Perspective: Leveraging Domain Knowledge for Tabular Machine Learning in the Medical Domain

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Abstract

There has been limited exploration of how domain knowledge can be effectively integrated into machine learning for medical tabular data. Traditional approaches often rely on non-generalizable processes tailored to specific datasets. In contrast, recent advances in deep learning for language and tabular data are leading the way toward more generalizable and scalable methods of domain knowledge inclusion. In this paper, we first explore the need for domain knowledge in medical tabular data, categorize types of medical domain knowledge, and discuss how each can be leveraged in tabular machine learning. We then outline strategies for integrating this knowledge at various stages of the machine learning pipeline. Finally, building on recent advances in tabular deep learning, we propose future research directions to support the integration of domain knowledge.

1 Introduction

Tabular data plays a fundamental role in the medical field, capturing patient-specific details such as demographics, medical history, biomarkers, and diagnostic codes (Mao et al., 2024). Many clinical machine learning models rely on this data for tasks such as disease diagnosis (Ahsan et al., 2022) and adverse events prediction (Tomašev et al., 2021).

However, developing these models poses unique challenges. For instance, models can often learn shortcuts when modeling the data, leading to potentially harmful decisions. Caruana et al. (2015), for example, show that a model trained to predict pneumonia risk can incorrectly identify asthma as a protective factor. This error can occur because asthmatic patients generally receive more aggressive treatment, leading to better outcomes.

In contrast to clinicians who draw on prior training and domain expertise, models are typically developed with limited prior knowledge (Moor et al., 2023). They rely on statistical associations between input features and targets and do not understand the underlying physiology (Moor et al., 2023). Learning these associations can be further complicated by the heterogeneous features and complex interactions present in medical datasets (Ruan et al., 2024).

The lack of knowledge can also hinder the development of models for specialized medical tasks (Moor et al., 2023), as it can limit their ability to perform reliably in various clinical settings. In addition, inconsistencies in data standardization of medical datasets (Ahmadian et al., 2011) can be a barrier to the generalizability of models across medical environments.

This paper explores how the integration of domain knowledge into machine learning for medical tabular data can help address these challenges. In particular, it can guide variable selection (Wu et al., 2022), mitigate data quality issues (Curé, 2012) and help establish consistent standardization (Shi et al., 2021). It can also help ensure that models meet natural laws and regulatory requirements, which data-driven approaches may ignore (Von Rueden et al., 2021). Ultimately, this could support the translation of machine learning into clinical practice, a hurdle many existing models have yet to overcome (El Naqa et al., 2023).

Despite the widespread use of tabular data in healthcare, to our knowledge, there has been no comprehensive investigation of domain knowledge integration for medical tabular data. In this paper, we first detail the types of medical domain knowledge and their potential uses. We then provide an overview of strategies for incorporating medical domain knowledge into tabular machine learning at all pipeline stages. In particular, we investigate how recent methods in table representation learning, such as foundation models (Hollmann et al., 2023a) or LLM-based table representation (Sui et al., 2024), can be adapted for this purpose. Finally, we suggest promising research directions

for automated knowledge integration in clinical machine learning for medical tabular data.

2 Related Works

Domain knowledge encompasses relevant information about the machine learning task, including relevant features, taxonomies, logical constraints, and probability distributions (Dash et al., 2022). It is also referred to as background or prior knowledge. Domain knowledge has been incorporated into various fields of machine learning, such as physics and engineering, where it is used to combine data with mathematical and physics-based models (Karniadakis et al., 2021; Willard et al., 2022).

In the medical domain, the importance of integrating domain knowledge has been increasingly recognized (Mao et al., 2024; Leiser et al., 2023; Von Rueden et al., 2021), especially in areas such as medical imaging (Xie et al., 2021). While previous work has shown that domain knowledge can benefit tabular clinical decision systems (Sirocchi et al., 2024), it is often poorly integrated into clinical machine learning pipelines and requires custom algorithms (Sirocchi et al., 2024).

