RESEARCH PAPER

Neural Joint-Distribution Network for Competing Risks of Death and Transplantation in Primary Biliary Cholangitis

Hardik Molia
Associate Professor, Computer Engineering,
Government Engineering College – Bhavnagar, Gujarat, India
Email: hardik.molia@gmail.com

ABSTRACT
Primary Biliary Cholangitis (earlier called Primary Biliary Cirrhosis) is a chronic disease in which the body's own immune system slowly destroys the small bile ducts inside the liver. Predicting how long a patient with severe Primary Biliary Cholangitis will survive is a difficult task. In many cases, a patient does not die naturally but receives an emergency liver transplant because of liver failure. Existing machine learning-based solutions focused on biliary cirrhosis target either the patient's death or the need for a liver transplant. Although both events seem independent, ignoring the transplantation possibility and focusing only on death misleads the prediction model. In this research, a Neural Joint-Distribution Network (NJDN) is proposed to calculate both the probability of natural death and the probability of needing an urgent transplant simultaneously. The proposed solution is trained and tested on the Mayo Clinic Primary Biliary Cirrhosis dataset. The results show that the proposed solution outperforms traditional models, providing doctors with clear, actionable timelines to plan life-saving surgeries well in advance.
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1. INTRODUCTION

Primary Biliary Cholangitis (PBC) (earlier called Primary Biliary Cirrhosis) [1-2] is a progressive autoimmune disease that targets the liver. In this disease, the patient's own immune system mistakenly attacks and slowly destroys the small bile ducts inside the liver. Because bile cannot flow properly, it builds up and damages healthy liver tissue. Over time, this toxic accumulation leads to severe scarring, known as cirrhosis, which can eventually cause total liver failure. Predicting how long a severely ill patient will survive is an incredibly difficult task due to the presence of competing risks. In real-world clinical environments, a severe patient may not reach the natural endpoint of death, but instead undergoes an emergency liver transplant as a life-saving measure. Accurate timelines allow hepatologists to optimize clinical care and manage medical interventions.

In recent years, researchers have shown growing interest in proposing prediction models for healthcare applications based on statistical or machine learning approaches. To the best of our knowledge, the majority of existing Primary Biliary Cholangitis (PBC) prediction models focus either on predicting survival or the requirement of a liver transplant in isolation. Logically, a liver transplant should be treated as a critical milestone indicating that a patient's condition had become severe, necessitating surgical intervention to prevent mortality. In traditional survival models, however, a patient's data up to the point of liver transplantation does not receive the necessary attention during model training. Most of the time, the model treats these patients exactly the same as patients who recovered without a transplant, or those who dropped out or moved away from the study. When an algorithm ignores the liver transplantation possibility, it also ignores learning how a patient's biological system was on the verge of collapse and surgical intervention was needed in emergency. When an algorithm treats liver transplantation as a non-informative event, it fundamentally fails to learn the critical biological thresholds that precede liver failure. A key contribution of this research work is the formal introduction of liver transplantation as an independent clinical event.

This research proposes the Neural Joint-Distribution Network (NJDN) for the prediction of death and transplantation in Primary Biliary Cholangitis. The solution is referred to as NJDN-PBC for the rest of this paper. NJDN-PBC calculates the probability of natural death and the probability of urgent liver transplantation across a discrete time horizon, structured as a calendar of 5 years. NJDN-PBC is trained, optimized, and validated using the landmark Mayo Clinic Primary Biliary Cirrhosis dataset. To demonstrate its effectiveness, NJDN-PBC is experimentally evaluated against both a traditional statistical method and a standard deep learning algorithm. NJDN-PBC's performance is compared against the Cox Proportional Hazards model, which serves as the traditional clinical baseline for competing risks, and DeepSurv, a standard deep survival neural network that ignores transplantation dependencies by treating them as random dropouts.

This paper is organized as follows. Section 2 discusses the related work. Section 3 presents the NJDN-PBC architecture and the dataset used for its evaluation. Section 4 provides the implementation details and performance analysis. Section 5 discusses the conclusions and future work.

