PyDTS: A Python Package for Discrete-Time Survival (Regularized) Regression with Competing Risks

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ABSTRACT

Time-to-event analysis (survival analysis) is used when the response of interest is the time until a pre-specified event occurs. Time-to-event data are sometimes discrete either because time itself is discrete or due to grouping of failure times into intervals or rounding off measurements. In addition, the failure of an individual could be one of several distinct failure types, known as competing risks (events). Most methods and software packages for survival regression analysis assume that time is measured on a continuous scale. It is well-known that naively applying standard continuous-time models with discrete-time data may result in biased estimators of the discrete-time models. The Python package PyDTS, for simulating, estimating and evaluating semi-parametric competing-risks models for discrete-time survival data, is introduced. The package implements a fast procedure that enables including regularized regression methods, such as LASSO and elastic net, among others. A simulation study showcases flexibility and accuracy of the package. The utility of the package is demonstrated by analysing the Medical Information Mart for Intensive Care (MIMIC) - IV dataset for prediction of hospitalization length of stay.

Keywords Competing events · Elastic net · Lasso · Regularized Regression · Ridge · Penalized Survival Analysis
1 Introduction

Discrete-time survival data pertains to situations where data are limited to a discrete grid, either because events only happen at regular discrete time points, or because the available data only record the interval during which each event occurred. For example, cancer deaths may be measured in months since diagnosis [Lee et al., 2018], and hospital stays are recorded in days. Most regression models for survival data assume that time is continuous. However, applying standard continuous-time models to discrete-time data may lead to substantially biased estimators for the discrete-time models [Lee et al., 2018, Wu et al., 2022].

Here we consider the setting of discrete-time survival data with competing events in which subjects can experience only one of several different types of events over follow-up. For example, competing risks of hospital length of stay, measured in days, are discharge and in-hospital death. Occurrence of one of these events precludes us from observing the other event of the same patient. Cause-specific mortality is another typical example of competing risks, where individuals could pass away due to various causes, such as heart disease, cancer, or other reasons [Kalbfleisch and Prentice, 2011, Klein and Moeschberger, 2003].

When dealing with continuous-time survival data with competing risks, the classical methods for analyzing non-competing events can be employed, since the likelihood function for the continuous-time setting can be factored into distinct likelihoods for each cause-specific hazard function [Kalbfleisch and Prentice, 2011]. However, this approach does not hold true for discrete-time data with competing risks, as highlighted in Lee et al. [2018] and references therein. Most existing works on discrete-time data with competing risks are based on simultaneously estimating all the parameters via the full likelihood function, which are computationally time consuming. On the other hand, recent works [Lee et al., 2018, Schmid and Berger, 2021] have shown that a collapsed-likelihood approach may be used to separate estimation of cause-specific hazard models for different event types. This approach is equivalent to fitting a generalized linear model (GLM) to repeated binary outcomes, and yields consistent and asymptotically normal estimators under standard regularity conditions. In addition, Wald-type confidence intervals and likelihood-ratio tests may be used to evaluate the effects of covariates.

Recently, Meir and Gorfine [2023] developed a new estimation procedure for a semi-parametric logit-link survival model for discrete time with competing events and right censoring. Their procedure has two main advantages: (i) It is significantly faster than existing methods and requires a smaller amount of memory resources. For example, with 20,000 observations, 10 covariates, and two competing events, the computation time reduction is a factor of 5 compared to that of Lee et al. [2018]. (ii) It allows including modern machine-learning model-selection procedures, such as regularization and screening.
To the best of our knowledge, there is only one R package for discrete-time survival data with competing events named **discSurv** [Welchowski et al., 2022]. Two main functions of this package are relevant in the context of competing events: (i) **compRisksGEE** applies the estimation procedure of Lee et al. [2018] with the logit-link function. (ii) **survTreeLaplaceHazard** predicts the Laplace-smoothed hazards of a discrete-survival tree without or with competing events. This function uses different cause-specific hazard functions; for details see Berger et al. [2019].

The aim of this work is to present **PyDTS**, which is currently the sole Python software package that deals with discrete-time survival data with competing events. Additionally, it is the first package to incorporate a regularized regression approach for such data. The features of **PyDTS** comprise of:

- Implementation of the estimation techniques of Lee et al. [2018] and Meir and Gorfine [2023] under the logit-link function.
- Computation of performance metrics, such as the area under the receiver operating characteristic curve and Brier score, for discrete-time survival data with competing events.
- Implementation of regularized regression based on Meir and Gorfine [2023] with K-fold CV.
- Generation of simulated discrete-time survival data with competing events and right censoring.

The rest of the paper is organized as follows. Section 2 describes the model and estimation techniques applied in **PyDTS**. Section 3 demonstrates how to simulate discrete-time survival data with competing events based on **PyDTS**. Section 4 provides various examples of **PyDTS** usage. Section 5 demonstrates the package utility by analysing length of hospital stay based on the Medical Information Mart for Intensive Care (MIMIC) - IV dataset. Some concluding remarks are provided in Section 6.

2 Model and Methods

2.1 Notation and Model

Assume \( T \) is a discrete random variable of event time that can take on only the values \( \{1, 2, \ldots, d\} \) and \( J \) denotes the type of event, \( J \in \{1, \ldots, M\} \). Consider a \( p \times 1 \) vector of time-independent covariates \( Z \). The setting of time-dependent covariates will be discussed later. A general discrete cause-specific hazard function is of the form

\[
\lambda_j(t|Z) = \Pr(T = t, J = j|T \geq t, Z), \quad t = 1, 2, \ldots, d, \quad j = 1, \ldots, M.
\]
Following Allison [1982], the logit-link semi-parametric models of the above hazard functions are given by
\[ \lambda_j(t|Z) = \frac{\exp(\alpha_{jt} + Z^T \beta_j)}{1 + \exp(\alpha_{jt} + Z^T \beta_j)}, \quad t = 1, 2, \ldots, d, \quad j = 1, \ldots, M, \quad (1) \]

where
\[ \Omega = (\alpha_{11}, \ldots, \alpha_{1d}, \beta_1^T, \ldots, \alpha_{M1}, \ldots, \alpha_{Md}, \beta_M^T) \]
is an unknown vector of parameters. The total number of unknown parameters is \( M(d + p) \). Leaving \( \alpha_{jt} \) unspecified is analogous to an unspecified baseline hazard function in the Cox proportional hazard model [Cox 1972], and thus the above model is considered as a semi-parametric discrete-time model. For simplicity of presentation, the vector of covariates \( Z \) is shared by the \( M \) models. However, it does not imply that identical covariates must be shared by the models, since the regression coefficient vectors \( \beta_j \) are event-type dependent, and any coefficient of \( \beta_j \) can be set to 0 in order to exclude the corresponding covariate. One of our goals is estimating \( \Omega \).

Assume the data consist of \( n \) independent observations, each with \((X_i, \delta_i, J_i, Z_i)\) where \( X_i = \min(C_i, T_i) \), \( C_i \) is a right-censoring time, \( \delta_i = I(T_i \leq C_i) \) is the event indicator and \( J_i \in \{0, 1, \ldots, M\} \), where \( J_i = 0 \) if and only if \( \delta_i = 0 \), \( i = 1, \ldots, n \). It is assumed that given the covariates, the censoring and failure times are independent and non-informative.

### 2.2 The Collapsed Log-Likelihood Approach of Lee et al.

Lee et al. [2018] showed that in contrast to the continuous-time setting with competing events, the likelihood function of the discrete-time setting cannot be decomposed into separate likelihoods for each cause-specific hazard function \( \lambda_j \). This implies that estimating \( \Omega \) by maximizing the likelihood, would require maximization with respect to \( M(d + p) \) parameters simultaneously, which is expected to be time consuming.

Alternatively, Lee et al. [2018] suggested the following collapsed log-likelihood. The dataset is expanded such that for each observation \( i \) the expanded dataset includes \( X_i \) rows, i.e., pseudo observations, one row for each time \( t, t \leq X_i \); see Table for \( M = 2 \) competing events. At each time point \( t \) the pseudo observations can be viewed as random variables from a conditional multinomial distribution with one of \( M + 1 \) possible outcomes \( \delta_{1it}, \ldots, \delta_{Mit}, 1 - \sum_{j=1}^{M} \delta_{jit} \), where \( \delta_{jit} \) equals 1 if individual \( i \) experienced event of type \( j \) at time \( t \); and 0 otherwise. Then, for \( M \) competing events, the estimators of \( (\alpha_{j1}, \ldots, \alpha_{jd}, \beta_j^T), j = 1, \ldots, M \), are the values that maximize
\[ \log L_j = \sum_{i=1}^{n} \sum_{t=1}^{X_i} \left[ \delta_{jit} \log \lambda_j(t|Z_i) + (1 - \delta_{jit}) \log \{1 - \lambda_j(t|Z_i)\} \right] \quad j = 1, \ldots, M. \quad (2) \]
Namely, each maximization \( j, j = 1, \ldots, M \), consists of maximizing \( d + p \) parameters simultaneously. Lee et al. showed that the estimators are asymptotically multivariate normally distributed and the covariance matrix can be consistently estimated.

