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Chapter 3: Machine learning in clinical decision-making: Shaping the future of treatment plans

3.1 Introduction

Clinical decision making – personal characteristics lead to the planning of effective treatments. Personalized medicine has become popular and has created new opportunities in clinical situations in recent years. Personalized realistic and appropriate health improvement plans for patient health conditions are considered as an important component of shared decision making. However, planning and taking effective action largely depend on the empirical judgment of the clinicians in clinical situations, and objective health improvement planning that is beneficial to both patients and clinicians is difficult. New data-driven treatment planning frameworks that can effectively plan health improvement processes to a practical level are proposed. There are public plans and models that propose treatment motion plans where it is possible to confirm that the planned motion plans are actionable and are in good agreement with clinical knowledge for the improvement of objective health factors. In addition, the proposed action helps clinicians to easily take patient-acceptable actions. Clinical outcomes show that the proposed planning motion plans effectively improve health factors. Finally, comparisons with conventional designs and encoding motion plans are performed for fixed-time set control functions. The results show that the proposed encoding motion plan can effectively improve the control objective by extending the action time by taking a feasible improvement action in time to compare the conveniences with the fixed-time set control function. Despite the numerous recent successes, it is still largely unclear how ML can support clinical decision-making. Ideally, after taking any data into account, it would be possible to classify the patient under the correct diagnosis. In human decision-making, a clinician would ideally explore all the available data and compare them to patients they have seen before or were trained to recognize. Because of this, numerous personal factors such as the knowledge and experience of the clinician, the time available, the noisy communication of diagnostic results, and even mood may bias the decision. For standardization, many professional organizations provide guidelines on how to manage patients under the best available evidence. This accumulation of evidence is generally based exclusively on data obtained from large cohorts of patients and, in general, corresponds to the average behavior of the population. However, these guidelines often ignore a large number of factors, both personal – sex, age, genetic predisposition, among others – and environmental – lifestyle, diet – that may be of relevance.

3.1.1. Background and Significance

Realizing the potential of ML in the medical sector and motivated by the previous works, much pioneering research has been conducted on tailored models that can explain black-box models as a post hoc analysis. Yet it is still nascent to investigate how to cast the medical requirements into ML models. If the aim is to provide assistance in clinical decision-making in terms of causal relation with model prediction, specific portable knowledge is required from the model. Unlike pattern interpretation, treatment processes should suggest medical actions corresponding to the input. For example, to support clinical decision-making, the blood test should be conducted to screen for possible diseases, or a rehabilitation process should be taken for an orthopedic patient. Designed models aim to explicitly estimate the treatment processes as a function of input and output. Quantitative evaluation is made on a diverse and uneven benchmark by analyzing the impact on predictive performance of the proposed models in addition to goodness-of-fit of the computed treatment processes. Overall, patient-tailored post-procedures should be built to make the black-box model actionable for practical use simultaneously and still highly predictive over the inputs. (Komaragiri, 2022; Chakilam, 2022; Malempati, 2022).

3.2. Overview of Machine Learning

As the best answer to a patient's treatment program should always rely on evidence-based recommendations, adversarial lifestyle interventions are a powerful aid to learn from metadata patient questions, increasing the statistical performance of clinical decision-making. The practical meaning for the involvement of machine learning in crafting a treatment plan for a patient could be in digitizing their meta-clinical history and allowing all credible evidence-based interventions to be scanned in, a model run multiple times on each patient and best programs devised as the top N statistically significant tests. Integrated Behavioral Health records have been analyzed for a large number of UK patients to determine the onset of treatment derived from machine-mediated treatment recommendations generated sophisticated treatment plans applying adversarial lifestyle interventions. Requirements allow for 17 unique or adapted lifestyle treatment plans to be devised, all of demonstrable equivalence to UK NHS recommendations based on the full clinical histories of 300k de-identified patients, and the same machine-mediated treatment plan is then compared against 1101 complex case files, each providing a patient history of moderate-to-severe ailment, in order to compare the statistically significant treatment list recommended by the model against outcomes in the NHS database. The occupation with which some ID-matches can be made allow any reported outcome to be mapped onto the standard treatment program, a binary flag of admission within 9 months, adoption of suggested treatment, or a death within 6 years. These findings are then correlated with admission date in order to estimate efficacy gradients of treatments as a function of time. (Challa, 2023; Nuka, 2023)

