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Electronic Health Record Mining for Early Disease Risk Prediction

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Abstract: ***Mining electronic health records (EHR) for patterns predictive of the onset of diseases and clinical events has the potential to generate knowledge that supports the identification of at-risk patients in the early stages of disease evolution. The HPC-ML-HAZARD project aims to design, build, and evaluate predictive models that are applicable in clinical settings. The early identification of patients at risk facilitates interventions, system-level management, and ultimately the prevention of excess morbidity and mortality. Furthermore, early risk prediction has potential implications not limited to the patients identified, including informing and optimizing the allocation of hospital resources. The use of EHRs for early prediction of diseases has received relatively little attention compared to other uses, especially considering the potential clinical significance. The prospect of identifying patients at risk before the onset of disease or clinical complications is enticing, as it provides an opportunity to implement preventive measures, support systems, and clinical research to clearly identify preclinical disease stages.***

Keywords: Electronic health records (EHRs), Early warning systems, Risk stratification, Impact on clinical outcomes, Risk evolution

1. Introduction

Early risk prediction for a wide range of diseases based on EHR data helps clinical decision-making, facilitates preventative action, and promotes better patient outcomes. This area of research, called EHR mining, uses the growing quantities of structured and unstructured data recorded on patients over the course of their lifetime to provide early predictive models for a range of diseases.

EHR mining requires careful consideration of model development and application to integrate these predictive models into everyday clinical practice. Key processes include ensuring data quality (which reflects upon risk prediction model quality), ensuring appropriate modelling approaches are applied to support detection at various stages of disease progression, capturing evolving patient risk over time and integrating the prediction of multiple diseases across different data modalities. Applying these methods has the potential to transform predictive modelling in a clinical context—from decision support to alerting- improving patient care while reducing the burden on healthcare systems.

1.1 Background and Significance

"EHR mining provides the means to analyze past health care data to determine which patients are at risk of developing disease in the future. The earliest possible prediction allows for the most proactive mitigation strategy. The clinical literature documents the vast number of risk prediction models that have been developed and validated, across an equally diverse range of diseases. These efforts, however, have been confined to predicting a single disease. Such single-disease prediction models cannot be implemented to suggest the patients who would benefit from intervention, because clinical care is not organized by disease but by a holistic view of the person. There has been much less focus on mining EHR data for the purpose of creating risk prediction equations for a large number of diseases or for large panels of diseases. Exploring EHR data across multiple diseases is useful for diving deeper into EHR data and for truly personalized medicine; thus, risk prediction models of multiple diseases can be built and advanced machine learning and statistics techniques can be utilized to explore and visualize the EHR data. The practical outcome of these efforts is a predictive model that can be turned into an alerting system- an alerting system that informs the physician of the patients attending his or her clinic that are at risk of negative events that can be prevented or mitigated with timely and appropriate management."

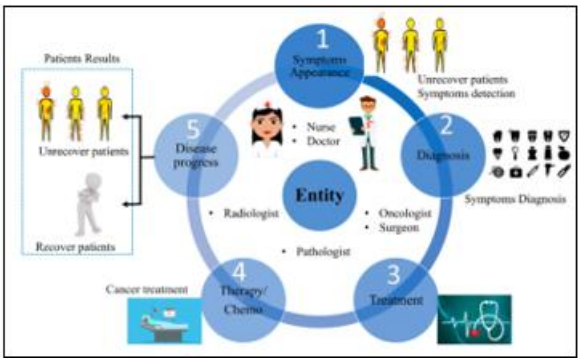
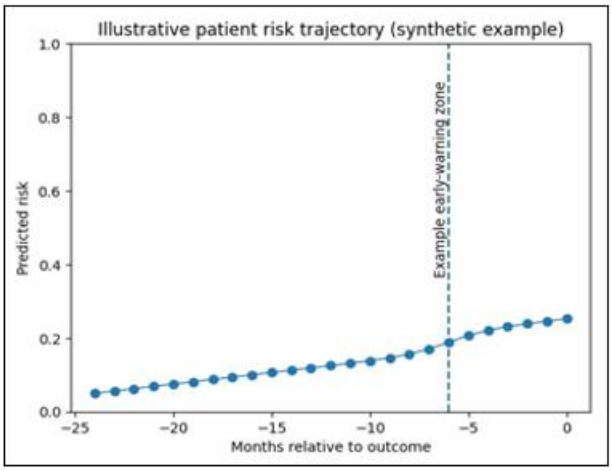