Xie et al. (2021) identify three challenges hindering the adoption of domain knowledge in medical computer vision models, which are also relevant to tabular data: identifying relevant sources, selecting appropriate representations, and integrating them into deep learning models.

3 Medical Domain Knowledge

In this section, we build on prior work in machine learning and domain-informed models (Von Rueden et al., 2021; Mao et al., 2024) to propose a categorization of medical domain knowledge.

3.1 Patient Data

Definition Patient data encompasses a wide range of health-related information, such as demographics, laboratory values, and vital signs. These data are commonly stored in systems like Electronic Health Records (EHRs).

The accessibility of patient datasets can vary considerably. MIMIC (Johnson et al., 2023) or UK Biobank (Sudlow et al., 2015) are available to researchers through application procedures, while most datasets are only accessible within individual institutions. These datasets may reflect the biases of specific patient populations. Other sources, such as population-wide health statistics, from initiatives like the Global Burden of Disease (Vollset et al., 2024), can provide context to assess generalizability. In addition, knowledge graphs can be developed from datasets such as cancer registries to understand the variation in outcomes (Hasan et al., 2019). Furthermore, biomedical databases that capture gene-gene or protein-protein interactions encode biological relationships and can serve as prior knowledge to inform downstream model training and inference (Wysocka et al., 2023).

Representation Patient data is often represented by datasets of various modalities that can be used to train or pre-train medical models.

Integration Patient data can be used for training and subgroup analyses, bias detection, and generalizability evaluation across diverse cohorts. Patient statistics can also inform feature engineering.

3.2 Formal Knowledge

Definition Formal knowledge encompasses established biomedical and scientific information recognized by scientific consensus. It originates from authoritative sources, such as medical textbooks or clinical guidelines, which can establish standardized procedures for clinical practice.

Formal knowledge can be *quantitative*, often represented through mathematical models that estimate biomarker dynamics or disease progression, such as pharmacokinetic models of drug absorption (Lin and Wong, 2017) or tumor growth models (Albano and Giorno, 2006; Tabatabai et al., 2005). Known clinical thresholds (e.g., defining sinus tachycardia as heart rate $\geq$ 100 bpm at rest (Page et al., 2016)) can guide data encoding and interpretation. Additionally, quantitative rules support data quality control by flagging physiologically implausible values.

Formal knowledge can also be *qualitative*, capturing the known interactions of patient characteristics. For instance, diagnosing delirium relies on behavioral and cognitive changes assessed through mental status exams (Tieges et al., 2018). Similarly, clinical gestalt refers to the ability of a physician to synthesize signals such as facial expressions or posture to form early diagnostic impressions (Cramer et al., 2025). Though laboratory tests often confirm a diagnosis, initial suspicion can stem from these assessments, such as hyperpigmentation in vitamin B12 deficiency (Brescoll and Daveluy, 2015).

Representation Formal knowledge can be represented as rules, lookup tables (e.g., scoring ranges, reference intervals), and flow charts or other categorical mappings for qualitative associations.

Integration Formal knowledge can be used for feature engineering, data cleaning, encoding medical relationships, integrating medical constraints, and validation.

3.3 Medical Semantics

Definition Medical semantics refers to standardized representations of biomedical concepts that support interoperability between datasets.

In tabular medical datasets, biomedical concepts are often expressed in varying forms, through free text and different coding systems. This variability can hinder the generalizability of machine learning models. To address this, semantic frameworks like SNOMED CT (Chang and Mostafa, 2021) and the Unified Medical Language System (UMLS) Lindberg et al. (1993) offer structured vocabularies and ontologies (Gaudet-Blavignac et al., 2021). LLMs can also generate medical semantic embeddings that enrich tabular data with contextual meaning. For example, Michalopoulos et al. (2021) introduce UmlsBERT, which incorporates domain knowledge from UMLS by linking terms with shared concepts and semantic types.

