pathways, toward proactive patient monitoring and support strategies that seek to predict the likelihood of disease onset or exacerbation using predictive analytics models from individual patient data, as well as adjust for the risk of imminent disease onset or worsening through decision support tools based on care pathways. These proactive strategies are also being enhanced by intervention delivery via telehealth and virtual care systems that utilize both sensor data and human interactions to monitor and ameliorate the risk of disease onset or exacerbation.

#### 1.1. Background and significance

Efforts currently underway to prevent, detect, and treat disease have become increasingly challenging. Rising costs of healthcare delivery, poor care quality for chronic diseases, and inefficient allocation of resources to pathologies have led to a renewed interest in the implementation of Clinical Pathways (CPs). A CP is a knowledge-based approach to the standardization of decision making in clinical practice that is designed to reduce both unnecessary variability in the delivery of care and housing several other purported benefits. CPs provide an avenue to transform care delivery into a more efficient and desirable practice by guiding the activities to be performed in order to achieve favorable endpoints. Standardized CPs, promoting the delivery of optimal care, can maximize the probability of achieving successful outcomes while minimizing the costs of sub-optimal care. Moreover, the creation of CPs is aligned to the challenging objective of controlling the costs of care delivery, while guaranteeing the quality of the services.



Fig 1: AI-Powered Clinical Pathway Optimizer for Personalized Healthcare Treatment Planning.

It is now widely acknowledged that this approach alone has reached its limits of effectiveness. Variations in patient characteristics, evolution of knowledge about the natural history of diseases, technological innovations, and others, all may justify deviations from the standardized CP. As a matter of fact, clinical and decision support systems traditionally have not incorporated variability due to case-mix differences, or have only partially addressed it. The incorporation of tools that help to personalize CPs on the basis of patient characteristics and circumstances may represent a new avenue to enhance the implementation of these types of processes in daily medical practice. In other words, the controlled personalization of CPs is required to accomplish their goals. Such a modeling environment can be harnessed to model these types of processes under a new concept that is called Case-mix Based Optimized Personalization. The integration of AI and decision support tools, along with process modeling for CP development and reconfiguration, can also help increase the synergy between computer modeling and the CP design and development problem. Such integration should also assist in speeding up the now relatively lengthy and costly problem of CP design and approval.

#### 2. Literature Review

For an organization trying to reduce clinical variance and improve efficiency and patient experience, implementing clinical pathways or care pathways is a rational first step. Structuring healthcare delivery to optimize efficiency, consistency, and quality of care has long been sought in various healthcare conditions. Clinical pathways are interdisciplinary treatment plans, dealing with selection and timing of actions linked together to provide a structured care plan for a well-defined group of patients with a specific disease process.

Clinical Pathways standardize and synchronize medical actions aiming to reduce patients' hospitalization length, costs, and/or complications whilst increasing the quality of care. Currently, the clinical pathway's structure focuses on creating an optimal healthcare process regarding quality, probability, and time. Despite the benefits associated with CP implementation, several barriers hinder their success.

The literature describes various aspects of CP optimization, including pathways describing the optimal sequence of actions that a patient will go through; the effect in length of stay of the execution of care pathways; the cost-effectiveness role of CPs; the minimization of clinical pathway budgets, etc.

#### 2.2. AI in Healthcare

Artificial Intelligence identifies algorithms techniques where computer systems prove capable of intelligent behavior. AI allows machines to mimic humans and perform tasks such as problem-solving, speech recognition, scheduling, pattern recognition, and prediction. AI's most promising techniques in health science are machine learning and deep learning. Recent advances in AI provide accurate and efficient analysis of large amounts of high-dimensional data, making it a valuable method for assisting or replacing human intelligence in clinical settings.

AI also increases efficiency in data management, as a consequence, improving the implementation of predictive models in clinical pathways. However, the black box nature of many established algorithms makes them inadequate to assist care or do risk stratification. Hence, the merge of explainable artificial intelligence with the clinical pathway research field might lead to a more profound impact in this line of research. Even when models that are xAI compliant are utilized, additional work is needed to transfer the model into the clinical scenario.

Within the healthcare area, several combine AI and clinical pathways research. Some described the use of AI models to detect which patient outcomes were related to the execution of different clinical pathways applied to the same patient population. Others managed to reduce unnecessary costs and adverse outcomes by combining AI and CPs.

#### 2.1. Overview of Clinical Pathways

In healthcare, clinical pathways are tools used to optimize and standardize care delivery. Clinical pathways are defined as multidisciplinary management tools that are used to facilitate the implementation of clinical guidelines at the local level and link patient characteristics with expected outcomes. Clinical pathways document and standardize expected plans for care delivery by various disciplines during the patient's hospitalization. Clinical pathways can be described as detailed, specific plans for a particular patient condition, used to predict outcomes, determine resource utilization, ensure interprofessional coordination, improve quality, optimize costs, evaluate resource use, attain clinical outcome goals, set quality benchmarks, drive and shape change, and reward providers based on results. Clinical pathways are defined as explicit views of optimal care for a given patient population with a specific diagnosis over a specified time period. Clinical pathways may also be referred to as critical pathways, care maps, integrated care pathways, interdisciplinary pathways, care pathways, clinical paths, clinical path management, patient management plans, fast-track protocols, and case management protocols.

While definitions of clinical pathways can differ, all strive to define the processes of care for specific patient populations with specific diagnoses over specified time periods, helping to initiate, coordinate, and negotiate the patient-specific course of care. Clinical pathways document and standardize expected plans for care delivery by various disciplines during the patient's hospitalization. Initially implemented in the area of post-acute care for hospital patients, some of the latest advancements of clinical pathways seek to enhance the collaborative practice coordination of the entire interdisciplinary team throughout the continuum of care, with the objectives of achieving desired health outcomes.

#### 2.2. AI in Healthcare

Artificial Intelligence (AI) has become a transformative force in many domains, in recent years, it has found many applications in healthcare. AI is proving to be a beneficial improvement to computer systems and applications that are traditionally dependent upon human intelligence. AI has increased the ability of humans to solve the increasingly complex problems which remain unresolved by conventional means. The term AI depicts a machine and computer programs designed to learn, think, evaluate, and discuss the solution to the talked problems. Correct AI enhances the capability of machines that can imitate and modify the person's activities. AI can also be defined as machines performing activities which require human intelligence.