2. RELATED WORK

2.1 Artificial Intelligence, Machine Learning, and Deep

Learning in Healthcare

Artificial Intelligence (AI), Machine Learning (ML), and Deep Learning (DL) have transformed many areas of healthcare by improving the accuracy, speed, and efficiency of medical services. These technologies are widely used for disease diagnosis, medical image analysis, patient risk prediction, and personalized treatment planning. AI-powered systems can assist doctors in detecting diseases such as cancer, diabetes, and heart conditions at an early stage. Robotic-assisted surgeries help surgeons perform complex procedures with greater precision and reduced recovery time. Predictive models are used to forecast disease progression, hospital readmissions, and patient survival outcomes. AI is also applied in drug discovery, healthcare management, remote patient monitoring, and evaluating clinical performance, enabling better decision-making and improved patient care. Although AI, ML, and DL are increasingly used in healthcare, improving their accuracy and efficiency remains an important research area because healthcare applications require highly reliable and precise decisions [3-7].

2.2 Deep Learning for Survival Analysis

Researchers have shown keen interest in formal explorations of how to use deep learning for the purpose of survival analysis (time to event analysis). Several contributions are referred to discuss how well deep learning can be used for different types of data. Some of the recent contributions are summarized in this section.

DeepHit [8], Dynamic-DeepHit [9] , and DeepCompete [10] are deep learning models for survival analysis with competing risks, but they differ in their treatment of time and data. DeepHit learns the distribution of survival times directly without making any assumptions about the underlying stochastic process. It offers static data with discrete time domain based joint distribution of event and time. Dynamic DeepHit learns associations between the longitudinal data and the various associated risks in a fully data-driven fashion. It offers longitudinal data with time domain based dynamically updated joint distribution. DeepCompete learns risk specific cumulative hazard functions using static data with continuous time. Feature Selection for Survival Analysis [11] is proposed to address the issue of performance degradation due to presence of many irrelevant features. FilterDeepHit^{+} [11] is a hard feature selection approach that identifies the most important features and removes less relevant ones before the training. It is based on the selection of different features for different competing risks. SparseDeepHit^{+} [11] is a soft feature selection approach. Instead of removing features completely, it adds a sparse layer at the beginning of each subnetwork. This layer assigns a learnable weight to every input feature. HybridDeepHit^{+} [11] trains DeepHit first then measures importance by randomly permuting each feature. It selects features that most affect model performance. A dynamic prediction framework for competing-risk survival analysis [12] using multiple longitudinal biomarkers is proposed to continuously update the probability of experiencing an event as new measurements become available.

2.3 Prediction Models for Primary Biliary Cholangitis (PBC)

This section discusses various AI / ML / DL based prediction models proposed by various researchers for Primary Biliary Cholangitis (PBC). Table-1 compares and summarizes these approaches.

Table-1 Prediction Models for Primary Biliary Cholangitis (PBC)

Purpose	Main Feature(s)	Algorithm(s)
Survival & Prognosis Prediction [13]	Identification of low-risk and high-risk patients so treatment strategies can be decided.	Random Survival Forest
Survival & Prognosis Prediction [14]	Predicts transplant-free survival and identifies prognostic markers.	Random Survival Forest
Survival & Prognosis Prediction [15]	Focuses on predicting early-stage patient outcomes (Survival vs. Non-survival).	Support Vector Machine, Decision Tree, Random Forest, Logistic Regression, Neural Networks
Survival & Prognosis Prediction [16]	Prediction of stage of PBC for advancing therapeutic diagnosis.	Ensemble Model with 12 Algorithms Such as Catboost, Extra Trees
Survival & Prognosis Prediction [17]	Prediction of survival possibility of a patient.	Decision Tree, Random Tree, Random Forest, Naïve Bayes.
Survival & Prognosis Prediction [18]	Prediction of 1 year mortality possibility of a patient.	Random Survival Forest and Support Vector Machine
Treatment Response Prediction [19]	predict treatment responders (e.g., to Ursodeoxycholic Acid) from pretreatment data.	Random Forest, Extreme Gradient Boosting, Decision Tree, Naïve Bayes, Logistic Regression
Treatment Response Prediction [20]	Multicenter cohort study validating an ML model to identify biochemical response (Paris II criteria) based on pretreatment markers like total bilirubin, total protein.	Extreme Gradient Boosting
Risk Stratification [21]	ML identified four clusters of patients characterized by different phenotypes and long-term prognosis.	Clustering
Risk Stratification [22]	Focuses on generating explainable, logic-based classification rules to accurately stratify the associated genetic risk.	Logic Learning Machine