Figure 1: Electronic Health Record

2. Background and Rationale

An overarching goal of predictive models is to provide early indications of future events. A natural application of such models is to signal potential risk of disease onset at a point in time before the disease is diagnosed. This would allow practitioners to proactively intervene and potentially divert health-care resources away from the development of disease. The area of disease risk prediction has received considerable

attention within the machine learning community, with many papers addressing some form of early disease risk prediction. Research efforts along these lines have been termed early disease risk prediction, early disease risk modelling or early disease risk estimation. Although formal definitions vary, central to early risk prediction is the aim of forecasting the likelihood of developing disease in the future. Accordingly, the predictions aim to indicate the risk of an underlying disease approximately six to thirty months before clinical diagnosis. Several approaches have sought to predict disease onset risk using machine learning techniques trained on electronic health record data. Intuitively, predicting disease risk in the months to years prior to diagnosis is clinically most relevant. As such, these models are of direct clinical utility and supplement, rather than replace, traditional methods of diagnosis.



2.1. Research design

The study aims to conduct an early-disease-risk-prediction study using clinical text and structured features. It combines four prediction modeling families, addressing a key gap where many early-prediction studies predict risk between two specific disease transitions. The empirical investigation is guided by two hypotheses: 1) at-risk patients can be identified with a considerable lead time, and 2) risk levels evolve over time. The empirical investigation is scoped to conditions with sufficient clinical notes and structured data capable of predicting risk. The investigation addresses validity and reliability by employing cross-validation, internal and external time-based replication, and quantifying bias-fairness trade-offs across the four modeling families. The study is expected to contribute to ongoing EHR-utilization efforts by demonstrating an end-to-end EHR-structural-text-sourced risk-identification framework that can identify individual-risk-level trajectories over time.

The proposed framework forecasts future patient conditions utilizing both clinical text and structured features. Recognizable clinical notes such as clinical summary/diagnosis, pathology, and procedures within clinical narratives are paired with other features, including demographics, diagnosis, medical history, medications, lab tests, and imaging investigations, forming different modeling families: supervised learning-set and time-to-event prediction-set for a predefined pair of diseases as well as multi-modal sequence-modeling-and-risk-trajectory-frameworks employing Temporal Convolution Networks (TCN) and a Natural Language Processing representation suitable for sequential text processing. The common tutorial discusses scaling, showcases applications, and explores the extension of both training- and time-trajectory-based modeling families across the entire healthcare database for other disease-trajectory patterns.

Equation 1: Data setup and notation (what the paper's pipeline implies)

Let:

- Patient index: $i = 1, \dots, N$
- Outcome (diagnosis / event) time for patient i: t_i^*
- We look backward D windows before outcome: $k \in \{-D, \dots, -1\}$
- Window length: Δ (e.g., 1 month, 3 months, etc.)
- Window k corresponds to time interval: $W_{i,k} = [t_i^* + k\Delta, t_i^* + (k+1)\Delta)$

From each window you compute a feature vector (counts, last observed value, mean, max, presence/absence, etc.):

$$\mathbf{x}_{i,k} \in \mathbb{R}^p$$

Then the full temporal representation is a sequence:

$$\mathbf{X}_i = (\mathbf{x}_{i,-D}, \dots, \mathbf{x}_{i,-1})$$

This corresponds to the paper's "divide time interval into equal-length windows moving toward the outcome; construct risk estimates."