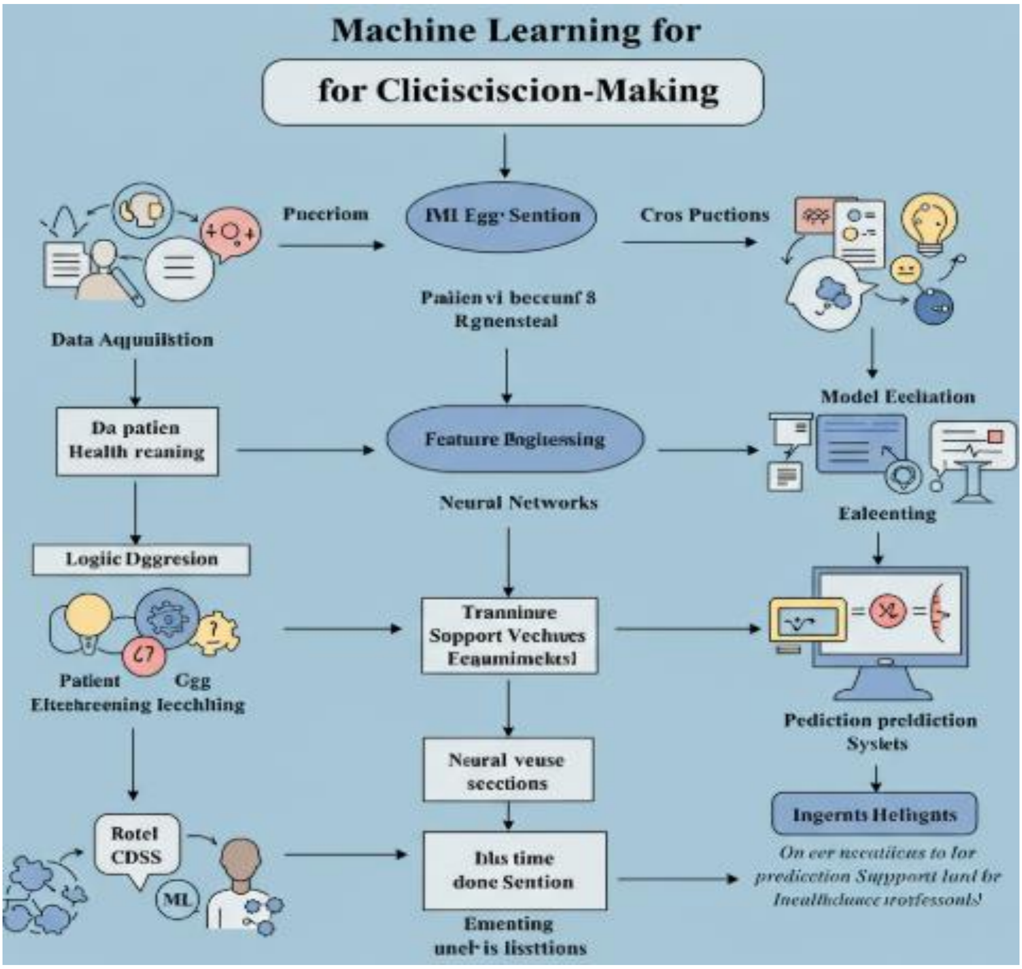

Fig 3.1: Machine Learning for Clinical Decision-Making

3.2.1. Definition and Key Concepts

Since the birth of the digital computer in the early 1940s, the field of artificial intelligence (AI) has captivated the collective imagination of scientists, science fiction writers and the general public. The promise of machines capable of human-like thinking and reasoning has driven research in this field with steady government funding, producing significant technical advancements, such as the development of the first programs that could asymptotically solve complex games or symbolic manipulation. Nonetheless, creating machines that can emulate higher human reasoning and introspection has proven to be elusive. Recent years have seen the rise of machine learning, an approach that focuses on inducing statistical models from data in order to make predictions rather than encoding explicitly programmed knowledge. The application of machine learning in high-level cognition problems has received interest, but has been met with skepticism from the artificial intelligence scientific community. Machine learning models have achieved superhuman performance in board games, video games, poker and other tasks. State-of-the-art models in text summarization, automatic translation and question answering have been developed. Nonetheless, training deep learning models requires large amounts of data and computational power. Projects have focused on creating applications of machine learning models to real world problems with significant limitations. For example, the models created are used to predict future events using data that is available only after such events have already occurred. Furthermore, most results have not been independently reproduced, the data and code used is rarely available, and the results tend to degrade over time. Effectively translating research results to the clinic requires reproducibility and robustness, thus researchers need to focus on the veracity and generalization of their models.