Transplant Need Prediction [23]	Prediction of urgent liver transplant need for appropriate treatments.	Logistic Regression, K-Nearest Neighbors, Naïve Bayes, Random Forest, and Extreme Gradient Boosting
Discrimination [24]	Discrimination between autoimmune hepatitis and primary biliary cholangitis.	Deep Learning Model (Autoimmune Liver Neural Estimator (Alne))

2.4 Literature Review Observations

This section lists the conclusive observations at the end of the literature review that was the main motivation to carry out this research work.

Appropriateness of AI / ML / DL for Healthcare: It has been observed that though AI / ML / DL based healthcare applications are found to be acceptably accurate and are being deployed in real-world applications, efforts for improvements should be continued, especially for rare diseases such as Primary Biliary Cholangitis (PBC).

Primary Biliary Cholangitis (PBC) is a rare disease for which it is extremely difficult to arrange a very large dataset to work with. Moreover, combining multiple individual datasets together may introduce heterogeneity and inconsistencies due to differences in patient demographics, data collection procedures, and clinical practices. Most of the proposals discussed in Section 2.3 are based on datasets that are limited to a specific geographical area or hospital.

The majority of the existing AI / ML / DL based solutions for Primary Biliary Cholangitis (PBC) are targeted towards solving a single task such as survival prediction or liver transplant prediction. Some solutions are based on prediction of effectiveness of treatment, etc. It may be better to combine multiple tasks together and build a model that tries to predict them simultaneously.

3. NJDN-PBC – PROPOSED SOLUTION

3.1 The Dataset

NJDN-PBC is trained, optimized, and validated using the landmark Mayo Clinic Primary Biliary Cirrhosis dataset [25]. This dataset is of 17 features, 2 targets, 1 identifier with 418 instances. Because PBC is a rare, orphan autoimmune disease, gathering massive amounts of data is structurally difficult. So, this dataset is found suitable for our work. The details of features and targets are shown in Table-2 [25].

Table - 2. Mayo Clinic Primary Biliary Cirrhosis dataset [25]

Variable	Role	Type	Description
ID	ID	Integer	Unique Identifier
N_Days	Target	Integer	Number of Days between Registration and Final Status
Status	Target	Categorical	Final Status of Patient: C (Censored) or CL (Censored due to Liver Transplant) or D (Death)
Drug	Feature	Categorical	Type of Drug: D-penicillamine or Placebo
Age	Feature	Integer	Age of Patient (Days)
Sex	Feature	Categorical	M (Male) or F (Female)
Ascites	Feature	Categorical	Presence of Ascites: N (No) or Y (Yes)
Hepatomegaly	Feature	Categorical	Presence of Hepatomegaly: N (No) or Y (Yes)
Spiders	Feature	Categorical	Presence of Spiders: N (No) or Y (Yes)
Edema	Feature	Categorical	Presence of Edema: N (No Edema and No Diuretic Therapy for Edema) or S (Edema Present Without Diuretics, or Edema Resolved by Diuretics) or Y (Edema Despite Diuretic Therapy)
Bilirubin	Feature	Continuous	Serum Bilirubin (mg/dl)
Cholesterol	Feature	Integer	Serum Cholesterol (mg/dl)
Albumin	Feature	Continuous	Albumin (gm/dl)
Copper	Feature	Integer	Urine Copper (ug/day)
Alk_Phos	Feature	Continuous	Alkaline Phosphatase (U/liter)
SGOT	Feature	Continuous	SGOT (U/ml)
Tryglicerides	Feature	Integer	Tryglicerides

Platelets	Feature	Integer	Platelets per Cubic (ml/1000)
Prothrombin	Feature	Continuous	Prothrombin Time
Stage	Feature	Categorical	Histologic Stage of Disease (1, 2, 3, of 4)

3.2 Data Preprocessing and Feature Engineering

Raw clinical datasets often contain missing entries, varying measurement scales, and complex temporal formats that should not be fed directly into a deep learning model. To ensure numerical stability and optimal gradient descent during training, data preprocessing using Python is done as below.