A2) Prediction target definitions

The paper mentions both:

- **Binary within-horizon labels** ("hospitalized within t months")
- **Time-to-event labels** (time until onset, censoring)

Binary within horizon H:

$$y_i^{(H)} = \begin{cases} 1, & \text{if event occurs in } (t_0, t_0 + H] \\ 0, & \text{otherwise} \end{cases}$$

Time-to-event:

- T_i: event time (or last follow-up time)
- $\delta_i \in \{0,1\}$: event indicator (1=event observed, 0=censored)

3. Data Sources and Preprocessing

EHR data from different institutions are leveraged to extract clinical information for predictive modeling. Patients of each underlying disease form the positive instance set, whereas the positive set is generated in 1:1 proportion from the remaining population for each disease under consideration. Several patient and patient-trajectory characteristics are mined as features from the clinical data; the features not only represent the patients but also the temporal nature of the EHR data. Age, sex, diagnosing codes, medication intake, imaging notes and relevant clinical

lab results are extracted as features from the patient data. The time-series sample is constructed on the drawn patients up to a certain time frame/age set and using the time-series window size as features for supervised temporal predictive modeling in order to understand how prematurely the disease can be diagnosed based on clinical symptoms. Missing data is imputed for different feature groups and thus, patients are represented with (i) The diagnosed code, (ii) The medication history and (iii) Previous lab-result for supervised Temporal predictive modeling.

Data quality is of utmost importance for any analytical exercise, especially predictive modeling. Data cleaning and data quality assessment steps have been specially emphasized during preprocessing. The reliability of Orthopedic imaging notes and Lab-Result Diagrams is checked and outlier removal is performed for better prediction assurance. Data from different institutions are not always available with the same set of coding thus proper harmonization is carried out for modeling and analyzing in a better manner. The Diagrams are prepared using the ICD, GRDo and other respective coding standards for representation convenience. For prediction, the data set is reshaped and prepared in a proper manner so that all the analysis can be done without any ambiguity and proper results can be fetched.

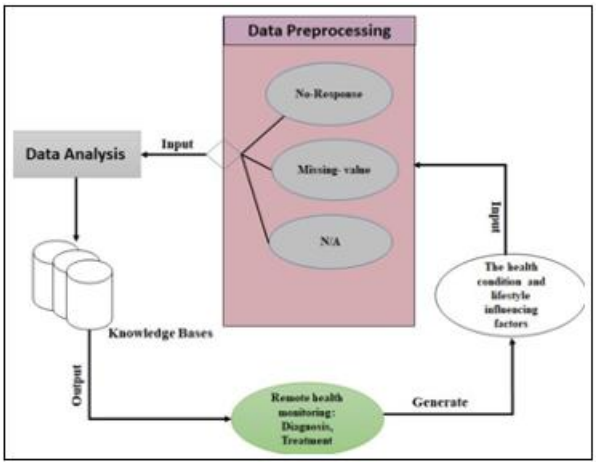


Figure 2: Data Preprocessing architecture

3.1 Data Extraction from Electronic Health Records

The study draws on data from Clinical Tables (2017-2019), HealthGraph (2007-2020), MIMIC-III (2001-2012), NYU School of Medicine IRS Data Haven (2006-2019), PHIS (2005-2018), PhysioNet (2001-2012), PubMed (2002-2019), SEER (1973-2020), and the Yale Open Data Access project. Individual encounters are captured within four years of birth and twenty years of life. Internment, social service, and funeral planning records are excluded from the data. For longitudinal predictions of developing adult-onset illnesses, encounters before age twenty-five are considered. Each hospital features a unique set of available structured electronic health data; unstructured notes support the individual-level chronological trajectory feature limited-duration predictive models. Demographic and social information has been gathered from the Social Vulnerability Index.

Data quality is essential for prediction success. Missingness in each feature is analyzed to a confidence level of 80% or higher, and records with a lower confidence are filtered out. Outliers are identified through univariate analysis; biological implausibilities and extreme observations are imputed. Features with different underlying definitions, such as ICD-9-CM and ICD-10-CM, are harmonized. Diagnoses, lab tests, and medication prescriptions are standardized using the corresponding ICD-10, RxNorm, and Logical Observation Identifier Names and Codes mappings. Paths in the HealthGraph dataset terminate when a patient reaches age seventy-five or dies. The natural language processing tools in the MIMIC-III dataset are used along with other underlying medical terminologies to process the free-text notes in ČSN.