Representation Medical semantics can be represented through ontologies and dictionaries or captured by using biomedical language models.

Integration Medical semantics can be used for preprocessing, standardization, or to enrich existing data with semantic hierarchy or similarity.

3.4 Experimental Medical Findings

Definition Experimental medical findings derived from data analyses, clinical studies, or trials often reveal potential interactions between biomedical concepts, even if causal relationships are not yet established or still require scientific consensus. For example, current evidence from controlled exposure studies in children supports an association between adverse behavioral outcomes and synthetic food dye (Miller et al., 2022). Experimental findings are typically also compiled in clinical guidelines used by physicians. They are classified into multiple categories of recommendations (Class I, IIa, IIb, II and III) and levels of evidence (A, B, or C) (McDonagh et al., 2023). These findings can serve as hypotheses to guide the design of machine learning models.

While clinical guidelines can be difficult to interpret due to their length and variations in format (e.g., text, flowcharts, tables), advances in retrieval augmented generation models lead the way towards a more efficient extraction of relevant information (Kresevic et al., 2024).

Representation: Experimental findings can be represented as soft rules with confidence scores, probabilistic associations, or model priors.

Integration Experimental findings can be used to incorporate promising hypotheses that are supported by preliminary evidence. It may be used to explore feature relationships during feature engineering, prioritize variables during feature selection, and introduce soft constraints during model training or validation.

3.5 Professional Insights

Definition Reasoning developed by experienced clinicians provides essential context when interpreting information. With years of clinical experience, even limited data can be synthesized to make a diagnosis (Groves et al., 2003). This is demonstrated, for example, by optometrists outperforming novices in diagnosing glaucoma when data is limited (Ghaffar et al., 2025).

Expert insight is particularly valuable for identifying potential confounding factors when developing machine learning models for clinical use. For instance, patients nearing the end of life may establish legal directives, such as Do Not Resuscitate (DNR) orders, to limit medical intervention by their wishes (Schmidt et al., 2015). However, such directives are often not recorded in structured datasets and may be communicated only verbally.

Representation Professional insight can be formalized through rules, thresholds, or guidelines derived from expert interviews or consensus (e.g., expert surveys).

Integration Expert input can inform data collection through the design of study protocols and guide the selection and construction of features. It also plays a key role in validating models, interpreting outliers, and enabling feedback loops for iterative refinement.