The introduction of AI in healthcare has gradually become a vibrant area of private and public interest. AI in healthcare, and in particular, Deep Learning (DL), has experienced a dramatic increase in efficiency, performance, and effectiveness in the disparate healthcare domain. The development of healthcare AI in the last decade has been influenced mainly by the rapid expansion of computing and processing capabilities, availability of massive data, and commercial opportunities generated by the global aging challenge, the increasing burden of chronic diseases, and a wide range of unfulfilled demands for improving and optimizing the outcomes and reducing costs of clinical practice. AI in healthcare has shown

promising performance in many tasks and areas such as Computer Vision, Robotics, Virtual Agents, Data Mining, and Patient Health Informatics, Clinical Decision Support, Active Learning, Reinforcement Learning, and Internet of Medical Things.

#### 2.3. Personalized Treatment Approaches

As previously reported, the wide interindividual variability in closely related topics such as drug disposition, genetic polymorphism, metabolism, and drug targets are the foundation for developing personalized medicine. However, the complexity of the disease dynamic conditions, combined with those before mentioned factors, is the motivation for the exponential increase in the use of AI. Nevertheless, increasing AI complexity should not overshadow the preclinical and clinical development validation requirements and should be increasingly a complementary approach and not a replacement for the present scientific methods. It is understandable that the predictions from AI are unrealistic. However, several approaches increasingly use the characteristics that AI provides. Omics signatures that need to be statistically validated, diagnostic-oriented classical approaches and with a validated, regulatory-approved outcome.

AI technology can improve the treatment of many diseases; however, there are some particularities related to psychiatric illnesses mainly related to the vast number of factors involved in diseases' development and duration, biased toward a significant number of undiagnosed patients. It must be highlighted that even if an external validity is later proven by other datasets, the AI results must be analyzed carefully. However, studies have demonstrated the power of the AI in identifying biomarkers and in developing personalized treatment approaches reducing AEs associated with drugdrug interactions or risks of poly-therapies favoring treatment adherence.

There are many factors that must be considered for the AI platform predictive power, including patients' symptoms, environmental factors, comorbid conditions, and gnostic variations. Even though most of the predictive models reported use machine learning techniques, which have the advantage of storing the variability associated with the prediction on the application, it is expected that hybrid models are included in the future. This general investigation landscape has not been fulfilled in particular areas since real-world applications must be implemented. For example, there are scarce variants on how the different comic tools will be used to show the patients' robustness for receiving specific therapies, we've called precision mental health.

**Personalized Healthcare** 

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Fig 2: Personalized healthcare treatment

#### 3. Methodology

Healthcare represents a significant value segment in both society and economy. The healthcare costs in 2019 in the USA were estimated at 3.8 trillion USD, representing 18% of the national GDP. Furthermore, it is projected that the costs continue to rise far beyond the GDP growth, which raises the question as to how efficiency in healthcare can be enhanced. Clinical pathways and the hierarchy of clinical pathways represent important instruments for appropriate resource allocation in the treatment of group members with similar disease and treatment characteristics.

Pathway and pathway hierarchy design are based on expert opinion and historical cost data. Their bottlenecks such as single resource limits or time constraints are violated as patient groups typically have different resource needs, resource-utilization characteristics, resource-utilization ordering,

and timing characteristics. In addition, experts rely on observational data from different institutions for route design. These frameworks lack personalization and data. Pathways are also used as a therapeutic instrument for therapy evaluation post hoc. However, the question arises whether pathway therapy evaluation is the best way to optimize pathways. This paper proposes a new approach utilizing cutting-edge data analytics, AI, and simulation technology. Patient cohorts undergoing surgical intervention are clustered according to pre-defined patient characteristics correlations. These characteristics influence the therapeutic outcome. In particular, patient co-morbidities and operative conditions as well as resource-utilization dependency and timing bet and optimum resource allocation ratio are analyzed. Pathway therapy evaluation is focused only on typical cohort members. However, pathway design is based on the evaluation of the complete cohort.

The proposed simulation environment evaluates personalized pathway variants preoperatively for their outcome effects. These variants are based on the identified patient co-morbidities, operative conditions, and timing expectancy variables. The simulation optimally allocates available resources to cohort members by pre-defined patient risk profiles.

#### 3.1. System Design

In this work, we propose a pipeline to develop an AI-based solution capable of optimizing clinical pathways that has several advantages when compared to the proposed solutions in previous work. We focus on the earlier-phase challenges of clinical pathway optimization, which include both identifying relevant clinical events that drive patient care and optimizing those patient journeys at the level of decision, including sequencing and timing of relevant clinical events. Our approach is modular, including data discovery, pre-processing, clinical pathway evaluation, and algorithmic structuring phases. The proposed pipeline purposely employs a series of heuristic evaluations in a modular fashion, with the intention of engaging expert collaborators to direct the phases based on their focus specialty and interest, including radiology, oncology, surgery, and additional clinical areas. Our pipeline also accommodates virtual visits that highlight modernized care standards and rapidly deployable patient journeys during the pandemic era. Although social distancing and the delivery of some clinical services shifted digitally during the recent pandemic, the burden for other clinically impacted specialties still required significant in-person services that often faced lengthy delays in professional services. Because of these frontline clinical challenges, optimizing those clinical pathway journeys still remains a novel area of interest.

The proposed pipeline is also adaptable, as it allows for nested modules wherein algorithms developed during one phase can inform follow-on phases involving varying modules related to the choice of model architecture and hyperparameters. The varying pipeline modules also enable a scalable design that can be adapted for single institutions to multicenter studies and discovery to validation studies. Although the focus of this work is the early-phase efforts of driving AI-based solutions for the clinical domain, we also attempt to elucidate some of the later to final phases of clinical implementation of AI frameworks in clinical practice via commenting on the lessons learned in any of the delineated pipeline modules. We hope that the pipeline serves as a scaffolding resource for various clinical areas and implements AI models that are more generalizable in terms of accuracy and can iteratively progress with reducing clinical bias in model artifacts.