3.2 Data Cleaning and Normalization

Examining EHRs for early risk prediction presents high potential. Nevertheless, exploring temporal disease risk trajectories across a range of diseases is still nascent. Therefore, temporal modeling of the predicted risk proposition has gained increasing attention. Model predictions can be visualized as interpreted trajectories, showing how a patient's risk changes over time and allowing prediction windows to be opened or closed dynamically. Recent research has also explored the temporal aspect of risk prediction using different modeling families, predicting risks in a time-to-event setup. Although these analyses capture changing risks, the predictions are not designed to be predictive trajectories. Formalizing the notion of risk trajectories- the combination of a temporal model, prediction windows, and change over time—enables the utilization of disease risk prediction in a more versatile fashion. Risk predictions of different diseases can also be addressed jointly- for example, when predicting presence across multiple diseases or predicting comorbidities.

EHRs present a rich repository of data that can be employed in predictive modeling. However, direct application of these records often suffers from data quality issues. Missing data is frequently encountered during data analysis activities. Decision-making under uncertainty with respect to such missing data can potentially lead to incorrect conclusions, especially when such activities are not properly communicated. The impact of missing data can be tackled by numerous approaches, including imputation, data augmentation/creation, and proper adaptation of the methodology. Outlier identification and treatment are equally important, as extreme values might dominate the results. Data harmonization across data sources, clinical departments, and even devices is essential when data are pooled together. Furthermore, when dealing with various codes (such as ICD-10), standardization to a common one improves integration. The internal quality of data is often assessed by different techniques.

3.3 Feature Engineering and Representation

The feature sets constitute the information repositories from which disease risk predictors are derived. The relevant characteristics generally fall into five distinct categories: demographics (e.g., age, sex, race, ethnicity), clinical diagnoses, medications, laboratory tests, and imaging report notes. The upcoming steps enable the generation of the risk signals at any user-defined time window points. The temporal aspect of these features determines the representations that transition from the high-dimensional form widely used in statistical settings to lower-dimensional forms suitable for samples and deep learning models. The final component uses a variation of the Optimal Feature Set technique, with additional refinements introduced for sequence modeling when the target risk increases during the sequence.

The admissibility of any feature depends on the availability across the subjects for the complete time span of interest. Therefore, missing features at an instance can severely limit the analysis. Accordingly, a time lag between the feature vectors and the actual risk may address the missing occurrence of important preceding indications before the disease arrives. In the case of reliable predictors that occur well earlier than the actual disease, such as A1C before the onset of type 2 diabetes, the principal sequence risk may have been present at least since the first appearance of the predictor. This poses a clear challenge in clinical practice since risk modeling is usually done for the present time, although technically possible. Therefore, modeling cadences will be required for clinical use- not unlike the industry practice of generating quarterly banking alerts on a customer portfolio.

4. Methodological Framework

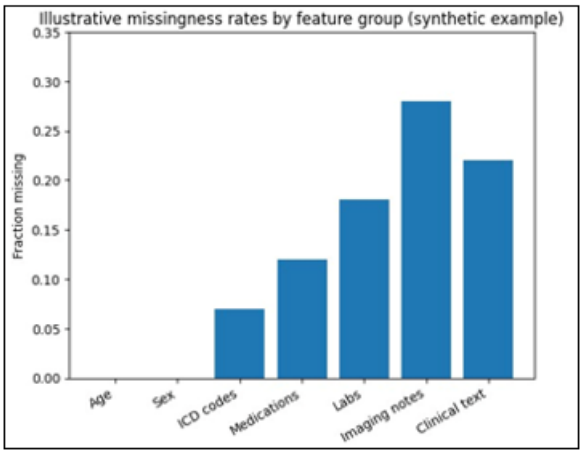
The methodological framework encompasses both predictive modeling and temporal analysis. For the first part, predictions for multiple diseases and conditions are modeled as supervised machine-learning tasks. Apart from common indicator classes (e.g., yes/no), modeled labels can also capture time-to-event information, with patients being hospitalized within t months for a specific disease. Some approaches consider all signals as a single modality, whereas other methods treat cues from different modalities separately. A multitude of algorithms are implemented, with performances assessed against separate datasets and benchmarked against model types- tabular, sequence-to-vector, and joint multi-modal- that are simpler, easier to control, and/or more interpretable.

