PT-MESS: a Problem-Transformation approach for Multi-Event Survival analySis

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Outline

- Survival analysis
- PT-MESS
- Experiments
- Conclusions

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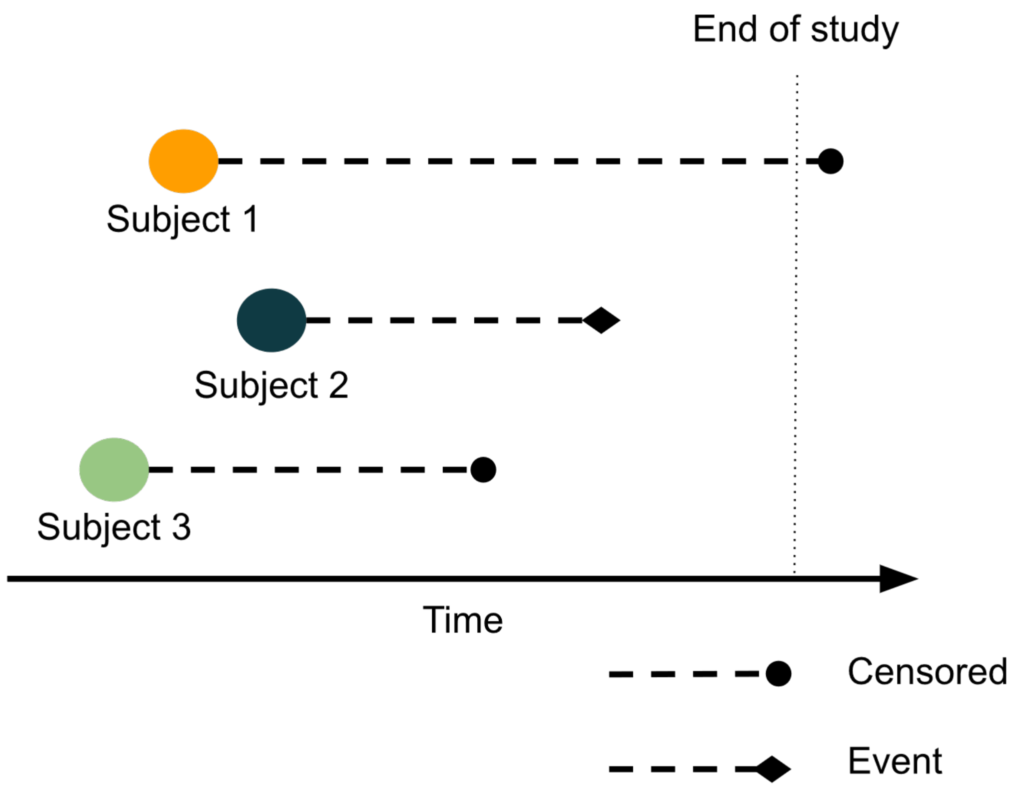
Survival analysis (SA)

- The value of interest is time to (one or multiple) event
- Part of the population does not experience the event during follow up
  - Right censoring:
    - have not (yet) experienced the relevant outcome
    - are lost to follow-up during the study period



Censoring as data scarcity

Patient	X	T (days)	δ
1	0.5	10	1
2	4.0	6	0
3	1.2	15	1
4	2.6	17	0
…	…	…	…

The patient does experience the event during follow-up after ten days

The patient is lost to follow-up after 17 days:

- The patient might experience the event after the follow-up
- The patient might never experience the event

Multi-event survival analysis

- Existing standard approaches mainly deal with specific settings namely (semi-) competing risk or repeated events
  - Assumptions regarding order and exclusivity of events
    - Competing: Time to death due to cardiac arrest or cancer
    - Semi-competing: Diagnose of ICU-AW, diagnose of sepsis or death
    - Repeated: Time to (re)admission to ICU