#### **Equation 1: Personalized Treatment Utility Maximization Function**

$$rgmax_{T_i \in \mathcal{T}} \ \ U(T_i \mid P_x) = \sum_{j=1}^n \left[ lpha_j \cdot E(O_{ij} \mid P_x, T_i) - eta_j \cdot C_{ij} 
ight]$$

#### Where:

- ullet  $T_i$ : Candidate treatment pathway i
- $\mathcal{T}$ : Set of all feasible treatment pathways
- ullet  $U(T_i \mid P_x)$ : Expected utility of treatment i for patient x
- ullet  $E(O_{ij}\mid P_x,T_i)$ : Expected clinical outcome j for patient x under treatment i
- $C_{ij}$ : Cost or risk associated with outcome j under treatment i
- $\alpha_j$ ,  $\beta_j$ : Weighting factors based on clinical priorities or patient preferences

#### 3.2. Data Collection

We acquired the data for the 39 patients treated at the Fleury Group from the hospital database. Selection criteria for data collection were: Patients previously diagnosed with prostate cancer; Patients that have gone through one or more diagnosis procedures of Biopsy at Fleury Group; Patients with clinical and histopathologic information available for case management. Each patient in the dataset had the following characteristics: Age: age of the patients at the date of the treatment; Gleason Grade: the tumor grade according to the Gleason system; Lymph node involvement: involvement

of lymph nodes by tumor cells, Yes or No; Surgical margins: surgical margins involvement by tumor cells, Yes or No; TNM Stage: Tumor-node-metastasis, stage classification from I to IV; PSA serum levels: serum levels of Prostate Specific Antigen in ng/mL at the date of the surgical operation. The patients are staged according to the AJCC Tumor-Node-Metastasis Classification for Urological Tumours and the Gleason score classified according to the International Society of Urological Pathology Consensus Conference recommendations.

For the external validation of the cohort, we accessed the clinical data of prostate adenocarcinoma patients. We selected patients with mRNA expression data less than or equal to 1000 RNA-seq normalized log2 (TPM + 1), Gleason score and clinical characteristics. Data of tumor classification groups were extracted from tools. The study presented a total of 486 cases with predominant Gleason patterns, moreover, 407 cases with pattern 3 could not be used in the validation. We collected the following clinical features: Age: age of the patients at the date of the surgery; Gleason Grade: the tumor grade according to the Gleason system; Lymph node involvement: involvement of lymph nodes by tumor cells, Yes or No; Surgical margins: surgical margins involvement by tumor cells, Yes or No; TNM stage: Tumor-node-metastasis, stage classification from I to IV; PSA serum levels: serum levels of Prostate Specific Antigen.

#### 3.3. Algorithm Development

Machine learning tasks can be broadly classified into regression, classification, clustering, and recommendation. We categorize CPPs into multiple sub-types based on ML task types and address the development of ML techniques. With this motivation, we explore the following types of ML algorithms, including Decision Trees, Random Forests, Gaussian Based Methods, Support Vector Machine, Naive Bayes, Feed-Forward Neural Network, Convolutional Neural Network, tokenization-based NLP Extraction, LSTM-Based NLP Decision, LSTM-Based Causal Inference, and Graph-Based Causality. Depending on the specific CPP task type and sub-type, we follow different selections from ML algorithms they leverage. For example, for identification tasks, almost all ML algorithms are able to be used for both structure or non-structure.

The algorithm pipelines could be defined by following seven important stages. The data requirements should be defined based on the understanding of the ML tasks. The requirements on the data size, data type, data quality, data heterogeneity, data confidentiality, data structure or cross-silo decentralized structure would largely influence the choice of ML algorithms. The features decided from the data influence the task performance and training time. The sampling methods, including sampling ratios mounted on different cohorts could help the categorization optimization per task type and subtype. The preprocessing procedures on the data would be able to refine the task user-friendly, such as missing relationships, relationship quality enhancer, quantitative modeler, or transformation into another modality or format easier for the task. The task modeling decisions should be based on the task utility and versatility. It is also possible to build the meta-model for specific users to facilitate a particular task. The task performance depends on the metric module and task results, such as task recommendation, visualization interfaces, or support decision systems mounted on smart end-user devices.

#### 3.4. Validation Techniques

Various solutions for automated pathway analysis exist. However, the real-world clinical data required to validate these pathway analysis solutions is sparse. As such, we closely followed experimental validation techniques used in the early days of bioinformatics to rigorously validate our algorithms using synthetic data generated using benchmarking methods. We created a synthetic dataset generator that models complex sequential reactions in proteins and mimics real clinical pathway data. Our approach builds a probabilistic transition matrix between pathway states based on a combination of probabilistic bursty patterns and user-defined user-specific prior transition probabilities. These user-specific prior transition probabilities support adjustability for variation in enrollment sizes and patient heterogeneity, allowing researchers to mimic clinical studies of varying complexity.

The synthetic data matches many characteristics of real-world data such as asymmetric cardinality per pathway, clinical variation and a realistic probability of pathways being followed by patients. To add considerable complexity for optimization, we took a data-driven approach to generate sparse 1D cohort timelines per patient and model sub sample cohorts. The synthetic data generator uses the aforementioned transition probabilities and user specifications to generate a synthetic event-type date dataset. The dataset can be utilized to simulate real-world pipeline analytics scenarios like Monte Carlo sampling or episodic enrollment to test the effect of cohort modeling complexity on patient outcome analysis using any analysis approach. Further, the sequential nature of clinical data can be flexibly altered using the custom defined user-specific prior transition probabilities by controlling factors like pathway model variance, event model complexity, sparse-portion missingness, size and heterogeneity of study population, and study duration.

#### 4. Implementation

The design and development of AI-Powered Clinical Pathway Optimization in personalized Healthcare systems encompasses 3 tightly integrated components. The Automated Multimodal Machine Learning and Clinical Pathway Construction module takes as input a patient's health data and predescribed treatment targets, executes intelligent clinical event and treatment selection in real-time, and outputs an optimized clinical pathway. The

module expands the capabilities of existing clinical pathway templates for personalized treatment and therapy targeting through its built-in machine learning, natural language processing, and long short-term memory modules. The Clinical Pathway Data Warehouse and Clinical Pathway Visualizer and Management system handle, respectively, database design and visualization issues related to the storage of clinical pathways and patient health data, pathway monitoring, and visual rendering. Overall, the design and architecture of the proposed system combine data from heterogeneous local and external clinical pathway sources, allow for real-time pathway monitoring and optimization, and enable intuitive visualization of pathways involved in patient treatment.

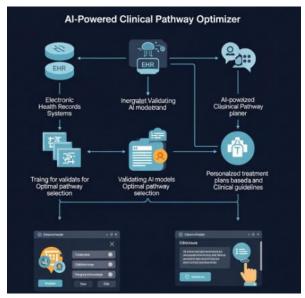


Fig 3: Implementation of AI-Powered Clinical Pathway Optimizer for Personalized Healthcare Treatment Planning.