4.1 Temporal Modeling and Risk Trajectories

The second methodological family incorporates the temporal dimension, relying on event sequences as key modeling cues. For supervised problems, disease-onset windows define positive cases, typically set at t = 1 month for long-term risk modeling and at t = 6–12 months for near-term prediction. Clinical risk trajectories are constructed by slicing time and deriving a sequence of temporally-aligned risk signals for each patient, capturing both cohort-level patterns and individual-level deviations. Lag effects of these pathway signals are accounted for using multiple signal pixels, and smoothed clinical trajectories can be represented in different forms. An alternative methodology models signals as observations that change over time, with risk factors specific to the t-th step in a t-step-ahead prediction problem.

4.2 Validation and Calibration

Methodological validation proceeds along multiple dimensions. Internal and external validation is performed, with multiple cross-validation setups applied to control for different levels of data leakage. Separate calibration plots assess temporal performance and fairness across age, gender, and race groups. The architecture seeks to avoid overfitting through careful regularization and dropout, and bootstrapping provides a further defense against noise. The resulting risk predictions can be sensitive to different definitions of labels, yet multiple robustness checks bolster their credibility.



4.3 Predictive Modeling Approaches

The modeling solutions encompass supervised risk prediction, time-to-event forecasting that considers early disease diagnosis, and multi-modal modeling applications. Algorithms from the quantitative data-mining literature are deployed for each family. The supervised models, including multi-layered perceptrons (MLPs), decision trees, and random forests, achieve high predictive performance. Leave-one-site-out, k-fold, and stratified cross-validation are used for validation in different settings. Attention to temporal aspects is crucial for modeling sequence data, and lagged and sliding-window windows of EHR records capture evolving disease risk.

The time-to-event prediction incorporates disease onset as an important macro-event but learns the disease risk-free pathway for all patients. Multi-modal forecasting joins the progression of categorical disease risk groups with a real-valued full risk measure. The calibration of results toward health equity requires validation on an appropriate subset or a set of external sites with different socio-demographic characteristics or teaching status. In all settings, careful evaluation through diverse operational metrics safeguards against overfitting or

other validation pitfalls. Redundancy of result evaluation not only reinforces confidence in the results but also strengthens the interpretation of contributing EHR features. Robustness checks examine the stability of results against partial data removal and disease-specific model training.

4.4 Temporal Modeling and Risk Trajectories

Capturing evolving disease risk over time is crucial for early prediction and intervention. In the proposed approach, each individual's health status during a specific period prior to the outcome is represented as a temporal sequence. Events from structured EHR data, such as diagnoses, medications, and laboratory test results, are arranged in chronological order relative to the date of the outcome. The time interval preceding the outcome is divided into equal-length windows that move along the timeline toward the outcome. The information from these windows is then used to construct risk estimates for the supported diseases. Due to the nature of the supporting algorithms, validation, and calibration properties, temporal effects are specifically considered for constant-time-to-event prediction problems. Prior to prediction, the development of disease-supporting models is similar to that of supervised learning; however, these models are designed to monitor the disease-free periods of the individuals present in the cohort. For each prediction step, the sequential deposition of features (−D, …, −1) reveals how the risk for the occurrence of the disease-type label evolves over time and consequently acts on different time-to-event prediction methods and data-affine algorithms.

Short-term longitudinal data (e.g., past 24 months, 30 days) are best suited for modeling the prediction-population timeline. The sequence in the previous structure lacks lag effects, which capture how information at previous time points influences predictions at later time steps and is essential for time-invariant prediction problems. Furthermore, these sequences do not properly reflect how an individual's temporal changes influence their risk of subsequent diseases. A temporal modeling approach enables these aspects of the data to be accurately addressed, ensuring consistent prediction population–risk trajectory mapping. For risk predictive modeling, two families of methods are adopted: (1) non-modular data-affine methods, which predict the expected time to the occurrence of diseases, and (2) multi-modular methods not constrained by the presence of additional information about undergoing events.