3.2.2. Types of Machine Learning

Machine learning has moved from being pie-in-the-sky to a practical aspect of drug discovery, including real applications every day. It can be used in a variety of ways, including predicting risks or segmenting patients to guide better diagnostic processes or targeted treatments. While the use of artificial intelligence and machine learning holds promise for improved efficiency and patient outcomes, several uncertainties remain about the correct uses and implementation in the clinic. There are also significant barriers to successfully and safely integrating these techniques that must be overcome for their full potential to be realized. There are many different types of machine learning that can be undertaken. There can be supervised or unsupervised learning. Supervised learning looks at previous examples, with a target variable that is then learned. This could be a classification problem with discrete outcomes or a regression problem for continuous outcomes. Alternatively, in unsupervised learning there is no target. The learning is from the examples themselves, which naturally cluster into different unknown classes. Clinical predictive modelling would often be looked at in a supervised sense, where we have a dataset of patients and outcomes, and are particularly interested in how they are related. An algorithm is then used to learn a link between the two, which can be evaluated and tested (usually in terms of discrimination or calibration). There is an ever-growing amount of physical examination data stored in digital format, which provides an ideal platform for machine learning approaches to help understand a patient's health condition and facilitate personalized disease treatments. In health care this will involve a patient who has a specific outcome, and the possibility to learn underpinning rules to make predictions about potential future walking diagnoses. With a move to 'big data' and an increasing ability to store and manipulate it, there is an opportunity to learn from that data in a more sophisticated way.

3.3. Clinical Decision-Making Process

Given the exponential growth of technologies in recent years, the possible planning of a treatment plan to achieve health improvement for each individual using a proper risk model becomes realistic. This subject is new, and its exploration has not been sufficiently discussed in the literature. One of the main barriers is the difficulty of identifying actionable planning from a wide variety of treatment processes. Another is an empirical judgment of clinical consideration. To some extent, the framework from machine learning with an emphasis on its interpretability has become possible. A comprehensive picture is naturally not actionable for health improvement, so there is a rational need to identify planning from this. Most existing empirical planning methods are analytical solutions, and they are often not able to cover a wide variety of treatment plans. One such example is the mobile web application that found plans based on a linear combination of the basis functions. It has been shown that computed plans are actionable and they are composed of only a few basis functions. There is a significant gap in actionable planning and theoretical studies, and it is unclear whether this plan is consistent with clinical knowledge. There is demand for a new planning framework that is automatically computed from comprehensive information and can identify a reasonable number of actionable treatment processes. Clinical decision making by cardiologists, as well as by most medical specialists, is incredibly complex but based on building a mental model of an individual patient's state to recommend actions to benefit that patient's health. Machine Learning methods have shown great potential for advanced data processing and feature extraction that improve diagnostic and treatment results.