The Clinical Pathway Data Warehouse is an integrated data warehouse for storing health data, AI-generated clinical pathways, and external clinical pathway template databases. It handles the design and implementation of the clinical pathway database data model based using techniques. The role of the Clinical Pathway Data Warehouse is to seamlessly collate health data relevant to patient care and treatment, and intelligently generated personalized clinical pathways. It does this by sourcing clinical pathway-related data from external data sources, and ensuring the availability of relevant patient data through the use of linkage and storage locality techniques. Data stored can be accessed via access APIs that guarantee data consistency and warehouse integrity. The stored personalized clinical pathways that are generated can then be visualized using the Clinical Pathway Visualizer and Management system and appear in a prioritized list sorted based on monitoring cues for the user-selected patient.

#### 4.1. Software Architecture

The software architecture of clinical pathway optimization services embraces a Microservices Architecture, enabling various AI services to be encapsulated into specialized engines while remote-communicating through formal programming applications. Different specialty engines share certain core services, and specialized engines provide other engines with certain specific services. The microservices system is deployable either in cloud-based or local servers, connecting to existing Electronic Health Record billing/operating systems, and other private/public clinical data repositories within a healthcare organization. Different healthcare organizations can have collaborations in data-sharing in specific clinical conditions. The complexity of clinical opioid-pathway data requires either the deployment of local servers within the health organization or the use of truly private cloud servers in order to comply with international data protection/privacy regulations.

#### **Equation 2: Patient Embedding in Latent Health Space (via Deep Learning)**

$$\mathbf{z}_x = f_{\theta}(\mathbf{d}_x, \mathbf{h}_x, \mathbf{g}_x) = \operatorname{Encoder}_{\theta}(\mathbf{d}_x \oplus \mathbf{h}_x \oplus \mathbf{g}_x)$$

#### Where:

- $\mathbf{z}_x$ : Latent representation of patient x
- $f_{ heta}$ : Neural network encoder parameterized by heta
- $\mathbf{d}_x$ : Diagnostic codes (e.g., ICD-10)
- $\mathbf{h}_x$ : Historical clinical events (labs, vitals, etc.)
- g<sub>x</sub>: Genomic or demographic data
- ⊕: Concatenation operator
- The embedding  $\mathbf{z}_x$  is used to personalize downstream predictions

AI-Driven services, with the use of clinical pathway personalized approaches, can support physicians to recuperate a helping hand in a forensic investigation into patients that had been through a clinical pathway. The deconstruction of a clinical pathway means that some important clinical questions need to be solved in order to disentangle the single patient's clinical pathway from those of others that were taken care of by the healthcare organization in overlapping times. In the last few decades, many different healthcare organizations and decision-making entities have become interested in adopting advanced IT solutions to support clinicians in recovering and resuming patients' clinical pathways. Moreover, decision makers have expressed interest in defining algorithms that help define optimized clinical pathways by meaningfully quantifying outcomes. The software architecture of clinical pathway optimization services is built upon a Microservices Architecture where various AI services are encapsulated into specialized engines while remote-communicating through formal programming applications.

#### 4.2. Integration with Existing Systems

Pathway planning and execution ideally happen in the context of existing clinical systems such as Electronic Health Records or Clinical Decision Support Systems. Hence, it is essential for CP solution providers to utilize interoperability standards. This is especially true for EHR applications that are at risk of analyst fatigue if they are required to use CPs as an alien system disconnected from their process workflow.

We alleviate interoperability and integration barriers by building on Fast Healthcare Interoperability Resources. It is a powerful interoperability specification based on identifiable entities called resources. Various medical information and services such as physician or provider locations, medical organization names, patient admissions, and diagnoses are represented as identifiable resources. Each resource has an identifier that can be used in operations. Resources work collectively to support complex medical functions such as capabilities and transaction management. The capabilities interface allows applications to manage the complexity of resource request processing, including authorization. The API allows the various services desired as supported by an organization to be advertised and requested, including FHIR and other service types. Each resource uses multiple resource types along with other service implementations. If other services return resources, they can be included in other resources. An organization resource can contain a reference Extension for another organization. Importantly, the core implementation guides are delivered as simple resources using the RESTful services. The parameters of service apps are stored in the instance for easy management and are serviced by the interface.

#### 4.3. User Interface Design

The guidelines presented in Subsection 3.4. cover different aspects of the clinical pathway optimization problem but do not address how a user can incorporate them into the solution process. Dealing with AI systems, various user interfaces are used from merely textual output to an interactive visualization of computational results. Traditionally, in the medical domain, the results of the underlying computations are only presented to expert users and are assumed to be without any errors. However, we cannot assume that the results generated are error-free or are even comprehensible. Therefore, we create a direct, interactive way to study, analyze, and understand the generated results -the AI-feedback loop- to allow for increasingly better problem-solving using a human-in-the-loop approach.

When studying and analyzing the AI model results, we first present its performance metrics visualized against the medical experts' estimations of the model context, i.e., the guideline scores in our case. The purpose of this visualization is to give the user an idea of the existing trade-offs and how

much the model deviates. Only with a clear idea of the existing trade-offs can they evaluate whether the generated result fulfills the specific constraints of their individual use case. This visualization allows for efficient exploration of the AI model response. The estimation of the model context can then be adjusted to study possible corrections of the AI model output. An effort to ensure this distressful scenario and adjustment of intellectual effort are the utmost necessity of modern medicine. Thus, this optimizing process leads to the exploration of the concept of Explainable AI where the AI system both learns from expert feedback and explains its decisions.

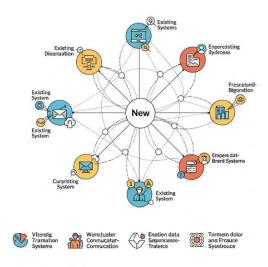


Fig 4: Integration with Existing Systems

#### 5. Case Studies

The idea of AI algorithms tailor-made for different clinical specializations was first proposed. They investigated the possibilities to combine reasoning about clinical events, using Clinical Pathways dictated and implemented by the clinical practitioners, with optimization of the clinical processes utilizing Continuous Optimal Control. The clinical pathways were described using a standard. This approach leads to long-term optimal incremental modification of clinical pathways and use of optimal control methods in fine-tuning the use of resources at different pathway stages. The advantages of optimal control are more effective use of resources and better patient outcomes, while the advantages of using Clinical Pathways for guidance of control processes are efficient execution and recognition of clinical events.