Handling Missing Values: For clinical features containing missing observations (such as serum cholesterol or copper levels), median imputation is applied rather than instance deletion to preserve the size of the dataset.

Categorical Encoding: For clinical features having binary outcomes (such as sex, presence of ascites, hepatomegaly, and blood vessel spiders), mapping to a 0/1 format is done. For multi-category nominal features (such as severe edema classifications), one-hot encoding is done.

Special Attention to Categorical Feature "Drug": As per the dataset, 158 patients received D-penicillamine, 154 patients received a placebo, and the remaining 106 patients were simply tracked to observe the natural progression of the disease. If categorical encoding was done, then it would consider the unassigned tracking state as a third clinical category that could mislead the training. As the drug is included in the dataset as an intervention, not as a parameter of the patient's profile, its categorical encoding is not done and this feature is not used for training.

Feature Standardization: To standardize the ranges of all numerical features, they are normalized using standard scaling to have a mean of 0 and a standard deviation of 1.

Time Binning: The total tracking time (N_Days) is divided into 5 equal-sized groups representing a 5-year timeline. This allows the model to predict exactly which year a patient will experience an event, turning a continuous number of days into a clear 5-year calendar using a statistical method called quantile slicing.

Updated Feature Set: As discussed earlier, we initially had 17 features. One feature ("Edema") is one-hot-encoded as three features. One feature ("Drug") is dropped. So total features to be used for training is 18.

3.3 NJDN-PBC Architecture

The NJDN-PBC Architecture (Neural Joint-Distribution Network) is a deep learning model designed to predict how a liver disease patient's condition will evolve over a five-year period. Instead of looking at survival or transplants as separate, isolated events, it evaluates them together as competing risks. The architecture is divided into three main sections:

The Input Layer: NJDN-PBC received input of 18 features (as discussed in section 3.2) from patient's medical history at a single point of time. These 18 features remain pre-processed (as discussed in section 3.2) before provided to the input layer.

The Shared Context Hidden Layers: There are two hidden layers. First hidden layer (64 Nodes) expands the 17 inputs to map out complex and hidden patterns. It uses a dropout rule to prevent the model from simply memorizing the training data. Second Hidden Layer (32 Nodes) shrinks the data to represent patient's overall liver health.

The Joint-Distribution Output Matrix (The 5-Year Calendar): Patient's overall health is presented as a grid of 11 output slots. These slots represent a mutually exclusive timeline over a 5-year tracking window as shown in Table 3.

Table 3. 5 Year Tracking Window

Slots	Purpose
Slots 1 to 5 (Transplant Horizon)	The probability that the patient will require an urgent liver transplant during Year 1, Year 2, Year 3, Year 4, or Year 5.
Slots 6 to 10 (Mortality Horizon)	The probability that the patient will face natural mortality during Year 1, Year 2, Year 3, Year 4, or Year 5.
Slot 11 (Survival Cushion)	The probability that the patient will survive past the entire 5-year window without needing a transplant or facing mortality.

It is to be noted that the Joint-Distribution network here does not calculate independent joint probabilities; instead, it outputs the simultaneous probability distribution of the time-of-event and type-of-event combined.

The Global Balancing: The defining feature of NJDN-PBC is the Global SoftMax applied at the end to force the probabilities across all 11 output slots to compete against each other so that their combined total always equals exactly 100%.

Figure [1] (generated for better visualization using Gemini (Google) based on author-provided contents for steps) shows overall process.