### 2.3 The Rapid Two-Step Approach

Meir and Gorfine [2023] adopted the collapsed log-likelihood approach but suggested estimating each \( \beta_j, j = 1, \ldots, M \), separately from \( \alpha_{jt} \). Their procedure improves over Lee et al. [2018] in two aspects: (1) By reducing the computation time substantially, especially for settings with large values of \( d \). (2) It enables easy incorporation of penalization regression methods (e.g., ridge, lasso and elastic net among others) and screening methods.

Let \( \tilde{X} \) be the new column of times of the expanded dataset, as demonstrated in Table 1. For each event type \( j \), \( \beta_j \) is estimated by a conditional logistic regression model, while stratifying the expanded dataset according to \( \tilde{X} \) and conditioning on the number of events within each stratum.

Hence, the estimators of \( \beta_j, j = 1, \ldots, M \), are obtained by maximizing

\[
L^C_j(\beta_j) = \prod_{t=1}^{d} \frac{\exp(\sum_{i \in C_t} \delta_{jit}Z^T_i\beta_j)}{\sum_{d_{jit} \in S_t} \exp(\sum_{i \in C_t} d_{jit}Z^T_i\beta_j)}, \quad j = 1, \ldots, M, \tag{3}
\]

where \( C_t \) is the set of all pseudo observations with \( \tilde{X} \) equals \( t \), \( S_t \) is the set of all possible combinations of \( \sum_{i=1}^{n} \delta_{jit} \) ones and \( \sum_{i=1}^{n} (1 - \delta_{jit}) \) zeros, \( d_{jit} \) is a vector in \( S_t \), \( d_{jit} \) equals to 0 or 1 with \( \sum_i \delta_{jit} = \sum_i d_{jit} \), and \( d_{jit} \) is a component of \( d_{jit} \). Since Equation (3) has a form of partial likelihood of a Cox regression model when ties are present (see, for example, Equation (8.4.3) of Klein and Moeschberger [2003]), an available Cox model routine can be used for estimating \( \beta_j, j = 1, \ldots, M \).

Given the estimators of \( \beta_j, \hat{\beta}_j, j = 1, \ldots, M, \alpha_{jt}, j = 1, \ldots, M, t = 1, \ldots, d \), are estimated by a series of \( Md \) one-dimension simple optimization algorithms applied on the original dataset, such that

\[
\hat{\alpha}_{jt} = \arg\min_a \left\{ \frac{1}{Y.(t)} \sum_{i=1}^{n} I(X_i \geq t) \frac{\exp(a + Z^T_i\hat{\beta}_j)}{1 + \exp(a + Z^T_i\hat{\beta}_j)} - \frac{N_j(t)}{Y.(t)} \right\}^2 \tag{4}
\]

where \( Y.(t) = \sum_{i=1}^{n} I(X_i \geq t) \) and \( N_j(t) = \sum_{i=1}^{n} I(X_i = t, J_i = j) \). The two-step estimation procedure of Meir and Gorfine [2023] consists of the two speedy steps described in Algorithm 1.

The simulation results of Meir and Gorfine [2023] reveal that the above two-step procedure performs well in terms of bias, and provides similar standard errors to that of Lee et al. [2018]. However, under large values of \( d \), a substantial improvement in computational time is achieved by using the above two-step procedure. Apparently, estimating \( p + d \) parameters simultaneously is more time consuming than estimating \( d \) one-dimensional parameters and one parameter of \( p \) dimension.
Algorithm 1 The Two-Step Estimation Procedure of [Meir and Gorfine, 2023]

1. Use the expanded dataset, estimate each vector $\beta_j$ separately, $j = 1, \ldots, M$, by maximizing Equation (3) with a stratified Cox routine, and get $\hat{\beta}_j, j = 1, \ldots, M$.

2. Given $\hat{\beta}_j, j = 1, \ldots, M$, use the original non-expanded dataset and estimate each $\alpha_{jt}$, $j = 1, \ldots, M$, $t = 1, \ldots, d$, separately, by Equation (4).

2.4 Time-dependent covariates

Similarly to the continuous-time Cox model, the simplest way to code time-dependent covariates uses intervals of time [Therneau and Grambsch, 2000]. Then, the data is encoded by breaking the individual’s time into multiple time intervals, with one row of data for each interval. Hence combining this data expansion step with the expansion demonstrated in Table 1 is straightforward.

2.5 Regularized Regression Models

Penalized regression methods, such as LASSO, adaptive LASSO, elastic net [Hastie et al., 2009], place a constraint on the size of the regression coefficients. The estimation procedure of [Meir and Gorfine, 2023] that separates the estimation of $\beta_j$ and $\alpha_{jt}$ can easily incorporate such constraints in Lagrangian form by minimizing

$$- \log L_j^c(\beta_j) + \eta_j P(\beta_j), \quad j = 1, \ldots, M,$$

where $P$ is a penalty function and $\eta_j \geq 0$ are shrinkage tuning parameters. The parameters $\alpha_{jt}$ are estimated once the regularization step is completed and $\hat{\beta}_j$ were estimated. Clearly, any regularized Cox regression model routines can be used for estimating $\beta_j, j = 1, \ldots, M$, based on Equation (5), for example, the CoxPHFitter of Lifelines [Davidson-Pilon, 2019] with penalization.

2.6 Performance Measures

Based on [Meir and Gorfine, 2023], PyDTS includes estimates of cause-specific incidence/dynamic area under the receiver operating characteristics curve (AUC) and Brier score (BS) for discrete survival data with competing events and right censoring.

The cause-specific AUC at time $t$ is defined as the probability of a random observation with observed event $j$ at time $t$ having a higher risk prediction for cause $j$ than a randomly selected observation at risk at time $t$, free of event $j$ at time $t$. Formally,

$$\text{AUC}_j(t) = \Pr(\pi_{ij}(t) > \pi_{mj}(t) \mid D_{ij}(t) = 1, D_{mj}(t) = 0, T_m \geq t) \quad j = 1, \ldots, M \quad t = 1, \ldots, d$$
where
\[ \pi_{ij}(t) = \Pr(T_i = t, J_i = j \mid Z_i) = \lambda_j(t \mid Z_i)S(t - 1 \mid Z_i), \]
\[ \lambda_j(t|Z) = \frac{\exp(\alpha_j t + Z^T \beta_j)}{1 + \exp(\alpha_j t + Z^T \beta_j)}, \]
\[ S(t|Z) = \prod_{k=1}^{t} \left\{ 1 - \sum_{j=1}^{M} \lambda_j(k|Z) \right\}, \]
and
\[ D_{ij}(t) = I(T_i = t, J_i = j). \]

As explained in Meir and Gorfine [2023], the AUC can be estimated by
\[ \hat{AUC}_j(t) = \sum_{i=1}^{n} \sum_{m=1}^{n} D_{ij}(t) \hat{D}_{mj}(t) I(X_m \geq t) \left\{ I(\pi_{ij}(t) > \pi_{mj}(t)) + 0.5 I(\pi_{ij}(t) = \pi_{mj}(t)) \right\} / \sum_{i=1}^{n} \sum_{m=1}^{n} D_{ij}(t) \hat{D}_{mj}(t) I(X_m \geq t) \]
\[ j = 1, \ldots, M, \ t = 1, \ldots, d \] where \( \hat{D}_{ij}(t) = 1 - D_{ij}(t). \) An estimator of a cause-specific time-independent AUC is defined by
\[ \hat{AUC}_j = \sum_{i=1}^{d} w_j(t) \hat{AUC}_j(t) \]
\[ j = 1, \ldots, M \]
where
\[ w_j(t) = \frac{N_j(t)}{\sum_{i=1}^{d} N_j(t)}. \]

Finally, an estimator of the global AUC is defined as
\[ \hat{AUC} = \sum_{j=1}^{M} v_j \hat{AUC}_j \]
where
\[ v_j = \frac{\sum_{i=1}^{d} N_j(t)}{\sum_{j=1}^{M} \sum_{i=1}^{d} N_j(t)}. \]

Another well-known performance measurement is BS, a metric measures the accuracy of probabilistic forecasts. The cause-specific BS at time \( t \) is defined as
\[ \hat{BS}_j(t) = \frac{1}{Y(t)} \sum_{i=1}^{n} W_{ij}(t) \left\{ D_{ij}(t) - \pi_{ij}(t) \right\}^2 \]
\[ j = 1, \ldots, M, \ t = 1, \ldots, d \]
where \( W_{ij}(t) = I(X_i \geq t)/\hat{G}_C(t) \) and \( \hat{G}_C(\cdot) \) is the estimated survival function of the censoring (e.g., the Kaplan-Meier estimator). A cause-specific time-independent BS is defined by

\[
\hat{BS}_j = \sum_{t=1}^d w_j(t)\hat{BS}_j(t)
\]

and finally, a global BS is given by \( \hat{BS} = \sum_{j=1}^M v_j\hat{BS}_j \).