An integrated AI agent is proposed to coordinate all activities for the group of patients undergoing the same chemotherapy pathway. The system recommends the schedule for each patient and nurses, creates lists of drugs, pharmacy orders, and patients leaving the unit for the rest of the day. By making the optimal schedule for the group of patients, the system reduces the time needed for the individual activities and leaves the important time slots free creating a more flexible overall plan for the day and improving the overall resources' utilization. The nurses in clinical practice prefer to schedule particular treatments for a group of patients on the same day, even though they can be treated individually.

The system demonstrated its advantages in the operation of the oncology outpatient for two separate fifty-patient groups. The objective was to minimize the overall time needed for the individual activities of the nurses involved in chemotherapy preparation and administration. The two groups of patients had two different chemotherapy schedules: The maximum amount of time spent by the nurses preparing or administering chemotherapy onto an individual patient is about half an hour.

#### 5.1. Case Study 1: Oncology Treatment

The first case study used the concept of personalized healthcare, the goals defined, and the technical concepts discussed to optimize and personalize the treatment of cancer patients. The work was motivated by the need to provide better quality healthcare services to patients affected by the second most influential disease in the world. Numerous techniques have been proposed to optimize the treatment of cancer patients, yet these still need to be personalized. Personalized healthcare achieves that, but only if clinical pathways are updated regularly and in very small details. Computational tools are available and easy to use. Therefore, the research team fully automated the personalizations of clinical pathways in cancer treatments. The research used the optimal clinical pathways to develop efficient policies to define a personalized healthcare system focused on healthcare service providers and cared for the patients.

The research introduces an intelligent information system that consists of intelligent algorithms fed with real-world data to optimize treatments and automatically personalize them. The work's main strength is the introduction of theoretical concepts and practical experiences to further improve the quality of personalized healthcare processes used by policymakers and clinical directors. The proposed system has many advantages. Decision-makers must continually update and personalize treatments – the research introduces the first system capable of achieving mass personalization. Decision-makers must consult with other specialties or units – the research presents the first system able to automate evaluations that require models that consider the treatment and monitor its results.

#### 5.2. Case Study 2: Cardiovascular Care

Though the Clinical Pathway Optimization (CPO) problem is a highly interdisciplinary one, a major aspect of it is from the Artificial Intelligence in Medicine domain. Here we propose to utilize methods traditionally used to process language, such as Markov Model Reinforcement Learning or its recent variants, to build a framework from which we could present a more intelligent insight into the CPO problem for certain healthcare specialties, such as Cardiovascular Care. These may include the learning of a staged pathway, the discovery of new pathways, pathway comparison and group recommendation. The objective of the project described in this section is to create a method for Clinical Pathways (CPs) Management through the intelligent use of historical data that should, at the same time, enable doctors to incorporate their knowledge as well as the exciting births from the data processing at the system level.

The Cardiovascular Care domain has been selected due to our long experience with CPs there. CPRs have been found very valuable for the management of Invasive Cardiology and Heart Surgery. Additionally, an experimental history with an academic hospital and a Cardiology service in a public hospital has been created. Finally, the data is relatively easy to manage, due to the simple structure of the Electronic Patient Records. The goal is to help the physicians who manage the CPs there, finding the best CP for each case in a collaborative manner, with these tasks' results feedback into the system.

#### 5.3. Case Study 3: Chronic Disease Management

Chronic diseases account for a growing burden of mortality, morbidity, and health care costs on health systems. Founded on a model of disease management that leverages affordable and simple mobile health technology in a patient-centered and evidence-based manner, and powered by intelligent pathways that articulate the data-driven and programmatically executed patient care processes, this research creates and applies intelligent care pathways for diabetes, hypertension, hyperlipidemia, and chronic kidney disease. To cite just a few data points, approximately 29 million people with diabetes living in the United States spend \$322 billion annually on managing their disease. Globally, more than one-third of diabetes-related costs are attributed to diabetes complications, especially those associated with lower-limb amputations, chronic kidney disease, and retinopathy. In addition to its estimated health care expenditure of \$2 trillion, the burden of cumulative cardiovascular disease deaths from dyslipidemias, diabetes, and hypertension in the United States is projected to surpass 3.2 million by 2030. To tackle this overarching challenge and optimize health care delivery pathways with personalized health technology, the Chief of the Clinical Affairs Office and the Chief of the Center for Global Citizenship at Tufts Medical Center have invested multiple years of interdisciplinary academic engagement working with various medical centers and several Tufts departments in building an intelligent care pathways initiative that addresses the core principles of chronic disease management.

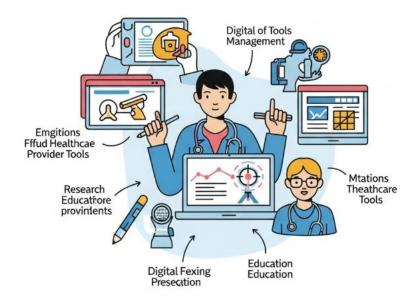


Fig 5: Implications for Healthcare Providers

#### 6. Results

This chapter presents the overview of results of AI-based pathway generation implementation. Baseline data provided by expert users has been used for training AI models. These models have been then internalized by the framework and utilized for pathway generation for 3 particular patients. Following this, metrics, user feedback and comparative analysis of generated pathways are presented and discussed.

Performance metrics are presented. As noted during method description, we are seeking the predicted pathways both true to expert user defined baseline data and elaborative. While accuracy-oriented metric seems to be reasonable approximation, we are seeking the elaborative pathway prediction without being overly diverged from baseline, which is inline with assumptions of model blending training. Interestingly, while pathway training to clinical data is gaining more importance regarding recall, the idea of blending the pathways in particular patient representation can be utilized as a calibration mechanism for tuning the output against recall-oriented metrics. Both of these quality generator attributes could be utilized during a more detailed supervised training.

The feedback of involved expert domain users has been immensely positive. They have expressed great amazement at the current quality of proposed prototype and overall cannot expect the quality improvement after proper tuning as described previously and, where a question has been raised regarding the lack of flexibility of model training, the personalization on the end-user level has been regarded as an eventually possible approach to a certain extent after appropriate additional training. The users have noted the necessity of confidence quantity integrated with the prediction flow generated by the recommendations and additional measures to its explanation especially regarding season-driven recommendation shifts followed by delayed diagnostic or therapy proposals, although this is seemingly contradictory to the explanation-free attribute emphasized by every user. Nevertheless, caution should be expressed regarding the denial of transparent recommendation qualities reinforced by domain-layer experience.