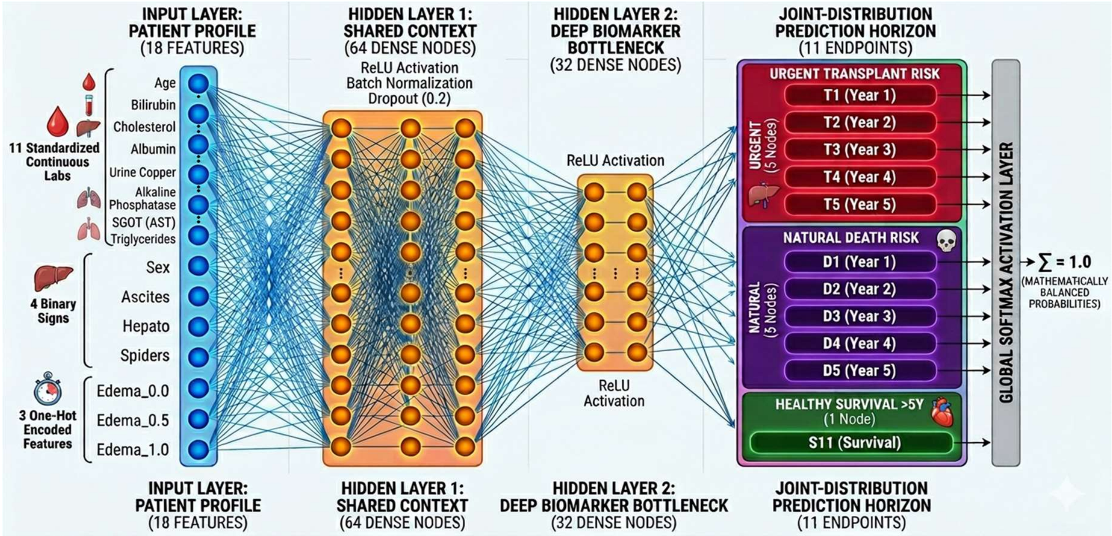

Figure 1 - NJDN-PBC Architecture

4. IMPLEMENTATION AND RESULT

4.1 Implementation

The NJDN-PBC Architecture (Neural Joint-Distribution Network) is implemented with Python-3 [26-27]. The neural network is implemented using PyTorch. numpy, pandas, sklearn are used for data pre-processing, data splitting and result analysis. lifelines, a complete survival analysis library completely written in Python is used to implement CoxPHFitter - Cox Proportional Hazards Fitter. PyTorch is used to implement DeepSurv - Standard Deep Survival Network.

Performance evaluation of NJDN-PBC is done with two approaches: Traditional Statistical Model (CoxPHFitter - Cox Proportional Hazards Fitter) and Standard Deep Survival Network (DeepSurv).

CoxPHFitter is a traditional statistical tool used in Python to estimate how different patient features affect the time it takes for an event, like death, to occur. It is based on the classic Cox Proportional Hazards model, which assumes that a patient's risk is a simple, linear combination of their health metrics. In this research, it calculates baseline risk scores by looking at each event independently, but it treats alternative events as simple dropouts rather than true competing risks.

DeepSurv is a modern deep learning model designed to predict survival risk by upgrading the traditional Cox model with a neural network. Instead of assuming patient risks are strictly linear, it uses hidden network layers and non-linear activation functions to discover complex interactions between health features. It trains by using a custom partial log-likelihood loss function that actively ranks patients, ensuring those who experience an event sooner are assigned a higher risk score.

Evaluating NJDN-PBC with these two models is sufficient because they cover both sides of the machine learning spectrum: CoxPHFitter represents the traditional baseline whereas DeepSurv represents the state-of-the art baseline. These two modes are mentioned as CoxPHFitter-PBC and DeepSurv-PBC respectively.

4.2 Comparative Analysis as Survival Model

The Concordance index (C-index) is a s metric used to evaluate the performance of a predictive model that is based on survival analysis. It ranks the risk or event times of individuals to measure how well a model predicts the relative ordering of survival times.

C−Index= Number of concordant pairs / Number of comparable pairs

Where, Concordant pair is considered when the model correctly ranks two patients according to their observed survival times. Comparable pair is any valid pair of patients that can be meaningfully compared considering survival times. C-Index of 1 is perfect prediction, 0.5 is random prediction and less than 0.5 is worse than random prediction. The comparative analysis of CoxPHFitter-PBC, DeepSurv-PBC and NJDN-PBC in terms of survival models with C-Index is presented in Figure 2, 3, 4.