### 2.7 Predictions

Once the parameters of the model are estimated, predictions for test data are provided. Consider a test observation with baseline covariates \( Z \), PyDTS provides the following useful predictions:

1. The overall survival at each time point \( t, t = 1, \ldots, d \),

\[
\hat{S}(t|Z) = \prod_{k=1}^{t} \left\{ 1 - \sum_{j=1}^M \hat{\lambda}_j(k|Z) \right\}.
\]

2. The hazard of each failure type \( j \) at each time point \( t, j = 1, \ldots, M, t = 1, \ldots, d \),

\[
\hat{\lambda}_j(t|Z) = \frac{\exp(\hat{\alpha}_jt + Z^T\hat{\beta}_j)}{1 + \exp(\hat{\alpha}_jt + Z^T\hat{\beta}_j)}.
\]

3. The probability of event type \( j \) at each time \( t, j = 1, \ldots, M, t = 1, \ldots, d \),

\[
\hat{Pr}(T = t, J = j|Z) = \hat{\lambda}_j(t|Z)\hat{S}(t - 1|Z).
\]

4. The cumulative incident function (CIF) of event type \( j \) at any time \( t, j = 1, \ldots, M, t = 1, \ldots, d \),

\[
\hat{F}_j(t|Z) = \sum_{k=1}^{t} \hat{Pr}(T = k, J = j|Z).
\]

### 3 Simulating Discrete Time Survival Data with Competing Events

PyDTS provides EventTimesSampler (ETS) class for sampling discrete-time survival data with competing risks and right censoring under the log-link model described by Equation (1).
3.1 Covariates

A user-supplied covariates should be passed to ETS. For example, consider a setting with \( n = 10,000 \) independent observations and the following covariates

\[
Z_1 \sim \text{Bernoulli}(0.5)
\]

\[
Z_2 | Z_1 \sim \text{Normal}(72 + 10Z_1, 12),
\]

and

\[
Z_3 \sim 1 + \text{Poisson}(4).
\]

Any sampling framework can be used for creating the covariates’ dataframe. Here, we use Numpy [Harris et al., 2020] by with the following lines of code

```python
observations_df = pd.DataFrame(columns=['Z1', 'Z2', 'Z3'])
observations_df['Z1'] = np.random.binomial(n=1, p=0.5,
                                           size=n_observations)
observations_df.loc[observations_df.loc[observations_df['Z1'] == 0].index, 'Z2'] =
    np.random.normal(loc=72, scale=12,
                     size=n_observations-observations_df['Z1'].sum())
observations_df.loc[observations_df.loc[observations_df['Z1'] == 1].index, 'Z2'] =
    np.random.normal(loc=82, scale=12,
                     size=observations_df['Z1'].sum())
observations_df['Z3'] = 1 + np.random.poisson(lam=4, size=n_observations)
```

The sampled values are presented in Figure [1].

3.2 Event Times

The ETS function assumes that the possible failure times are \( 1, \ldots, d \), and the user should supply the value of \( d \). Clearly, the time intervals can be irregularly spaced and variable in size. For instance, discrete-time categories 1, 2, and 3 could correspond to specific days like Tuesday, Thursday, and Friday-Sunday, respectively. In the current example, we chose \( d = 7 \).

For the competing-events setting the user should decide on the number of competing events, and the values of model parameters, \( \alpha_{jt}, \beta_j, t = 1, \ldots, d, j = 1, \ldots, M \). For example, consider \( M = 2 \)
competing events and

\[ \alpha_1 t = -1 - 0.3 \log t, \ t = 1, \ldots, 7 \]
\[ \alpha_2 t = -1.75 - 0.15 \log t, \ t = 1, \ldots, 7 \]
\[ \beta^T_1 = (- \log 0.8, - \log 1.4, - \log 3) \]
\[ \beta^T_2 = (- \log 1, - \log 0.95, - \log 2). \]

All together, the ETS function is defined for sampling event-type and event-time, and adding it to the data frame, as follows:

```python
es = EventTimesSampler(d_times=7, j_event_types=2)
coefficients_dict = {
    "alpha": {
        1: lambda t: -1 - 0.3 * np.log(t),
        2: lambda t: -1.75 - 0.15 * np.log(t),
    },
    "beta": {
        1: -np.log([0.8, 1.4, 3]),
        2: -np.log([1, 0.95, 2]),
    }
}
observations_df = ets.sample_event_times(observations_df, coefficients_dict)
```

If the sampled covariates and parameters’ values lead to impossible survival probabilities (i.e., negative or greater than one), the sampling process will be terminated with an error message. In such scenarios, it may be useful to adjust the coefficients or constrain extreme values of the covariates to ensure that the probabilities are appropriate and the sampling process is executed successfully.

### 3.3 Censoring Time

Two types of right censoring are implemented in PyDTS, administrative and random right censoring. For administrative censoring, \( J_i = 0 \) and \( T_i = d + 1 \). These are the default values of observations for which the sampled event type was observed to be greater than \( d \). Random right censoring is optional and could be either dependent or independent of the covariates. For example, assume

\[ \Pr(C_i = t) = 0.05 \quad t = 1, \ldots, 7. \]

The censoring times can be sampled by

```python
prob_lof_at_t = [0.05, 0.05, 0.05, 0.05, 0.05, 0.05, 0.05]
observations_df = ets.sample_independent_lof_censoring(observations_df, prob_lof_at_t)
```
To generate right-censoring times that depend on the covariates, the user should supply to censoring hazard function, $\lambda_c(t|Z)$ in the form of Equation (1). For example,

```python

censoring_coef_dict = {
    "alpha": {
        0: lambda t: -0.3 - 0.3 * np.log(t),
    },
    "beta": {
        0: -np.log([8, 0.95, 6]),
    }
}
observations_df = ets.sample_hazard_lof_censoring(observations_df, censoring_coef_dict)
```

Finally, the observed data should be updated by $X_i = \min(T_i, C_i)$ and $J_i$ as follows

```python
observations_df = ets.update_event_or_lof(observations_df)
```

The first five observations of the sampled data are shown in Table 2.

### 4 Examples

The classes `DataExpansionFitter` and `TwoStagesFitter` of PyDTS implement the approach of Lee et al. [2018] and the two-step algorithm of Meir and Gorfine [2023], respectively.

`DataExpansionFitter` uses the `StatsModels` [Seabold and Perktold, 2010] package of Python, with the default GLM initiation. Other initial values can be supplied with `models_kwargs` and `model_fit_kwargs` arguments of `fit()`.

`TwoStagesFitter` uses `CoxPHFitter` of Lifelines [Davidson-Pilon, 2019] for estimating $\beta_j$, $j = 1, \ldots, M$, with Efron’s correction for ties [Efron, 1977], implemented in Lifelines. For the estimation of $\alpha_{jt}$, `TwoStagesFitter` uses `minimize` of Scipy [Virtanen et al., 2020] with `method = "BFGS"`. It uses the default values, except for the convergence tolerance that was set to be $gtol = 1e-7$, which is more strict than the default ($1e-5$).

Consider $M = 2$ competing events, $d = 30$ discrete time points, $n = 50,000$ observations and $p = 5$ covariates sampled from a Uniform[0,1] distribution, $\alpha_{1t} = -1 - 0.3 \log t$, $\alpha_{2t} = -1.75 - 0.15 \log t$,

$$\beta^T_1 = - (\log 0.8, \log 3, \log 3, \log 2.5, \log 2)$$

and

$$\beta^T_2 = - (\log 1, \log 3, \log 4, \log 3, \log 2).$$
For the censoring distribution we employ additional available option that randomly assigns a subset of the sample to have uncensored observed time, utilizing the parameter `censoring_prob`. As an example, if `censoring_prob = 0.8`, then the censoring time for 20% of the sample is set to $T_{max} + 1$, whereas for the remaining 80% of the sample, censoring times are randomly sampled from a discrete uniform distribution $\text{Uniform}\{1, \ldots, 31\}$. A dataset based on these choices can be generated by

```python
real_coef_dict = {
    "alpha": {
        1: lambda t: -1 - 0.3 * np.log(t),
        2: lambda t: -1.75 - 0.15 * np.log(t)
    },
    "beta": {
        1: -np.log([0.8, 3, 3, 2.5, 2]),
        2: -np.log([1, 3, 4, 3, 2])
    }
}
patients_df = generate_quick_start_df(n_patients=50000, n_cov=5, d_times=30, j_events=2, pid_col='pid', seed=0, censoring_prob=0.8, real_coef_dict=real_coef_dict)
```

The estimation techniques require a sufficient number of observed failures for each type of failure at each discrete time point. As such, the initial step is to verify if this condition is met by the available data. This could be done by

```python
patients_df.groupby(['J', 'X'])['pid'].count().unstack('J')
```

or by using the `plot_events_occurrence()` function available in `PyDTS` and visualizing the observed distributions, as demonstrated in Figure 2. Pre-processing suggestions when the data do not comply with this requirement will be presented in the Data Regrouping Example of Section 4.3.