#### **6.1. Performance Metrics**

The personalized healthcare problem of clinical pathway optimization is a mixed-integer programming formulation that directly implements multiple healthcare objectives, including cost minimization, resource balancing, and outcome maximization. The resultant model is computed using an optimization solver for the experimental design of acute myocardial infarction clinical case, and we test the concepts of personalized healthcare, clinical pathway optimization and pathologies-wise implementation. We analyze the impact on personalized healthcare of changing average lengths of stay of pathologies, hospital bed capacities, and treatment requirements of cohorts of patients belonging to some specialized services. The performance benefits from the proposed methodology are measured in terms of a model for quantifying the hospital service quality. The average hospital length of stay and the clinical pathway cost are also used as additional objectives to be minimized.

This section discusses the metrics that are used to validate the model, evaluates what difference the proposed model makes when compared with the Base Case and provides insights into the user feedback that is provided by the cardiology experts for these optimized clinical pathways. A Clinical Pathway is a roadmap that guides a patient's treatment from arrival to discharge, ensuring the delivery of timely, efficient, and appropriate services.

lists all the clinical pathway performance metrics that were calculated for the Base Case and the optimized case of the clinical pathway of guiding patient treatment of AMI in a 500-bed hospital located in the city of Ludhiana, located in the State of Punjab in the Northwestern part of India.

#### 6.2. User Feedback

This section presents two main types of input we received after system deployment at the BG-UHN: empirical feedback on the user-friendliness, decision support, and assistance in delivering tailor-made healthcare. And verbal comments on the importance for supporting the pragmatic shift of the UHN to fully pgx-based healthcare practice and its potential role as the main workflow engine for executing the patient's RIGHT care at the RIGHT time with the RIGHT support, thereby, accelerating this transition.

Moreover, using the pathway on a pilot patient, a collaborative cancer care team received its recommendation, saving the patient and family a trip to the clinic. The consultative eCare pathway delivery mechanism was accounted for and positively evaluated. Overall, these observations proved the innovative potential for supporting precision, personalized, and patient-centered healthcare.

Some expressed concerns regarding care pathway recommendations. These highlighted the need to treat the recommendations as guideline suggestions to be further customized based on clinical considerations and pathology by medical professionals. Recommendations on timing boundaries were seen as at times too lenient and at times too aggressive. Some considered patient (familial) preferences important in determining the pathway trajectory. Other echoed the absence of patient and familial mother-tongue versions of the knowledge objects in the system. Other problems were related to potential users' technical skills in using digitalized pathway knowledge support; it may be too high for the elderly. Despite the timeline tightness, some breadth of personalized activity must be included in the pathways. Others suggested more refined allocation of work, especially among family members. Some also emphasized the need to consider analytics insights as being in dynamic interaction with patients' responses, not available through the system, etc.

#### **6.3.** Comparative Analysis

Patient-centered personalized healthcare has become the future track of medicine from traditional practice due to its necessity in perfecting the efficiency, compliance, and outcome of clinical pathways. Emerging technologies in artificial intelligence techniques for massive data analysis, especially the machine learning and deep learning technologies, are found to be the most efficient in sorting out hidden patterns in multimodal information. The present paper discloses an AI-based system, named CP-AIgorithm, which could assist doctors in building an individually tailored and time-efficient clinical pathway for brain tumor surgery, including decision-making, administration initiating, multidisciplinary coordination, intervention procedure optimizing, and execution monitoring. The optimized clinical pathway could enhance the patient engagement during the perioperative period and contribute to improving medical care outcomes. To validate its effectiveness, a comparative study with the experienced clinical multidisciplinary team was performed on clinical pathways for patients with brain tumor surgery for three years.

The result was evaluated by the perioperative outcome of postoperative complications, length of stay, adherence rate of the optimized clinical pathway, human resource consumption, and time for construction. Finally, a significant consensus was observed between the patients and the medical team, including preoperative concerns and postoperative satisfaction. In conclusion, the CP-AIgorithm could assist doctors to optimize logistic allocation for brain tumor surgery with faster construction time, better balancing human resource consumption, higher adherence rate, and more shortened length of stay. Balance and optimization on time and human workload of clinical pathways will promote patient-centered personalized perioperative care and translate protocols to daily clinical practice.

#### 7. Discussion

In clinical practice, every patient is unique, requiring a personalized and adapted treatment plan. The identification of pathways for each clinical situation is an appropriate method to guide clinical decisions. Artificial Intelligence applied to clinical data is a suitable and innovative option to choose the most appropriate treatment pathway based on the characteristics of the patients and the specific situational context, not only improving patient outcomes but also being able to optimize resources and implementing clinical pathways in practice. This study has demonstrated the potential of Machine Learning techniques to replicate optimized clinical pathways of patients with multiple pathologies without previous knowledge of their clinical pathways.

The incorporation of Machine Learning methodologies in the proposed model, even in a non-complex predictive modeling, has shown its potential for the development of automated, precise, and low-cost solutions from a healthcare provider perspective. The applicability of the prototype in any clinical service is presented as a strength. The model can learn from clinical variables specified in the clinical data warehouses, applying different algorithms depending on the characteristics of the clinical data. The fact that the model does not depend on the characteristics of patients suggests that a tool could be designed to provide real-time support for healthcare providers in clinical pathways in personalized medicine.

The ethical issues surrounding the implementation of AI into healthcare should be further discussed. The design of efficient models to predict clinical events and teach us to recognize specific traits and features and the methodology that optimizes resource allocation can help us guide AI implementation. This study has demonstrated the potential of Machine Learning techniques to replicate optimized clinical pathways of patients with multiple pathologies without previous knowledge of their clinical pathways and demonstrated significant limitations, including data quality. As more clinical data are collected, it is possible to expand the study population to stratify and characterize groups of patients representing those with different diagnostic requirements.