Equation 2: Supervised risk prediction equations (tabular models)

Goal: model probability of event within horizon H:

$$p_i = \Pr(y_i = 1 \mid \mathbf{x}_i)$$

Step 1: linear score

$$z_i = \beta_0 + \boldsymbol{\beta}^{\top}\mathbf{x}_i$$

Step 2: map to $[0,1]$ with sigmoid

$$\sigma(z) = \frac{1}{1+e^{-z}} \quad \Rightarrow \quad p_i = \sigma(z_i) = \frac{1}{1+e^{-(\beta_0+\boldsymbol{\beta}^{\top}\mathbf{x}_i)}}$$

Step 3: odds and log-odds form (derivation)

Odds:

$$\frac{p_i}{1-p_i}$$

Using $p_i = \frac{1}{1+e^{-z_i}} \Rightarrow 1-p_i = \frac{e^{-z_i}}{1+e^{-z_i}}$,

$$\frac{p_i}{1-p_i} = \frac{\frac{1}{1+e^{-z_i}}}{\frac{e^{-z_i}}{1+e^{-z_i}}} = e^{z_i}$$

Taking log:

$$\log\left(\frac{p_i}{1-p_i}\right) = z_i = \beta_0 + \boldsymbol{\beta}^{\top}\mathbf{x}_i$$

That is the classic "risk equation" used in clinical prediction.

Likelihood for one sample:

$$\Pr(y_i \mid p_i) = p_i^{y_i}(1-p_i)^{(1-y_i)}$$

Log-likelihood:

$$\log\Pr(y_i \mid p_i) = y_i \log p_i + (1-y_i)\log(1-p_i)$$

Negative log-likelihood (loss):

$$\mathcal{L}_i = -[y_i \log p_i + (1-y_i)\log(1-p_i)]$$

Average over dataset:

$$\mathcal{L} = \frac{1}{N}\sum_{i=1}^{N}\mathcal{L}_i$$

Regularization (paper mentions regularization/dropout broadly in validation context):

- L2: $\mathcal{L}_{\text{reg}} = \mathcal{L} + \lambda \parallel \boldsymbol{\beta} \parallel_2^2$
- L1: $\mathcal{L}_{\text{reg}} = \mathcal{L} + \lambda \parallel \boldsymbol{\beta} \parallel_1$

4.5 Validation and Calibration

Internal and external validation strategies assess potential performance in novel clinical settings. Temporal aspects of predictive modeling introduce additional challenges; distinct patients can be represented at different points in time, forming a naturally stratified training/validation/test split. In addition to employing patient cohorts for validation, internal stratified cross-validation will be harnessed whenever the size of the cohort allows for it. Besides ensuring proper evaluation of models, the need to avoid overfitting will be addressed by dedicated model flexibility and complexity controls. Based on previous work, prediction performance is expected to be highly sensitive to model flexibility and tuning strategies are required to mitigate this effect.

Calibration plots visualize and evaluate the correlation between predicted probabilities and actual event frequencies. Moreover, these plots enable simple fairness checks for classifier decisions in multi-class settings based on discretizing predicted probabilities. Fidelity assessments are especially important for models with good accuracy on independent test sets but limited calibration capabilities, which may hinder deployment because real-world operational costs are not adequately reflected by the underlying measures of classification success. Independent calibration datasets and calibration methods may not always be available; therefore, various calibration methods will be explored. In addition to general purpose calibration methods that can be used independently of the modeling algorithm,

dedicated approaches catering to the forecasting methodology and the prediction task directly will also be investigated.

5. Privacy, Ethics, and Governance

Privacy, confidentiality, and impartiality concerns arise in many data-driven research projects, especially when personal data may be involved. In this project, the potential privacy risks associated with using European health data containing sensitive personal information are considerable, especially in view of the substantial differences in the treatment of privacy across the EU member states: for example, in the UK, public health authorities often share health-related data easily and with little concern about privacy, while in Germany these data may be shared only in exceptional situations or when the identity of individuals cannot be revealed. Consequently, specific considerations are needed to avoid ethical and legal issues. The principles behind health-related data privacy in Europe are universal: data should be anonymized, directly or indirectly, and individual patients' consent must be obtained whenever there is reason to suspect possible breaches so that their privacy remains primarily the responsibility of the researcher.

The patients' consent for using the EHRs must therefore be obtained as part of the work. Consent forms should explain how the data will be used, rules for patient privacy, the expectations of proof of risk, the possible need for false alerts, data governance, and requirements for the approval of external consortia for the use of the EHRs. The focus should lie on health data privacy concerns, particularly in relation to the functioning of the European Data Protection Board, which ensures conformity with the General Data Protection Regulation. Ethical approval has been granted by the respective institutional review boards in compliance with the Declaration of Helsinki. Data governance structures should guarantee the absence of data breaches in the conducted research. During the research phase, all data are treated as redacted data according to the risk management process. Permission for the proposed use of EHRs has been requested and accepted via GDPR Article 6 compliance for public use of EHRs in a general health risk context.