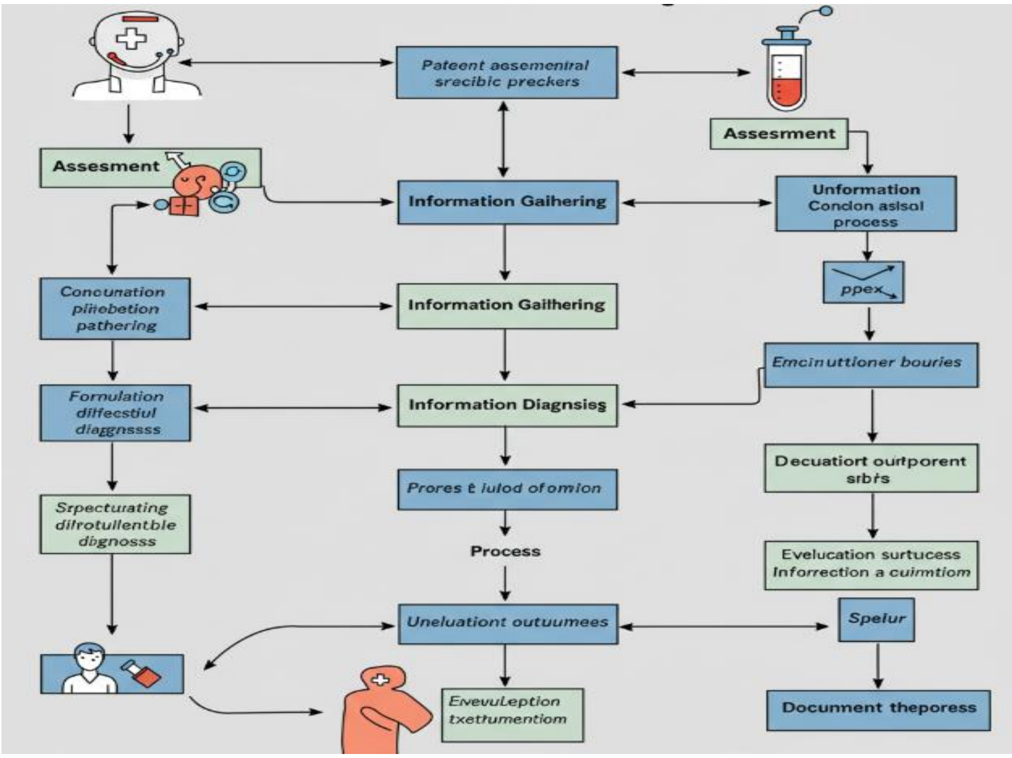

Fig 3.2: Clinical decision-making

3.3.1. Traditional Approaches

Recently, direct-to-consumer testing has been putting individuals on both sides of those conversations in a difficult position. Sometimes it has identified previously unknown genetic risks that need follow-up evaluation — and sometimes it has overattributed risks, creating a problem of its own. A number of genetic counselors said they had had patients come to them with direct-to-consumer test results that were alarmingly incorrect. Counseling with a genetic professional can help verify results and provide follow-up testing where needed. But people who aren't prepared to have those conversations aren't necessarily well-served by the tests in the meantime. Even for people prepared to have those conversations, those overreactions can have real effects. Most of the variants on a direct-to-consumer test involve fairly common diseases with more complex genetics. People may be influenced by the results of a direct-to-consumer test in ways that don't have any basis in the clinical care of their condition, and that's based on seeing past examples. Such tests can cause anxiety, and, more subtly, they can contribute to a phenomenon that specialists refer to as lived experience disease. That's when people who aren't sick believe that they are because their minds are so focused on watching for possible symptoms of a possible condition. The phenomenon weakens workforces as people react to their test results by shifting to parttime work or stop working, even when larger scale repeated studies do not support the idea that working play tiddlywinks? Many say that this is just an urban legend. At the same time, specialists also report scenarios in which parents of a child with a rare disease had to sell a house because, after a direct-to-consumer test wrongly suggested that the child might have a fatal disease, they quit their jobs and sought permanent treatment for the child abroad.

3.3.2. Role of Data in Decision-Making

Clinical decision-making is the keystone of evidence-based medicine and a milestone in achieving personalized treatment. Generally, it is based on the relevant medical guideline undergoing diagnostic and treatment steps, which lead from medical facts to appropriate treatment. In choosing the treatment alternatives, a large number of factors should be taken into consideration, such as guideline-based care pathways, incomplete data, financial constraints, or patient preferences. However, it is difficult to have all these factors and comprehensively consider them during the clinical decision-making process. An elegant approach is to model clinical decision-making problems into a well-defined optimization framework, which can take into account both objective, clinical, and subjective patient-specific factors simultaneously. Given that the rise of a data-driven approach is modifying the healthcare field, and many diagnostic and therapeutic decisions lie on the analysis of large amounts of data; the new framework of clinical decision-making HIPPATP is proposed to plan treatment processes based on routinely collected data. HIPPATP is the first to deal with the planning of the treatment process, leading towards the actionable and goal-reaching treatment. Since the improvement of health is not guaranteed through the executed treatment sequence of actions or optimal reactions, a surrogate Bayesian model is introduced. The rationale is that, by predicting the likelihood of actionable and successful treatments with the developed Bayesian method, possible future strategies can be recommended to clinicians. It is computationally demonstrated that the treatment plans consist of well-structured executable clinical treatment actions and substantially contribute to lowering the blood pressure, which agrees with the existing anti-hypertensive treatment approach in Japanese Clinical Guidelines. The feasibility and consolation with the existing clinical knowledge of HIPPATP-ascertained treatment processes are supported since clinicians have successfully executed 35% of the recommended treatment actions for 60% of the patients.