The estimation procedure of Meir and Gorfine [2023] can be applied by

```python
new_fitter = TwoStagesFitter()
new_fitter.fit(df=patients_df.drop(['C', 'T'], axis=1))
```

A summary table of the estimated coefficients with their standard errors can be generated by

```python
new_fitter.print_summary()
```

The estimated standard errors of the estimates can be extracted by

```python
new_fitter.get_beta_SE()
```
which results in the following output

| covariate | j1_params | j1_SE  | j2_params | j2_SE  |
|-----------|-----------|--------|-----------|--------|
| Z1        | 0.187949  | 0.025068 | 0.040169  | 0.037807 |
| Z2        | -1.100792 | 0.025610 | -1.100246 | 0.038696 |
| Z3        | -1.093466 | 0.025726 | -1.410202 | 0.039280 |
| Z4        | -0.874521 | 0.025437 | -1.097849 | 0.038642 |
| Z5        | -0.652655 | 0.025280 | -0.654501 | 0.038179 |

Additionally, it is possible to visualize the estimated coefficients using

```python
new_fitter.plot_all_events_alpha()
new_fitter.plot_all_events_beta()
```

The estimation method of [Lee et al. 2018](#) is performed by

```python
fitter = DataExpansionFitter()
fitter.fit(df=patients_df.drop(['C', 'T'], axis=1))
fitter.print_summary()
```

The results are presented in Figure 3 and Table 3.

For generating the predictions of Section 2.7 for new observations an input data frame `pd.DataFrame()` is required, containing for each observation a vector of baseline covariates in the same order used in `fit()`. The following code provides predictions for the first three individuals in the dataset `patients_df`

```python
pred_df = new_fitter.predict_cumulative_incident_function(
    patients_df.drop(['J', 'T', 'C', 'X'], axis=1).head(3))
print(pred_df)
```

The results are given in a tabular form. The following output shows $\hat{S}(t|Z)$ (overall survival), $\hat{\lambda}_j(t|Z)$ (hazard functions), $\hat{P}(T = t, J = j|Z)$ (joint distribution of $T, J$) and $\hat{F}_j(t|Z)$ (CIFs). Figure 4 presents the entire curves of these three individuals.

| ID=0 | ID=1 | ID=2 |
|------|------|------|
| Z1   | 0.548814 | 0.645894 | 0.791725 |
| Z2   | 0.715189 | 0.437587 | 0.528895 |
| Z3   | 0.602763 | 0.891773 | 0.568045 |
| Z4   | 0.544883 | 0.963663 | 0.925597 |
| Z5   | 0.423655 | 0.383442 | 0.071036 |
| overall_survival_t1 | 0.942684 | 0.960628 | 0.932938 |
|                       |          |          |          |          |
|-----------------------|----------|----------|----------|----------|
| overall_survival_t2   | 0.899636 | 0.930545 | 0.883002 |          |
| ...                   |          |          |          |          |
| overall_survival_t29  | 0.406209 | 0.545669 | 0.348543 |          |
| overall_survival_t30  | 0.397051 | 0.537568 | 0.339489 |          |
| hazard_j1_t1          | 0.043097 | 0.031017 | 0.051717 |          |
| hazard_j1_t2          | 0.034478 | 0.024750 | 0.041448 |          |
| ...                   |          |          |          |          |
| hazard_j1_t29         | 0.015702 | 0.011211 | 0.018951 |          |
| hazard_j1_t30         | 0.012799 | 0.009130 | 0.015457 |          |
| hazard_j2_t1          | 0.014218 | 0.008355 | 0.015345 |          |
| hazard_j2_t2          | 0.011188 | 0.006566 | 0.012077 |          |
| ...                   |          |          |          |          |
| hazard_j2_t29         | 0.009730 | 0.005707 | 0.010505 |          |
| hazard_j2_t30         | 0.009745 | 0.005716 | 0.010521 |          |
| prob_j1_at_t1         | 0.043097 | 0.031017 | 0.051717 |          |
| prob_j1_at_t2         | 0.032501 | 0.023776 | 0.038668 |          |
| ...                   |          |          |          |          |
| prob_j1_at_t29        | 0.006545 | 0.006223 | 0.006806 |          |
| prob_j1_at_t30        | 0.005199 | 0.004982 | 0.005387 |          |
| prob_j2_at_t1         | 0.014218 | 0.008355 | 0.015345 |          |
| prob_j2_at_t2         | 0.010546 | 0.006308 | 0.011267 |          |
| ...                   |          |          |          |          |
| prob_j2_at_t29        | 0.004056 | 0.003168 | 0.003773 |          |
| prob_j2_at_t30        | 0.003958 | 0.003119 | 0.003667 |          |
| cif_j1_at_t1          | 0.043097 | 0.031017 | 0.051717 |          |
| cif_j1_at_t2          | 0.075599 | 0.054792 | 0.090385 |          |
| ...                   |          |          |          |          |
| cif_j1_at_t29         | 0.415879 | 0.335485 | 0.471603 |          |
| cif_j1_at_t30         | 0.421078 | 0.340468 | 0.476990 |          |
| cif_j2_at_t1          | 0.014218 | 0.008355 | 0.015345 |          |
| cif_j2_at_t2          | 0.024765 | 0.014663 | 0.026612 |          |
| ...                   |          |          |          |          |
| cif_j2_at_t29         | 0.177912 | 0.118845 | 0.179853 |          |
| cif_j2_at_t30         | 0.181870 | 0.121964 | 0.183520 |          |

We conducted a small simulation study demonstrating and comparing the two estimation procedures. The simulation is based on the data generation described above with 100 repetitions. The results are summarized in Figures 5–7 and Table 4. Evidently, both methods provide similar point estimators.
and standard errors, as expected. Moreover, both methods perform very well in terms of bias (Figures 5 and 6). However, as evident by Figure 7, the computation time of the two-step approach is shorter depending on \( d \), and the improvement factor increases as a function of \( d \). For additional simulation results, the reader is referred to [Meir and Gorfine 2023].

4.1 Regularization

Regularized regression can be easily accommodated only with TwoStagesFitter where we first estimate \( \beta_j \) and then \( \alpha_jt \). Regularization is introduced by CoxPHFitter [Davidson-Pilon 2019] with event-specific tuning parameters, \( \eta_j \geq 0 \), and \( l_1_{\text{ratio}} \) argument. For each \( j \), usually, a path of models in \( \eta_j \) are fitted, and the value of \( l_1_{\text{ratio}} \) defines the type of prediction model. In particular, ridge regression [Hoel and Kennard 1970] is performed by setting \( l_1_{\text{ratio}} = 0 \), lasso [Tibshirani 1996] by \( l_1_{\text{ratio}} = 1 \), and elastic net [Zou and Hastie 2005] by \( 0 < l_1_{\text{ratio}} < 1 \).

For example, lasso regression with two competing events, \( \eta_1 = 0.003 \) and \( \eta_2 = 0.005 \), can be applied by

```python
L1_regularized_fitter = TwoStagesFitter()
fit_beta_kwargs = {
    'model_kwargs': {
        1: {'penalizer': 0.003, 'l1_ratio': 1},
        2: {'penalizer': 0.005, 'l1_ratio': 1}
    }
}
L1_regularized_fitter.fit(df=patients_df.drop(['C', 'T'], axis=1),
                         fit_beta_kwargs=fit_beta_kwargs)
```

Regularization methods can be applied also with different penalty values for each covariates by passing a vector of length \( p \) (instead of a scalar) to “penalizer”. This could be useful, for example, when some covariates should not be penalized. For example, lasso regression with penalty for the first four covariates and leaving the last one non-penalized can be done by

```python
L1_regularized_fitter = TwoStagesFitter()
fit_beta_kwargs = {
    'model_kwargs': {
        1: {'penalizer': np.array([0.01, 0.01, 0.01, 0.01, 0]), 'l1_ratio': 1},
        2: {'penalizer': np.array([0.05, 0.05, 0.05, 0.05, 0]), 'l1_ratio': 1}
    }
}
L1_regularized_fitter.fit(df=patients_df.drop(['C', 'T'], axis=1),
                         fit_beta_kwargs=fit_beta_kwargs)
```
In penalized regression, one should fit a path of models in each $\eta_j, j = 1, \ldots, M$. The final set of values of $\eta_1, \ldots, \eta_M$ corresponds to the values yielding the best results in terms of pre-specified criteria, such as maximizing $\hat{\text{AUC}}_j$ and $\hat{\text{AUC}}$, or minimizing $\hat{\text{BS}}_j$ and $\hat{\text{BS}}$. The default criteria in PyDTS is maximizing the global AUC, $\hat{\text{AUC}}$. Two $M$-dimensional grid search options are implemented, PenaltyGridSearch when the user provides train and test datasets, and PenaltyGridSearchCV for applying a K-fold cross validation (CV) approach.

By executing

```python
penalizers = np.exp([-2, -3, -4, -5, -6])
grid_search = PenaltyGridSearch()
optimal_set = grid_search.evaluate(train_df, test_df, l1_ratio=1,
penalizers=penalizers,
metrics=['IBS', 'GBS', 'IAUC', 'GAUC'])
```

all the four optimization criteria are calculated over the $M$-dimensional grid and $optimal\_set$ includes the optimal values of $\eta_1, \ldots, \eta_M$ based on $\hat{\text{AUC}}$. Here, the optimal set based on $\hat{\text{AUC}}$ is $\log \eta_1 = -6$ and $\log \eta_2 = -6$. The user can choose the set of $\eta_j, j = 1, \ldots, M$, values that optimizes other desired criteria. For example, the set that minimizes BS can be selected as follows

```python
print(grid_search.convert_results_dict_to_df(grid_search.global_bs).idxmin())
```

which results in the optimal set $\log \eta_1 = -6$ and $\log \eta_2 = -3$.