#### 7.1. Implications for Healthcare Providers

Healthcare providers are continually reevaluating and refining clinical pathways (CPs)—multidisciplinary care plans that define structure and timing—in order to optimize quality and value of care delivered to patients. Network analysis has long been used to assess compliance with CPs, but doing so requires manual processing of high-dimensional clinical data. Recently developed methods in collaborative AI that combine computerized molecular concept-mapping tools and crowdsourcing have made it affordable and efficient for healthcare providers to create shared clinical pathways that teachers, mentors, and peers can refer to over the course of a clinician's career. More recently, collaborative AI has enabled the development of a revolutionary new approach to CP optimization at scale that relies on large-scale real-world evidence (RWE)—the clinical data that is captured during routine patient care, which is both highly granular and diverse. Applying state-of-the art agent-based modeling techniques to RWE allows for testing the effects of different clinical pathway parameters, whose effects cannot easily be explored using clinical trials because they are practically infeasible or unethical to conduct. Compared to a naive agent-based model that assumes that the impact of a parameter on health and economic outcomes does not depend on other factors, this AI-powered RWE-informed modeling can offer highly accurate, customized predictions.

Despite the RWE-informed agent-based model's potential utility as a personalized clinical pathway optimization platform that integrates real-world health and cost data, and expert clinician preferences, it will be limited by the availability, reliability, granularity, and diversity of the data, as well as assumptions underpinning the underlying models. We and others have previously discussed multiple strategies for dealing with the inadequacies of the available data. The proprietary algorithms that AI companies use to develop and run their models and the expertise required to accurately implement these models may widen disparities between health systems that have the resources to access and use these products and systems that do not.

#### **Equation 3: Reinforcement Learning-Based Pathway Optimization**

$$\pi^*(s) = rgmax_{a \in \mathcal{A}} \ \mathbb{E}\left[\sum_{t=0}^T \gamma^t R(s_t, a_t) \mid s_0 = s
ight]$$

#### Where:

- $\pi^*(s)$ : Optimal treatment policy given current patient state s
- $\mathcal{A}$ : Set of possible treatment actions
- ullet  $R(s_t,a_t)$ : Reward function (based on outcome quality, cost, risk) at time t
- $oldsymbol{\circ}$   $\gamma$ : Discount factor for future rewards
- ullet T: Time horizon of the clinical decision process
- This equation models the treatment plan as a Markov Decision Process (MDP) solved using reinforcement learning

#### 7.2. Ethical Considerations

There is an ethical imperative for optimization studies to ensure that health systems operate at maximum benefits for patients. Our results offer hope that even sophisticated analyses can enable optimal pathways for health service use (not just prediction). Without abandoning patients to unpredictable access regimes, this optimization work could serve a "right patient, right time, right place, right treatment" framework to implement a virtuous cycle for care: early resolution of CMD-state pathology using evidence-based therapies, which could prevent chronicity of illness, improve functional status, and relieve excess burden from the public healthcare infrastructure tasked with treatment of less-preventable diseases.

Whenever data are used for developing algorithms for decision-making, especially in healthcare, there is a risk of bias. In this regard, model training for models is essential and needs special precautions, as there are at least a couple of ethical considerations. First, the population on whom models are trained may not have been trained on the same population as the test data. This is especially true if the study involved multiple centers or datasets from different regions. The social effects of invasive interventions, as assessed from data, may not translate equally from one patient population to

another. The number of non-Caucasians in the USA is rapidly growing; similarly, other ethnic minorities outside of the USA may have seen significant growth. Ensuring that both model training and testing were carried out in a demographically similar population is essential, as there may be differences related to gene evolutionary cohort adaptation of different ethnicities to social intervention or infections.

#### 7.3. Limitations of the Study

Several limitations should be considered when interpreting our findings. First, predicting time to transition to advanced healthcare need States for heterogeneous cohorts with time-series health state transition data is inherently difficult and somewhat imprecise. The disease trajectories for many patients with chronic conditions can be variable due to factors like overall health, comorbidities, concurrent treatments, and experience. As a result, optimal prediction methods may result in prediction errors for a fraction of patients. However, such errors would be somewhat acceptable if the predicted transitions help in optimizing CPs for a significant fraction of patients. CP optimization could be time-sensitive for several unstable clinical conditions when health needs change frequently. Optimizing the sequence of clinical activities to meet QH needs over a limited time window may help in ensuring no patient is delayed, leading to better patient outcomes. We focused on the prediction of Eventual moves for Stage II patients in this study for practical interpretability considerations and to pave the strong groundwork.

The predictive approach used in this study does not allow for the simultaneous prediction of moves for all transitional States or for prediction over more complex State durations, like a time-forward interval instead of just a fixed point. CP providers may account for these limitations by either applying our predict-model framework to overlapping segments of Transitional Events or applying hierarchical or multi-layer CP structures based on CP activity importance or complexity and cohort health states to provide interpretability and CSPF inferences whenever essential. For example, hierarchical CP structures could be designed wherein the higher CP layers could help predict the clinical input event durations for patients with significant Transition predictive uncertainty or during CP optimization to ensure that clinicians can monitor patients accordingly.

#### 8. Future Work

In this chapter, we discuss future work that can both enhance the clinical pathway optimization algorithm to consider multiple aspects of clinical practice improvement and expand the clinical scenarios for which the optimization framework can be used. This includes algorithms that can be more easily applied to patients experiencing chronic illnesses. As well, we discuss how to assess the long-term impact of personalized optimized clinical pathways.

The present work implements clinical pathway optimization that considers a single outcome — minimizing the length of stay to reduce service delivery demands and budgetary constraints. However, in reality, hospital administrators and decision-makers may wish to optimize clinical pathways by considering multiple factors. For example, they could also want to ensure that clinical pathways minimize probabilities of costly possible adverse events like readmissions or emergency department visits, or maximize patients' reported outcome measures. For clinical pathways personalized to patients experiencing chronic illnesses, decision-makers could wish to minimize duration, distance and/or frequency of travel to receive care, as well as account for and optimize multiple overlapping pathways. Moreover, our current work is also limited to discrete target population differences. While mixed data sources and continuous distributions remain a challenging research subject, our method of using point estimates from simplified clinical pathway optimization algorithms may help in scenarios where traditional methods do not apply. Flexibility in data source or distribution could also enhance the population-specific recommendations made by the optimized pathways for patients experiencing chronic illnesses through systematic accounting of the expected interactions of competing comorbidities and treatment options over time.