3.4. Integration of Machine Learning in Healthcare

Opportunities to improve patient outcomes, team performance, and reduce healthcare costs abound. Even with recent gains made in model interpretability and stiffer reporting requirements, a large gap remains between the accuracy of a model output, the trust clinicians can place in it, and its potential for doing harm left unchecked. In the evaluation of model functionality, the present focus is set on Machine Learning. Many more calculations are expected to be made towards automating the process of deciding the best treatment plan for a patient. Meanwhile, only a tiny subset of all Machine Learning (ML) meant for healthcare have been successfully integrated into the clinical space. Initiatives to develop models that are necessarily physician-led and informed run up against the reality that physicians are already overtasked. A critical assessment of models from a ML perspective is herein presented. The very real barriers that must be overcome prior to clinical implementation are detailed, as well as why it should be done despite the hurdles. A wish to see such technologies developed is shared, but the difficult path to that end is demarcated, hoping to direct research at a better target. It is contended here that it would be best to focus first on creating fully formed systems oriented towards one specific clinical problem, and second that training of these models should be carried out by a separate party after some proof of efficacy. The concept of a market of competing tools resoundingly declared.

3.4.1. Data Collection and Management

Clinical decision-making might soon depend on machine-learning algorithms and should be featured in training programs since medicine depends on medical research, clinical experience and decision-making. This will have to be accomplished by assessing data relevance, to be brought together and analyzed coherently and properly, organized in medical databases and ensuring it is reliably available for clinical decision-making, research, and teaching. Medical databases might be complex and essential for quality patient care to collect, organize, store, manage and present Canadian health data and should also be suitable for clinical decision-making and research. Software should be capable of epidemiologic, demographic, time-dependent patient history, signs, symptoms, laboratory test algorithms logic, practice guidelines, and problems, allergies and pharmacological profiles. Patient diagnosis and subsequent treatment should be automatically recommended and generated, supported by and consistent with current medical knowledge and guidelines, and it should also be time-sensitive. Physicians are warned that urgent antibiotics are prescribed and their actions might contraindicate medications and medical procedures or give rise to potentially adverse drug reactions . Concerning future optimization of clinical trial outcomes, clinician’s planning for new clinical trials should also resolve ways to maximize the rate of arriving at definitive findings, predict treatment effectiveness, examine therapy effectiveness in omitted patient populations, and predict harmful outcomes from the treatment. Proposed regimens should be dynamically adapted according to accumulated patient data, monitoring medical conditions and adverse events on a day-to-day basis. Based also on current medical progress, treatment exploration might increase based on linear, programmatic research traditions. Three elements are key in evidence-based medicine, called ‘best external clinical evidence’, which should amend medical expertise and the patients’ preferences and values. The program will be a new estimate, the described one for CNC machines or additional original research. Predictive models based on different mathematical paradigms have been devised to estimate patients’ medical conditions, regardless of the clinician diagnosis for evidence-based medicine. Notwithstanding, therapeutic decisions might also be informed by predictive models to estimate therapeutic outcomes. A great deal of methodological and analytical research has been pursued universally to ascertain treatments are different within treated and control arms. Notwithstanding, the best of the obtained methods have not been adopted and have had limited impact on clinical research and biomedical guidelines, which is attributed to the complex and outdated understanding of statistically analyzing trial data.

3.5. Case Studies of Machine Learning Applications

Analysing coronary vessels can reveal CVD and estimate its severity. Machine learning (ML) and computational geometry, including probability distributions, curvature-driven diffusion, and several differential geometric and topological notions, are combined to bridge the gap between these medical objectives. The resulting system estimates coronary bed locations, models vessel path, and provides a severity index, showing potential in the computer-aided diagnosis of CVD. Additional widespread infectious disease outbreaks are expected in the future. As an affordable and easy-to-apply intervention, washing hands with soap is recommended. A deep learning scheme is designed to check compliance passively. The resulting system operates on sequences captured by a single thermal camera and can detect faulty handwashing in real-time, showing promise in curtailing disease spread. Studies on visual discomfort suggest that it decreases image quality and adversely impacts the observer's capabilities. However, eye strain is also associated with increased visual effort and sustained accommodation, whose relation to viewing distances is still unclear. A system to study visual discomfort using a set of built-in measurements and a method to estimate viewing distances from the measured stereo-discharges is proposed. A comprehensive analysis with statistical validation across multiple sessions revealed good agreement between the actual distance and the estimated values. Improper viewing distances were found to be correlated with increased visual effort and decreased image quality. Further research in these directions could contribute to guidelines aiming to improve the observer experience across a broader spectrum of visual content, particularly on emerging display technologies. Partnering with the healthcare industry, firms have developed AI-based medical imaging software to provide fast and accurate diagnosis services. Inmates in Chinese prisons and labour camps have also been the subject of forced organ transplantations involving AI-developed organs. AI-generated drug information paraphrases and rewrites the Chinese version of the package insert monograph of FDA-approved drugs. AI algorithms are used in the construction of dynamic human face rotating images. Machine learning is deployed for the construction of text synthesis models. Despite beneficial impacts, the unrestrained use of AI and machine learning technology might infringe on individual rights such as privacy.