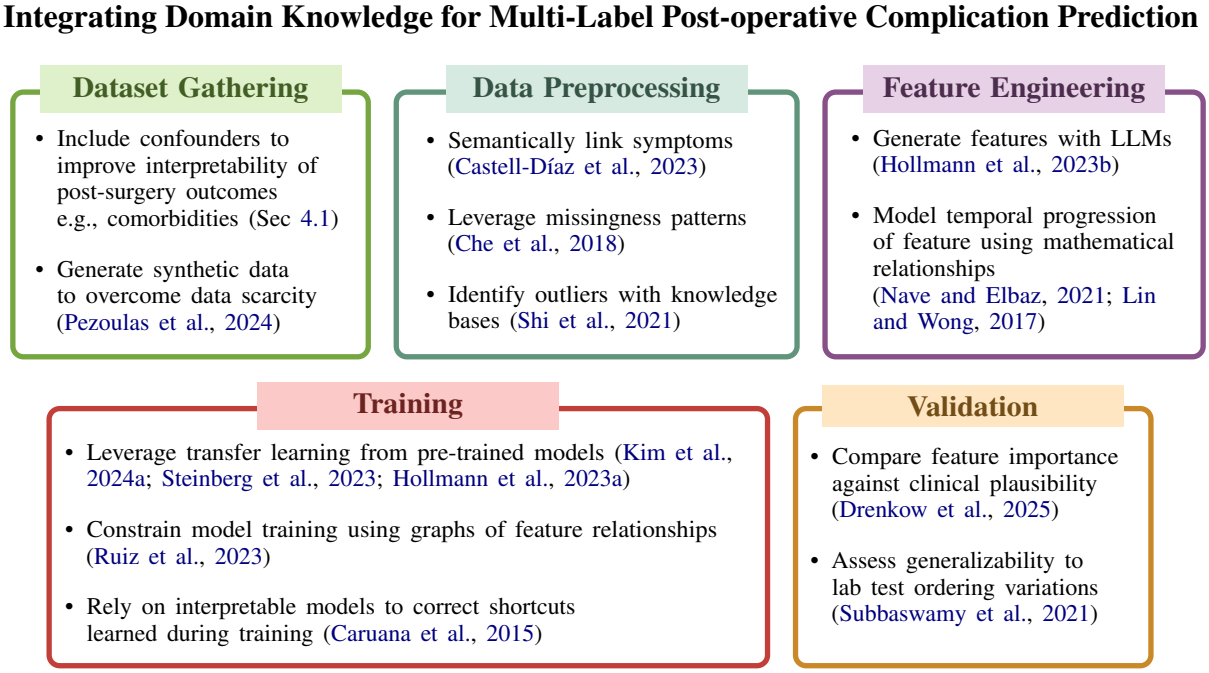

Figure 1: Possible integrations of domain knowledge for the use-case post-surgery complications prediction

4 Integrating Domain Knowledge

In Section 3, we explored the various forms of medical domain knowledge. Here, we examine each stage of the machine learning pipeline, from data collection to model validation, and highlight opportunities to meaningfully integrate domain expertise. We also focus on how advances in deep learning can be incorporated for domain knowledge integration and suggest promising research directions. In Figure 1, we provide an example of how domain knowledge can be integrated into the use case of post-surgery complications prediction.

4.1 Dataset Creation and Selection

Data collection Medical domain knowledge and professional insight are critical to data collection, especially in the case of *prospective studies*. Expert input (see Section 3.5) is essential when designing the study protocol, selecting data sources, defining patient populations, and determining which features to collect. Potential confounders should be considered during study design and data collection or assessed during analysis (Jager et al., 2008; Kahlert et al., 2017). A common strategy involves defining an a priori set of covariates to account for (Brookhart et al., 2010). For example, in a study investigating diabetes and ischemic heart disease, researchers could control for age by including only participants over 65 (Jager et al., 2008).

Beyond addressing confounders, incorporating additional relevant variables can help capture clinical context. Savchenko et al. (2023), for example, incorporate patient socio-demographic information to model the clinical dynamics of non-invasive bladder cancer treatment. Their inclusion yields an 8.14% performance gain over the baseline model lacking these features (Savchenko et al., 2023).

For *retrospective studies*, leveraging public datasets can also enrich training data. Factors such as demographic statistics can help select appropriate datasets. Ontologies can also be used to semantically categorize features, enabling table comparisons (Woźnica et al., 2024).

Synthetic data Synthetic data can help protect patient privacy or increase data size (Pezoulas et al., 2024). Bayesian networks can be used to generate synthetic patient data by modeling probabilistic relationships and latent variables (Tucker et al., 2020). These relationships can be informed by expert knowledge (Rabaey et al., 2024) or learned from existing datasets (Tucker et al., 2020). To ensure that the generated data maintains strong inferential properties, informative prior knowledge is essential to appropriately weight the different network structures (Young et al., 2009). Simulation-based methods can also leverage domain knowledge to generate data points. Deist et al. (2019) propose a technique that integrates prior knowledge using domain-informed kernels. The method performs well in low-data, high-dimensional set-

tings but is surpassed by data-driven approaches as training data increases. Shi et al. (2022), for instance, show that when data-driven methods use large amounts of data, they can generate synthetic data that closely resembles real data.