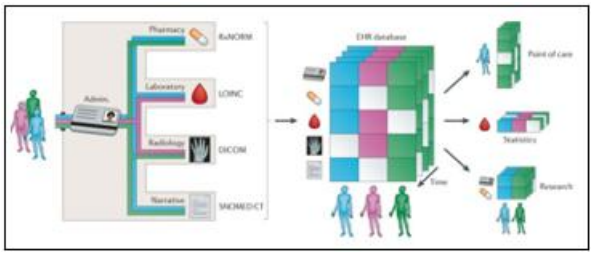


Figure 3: Privacy, Ethics, and Governance

6. Challenges and Limitations

Data quality constraints may prevent conclusions about risk for rare diseases, challenge generalizability beyond a specific setting or population, require caution in interpreting predictions, and hinder the application of some modeling families. Evaluation and mitigation strategies are proposed.
The use of clinical procedures and outcomes—particularly the presence of ICD codes—for prediction and risk trajectory construction introduces a bias toward modelling a population of patients already diagnosed with the predicted disease. Classification of non-cases at positive training or test set label time may be problematic, especially when negative diagnosis codes or study filtering is not complete. Such effects are assumed to lessen with accumulated patient years but are not a primary focus due to the datasets' diverse clinical contexts. High, low, and zero case prevalence settings also afford perspective on generalizability. Procedures or outcomes that are rare (e.g., MS, transplantation, hospitalization) or very rare should be modelled carefully, and conclusions avoided.

Data from specialties or settings with underlying bias may affect utility, such as orthopaedic cohorts modelling hip fracture. Data volume in a predictive context offers interpretability towards treatment or outcome, but specific modelling families expose the data not for assigning an individual risk but as a tool for decision support in the clinic, clinical risk modelling, risk permutation, or clinical alerting.

Equation 3: Time-to-event (survival) modeling equations

- **Survival function**

$$S(t) = \Pr(T > t)$$

- **CDF**

$$F(t) = \Pr(T \le t) = 1 - S(t)$$

- **Density**

$$f(t) = \frac{d}{dt}F(t)$$

- **Hazard**

$$h(t) = \lim_{\Delta t \to 0} \frac{\Pr(t \le T < t + \Delta t \mid T \ge t)}{\Delta t} = \frac{f(t)}{S(t)}$$

From $h(t) = \frac{f(t)}{S(t)}$ and $f(t) = -\frac{d}{dt}S(t)$,

$$h(t) = \frac{-S'(t)}{S(t)} \Rightarrow \frac{S'(t)}{S(t)} = -h(t)$$

Integrate from 0 to t:

$$\int_0^t \frac{S'(u)}{S(u)}du = -\int_0^t h\,(u)du \Rightarrow \log S(t) - \log S(0)$$

$$= -\int_0^t h\,(u)du$$

With $S(0) = 1$:

$$S(t) = \exp\left(-\int_0^t h\,(u)du\right)$$

C2) Cox proportional hazards model

Cox model:

$$h(t \mid \mathbf{x}) = h_0(t)\exp(\boldsymbol{\beta}^\top \mathbf{x})$$

So the survival is:

$$S(t \mid \mathbf{x}) = \exp\left(-\int_0^t h_0\,(u)\exp(\boldsymbol{\beta}^\top \mathbf{x})\,du\right)$$

$$= \exp\left(-\exp(\boldsymbol{\beta}^\top \mathbf{x})\int_0^t h_0\,(u)\,du\right)$$

Let:

$$H_0(t) = \int_0^t h_0(u)\,du$$

Then:

$$S(t \mid \mathbf{x}) = \exp\left(-H_0(t)\exp(\boldsymbol{\beta}^\top \mathbf{x})\right)$$

Risk of event by time t:

$$\Pr(T \le t \mid \mathbf{x}) = 1 - S(t \mid \mathbf{x})$$

This is the standard way to compute "probability of event within t months."