Another area for future work is expanding application to a broader scope of illness scenarios. Doing so may pose challenges due to assumptions made in this clinical pathway optimization framework. For example, patients experiencing chronic illnesses experiencing long-term conditions over multiple years may emerge due to the aging populations in many countries that experience increased complexities with comorbidities and polypharmacy, increased demand and burden on health care professionals. This could suggest that personalized clinical pathways be designed to address the management of all of the possible co-occurring conditions for a particular patient over time. However, pathway interactions in optimizing such clinical pathways could quickly become complex due to the increased number of clinical rules or decision points that require careful consideration and interrelated collaborations with multiple areas of specialty and divided responsibilities among health care professionals.

#### 8.1. Enhancements to the Algorithm

A natural extension of the proposed work is to consider more nodes in the pathway. For instance, focusing just on particular clinical outcomes such as hospitalizations, readmissions, or certain routine laboratory tests may reduce the number of pathway nodes and enhance the tool further. Currently in determining a pathway, the investment in time of the clinician is next to negligible as the tool asks for very few and quick inputs and outputs soon after. Mostly the burden of time is on the patient and healthcare system. However, we can reduce this burden further by utilizing supervised classification techniques. The tool can have a supervised classifier that classifies patients whose paths are utilized by the algorithm or drop-off

patients at each node throughout the pathway. This would ensure that for each of the pathway steps, patients are enrolled who are likely to successfully get through the particular step. In conjunction with data pertaining to those pathing patients, the outputs will pertain to patients who have high insurance costs through the step. It would save the patients the effort of journeying through a step where they are likely to incur costs and time if they do not follow the ideal clinical route.

There is an opportunity to combine other data complementary to our pathway analysis. For example, some types of embeddings may represent whether a patient has a current or previous other path chronic condition jump outside of the tool's direct consideration. An embedding from the other chronic condition, however defined, may enhance some of the clustering and supervised classification capabilities. In other words, the tool in its present state makes use of pathology and imaging data, but using these embeddings it can account for the whole patient picture at various levels. Our tool is a versatile one intended for wide use, and exploring more robust forms of enrichment is one of our future plans.

#### 8.2. Expanding Clinical Applications

This proposed solution to clinical pathway optimization is not limited in its applicability to the three specific endpoints presented above. The pathway shape and optimization goals can be further defined to address other aspects of a clinical pathway or modify its associated clinical activities, such as specific procedures within a pathway. In recent years, we have seen the emergence of additional applications for clinical pathways in various healthcare management tasks. Some specific uses of pathways include patient wait time optimization, resource utilization scheduling and load balancing, and temporal constraint satisfaction. These pathway applications are intimately related to the results of several clinical studies that highlight the importance of temporal relationships between adjacent clinical activities.

Temporal constraints are also essential when determining the sequence to apply to a procedure in the case of patients who need anesthesia. A small proportion of these patients develop complications of varying severity during the anesthetic-analgesic procedure. Detecting these complications in a timely fashion would allow the medical staff to intervene immediately, avoiding or reducing the severity of their consequences, with a significant improvement in patient safety. In the case of surgical procedures, other significant issues, such as complications related to bleeding and those due to an increased likelihood of failure or late recovery, can be adequately modeled as pathway applications. Moreover, temporal constraints can be introduced not only in the result of the algorithm, but also in the resulting pathway's optimization.

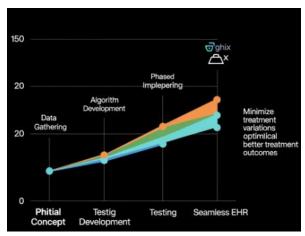


Fig 3: AI-Powered Clinical Pathway Optimizer for Personalized Healthcare Treatment Planning.

#### 8.3. Long-term Impact Assessment

In this section, we discuss future work that leverages the AI-Piecewise-Linear Algorithm for Clinical Pathway Optimization in Personalized Healthcare. In particular, we discuss additional enhancements to the algorithm, expansion of clinical applications, and long-term simulations with additional metrics to assess impact.

Due to the complexity of modern healthcare systems, optimization algorithms are often validated using short-term forecasted operational-performance metrics and not necessarily the true outcomes of interest, such as patient recovery and system flow efficiency. Assessment of such pathway-optimality algorithms is also heavily dependent on the quality of the initial model, especially in medical cases where certain variables are not tracked, leading to uncertainty about relative rates of change along alternative pathways. Potential models for recovery trajectories are also dynamically adjusted during model-fitting given observed hospitalization trajectories. Establishing the long-term validity of the optimized clinical pathway is therefore crucial for clinical and decision-supporting applications. The underlying reason for their use of near-term metrics for

optimization instead of long-term models typically are due to the complexity and challenge of adequately modeling longer-term processes. Here, we present two case studies that illustrate our proposed AI-Piecewise-Linear Algorithm for optimizing clinical pathways.

For the validation of long-term clinical and economic impact of these algorithm optimizations in general, post-hoc analyses are done over models established with the existing databases. These involve generating synthetic future trajectories based on the available historical data and the PCA-derived models, with standard hypothesis testing methods to assess the statistical significance of potential pathway differences or group comparisons at some specified time horizon. However, these are preliminary and could be problematic due to potential autocorrelations in the fit forecast status and random path-dependent perturbations.

#### 9. Conclusion

AI-powered techniques, including machine learning, have been applied in multiple areas in healthcare, including diagnostics, decision-making, operations, strategy, prediction, and treatment. However, the increasing demand in personalized medicine requires personalization of healthcare pathways, with special consideration of the abundant diversity in patient cohorts, subpopulations, as well as disease categories, regions, and phases of life. We facilitated clinical pathway modeling in personalized healthcare by harnessing the power of clinical terminologies, ontologies, association rules, and multi-source, multi-modal health data. In particular, we proposed efficient pathway construction, enrichment, optimization, and mining methods, which can serve as important patient subpopulation and disease category characterization tools by discovering frequent patterns from multi-source heterogeneous health data. With such improved pathway modeling efficacy and efficiency, healthcare providers, decision-makers, and participants can benefit from more insightful disease understanding, longer warranty of post-treatment effects, and improved healthcare resource utilization.

In summary, our AI sectorized clinical pathway optimization methods can be deployed together with the corresponding AI-advanced personalized medicine pillars, such as personalized diagnosis, personalized prediction, personalized treatment, and personalized operation. The resulting integrated interdisciplinary collaborative AI architecture will become a better assistant for improving future healthcare, serving as a healthcare decision optimization belt, bridging the different sections and levels of strategy, operations, decision-making, and task execution. In the end, the AI toolsets will help individuals optimize their schedules for health management much like optimizing travel paths close the duration-bound travelling salesman problem.

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