Large language models have also been proposed for synthetic data generation (Zhang et al., 2023). However, this approach should be further tested in the medical domain in terms of privacy preservation. Kim et al. (2024b) propose combining LLMs with attribute constraints to generate synthetic financial data. Yet, they notice that using constraints could reduce diversity in some attributes, which may cause issues for data with high variability. These findings may also be relevant for similar approaches in the medical domain.

While synthetic data is often used to replace or complement training data, it can also help train tabular models. TabPFN (Hollmann et al., 2023a), a transformer-based model for tabular tasks, is trained on a large number of synthetic datasets, reducing reliance on sensitive real-world data. Recent work has demonstrated that domain knowledge can improve its adaptability to specific data types. For example, Perciballi et al. (2024) enhanced TabPFN's performance on metagenomic data by modifying the generative model priors to better reflect the sparsity and variability of this domain. However, the high variability in their results indicates that further experimentation is needed.

Future Research When working with a small dataset, a common strategy is to identify semantically or structurally similar datasets that can be leveraged through transfer learning. Advances in semantic data type detection (e.g., Hulsebos et al. (2023)) could lead to more informed dataset selections when combined with medical ontologies.

Synthetic data offers another promising research avenue for bias mitigation and data augmentation. The explicit inclusion of domain knowledge could guide this process, especially for low-resource domains. However, more research is still needed to compare the various methods of synthetic data generation in terms of privacy preservation, fidelity, bias, and clinical relevance.

4.2 Data Preprocessing

Cleaning Clinical data often contains inconsistencies that require tailored preprocessing. While such issues are best mitigated through standardized data collection protocols, missing data and non-standardized entries remain common and are sometimes unavoidable.

Numerical values suffer from inconsistent units due to varying practices across laboratories and general practitioners (e.g., 'g/dL', '??', 'NULL') (Shi et al., 2021). Domain knowledge can guide semantic alignment and harmonization through the identification of valid unit conversions or the correction of implausible entries (e.g., checking whether values are in acceptable ranges). For instance, Shi et al. (2021) automatically derive conversion rates, detect outliers, and identify extreme ranges using literature and knowledge bases.

Categorical values also require standardization. For this, medical knowledge bases can provide structured vocabularies (Chang and Mostafa, 2021; Bodenreider, 2004), and dictionaries can define permissible value labels, helping flag and correct invalid entries (Pilowsky et al., 2024). Beyond rule-based methods, ontology embedding techniques can leverage clinical ontologies to generate vector representations of terms (Zahra and Kate, 2024; Castell-Díaz et al., 2023). These embeddings enable the suggestion of the semantically related post-coordinated expression (Castell-Díaz et al., 2023).

Using LLMs for automated tabular data cleaning could alleviate the need for tailor-made outlier detection and error correction algorithms (Bendinelli et al., 2025). However, (Bendinelli et al., 2025) observe that LLMs tend to use brute force for data cleaning. Providing contextual knowledge, such as partial guidance on how to correct an error, often improves the results.

Missing data A common approach to handling missing data is complete case analysis, which excludes patients with incomplete information. This can introduce selection bias when missingness is related to underlying clinical factors (Haneuse, 2016). Clinical insight is therefore essential to assess if missingness is occurring at random. In the case of longitudinal data, missingness patterns can be especially informative (Che et al., 2018). For instance, stable patients may have specific lab tests omitted (Raebel et al., 2016), or patients experiencing severe toxicity may be more likely to drop out of a clinical trial (Bell et al., 2014).

Medical context also informs the design of imputation strategies. Multi-omics correlations from external datasets can, for instance, help impute genetic data (Lin et al., 2016). More recently, LLM-based imputation methods have shown significant

improvement over baselines for data 'missing not at random' (Hayat and Hasan, 2024).

Future Research Preprocessing is crucial for ensuring interoperability, especially when combining datasets from multiple institutions where data quality often varies. In particular, poor standardization across datasets and a high rate of missing data impact the quality of tabular medical datasets. Current initiatives on the interoperability of healthcare databases aim to lessen the need for custom preprocessing (Semler et al., 2018).