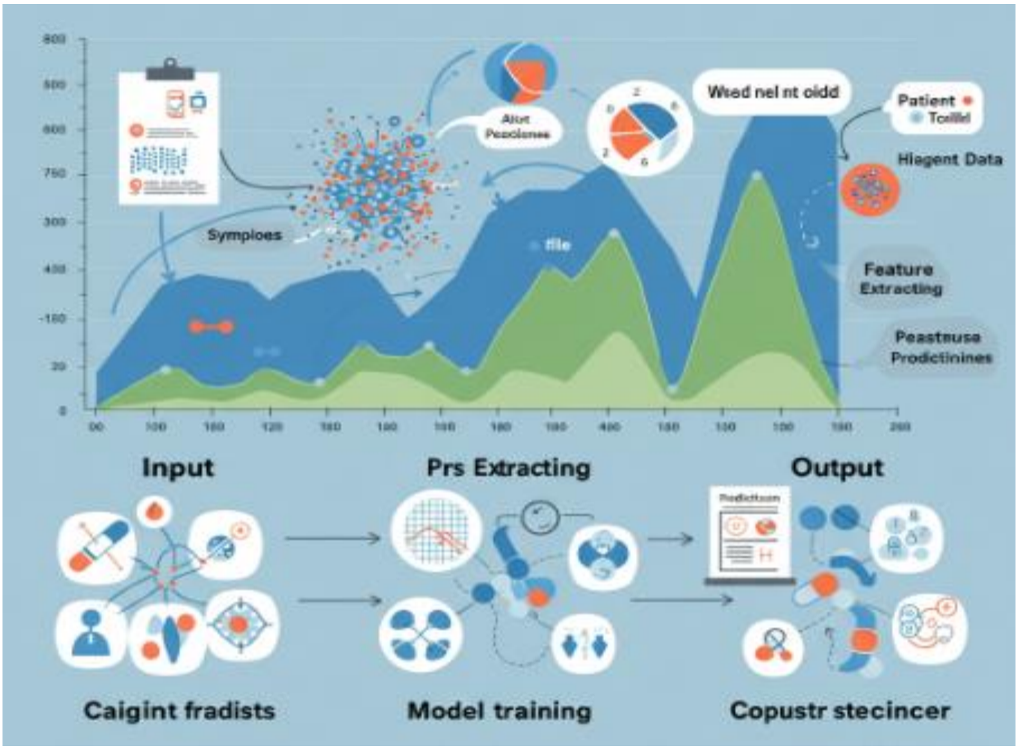

Fig : Machine Learning Predictive Model as Clinical Decision Support

3.5.1. Predictive Analytics in Patient Outcomes

This article would like to share a broad and comprehensive perspective on the impact of AI-predictive analytics on patient outcomes. The review covers the insights obtained regarding the influence of predictive models on patient outcomes and emphasizes the integral role of these models in the healthcare system. Wearables' data sources can be integrated into prediction models to ascertain the probability of rare outcomes. However, utilizing these widely collected data is still evolving. An overview of the methodologies used in the integrations, largely the usage of Bayesian or recurrent neural network models, is described.

This analysis was prompted by the commercialization of several medical wearables, which allow individuals to monitor their health proactively, and an increasing interest in a healthy lifestyle. The surge in utilization of such devices resulted in the creation of large, complex datasets that are still understudied. Although a number of published studies have sought to examine wearable data integration in prediction models, the strategies for using these data types are still under development.