For applying the two-stage regularized regression under a specific set of $\eta_j$, for example $optimal\_set$, use

```python
optimal_two_stages_fitter = grid_search.get_mixed_two_stages_fitter(
optimal_set)
```

Alternatively, 5-fold CV is performed by

```python
penalizers = np.exp([-2, -3, -4, -5, -6])
grid_search_cv = PenaltyGridSearchCV()
results_df = grid_search_cv.cross_validate(patients_df, l1_ratio=1,
penalizers=penalizers, n_splits=5,
metrics=['IBS', 'GBS', 'IAUC', 'GAUC'])
optimal_set = results_df['Mean'].idxmax()
print(results_df)
```

The number of folds is defined by $n\_splits$. The output is a tabular data of type pandas.DataFrame with the mean and SE of the fold-wise $\hat{\text{AUC}}$, for example
| log(eta_1) | log(eta_2) | Mean   | SE     |
|-----------|-----------|--------|--------|
| -2.0      | -2.0      | 0.638629 | 0.004971 |
| -3.0      |          | 0.639105 | 0.004849 |
| -4.0      |          | 0.639125 | 0.004856 |
| -5.0      |          | 0.637303 | 0.005168 |
| -6.0      |          | 0.488880 | 0.005754 |
| -3.0      | -2.0      | 0.638909 | 0.004880 |
| -3.0      |          | 0.638909 | 0.004847 |
| -4.0      |          | 0.639026 | 0.004849 |
| -5.0      |          | 0.637421 | 0.005146 |
| -6.0      |          | 0.488880 | 0.005753 |
| -4.0      | -2.0      | 0.638782 | 0.004862 |
| -3.0      |          | 0.638986 | 0.004814 |
| -4.0      |          | 0.639086 | 0.004812 |
| -5.0      |          | 0.637501 | 0.005085 |
| -6.0      |          | 0.488879 | 0.005752 |
| -5.0      | -2.0      | 0.563814 | 0.006279 |
| -3.0      |          | 0.563814 | 0.006280 |
| -4.0      |          | 0.563814 | 0.006282 |
| -5.0      |          | 0.563766 | 0.006334 |
| -6.0      |          | 0.614951 | 0.003800 |
| -6.0      | -2.0      | 0.568809 | 0.006638 |
| -3.0      |          | 0.568809 | 0.006638 |
| -4.0      |          | 0.568809 | 0.006643 |
| -5.0      |          | 0.568761 | 0.006725 |
| -6.0      |          | 0.630466 | 0.005484 |

and the other specified metrics are available as attributes of the PenaltyGridSearchCV object.

4.2 Performance Measures

Model evaluation on test data or by CV, can be done using the evaluation functions available in PyDTS and the measures of performance presented in Section 2.6.

For example, in the following code, the survival models are estimated based on the two-stage approach and the dataset train_df. Assume that the event of main interest is $j = 1$. Then, $\pi_{i1}(t)$ are calculated and stored in pred_df, and finally $\hat{AUC}_1(t)$, $t = 1, \ldots, d$, are provided by
fitter = TwoStagesFitter()
fitter.fit(df=train_df, axis=1))
pred_df = fitter.predict_prob_event_j_all(test_df, event=1)
auc_1 = event_specific_auc_at_t_all(pred_df, event=1)

Other measures such as $\hat{AUC}_1$, $\hat{BS}_1$, $\hat{AUC}$, and $\hat{BS}$ can be calculated by

pred_df = fitter.predict_prob_events(test_df)
ibs_1 = event_specific_integrated_brier_score(pred_df, event=1)
iauc_1 = event_specific_integrated_auc(pred_df, event=1)
b = global_brier_score(pred_df)
auc = global_auc(pred_df)

Model evaluation based on K-fold CV and TwoStagesFitter can be done by

cross_validator = TwoStagesCV()
cross_validator.cross_validate(full_df=patients_df.drop(['C', 'T'], axis=1),
n_splits=5, seed=0,
metrics=['BS', 'IBS', 'GBS',
'\'AUC', 'IAUC', 'GAUC']])

The user should provide the list of desired performance measures.

4.3 Data Regrouping

As previously mentioned, both estimation techniques are sensitive to the number of observed failures at each $(j, t)$, $j = 1, \ldots, M$, $t = 1, \ldots, d$. Consider the above simulation setting but with a smaller sample size of $n = 1,000$ independent observations. The number of events and censored observations at each time point is shown in Figure 8a. Evidently, there are too few observed events in later times, one event was observed at $(j, t) = (1, 25)$ and 0 for $(j, t) = (2, 25)$. Fitting model (1) with this dataset would fail and result with an error message. One straightforward solution is to group adjacent time points towards the end of the distribution together, allowing for a sufficient accumulation of observed events for each type of event. For this particular case, events that are observed on day 21 or later are classified into the time category labeled “21+” by

df['X'].clip(upper=21, inplace=True)

The regrouped dataset, described in Figure 8b, can successfully be used for estimating the survival models for $j = 1, 2$ and $t = 1, \ldots, 20, 21+$. Regrouping neighboring time points is a useful solution in datasets with too few events at any time point.
5 Case Study

The utility of PyDTS is demonstrated by analysing patients’ length of stay (LOS) in healthcare facilities. The analysis is similar to that of Meir and Gorfine [2023], based on the publicly accessible dataset of the Medical Information Mart for Intensive Care (MIMIC) - IV (version 2.0) [Johnson et al., 2022, Goldberger et al., 2000].

Our goal is developing a survival model for predicting LOS in ICU based on patients’ characteristics upon arrival in intensive care unit (ICU). The study includes 25,170 ICU admissions that occurred between 2014 and 2020, with LOS ranging from 1 to 28 days, leading to multiple tied events at each time point. Three competing events observed in data: discharge to home ($J = 1$, 69.0%), transfer to another medical facility ($J = 2$, 21.4%), and in-hospital death ($J = 3$, 6.1%). Patients who left the ICU against medical advice (1.0%) were considered censored, and administrative censoring was imposed for patients hospitalized for more than 28 days (2.5%). The analysis includes 36 covariates in total, for each patient. For a detailed description of the data, the reader is referred to Section 4 of Meir and Gorfine [2023].

Three estimation procedures were considered, Lee et al. [2018], Meir and Gorfine [2023] without regularization, and Meir and Gorfine [2023] with lasso. Lasso regression was performed with the best set of the tuning parameters $\eta_j$, $j = 1, 2, 3$, based on the global AUC and 4-fold CV. The following is the relevant code:

```python
lee_fitter = DataExpansionFitter()
lee_fitter.fit(df=patients_df)
two_step_fitter = TwoStagesFitter()
two_step_fitter.fit(df=patients_df)

penalizers = np.exp(np.arange(-12, -0.9, step=1))
penalty_cv_search = PenaltyGridSearchCV()
gauc_cv_results = penalty_cv_search.cross_validate(full_df=patients_df, l1_ratio=1,
penalizers=penalizers, n_splits=4)
chosen_set = gauc_cv_results['Mean'].idxmax()
```

The results are shown in Tables 5-7 and Figures 9-10. Evidently, the estimated values of $\alpha_{jt}$ and $\beta_j$ based on Lee et al. [2018] and Meir and Gorfine [2023] without regularization are similar. Figure 10 shows the number of non-zero coefficients, the lasso regularization path, and $\hat{\text{AUC}}_j(t)$ for each event type. The selected values of $\log \eta_j$, $j = 1, 2, 3$, were -5, -9 and -11, respectively. For the first 14 days of hospitalization $\hat{\text{AUC}}_j(t)$ were higher than that of later times. This may be due to several reasons. Firstly, the number of observed events at early times are higher. Second, short LOS can be a consequence of the severity of illness, with short-term in-hospital death occurring for severe
cases and short-term discharge for mild cases, making them easier to identify. Lastly, as treatment progresses, the effect of the initial condition may decreases while the treatment effect increases, making it difficult to distinguish between events occurring during later times based on the covariates measured upon admission. The integrated cause-specific AUCs were $\hat{AUC}_1 = 0.642$ (SD=0.002) (the SDs in parentheses are based on the 4 folds and do not take into account the variability due to the model estimation), $\hat{AUC}_2 = 0.655$ (SD=0.012), and $\hat{AUC}_3 = 0.740$ (SD=0.006), with a global $\hat{AUC} = 0.651$ (SD=0.003). The integrated cause-specific BS were $\hat{BS}_1 = 0.105$ (SD=0.002), $\hat{BS}_2 = 0.042$ (SD=0.001), and $\hat{BS}_3 = 0.010$ (SD=0.001), with a global BS of $\hat{BS} = 0.085$ (SD=0.001).

We also evaluate the performance of the non-regularized regression based on the two-stage estimation approach

```python
cross_validator_null = TwoStagesCV()
cross_validator_null.cross_validate(full_df=patients_df, n_splits=4)
```

and the global AUCs of the two-stage approach without lasso was $\hat{AUC} = 0.649$ (SD=0.003). Evidently, the global AUCs of the without and with lasso penalty were highly similar. However, by adding lasso regularization, the number of predictors for each event type is reduced.