Recent advances in table understanding methods that identify the semantic and syntactic types of cells (Zhang et al., 2020; Sun et al., 2021) represent a promising step toward developing end-to-end pipelines for automatic clinical data preprocessing. Further research on the use of medical vocabularies or ontologies in conjunction with LLMs could improve semantic interoperability. More broadly, LLMs are a promising research direction for automatized data cleaning and standardization. However, to our knowledge, they have not yet been applied to medical datasets with complex feature interactions. Thus, further adaptation and validation of this method to such datasets is necessary.

Although numerous statistical imputation techniques exist, many rely on the assumption that data is missing at random. This assumption often fails to account for the clinical context behind missingness. There is a growing need for frameworks that can represent the reasons behind missing data to address data 'missing not at random'. In cases where the underlying mechanisms can be known or approximated, mathematical models (e.g., pharmacokinetic models) could be leveraged to infer and impute specific features (Lin and Wong, 2017).

4.3 Feature Engineering

Feature selection and creation Domain knowledge is frequently integrated into feature selection, particularly in biomedical applications, where datasets often contain relatively few instances but many features. In this context, it can help reduce complexity and enhance model performance. The effectiveness of this approach depends on the use of accurate and contextually appropriate knowledge: Wu et al. (2022) show that well-curated, targeted domain knowledge yields superior results compared to indiscriminate application.

Domain knowledge can also be used to generate new features from existing ones. Features can be handcrafted based on clinical knowledge and, in particular, mathematical relationships. Nave and Elbaz (2021) train a machine learning model to predict tumor size over time. Their results showed that adding mathematical model outputs significantly improved performance: their tumor size prediction accuracy increased from 72.5% to 86.33%.

Hollmann et al. (2023b), on the other hand, use LLMs to engineer additional features automatically based on a dataset description. This approach can be further extended by integrating domain expertise. For example, an estimation of medication absorption could be calculated using baseline patient information (Rajagopalan and Gastonguay, 2003).

Table serialization Clinical data can also be serialized into text and processed using language models. This can allow models to extract semantically rich representations that might not be apparent through standard tabular processing alone. For example, Chen et al. (2023) apply this approach to prognosis prediction, leveraging medical knowledge from pre-training data to enrich tabular representations. Similarly, Slack and Singh (2023) propose a pipeline that integrates domain knowledge into LLM-based differential diagnosis prediction. They enrich tabular data with disease-specific instructions and show that including this can often significantly increase performance.

Future Research Language models offer a promising avenue for the automated engineering of additional features based on domain knowledge. However, their outputs may introduce biases, as careful assessment of these methods is still needed. For instance, Küken et al. (2025) observe that LLMs often rely too heavily on simplistic operations, such as addition, when generating features. Including information on formal relationships from domain knowledge to engineer features could be a way to avoid this bias.

While LLMs have been used for medical tabular tasks, they have yet to be extensively tested on clinical datasets with high-dimensional features. Multimodal approaches combining a language model and high-dimensional table representation may be more appropriate (AlSaad et al., 2024). However, current research on such multimodal models is still limited. In addition, using LLMs for feature engineering also requires more extensive testing of the potential propagation of training data biases.

4.4 Training

Leveraging graph representations Domain knowledge can be used to introduce clinically meaningful inductive biases during training, guiding models to learn patterns that align with established medical understanding. Graph representations of domain knowledge can encode structured relationships. For instance, Middleton et al. (2024) jointly process tabular data and knowledge graphs to identify therapeutic genetic targets. Similarly, Ruiz et al. (2023) encode prior knowledge in a graph structure, influencing how feature connections are learned—demonstrating efficiency in high-dimensional, low-sample settings such as genomics. The hierarchical structure of medical concepts has also been incorporated into knowledge graphs to improve single-cell classification (Mojarrad et al., 2024).