7. Applications and Implications for Clinical Practice

Well-designed EHR-based predictive models for early risk estimation of preventable diseases could improve patients' care pathways, quality of care, and health outcomes, and enable early interventions before crisis situations. Ultimately, they might reduce overall healthcare expenditures. In this context, the following scenarios describe potential clinical workflows:

1) Risk prediction as clinical decision support for personalized follow-up care: Based on the risk estimation of the next two years, care professionals could personalize the follow-up, e.g., in relation to the frequency of visits, incorporating higher frequencies or supporting communication with other professionals beyond general counseling.
2) Risk prediction trigger system with automatic alerts when divergence from trajectory is detected: Monitoring patients at risk of a particular disease, and issuing alerts when recent data show a significant increase in the disease's risk estimation, could lead to more timely identification. An additional alert, examining combinations of diseases that are predictive of the development of another disease, could help initiate follow-up.
3) Interactive predictive elicitation for the administration of prevention treatment: For some diseases like mental health diseases, predictive models could help clarify whether a prevention treatment should be recommended based on the risk. The healthcare team could be supported by an alert integrated into the predictive model.
4) Interactive predictive modality for both the care professional and the patient: Using predictive models to show patients their risk of future diseases (without invasion of privacy) could enhance health education and encouragement for active participation in implementing healthy lifestyles.

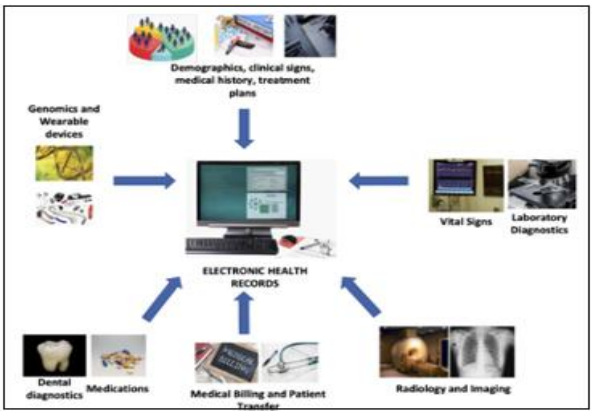


Figure 4: Applications and Implications for Clinical Practice

8. Conclusion

The last two decades have witnessed remarkable advances in health data collection, storage, and processing. Enhanced availability and affordability of electronic health records (EHRs) and associated clinical data have spurred research interest into data-driven health informatics applications. Nevertheless, despite the massive amounts of data continuously generated in health systems worldwide, clear and significant patient benefits in terms of disease prevention and risk management remain elusive. In particular, real-world applications of predictive models that can aid health systems and clinicians actively and accurately identify patients at risk of developing various health issues are scarce.

The work presented here represents a systematic, big-data-driven approach to EHR mining that finds its final form in predictive models for risk of developing 30 different health conditions, EHR mining applied to early risk prediction for 30 different health conditions, and an original framework for discovering risk-predictive temporal trajectories informed by patients' complete treatment history. Ongoing and future work promises further advances by scaling the current risk-prediction solution to integrate additional risk-predictive conditions and supporting an end-to-end clinical decision-support workflow.

8.1 Future Trends

Several trends and developments can be anticipated over the short- to medium-term horizon of three to five years. In the area of prediction modeling via EHR data mining, a greater emphasis on broader time-to-event risk predictions, rather than simple binary predictions, can be foreseen. The ability to capture temporal variation in risk is becoming increasingly important to clinical practitioners. The exploration of more sophisticated approaches, such as recurrent neural networks, may become feasible as larger longitudinal datasets become more widely available. Increasing model complexity, however, comes with the important trade-off of decreased interpretability of the predictors, and future work needs to explore methods that simultaneously consider both aspects.

Although relatively few papers have reported on the clinical deployment of prediction models derived from structured EHR data, it is easy to see how some of the approaches mentioned above could be integrated into clinical workstreams. Decision support workflows that yield a discrete output, such as an alerting mechanism that issues a recommendation or warning, tend to be the easiest approach for implementation. Indeed, the high stakes associated with predicting rare outcomes using currently available tools mean that patients likely would be mostly well engaged by, and receptive to, the heightened attention paid to their care when flagged for risk of a future acute myocardial infarction, end-stage renal disease, or a suicide attempt.

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