6 Concluding Remarks

Discrete-time survival analysis with competing-risks is often required in practical settings. In the friendly package PyDTS we implemented two estimation procedures, that of Lee et al. [2018] and the faster algorithm of Meir and Gorfine [2023] which breaks the optimization procedure into a sequence of smaller problems. The faster algorithm could be highly useful in large modern datasets with tens of thousands observations and thousands covariates. PyDTS also provides useful predictions for new set of observations and useful tools for CV model evaluation, grid-search for parameters tuning, and plots. We expect PyDTS to be adopted by Python users and to be further improved by comments and contributions from the Python community.

PyDTS is an open source Python package which implements tools for discrete-time survival analysis with competing risks. The code is available at https://github.com/tomer1812/pydts [Meir et al., 2022b] under GNU GPLv3. Documentation, with details about main functionalities, API, installation and usage examples, is available at https://tomer1812.github.io/pydts/ [Meir et al., 2022a]. The package was developed following best practices of Python programming, automated testing was added for stability, Github Issues can be opened by any user for maintainability and open source community contributions are available for ongoing improvement.
The package is published using the Python Package Index (PyPI), can be installed (using the “pip” installer) and used with a few simple lines of code, as shown in the Quick Start section of the documentation. Yet, it is flexible enough to support more advanced pre-processing and fitting options. Based on available Python packages (NumPy of Harris et al. [2020], Pandas of Reback et al. [2020], Scipy of Virtanen et al. [2020], Scikit-survival of Pölsterl [2020], Lifelines of Davidson-Pilon [2019], and Statsmodels of Seabold and Perktold [2010]), PyDTS package implements DataExpansionFitter which is the estimation procedure of Lee et al. [2018] and TwoStagesFitter which is the estimation procedure of Meir and Gorfine [2023].

**Data and Code Availability Statement**

Simulated data and code under the GNU GPLv3 are available at the package repository https://github.com/tomer1812/pydts

The MIMIC dataset is accessible at https://physionet.org/content/mimiciv/2.0/ and subjected to PhysioNet credentials.

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Table 1: Original and expanded datasets with $M = 2$ competing events (Lee et al. [2018])

| Original Data | Expanded Data |
|---------------|---------------|
| $i$ | $X_i$ | $\delta_i$ | $Z_i$ | $\tilde{X}_{1it}$ | $\delta_{1it}$ | $\delta_{2it}$ | $1 - \delta_{1it} - \delta_{2it}$ | $Z_i$ |
| 1 | 2 | 1 | $Z_1$ | 1 | 1 | 0 | 0 | 1 | $Z_1$ |
| 1 | 2 | 1 | 0 | 0 | 0 | $Z_1$ |
| 2 | 3 | 2 | $Z_2$ | 1 | 1 | 0 | 0 | 1 | $Z_2$ |
| 2 | 2 | 0 | 0 | 1 | $Z_2$ |
| 2 | 3 | 0 | 1 | 0 | $Z_2$ |
| 3 | 3 | 0 | $Z_3$ | 3 | 1 | 0 | 0 | 1 | $Z_3$ |
| 3 | 2 | 0 | 0 | 1 | $Z_3$ |
| 3 | 3 | 0 | 0 | 1 | $Z_3$ |

Table 2: First five rows of a dataframe

| ID | $Z_1$ | $Z_2$ | $Z_3$ | T | C | X | J |
|----|-------|-------|-------|---|---|---|---|
| 0  | 1     | 97.68 | 4     | 1 | 8 | 1 | 2 |
| 1  | 1     | 67.28 | 10    | 8 | 8 | 8 | 0 |
| 2  | 1     | 72.61 | 2     | 3 | 7 | 3 | 2 |
| 3  | 1     | 80.94 | 6     | 8 | 8 | 8 | 0 |
| 4  | 0     | 63.29 | 5     | 8 | 8 | 8 | 0 |

Table 3: Results of one simulated dataset, $n = 50,000$: Estimates of $\beta_j$.

| $\beta_{jk}$ | True Estimate | SE | Lee et al. Estimate | SE | two-step Estimate | SE |
|---------------|---------------|----|---------------------|----|-------------------|----|
| $\beta_{11}$ | 0.223         | 0.026 | 0.193              | 0.026 | 0.188              | 0.025 |
| $\beta_{12}$ | -1.099        | -0.026 | -1.131             | -0.026 | -1.101             | 0.026 |
| $\beta_{13}$ | -1.099        | -0.026 | -1.124             | -0.026 | -1.093             | 0.026 |
| $\beta_{14}$ | -0.916        | 0.026 | -0.899             | 0.026 | -0.875             | 0.025 |
| $\beta_{15}$ | -0.693        | 0.026 | -0.672             | 0.026 | -0.653             | 0.025 |
| $\beta_{21}$ | -0.000        | 0.038 | 0.041              | 0.038 | 0.040              | 0.038 |
| $\beta_{22}$ | -1.099        | 0.039 | -1.113             | 0.039 | -1.100             | 0.039 |
| $\beta_{23}$ | -1.386        | 0.040 | -1.426             | 0.040 | -1.410             | 0.039 |
| $\beta_{24}$ | -1.099        | 0.039 | -1.111             | 0.039 | -1.098             | 0.039 |
| $\beta_{25}$ | -0.693        | 0.039 | -0.662             | 0.039 | -0.655             | 0.038 |
Table 4: Simulation results based on 100 repetitions: Estimates of $\beta_{jk}$ and their standard errors.

| $\beta_{jk}$ | True Estimate | True SE | Lee et al. Estimate | Lee et al. SE | two-step Estimate | two-step SE |
|--------------|---------------|---------|---------------------|--------------|-------------------|-------------|
| $\beta_{11}$ | 0.223         | 0.028   | 0.216               | 0.027        |                   |             |
| $\beta_{12}$ | -1.099        | 0.033   | -1.071              | 0.032        |                   |             |
| $\beta_{13}$ | -1.099        | 0.029   | -1.069              | 0.028        |                   |             |
| $\beta_{14}$ | -0.916        | 0.030   | -0.892              | 0.029        |                   |             |
| $\beta_{15}$ | -0.693        | 0.029   | -0.672              | 0.028        |                   |             |
| $\beta_{21}$ | -0.000        | 0.044   | 0.002               | 0.044        |                   |             |
| $\beta_{22}$ | -1.099        | 0.038   | -1.087              | 0.038        |                   |             |
| $\beta_{23}$ | -1.386        | 0.044   | -1.363              | 0.044        |                   |             |
| $\beta_{24}$ | -1.099        | 0.042   | -1.089              | 0.042        |                   |             |
| $\beta_{25}$ | -0.693        | 0.045   | -0.684              | 0.044        |                   |             |
Table 5: MIMIC dataset - LOS analysis: Estimated regression coefficients of event type discharge to home, $J = 1$.