Other architectures In physics-informed neural networks, regularization losses can enforce expected behavior in a model's outputs (Cuomo et al., 2022). For example, Nguyen et al. (2020) introduce a domain-specific loss function based on the dose volume histogram from radiation therapy. They show that this loss improves results across most evaluation categories (Nguyen et al., 2020).

Using interpretable models can also help interpret patterns and use domain knowledge to correct potential unwanted shortcuts that conflict with clinical reality. For instance, Caruana et al. (2015) develop generalized additive models with pairwise interactions for a pneumonia detection task. When the model incorrectly learns, for example, that asthma lowers the risk of pneumonia, it can be addressed by reshaping the learned effect function to reflect the correct association.

Foundation model pre-training Through self-supervised pre-training, models can leverage the longitudinal nature of EHRs. For example, Steinberg et al. (2023) pre-train a time-to-event transformer-based model from EHRs medical codes. This helps model medical codes' semantic relationships and temporal dependencies representing diagnoses, medications, and procedures. Pre-training models on massive EHR datasets can help contextualize data with information not included in smaller task-specific datasets (Rasmy et al., 2021).

Future Research Grinsztajn et al. (2022) note that the underperformance of neural networks on tabular data may stem from a lack of inductive biases—especially when dealing with uninformative or noisy features, which are common in medical data. Future research could explore further the integration of inductive biases using graph or mathematical representations of domain knowledge. For example, Kim et al. (2024a) propose a new pre-training architecture for tabular data using graph representations, enabling improved transfer learning across structured datasets.

Additionally, given the growing interest in medical foundation models, it may be valuable to investigate how pre-training tasks can better exploit fine-grained relationships between clinical codes—potentially improving the quality of learned representations in structured medical data. In addition, though Steinberg et al. (2023) show improved results on pre-trained models compared to trained from scratch, the effect of the pre-training dataset should be studied in more depth. For instance, the impact of the size of the dataset or the distribution shift compared to the downstream task should be assessed. Furthermore, reinforcement learning with human feedback—used, for example, in natural language processing by (Ouyang et al., 2022)—could offer a way to adapt model behavior to clinical expertise, as also explored in other alignment strategies (Yao et al., 2023). This could also be leveraged for tabular datasets.

4.5 Validation

Validation of machine learning models incorporates explainability, generalizability, and bias analysis, which can be grounded in domain knowledge.

A survey by Tonekaboni et al. (2019) highlights that clinicians view *explainability* as a justification tool in clinical workflows. To that end, clinicians must be able to relate model features and outputs to medical reasoning. Explainability methods support clinicians in understanding which features the model considers vital for its decisions (Vimbi et al., 2024).

In addition, auditing frameworks (Drenkow et al., 2025) can enable structured identification of dataset "shortcuts" by comparing feature importance against clinical plausibility. Complementing this, medical literature and clinician insight offer valuable knowledge about known confounders or spurious correlations (Meng et al., 2022).

It is also important to assess model generalizability across patient populations and hospitals. One aspect is to appropriately select metrics and dataset splits. Expert insight can also provide information

into possible sources of dataset shift, such as variations in clinical workflows or patient populations. Subbaswamy et al. (2021) propose, for example, a method to evaluate how a model can generalize to shifts in laboratory test ordering.

Finally, it is also crucial to consider the baselines against which machine learning methods will be compared to, as even naive methods can show surprisingly good results. For instance, naive forecasting often shows competitive performance in financial forecasting tasks (Hewamalage et al., 2023). In clinical settings, domain knowledge could be used to construct naive rule-based baselines to validate clinical applications.

Future Research Although current explainability methods increase transparency and trust, they remain approximations of the model's internal logic, can introduce their uncertainties, and may not be suited for clinical decision validation (Ghassemi et al., 2021). Indeed, they cannot guarantee the correctness of predictions or justify their adoption in practice (Ghassemi et al., 2021).