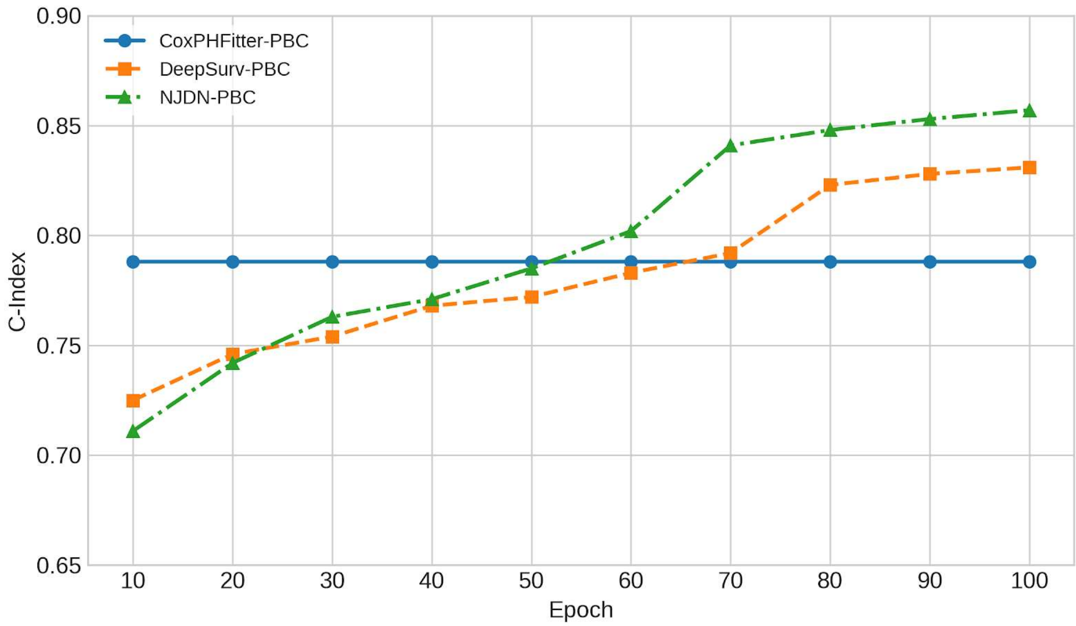

Figure 2 – C-Index (Death Prediction)

Figure 2 shows how efficiently the models learn to predict patient mortality over 100 training epochs. While the baseline CoxPHFitter-PBC remains completely static (epoch is not applicable) at a C-index of 0.788 due to its non-neural network nature, both deep learning models show steady learning curves. NJDN-PBC consistently maintains an upper hand throughout training, scaling up to a final peak C-index of 0.857 by epoch 100. DeepSurv-PBC follows a similar upward trajectory but finishes relatively lower at 0.831.

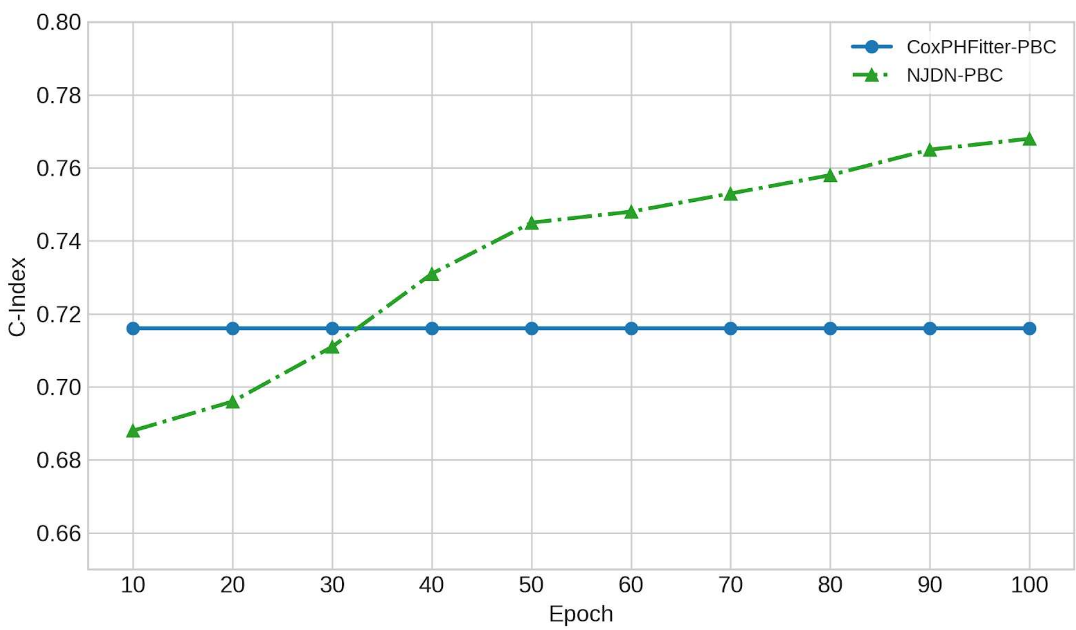

Figure 3 – C-Index (Liver Transplant Prediction) (Not Applicable for DeepSurv-PBC)