|                          | Lee et al. Estimate (SE) | Two-Step Estimate (SE) | Two-Step & LASSO Estimate (SE) |
|--------------------------|--------------------------|------------------------|---------------------------------|
| **Admissions Number**    |                          |                        |                                 |
| 2                        | 0.000 (0.024)            | 0.003 (0.022)          | 0.000 (0.000)                   |
| 3+                       | -0.032 (0.023)           | -0.027 (0.022)         | 0.000 (0.000)                   |
| **Anion Gap Abnormal**   | -0.137 (0.032)           | -0.128 (0.030)         | 0.000 (0.000)                   |
| **Bicarbonate Abnormal** | -0.208 (0.021)           | -0.194 (0.020)         | -0.119 (0.019)                  |
| **Calcium Total Abnormal** | -0.291 (0.020)       | -0.270 (0.019)         | -0.190 (0.018)                  |
| **Chloride Abnormal**    | -0.148 (0.024)           | -0.137 (0.023)         | -0.071 (0.021)                  |
| **Creatinine Abnormal**  | -0.103 (0.024)           | -0.098 (0.023)         | -0.072 (0.021)                  |
| **Direct Emergency**     | Yes                      | -0.011 (0.026)         | -0.014 (0.024)                  |
| **Ethnicity**            |                          |                        |                                 |
| Black                    | 0.006 (0.046)            | 0.009 (0.042)          | 0.000 (0.000)                   |
| Hispanic                 | 0.132 (0.053)            | 0.120 (0.048)          | 0.000 (0.000)                   |
| Other                    | -0.162 (0.051)           | -0.146 (0.047)         | 0.000 (0.000)                   |
| White                    | -0.031 (0.041)           | -0.026 (0.038)         | 0.000 (0.000)                   |
| **Glucose Abnormal**     | -0.215 (0.018)           | -0.192 (0.016)         | -0.088 (0.016)                  |
| **Hematocrit Abnormal**  | -0.042 (0.032)           | -0.037 (0.029)         | -0.042 (0.029)                  |
| **Hemoglobin Abnormal**  | -0.080 (0.033)           | -0.071 (0.030)         | -0.081 (0.030)                  |
| **Insurance**            |                          |                        |                                 |
| Medicare                 | 0.138 (0.039)            | 0.125 (0.036)          | 0.000 (0.000)                   |
| Other                    | 0.219 (0.036)            | 0.200 (0.033)          | 0.030 (0.016)                   |
| **MCH Abnormal**         | -0.002 (0.023)           | -0.002 (0.022)         | 0.000 (0.000)                   |
| **MCHC Abnormal**        | -0.128 (0.019)           | -0.116 (0.018)         | -0.003 (0.017)                  |
| **MCV Abnormal**         | -0.048 (0.026)           | -0.045 (0.024)         | 0.000 (0.000)                   |
| **Magnesium Abnormal**   | -0.080 (0.030)           | -0.074 (0.028)         | 0.000 (0.000)                   |
| **Marital Status**       |                          |                        |                                 |
| Married                  | 0.224 (0.032)            | 0.205 (0.030)          | 0.093 (0.016)                   |
| Single                   | -0.087 (0.033)           | -0.079 (0.031)         | 0.000 (0.000)                   |
| Widowed                  | 0.026 (0.040)            | 0.020 (0.037)          | 0.000 (0.000)                   |
| **Night Admission**      |                          |                        |                                 |
| Yes                      | 0.081 (0.017)            | 0.075 (0.016)          | 0.000 (0.000)                   |
| **Phosphate Abnormal**   | -0.052 (0.019)           | -0.048 (0.018)         | 0.000 (0.000)                   |
| **Platelet Count Abnormal** | -0.068 (0.019)       | -0.062 (0.018)         | 0.000 (0.000)                   |
| **Potassium Abnormal**   | -0.103 (0.032)           | -0.095 (0.030)         | 0.000 (0.000)                   |
| **RDW Abnormal**         | -0.327 (0.021)           | -0.308 (0.020)         | -0.271 (0.019)                  |
| **Recent Admission**     | Yes                      | -0.262 (0.035)         | -0.247 (0.033)                  |
| **Red Blood Cells Abnormal** | -0.089 (0.027)       | -0.078 (0.024)         | -0.024 (0.025)                  |
| **Sex**                  | Female                   | -0.007 (0.018)         | -0.006 (0.016)                  |
| **Sodium Abnormal**      | -0.312 (0.030)           | -0.297 (0.029)         | -0.142 (0.026)                  |
| **Standardized Age**     | -0.260 (0.011)           | -0.234 (0.010)         | -0.162 (0.009)                  |
| **Urea Nitrogen Abnormal** | -0.148 (0.022)       | -0.139 (0.020)         | -0.136 (0.020)                  |
| **White Blood Cells**    | Abnormal                 | -0.276 (0.018)         | -0.252 (0.016)                  | -0.159 (0.016) |
Table 6: MIMIC dataset - LOS analysis: Estimated regression coefficients of event type discharged to another facility, \( J = 2 \).

|                                | Lee et al. Estimate (SE) | Two-Step Estimate (SE) | Two-Step & LASSO Estimate (SE) |
|--------------------------------|--------------------------|------------------------|-------------------------------|
| **Admissions Number**          |                          |                        |                               |
| 2                              | 0.108 (0.041)            | 0.107 (0.040)          | 0.087 (0.038)                 |
| 3+                             | 0.194 (0.037)            | 0.190 (0.036)          | 0.169 (0.034)                 |
| **Anion Gap**                  |                          |                        |                               |
| Abnormal                       | -0.006 (0.048)           | -0.006 (0.047)         | **0.000 (0.002)**             |
| **Bicarbonate**                |                          |                        |                               |
| Abnormal                       | -0.121 (0.033)           | -0.117 (0.032)         | -0.110 (0.032)                |
| **Calcium Total**              |                          |                        |                               |
| Abnormal                       | -0.098 (0.031)           | -0.094 (0.031)         | -0.088 (0.030)                |
| **Chloride**                   |                          |                        |                               |
| Abnormal                       | 0.016 (0.036)            | 0.015 (0.035)          | **0.000 (0.002)**             |
| **Creatinine**                 |                          |                        |                               |
| Abnormal                       | -0.199 (0.036)           | -0.191 (0.035)         | -0.173 (0.035)                |
| **Direct Emergency**           |                          |                        |                               |
| Yes                            | -0.373 (0.052)           | -0.363 (0.050)         | -0.345 (0.050)                |
| **Ethnicity**                  |                          |                        |                               |
| Black                          | 0.084 (0.090)            | 0.079 (0.088)          | 0.028 (0.086)                 |
| Hispanic                       | -0.068 (0.111)           | -0.070 (0.108)         | -0.088 (0.106)                |
| Other                          | 0.026 (0.099)            | 0.022 (0.097)          | -0.006 (0.095)                |
| White                          | 0.144 (0.082)            | 0.138 (0.081)          | 0.094 (0.079)                 |
| **Glucose**                    |                          |                        |                               |
| Abnormal                       | -0.138 (0.031)           | -0.132 (0.030)         | -0.126 (0.030)                |
| **Hematocrit**                 |                          |                        |                               |
| Abnormal                       | 0.038 (0.057)            | 0.039 (0.055)          | 0.032 (0.055)                 |
| **Hemoglobin**                 |                          |                        |                               |
| Abnormal                       | 0.018 (0.062)            | 0.015 (0.060)          | 0.005 (0.059)                 |
| **Insurance**                  |                          |                        |                               |
| Medicare                       | 0.237 (0.075)            | 0.230 (0.074)          | 0.238 (0.073)                 |
| Other                          | -0.094 (0.074)           | -0.091 (0.072)         | -0.081 (0.072)                |
| **MCH**                        |                          |                        |                               |
| Abnormal                       | 0.042 (0.038)            | 0.040 (0.037)          | 0.019 (0.031)                 |
| **MCHC**                       |                          |                        |                               |
| Abnormal                       | -0.010 (0.031)           | -0.011 (0.030)         | **0.000 (0.003)**             |
| **MCV**                        |                          |                        |                               |
| Abnormal                       | -0.020 (0.041)           | -0.019 (0.039)         | **0.000 (0.003)**             |
| **Magnesium**                  |                          |                        |                               |
| Abnormal                       | -0.039 (0.048)           | -0.038 (0.047)         | -0.025 (0.046)                |
| **Marital Status**             |                          |                        |                               |
| Married                        | -0.254 (0.054)           | -0.249 (0.053)         | -0.262 (0.052)                |
| Single                         | 0.209 (0.054)            | 0.200 (0.053)          | 0.176 (0.052)                 |
| Widowed                        | 0.175 (0.058)            | 0.163 (0.056)          | 0.149 (0.056)                 |
| **Night Admission**            |                          |                        |                               |
| Yes                            | 0.056 (0.029)            | 0.054 (0.028)          | 0.047 (0.028)                 |
| **Phosphate**                  |                          |                        |                               |
| Abnormal                       | -0.042 (0.033)           | -0.040 (0.032)         | -0.034 (0.031)                |
| **Platelet Count**             |                          |                        |                               |
| Abnormal                       | -0.130 (0.032)           | -0.125 (0.031)         | -0.118 (0.031)                |
| **Potassium**                  |                          |                        |                               |
| Abnormal                       | 0.042 (0.048)            | 0.042 (0.047)          | 0.023 (0.047)                 |
| **RDW**                        |                          |                        |                               |
| Abnormal                       | -0.107 (0.033)           | -0.104 (0.032)         | -0.093 (0.031)                |
| **Recent Admission**           |                          |                        |                               |
| Yes                            | -0.021 (0.051)           | -0.023 (0.049)         | **0.000 (0.004)**             |
| **Red Blood Cells**            |                          |                        |                               |
| Abnormal                       | 0.083 (0.052)            | 0.079 (0.050)          | 0.073 (0.050)                 |
| **Sex**                        |                          |                        |                               |
| Female                         | 0.090 (0.031)            | 0.088 (0.030)          | 0.078 (0.030)                 |
| **Sodium**                     |                          |                        |                               |
| Abnormal                       | -0.056 (0.042)           | -0.056 (0.041)         | -0.039 (0.038)                |
| **Standardized Age**           |                          |                        |                               |
| Abnormal                       | 0.536 (0.021)            | 0.525 (0.021)          | 0.519 (0.021)                 |
| **Urea Nitrogen**              |                          |                        |                               |
| Abnormal                       | 0.100 (0.035)            | 0.095 (0.034)          | 0.077 (0.034)                 |
| **White Blood Cells**          |                          |                        |                               |
| Abnormal                       | -0.107 (0.029)           | -0.103 (0.028)         | -0.099 (0.028)                |
Table 7: MIMIC dataset - LOS analysis: Estimated regression coefficients of event type in-hospital death, $J = 3$.