Similarly, while valuable for evaluating model robustness and generalizability, cross-dataset testing assesses performance after distribution shifts have occurred. Future work could prioritize proactive strategies to build more resilient systems that mitigate or validate such shifts in advance, for instance, through synthetic data or causal modeling informed by clinical expertise.

In bias analysis, incorporating structured medical knowledge and recent experimental findings could help identify and address harmful shortcuts. Additionally, synthetic data could be used to generate slightly modified test datasets to assess the robustness of the model to changes that should not be medically relevant to outputs.

5 Discussion

As medical machine learning becomes increasingly prominent, incorporating domain knowledge is vital. Some approaches emphasize the scalability and diversity of large datasets, relying, for instance, on pre-trained models (Steinberg et al., 2023). Others prioritize the structured integration of domain knowledge using ontologies or graphs (Sirocchi et al., 2024). This becomes especially important when dealing with heterogeneous, high-dimensional, or noisy data.

However, access to expert input and curated databases can be limited, and integrating this knowledge effectively is often complex. In addition, clinical practices and medical understanding evolve, and relying on outdated ontologies or prior assumptions may introduce biases. Moreover, models trained on historical data may learn and reinforce prior clinical behaviors, leading to the risk of self-fulfilling prophecies in real-world decision support systems (De-Arteaga and Elmer, 2023). Furthermore, relying too heavily on domain constraints can unintentionally limit the discovery of novel patterns or rare cases. Thus, further empirical evaluations should assess the benefits of knowledge integration methods across medical datasets of different types and quality.

In general, we first recommend early discussions with medical partners to determine potential biases and confounders. While confounders can be unavoidable for retrospective studies, they should be recognized as limitations. Domain knowledge should also be included during data preprocessing to harmonize values following ontologies and guidelines or to assess the reasons for missing data and impute them accordingly. Domain knowledge can also engineer medically relevant features or integrate information from knowledge bases for feature selection. Moreover, model training can leverage pre-trained models or mathematical relationships. Finally, validation should be based on clinical expertise, and potential generalizability should be assessed for other patient populations or hospital settings.

While this process can be time-consuming, recent studies suggest that domain knowledge integration can be automated by leveraging foundation models for knowledge extraction (Kresevic et al., 2024) and its integration in the pipeline (Hollmann et al., 2023b). This paves the way toward scalable medical deep-learning models. Yet, medical foundation models also need to be evaluated in terms of privacy preservation, bias propagation, and generalizability. Recently, studies have led benchmarking efforts for scientific foundation models. Chen et al. (2024) show that while expert knowledge did not always improve code validity, it consistently increased success rates—supporting the idea that domain expertise can improve model outcomes, and its inclusion should be further studied for foundation models. However, medical machine learning on complex tabular datasets cannot rely yet on end-to-end LLMs.

Closer collaboration between the fields of healthcare and tabular machine learning could leverage

deep learning advances to design models that integrate domain knowledge more efficiently. Promising research directions include adapting and validating automated approaches for domain knowledge integration and transfer learning for tabular data (Kim et al., 2024a).

6 Limitations

The current study presents several limitations that should be acknowledged. The presented work is not a systematic review and does not aim to cover all relevant literature comprehensively. Thus, it has been influenced by the authors' experiences within the field of medical machine learning.

In addition, while we propose an overview and diverse examples for integrating domain knowledge into the medical machine learning pipeline, we do not offer concrete recommendations that are applicable to all use cases. Indeed, the appropriate approach may vary depending on the medical context and application. Therefore, we encourage interdisciplinary discussions between medical experts and machine learning practitioners to define a concrete guide collaboratively.

Moreover, the efficacy of the discussed methods of domain knowledge integration may vary according to data quality. We do not offer a systematic assessment of these integration methods on various data types, which would be valuable in gaining a deeper understanding of the impact of domain knowledge.

Finally, our focus was limited to tabular data. Integrating domain knowledge into multimodal machine learning models, which utilize data such as text, images, or time series, represents an important direction for future research, but was beyond the scope of this work.

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