Figure 3 shows how efficiently the models learn to predict patient liver transplant over 100 training epochs. This analysis is not applicable (NA) for DeepSurv-PBC because it lacks the multi-output architecture. While the baseline CoxPHFitter-PBC remains completely static (epoch is not applicable) at a C-index of 0.716 due to its non-neural network nature, NJDN-PBC consistently maintains an upper hand throughout training, scaling up to a final peak C-index of 0.768 by epoch 100.

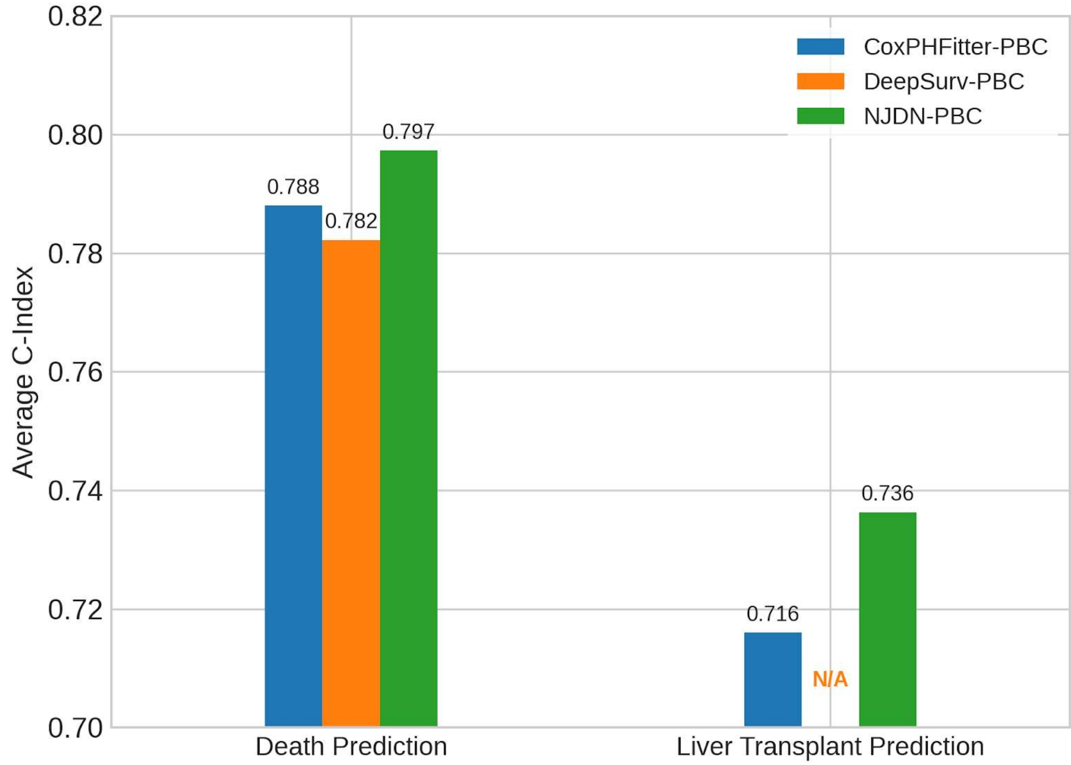

Figure 4 – Average C-Index Performance Analysis

Figure 4 shows how efficiently the models learn both the survival tasks (death and liver transplant) on average basis. The traditional statistical baseline, CoxPHFitter-PBC, performs moderately well but lacks the advantages of neural network. DeepSurv-PBC is unable to handle multi-output architecture so its result is present for death prediction only. NJDN-PBC achieves the highest overall performance with an average C-index of 0.797 for death prediction and 0.736 for liver transplant prediction.

Table 4 shows how efficiently NJDN-PBC performs for survival analysis. It is to be noted that the Benchmark score here is the height score observed so it is different from the average score mentioned in above-mentioned comparison.