3.5.2. Personalized Medicine

While there is a vast and growing literature on the application of machine learning to diagnostics and disease prognostication, perhaps the most exciting applications of machine learning for clinical decision-making relate to treatment plans. Proponents of precision medicine argue that traditional health science has focused too much on averages and not enough on individuals. In response to advances in machine learning technology, this argument suggests that outdated statistical tools may be less relevant to contemporary clinical decision making. The solution involves utilizing detailed longitudinal data on individuals, along with flexible machine learning approaches. The dream of precision medicine is to identify the best therapy for each person, while also freeing up clinicians to perform other important duties by automating tasks like diagnosis and prognostication — and with amazing accuracy. There have certainly been some breathtaking advances in medicine over recent years, and it is speculated that much of this would not have been possible without machine learning. However, claims about the transformative power of machine learning-based precision medicine often appear over-optimistic. Specifically, the use of statistical language that implies more certainty, confidence, and validity than is confirmed by available evidence is noted. An increasing number of these claims are being made by non-experts on the basis of studies published in non-technical outlets that do not provide sufficient evidence or transparent methodological details. In light of this, and in public interest, there is disagreement currently. Indeed, it is argued that it is now time to seriously realign expectations with reality in order to establish a more robust, transparent, and clear understanding with respect to the actual — and current — capabilities of machine learning-assisted precision medicine. As the over-emphasis on largely unrealistic promises already sometimes harms patients, refutations to five common myths or unsupported claims regarding machine learning-powered precision medicine are advocated.

3.6. Ethical Considerations

IDOMAL is an interdisciplinary Research Training Group at the University of Tübingen that aims at investigating how digitalization and machine learning are affecting the effectiveness of human experts in interpreting data and in relying on such interpretations to make complex decisions. Application areas range from the processing of online news, to remote sensing and econometrics, and to the analysis of medical brain images. Machine learning algorithms require the design of several free parameters; but the problem of calibrating them is still largely regarded as an art. Trusting an algorithm and using its output as a decision support can entail a considerable shift in the standard of proof usually expected in evidence-based medicine, opening novel ethical and legal issues. Such issues are notoriously demanding from a technical perspective and typically arise whenever algorithmic models involve an element of randomness and uncertainty. We would welcome suggestions about the relevance and impact of these problems in clinical diagnosis from a documentation and legal perspective, and about structuring a set of exemplary cases or simulations with which to identify those aspects more prone to controversy or litigation.

A rapidly increasing number of machine learning algorithms are deployed in diagnostic software as aids to clinical decision-making. How to shape awareness and handle concerns about the use of black-box technologies by laypersons and professionals.

3.6.1. Patient Privacy and Data Security

Data privacy and security are major concerns for any organization. Coveillance occurs when artificial intelligence is used to track, predict, and often control other intelligent systems, such as those used by individuals or businesses. Coveillance is in a very real sense the dominant underlying mode of AI use in the world today, employed by businesses and governments in myriad contexts ranging from predictive health algorithms and recommendation systems designed to drive consumer behavior to credit-scoring algorithms used in hiring or incarceration decision making. It has given rise to consumer-facing technologies developed by the pharmaceutical and insurance industries seeking to influence patient and consumer behavior, including machine-learning models that analyze health data and social media to target advertising. Data ownership is an issue in AI ethics and regulation, as there is a risk that individuals' data and autonomy could be eroded by large companies or governments. However, current models that prioritize algorithm audits, transparency and data privacy likely underestimate the threat of coveillance, which is characterized by the fact that the individuals and entities being tracked or manipulated do not have access to or control over the key intelligent systems at work. Instead, strategies for defending against coveillance require a greater emphasis on affirmative obligations concerning when, how, and why AI systems are used, including oversight and monitoring mechanisms such as interoperability and hard limits on the use of AI and its influence. Data transparency already encompasses a heterogeneous set of practices for making data available to other researchers and for ensuring the reproducibility of scientific claims. More standard practices include including in the main text or supplementary materials that provide access to the raw or post-preparation data, codebooks, or scripts; depositing data in general or domain-specific repositories; or simply including them as supplementary materials to the scientific publication. It is reasonable to expect an increase in demand for clearer, more detailed, and more systematized information about data collection, handling, and processing protocols.

3.6.2. Bias and Fairness in Algorithms

Biases and irrationality in human decision making based on irrelevant factors have been observed on countless occasions and in every context. Similarly, decision-making algorithms have been shown to discriminate based on irrelevant factors. Black defendants, white defendants, or any other attribute of the defendant. Explanations on generalizable reasons why either machine learning model, in principle, could be biased include the possibility that unfairness was encoded in the training data, statistical or data collection choices could be made that result in disadvantageous group outcomes, and one model type may be more reliant on variables that would have a disparate impact. Reassuringly, most initially concerning model types can be transformed into finished products with very high fairness post-hoc.