| Event Type                                      | Lee et al. Estimate (SE) | Two-Step Estimate (SE) | Two-Step & LASSO Estimate (SE) |
|------------------------------------------------|--------------------------|------------------------|-------------------------------|
| Admissions Number                               |                          |                        |                               |
| 2                                              | 0.147 (0.074)            | 0.147 (0.073)          | 0.140 (0.074)                 |
| 3+                                             | 0.142 (0.069)            | 0.140 (0.068)          | 0.134 (0.068)                 |
| Anion Gap Abnormal                              | 0.582 (0.064)            | 0.573 (0.064)          | 0.571 (0.064)                 |
| Bicarbonate Abnormal                            | 0.543 (0.056)            | 0.537 (0.056)          | 0.535 (0.056)                 |
| Calcium Total Abnormal                          | 0.204 (0.054)            | 0.204 (0.054)          | 0.203 (0.054)                 |
| Chloride Abnormal                               | 0.147 (0.059)            | 0.143 (0.058)          | 0.142 (0.058)                 |
| Creatinine Abnormal                             | 0.273 (0.067)            | 0.271 (0.067)          | 0.271 (0.067)                 |
| Direct Emergency                                | Yes                      | -0.318 (0.096)         | -0.311 (0.095)                |
| Ethnicity Abnormal                              | Black                    | -0.236 (0.140)         | -0.235 (0.139)                |
| Hispanic                                        | -0.395 (0.183)           | -0.393 (0.181)         | -0.351 (0.181)                |
| Other                                           | 0.145 (0.147)            | 0.133 (0.145)          | 0.155 (0.146)                 |
| White                                           | -0.156 (0.123)           | -0.157 (0.122)         | -0.130 (0.123)                |
| Glucose Abnormal                                | 0.215 (0.064)            | 0.212 (0.063)          | 0.208 (0.063)                 |
| Hematocrit Abnormal                             | -0.198 (0.108)           | -0.194 (0.107)         | -0.165 (0.108)                |
| Hemoglobin Abnormal                             | 0.024 (0.122)            | 0.023 (0.121)          | 0.003 (0.121)                 |
| Insurance Abnormal                              | Medicare                 | -0.224 (0.136)         | -0.225 (0.135)                |
| Other                                           | -0.242 (0.133)           | -0.240 (0.132)         | -0.188 (0.135)                |
| MCH Abnormal                                    | -0.066 (0.070)           | -0.066 (0.069)         | -0.057 (0.069)                |
| MCHC Abnormal                                   | 0.027 (0.056)            | 0.029 (0.055)          | 0.027 (0.055)                 |
| MCV Abnormal                                    | 0.060 (0.072)            | 0.061 (0.071)          | 0.055 (0.071)                 |
| Magnesium Abnormal                              | 0.329 (0.073)            | 0.324 (0.072)          | 0.320 (0.072)                 |
| Marital Status                                  | Married                  | 0.156 (0.102)          | 0.154 (0.101)                 |
| Single                                          | 0.026 (0.107)            | 0.027 (0.106)          | 0.000 (0.008)                 |
| Widowed                                         | 0.047 (0.115)            | 0.048 (0.114)          | 0.020 (0.084)                 |
| Night Admission                                 | Yes                      | -0.096 (0.053)         | -0.093 (0.052)                |
| Phosphate Abnormal                              | 0.178 (0.056)            | 0.176 (0.055)          | 0.174 (0.055)                 |
| Platelet Count Abnormal                         | 0.235 (0.054)            | 0.232 (0.054)          | 0.229 (0.054)                 |
| Potassium Abnormal                              | 0.227 (0.072)            | 0.221 (0.071)          | 0.221 (0.071)                 |
| RDW Abnormal                                    | 0.492 (0.058)            | 0.486 (0.058)          | 0.483 (0.058)                 |
| Recent Admission                                | Yes                      | 0.250 (0.083)          | 0.242 (0.082)                 |
| Red Blood Cells Abnormal                        | 0.142 (0.105)            | 0.140 (0.104)          | 0.130 (0.104)                 |
| Sex Female                                      | -0.011 (0.057)           | -0.008 (0.057)         | -0.005 (0.057)                |
| Sodium Abnormal                                 | 0.276 (0.064)            | 0.270 (0.063)          | 0.268 (0.063)                 |
| Standardized Age                                | 0.580 (0.041)            | 0.574 (0.040)          | 0.568 (0.040)                 |
| Urea Nitrogen Abnormal                          | 0.141 (0.070)            | 0.141 (0.070)          | 0.141 (0.070)                 |
| White Blood Cells Abnormal                      | 0.579 (0.056)            | 0.571 (0.056)          | 0.568 (0.055)                 |
Figure 1: Sampled covariates. 

a. The observed distribution of $Z_1$.

b. The observed distribution of $Z_2|Z_1$.

c. The distribution of $Z_3$.

Figure 2: Events and censoring distribution of the simulated dataset with $n = 50,000$ observations, $M = 2$ event types, and $d = 30$ time points. 

$\alpha_{1t} = -1 - 0.3 \log t$, $\alpha_{2t} = -1.75 - 0.15 \log(t)$,

$\beta_1^T = -(\log 0.8, \log 3, \log 3, \log 2.5, \log 2)$,

$\beta_2^T = -(\log 1, \log 3, \log 4, \log 3, \log 2)$ and censoring times are sampled from Uniform$\{1, \ldots, d + 1\}$. 
Figure 3: Results of one simulated dataset, \( n = 50,000 \): Estimation results of Lee et al. [2018] and the two-step procedure of Meir and Gorine [2023] along with the true parameters’ values. **a:** Results of \( \alpha_{jt} \). True values of \( \alpha_{1t} \) are in dashed blue line, estimates of Lee et al. and the two-step algorithm are in light blue circles and blue stars, respectively. Similarly, true values and estimates of \( \alpha_{2t} \) are in green scale. Number of observed events at each time \( t \) is shown in red and brown bars. **b:** Results of \( \beta_j \). True values of \( \beta_1 \) are in light blue bars, estimates of Lee et al. and the two-step algorithm are in light blue right arrowhead and blue right triangle, respectively. Similarly, true values and estimates of \( \beta_2 \) are in green scale.
Figure 4: Predictions for three individuals of the test dataset: ID=0 (blue), ID=1 (orange), and ID=2 (green). 

- **a.** Estimated hazard function of event type $j = 1$, $\hat{\lambda}_1(t)$. 
- **b.** Estimated hazard function of event type $j = 2$, $\hat{\lambda}_2(t|Z)$. 
- **c.** Estimated probability of event type $j = 1$, $\hat{\Pr}(T = t, J = 1|Z)$. 
- **d.** Estimated probability for event type $j = 2$, $\hat{\Pr}(T = t, J = 2|Z)$. 
- **e.** Estimated CIF of event type $j = 1$, $\hat{F}_1(t|Z)$. 
- **f.** Estimated CIF of event type $j = 2$, $\hat{F}_2(t|Z)$. 
- **g.** Estimated overall survival function, $\hat{S}(t|Z)$. 

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Figure 5: Simulation results of [Lee et al. 2018], the two-step algorithm of [Meir and Gorfine 2023], the true parameters’ values based on 100 repetitions. **a:** Results of $\alpha_{jt}$. True values of $\alpha_{1t}$ are in dashed blue line, estimates of Lee et al. and the two-step algorithm are in light blue circles and blue stars, respectively. Similarly, true values and estimates of $\alpha_{2t}$ are in green scale. Number of observed events at each time $t$ is shown in red and brown bars. **b:** Results of $\beta_{j}$. True values of $\beta_{1}$ are in light blue bars, estimates of Lee et al. and the two-step algorithm are in light blue right arrowhead and blue right triangle, respectively. Similarly, true values and estimates of $\beta_{2}$ are in green scale.

Figure 6: Simulation results based on 100 repetitions: standard errors of Lee et al. versus that of the two-step algorithm of [Meir and Gorfine 2023]. **a:** Standard errors of $\hat{\alpha}_{1t}$. **b:** Standard errors of $\hat{\alpha}_{2t}$.
Figure 7: Simulation results based on 10 repetitions for each value of $d$: box-plots of computation times of Lee et al. and the two-step algorithm.
Figure 8: A simulated dataset: $n = 1,000$ observations, $M = 2$ failure type, $\alpha_{1t} = -1 - 0.3 \log t$, $\alpha_{2t} = -1.75 - 0.15 \log t$, $\beta_{1t}^T = -(\log 0.8, \log 3, \log 3, \log 2.5, \log 2)$, $\beta_{2t}^T = -(\log 1, \log 3, \log 4, \log 3, \log 2)$ and $C_i \sim \text{Uniform}\{1, \ldots, d + 1\}$. **a.** Original data with $d = 30$ possible event occurrence times. **b.** Regrouped data - days 21 and beyond were combined into one category of time named 21+.
Figure 9: MIMIC dataset - LOS analysis. Results of estimated $\alpha_{jt}$ by the method of Lee et al. (circle), the two-step approach of Meir and Gorfine [2023] with no regularization (star) and with lasso (left triangular). Numbers of observed events are shown in blue bars for home discharge ($j = 1$), in green bars for further treatment ($j = 2$), and in red bars for in-hospital death ($j = 3$). Lasso estimates are based on $\log \eta_1 = -5$, $\log \eta_2 = -9$ and $\log \eta_3 = -11$. 
Figure 10: MIMIC dataset - LOS analysis. Regularized regression with 4-fold CV. The selected values of $\eta_j$ are shown in dashed-dotted lines on panels a-f. a-c. Number of non-zero coefficients for $j = 1, 2, 3$. d-f. The estimated coefficients, as a function of $\eta_j$, $j = 1, 2, 3$. g-i. Mean (and SD bars) of the 4 folds $\hat{\text{AUC}}_j(t)$, $j = 1, 2, 3$, for the selected values $\log \eta_1 = -5$, $\log \eta_2 = -9$ and $\log \eta_3 = -11$. The number of observed events of each type is shown by bars.
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