Table 4 - Comparison for Survival Models

Survival Analysis	Benchmark Model	Metric	Benchmark Model highest Score	NJDN-PBC Model highest Score	% of Improvement
Death Prediction	CoxPHFitter-PBC	C-Index	0.788	0.857	8.76 %
Death Prediction	DeepSurv-PBC	C-Index	0.831	0.857	3.13 %
Liver Transplant	CoxPHFitter-PBC	C-Index	0.716	0.768	7.26 %
Liver Transplant	DeepSurv-PBC	C-Index	Not Applicable	0.768	Not Applicable

4.3 Comparative Analysis as Classification Model

Accuracy, Precision and Recall are the most widely used classification metrics to evaluate prediction models. CoxPHFitter is a survival analysis model so it is excluded from this analysis. The comparative analysis of DeepSurv-PBC and NJDN-PBC in terms of survival models with accuracy, precision and recall is presented in Figure 5, 6.

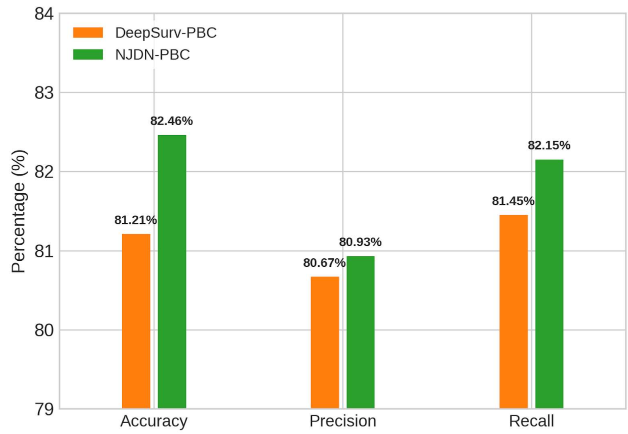

Figure 5 – Classificastion – Death Prediction

Figure 5 shows how efficiently models do classification as death prediction task. CoxPHFitter is a survival analysis model so it is excluded from this analysis. NJDN-PBC outperforms with 82.46% Accuracy, 80.93% Precision, and 82.15% Recall.

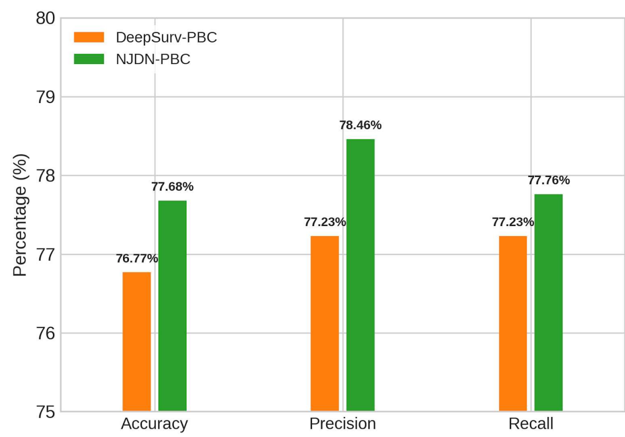

Figure 6 – Classificastion – Liver Transplant Prediction

Figure 6 shows how efficiently models do classification as liver transplant prediction task. CoxPHFitter is a survival analysis model so it is excluded from this analysis. NJDN-PBC outperforms with 77.68% Accuracy, 78.46% Precision, and 77.76% Recall.

5. CONCLUSION

This research work introduces NJDN-PBC (Neural Joint-Distribution Network for Primary Biliary Cholangitis) for the simultaneous prediction of death or liver transplant probabilities over a 5-year timeline. This solution aims to assist medical professionals by providing clear, actionable timelines to plan life-saving surgeries well in advance. The proposed model was evaluated against two benchmark models: a traditional statistical model (CoxPHFitter) and a standard deep survival network (DeepSurv). Performance was rigorously assessed across both survival and classification analyses. The results demonstrated that NJDN-PBC consistently outperforms both benchmark models in both evaluation paradigms. While deploying such a model in real-world clinical settings requires thorough validation from medical professionals, this study establishes a strong foundation for future translation. Moving forward, NJDN-PBC can be piloted in clinical environments to evaluate its practical efficacy. Furthermore, from an algorithmic perspective, the framework can be extended using alternative neural network architectures and validated against a wider array of baseline survival models.

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