The design, implementation and testing of a machine learning model must then be the focus of medical practitioners. We focus on a machine learning system that generates predictions to assist clinical decision-making in any modeling task of interest. This method highlights the 'neediest' patients who have an expected risk of some outcome. Many subsequent discussions concentrate on identifying what inferences can be drawn to ensure a model generates fair predictions. In doing so, methodological recommendations are driven by the three major comparability constraints, with different common subtypes. Similarly important, it is illustrated that modeling, in general, is biased. This has implications for most larger clinics and hospitals, emphasizing the importance of a prospective validation trial. Importantly, bias in the predictive model remains relevant when (and should be resolved before) deploying the telemedicine model.

3.7. Conclusion

Artificial intelligence (AI) has been adopted in various fields to assist strategy planning, e.g., games, marketing, and cybersecurity, leveraging reliable decision-making. In a clinical setting, a comprehensive strategy is required, including examination of prediction models while considering medical insight and crafting the treatment plan. However, there have been few reports of utilizing decisions derived from models in data-driven environments. In collaboration with medical professionals, a framework using a surrogate Bayesian model was influenced to generate a treatment process consisting of actions and conditions aimed at improving specific objective functions of individuals. The framework was also influenced to specify the timing of actions and conditions requiring personal values predetermined over a period.

Artificial intelligence (AI) has the prospective to transform fundamental operations in healthcare, from processing medical records to conducting advanced analysis—potentially approaching public health concepts. A critical challenge in the field is whether such models will be developed and implemented in ways that take into account the environment and meet the needs of stakeholders, including beneficiaries. In fact, implementing AI in healthcare is known to have slight overtones that it often brings out the fears of those it is designed to benefit. Many clinicians are interested that tools resulting from machine learning are technically incompatible with clinical practice. Nonetheless, disillusionment with progress is a great dismissal of AI implementation in healthcare. At a time when the dominant narratives reflect clinicians who are either unwilling to engage with statisticians or data scientists, the scope must be clear. People are in critical touch with patient confrontation and clinical indecision, pushing operations room conditions to adjustment and overseeing software modification, and routinely resorting to adjusted analysis consult. An earnest estimate of most pressing concerns, opportunities, and conditions to harness machine learning to improve the quality of care is presented.

3.7.1. Future Trends

In the last two decades, many important milestones have been achieved in clinical treatment, leading to increased survival rates, better prognosis, and improved life quality. However, the knowledge repository that individual human clinicians carry is limited and noise-intolerant. In contrast, computational models can learn using remarkable knowledge contained in datasets and cross-experience from many different clinicians. Moreover, reliable machine learning (ML) approaches avoid manual intervention bias, which normally takes place when working with guidelines. The translation of raw patient-specific information into a meaningful decision plan is called clinical decision-making (CDM). For a long time, CDM has been related to medical expertise. In human decision-making, specialists inspect patient data, previous records, and the current medical context. After exploring all the available information, a treatment plan is decided. When an onset patient is judged, the knowledge of prior examples on the probable effects of different treatments is particularly relevant. The probability of a treatment to benefit a patient, conditional on a given treatment (known as potential outcome), is what makes the disease and treatment effect estimable, and this is ultimately what the experts evaluate.

The uptake of ML in CDM is slower in comparison with other settings due to product and algorithm opacity, safety and privacy regulations, market restrictions, and ethical consideration. In pharmaceutical and medical device companies, outcomes are critical to obtain approval from the regulatory authorities. For the same reason, the pH in many hospitals is linked to hard outcomes. ModelState relies on a sequence of pivot models. At each time tβsc (vector of dimension C with valid data is present) the counterfactuals and the outcomes are stored and discretized on a finite grid {0, 1, …, Q}. Under the independence assumption between outcomes and counterfactuals, a joint distribution P(artβt) is defined, where a is included in {0, 1}Q C and the filters are the same size as the oblique matrix Ct. Counterfactuals and outcomes are related through the potential outcomes, {0, 1} CQ possible values of rca. The Or matrices contain the cause-effect relationships of fixed size N tB between rotated targets (outcomes and counterfactuals) and plat parameters (a flatten matrix Mt rotated to a, according to the pivot model). Given plat the cause-use event is defined as rtsc = δ(rt ;MtB sβ t C), and rid is dubbed when c ∉s can degrade without causing harm, e.g. removing a blinding or a filter.

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