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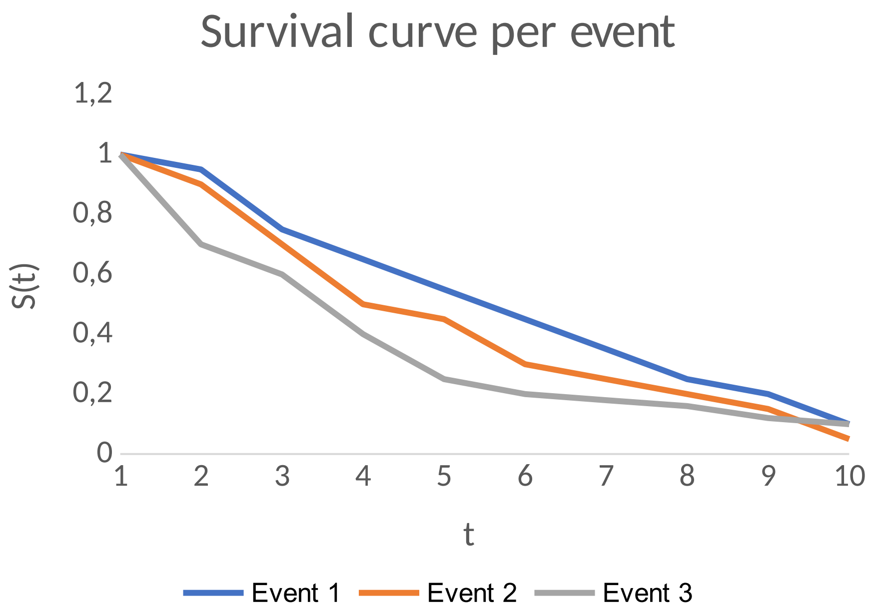
PT-MESS

- Encode multi-event SA as a multi-target regression task
  - Multi-target regression: regression with several targets
- Transform the typical SA outcome (time information + censoring into a single continuous value)
  - Take into account censored observations
  - Take into account survival distribution of the population in the encoding

Survival curve estimate

- We base our approach on the use of the Kaplan-Meier estimate of the survival curve per each event
  - Probability of not having experienced the event of interest *k* up to the time *t*
    - *d = number of events k at t*
    - *r = number of patients at risk of event k*
    - *at time t*

$$\hat{S}_k(t) = \prod_{j:t_j \leq t} \left(1 - \frac{d_k^{(j)}}{r_k^{(j)}}\right)$$



PT-MESS encoding

- Given observation *i* with time to event *k* (or censoring) encoded as o_k we define the following quantity:

$$\frac{\int_{t=0}^{o_k^{(i)}} \hat{s}_k}{\int_{t=0}^{\inf} \hat{s}_k}$$

Numerator → Restricted mean survival time, restricted to time o_k

Denominator → Expected time-to-event *k* for the entire population

- It expresses how early the observation *i* experience the event *k* (or is censored) w.r.t. the population distribution
  - Takes into account the censoring distribution

PT-MESS encoding cont'd

Multi-event SA

Patient	X	o_1	δ_1	o_2	δ_2
1	0.5	10	1	6	0
2	4.0	6	0	3	0
3	1.2	15	1	10	1
4	2.6	17	0	5	0
…	…	…	…	…	…

Multi-target regression

Patient	X	E_1	E_2
1	0.5	0.6	0.6
2	4.0	0.3	0.3
3	1.2	0.8	1
4	2.6	1	0.5
…	…	…	…

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Comparison methods

- Random Survival Forest-independent (RSFi)
- Inverse Probability of Censoring Weighting-independent (IPCWi)
  - Converts to binary classification
  - Removes censored data
- PT-MESS-independent (PT-MESSi)
  - Random Forest Regressor – variance as heuristic
- PT-MESS
  - Multi-target Random Forest Regressor

Datasets

Dataset (Setting)	Features	Instances	Events	Event (censoring rate)
MIMIC (S)	13801	3822	3	1 (.87), 2 (.91), and **3** (.92)
ADNI (S)	1917	1024	2	1 (0.82) and **2** (0.99)
CIBMTR (S)	9651	30	2	1 (0.82) and **2** (0.62)
ScrData (S)	2000	4	2	1 (0.34) and **2** (0.50)
Synthetic (I)	5000	15	2	1 (0.70) and 2 (0.71)

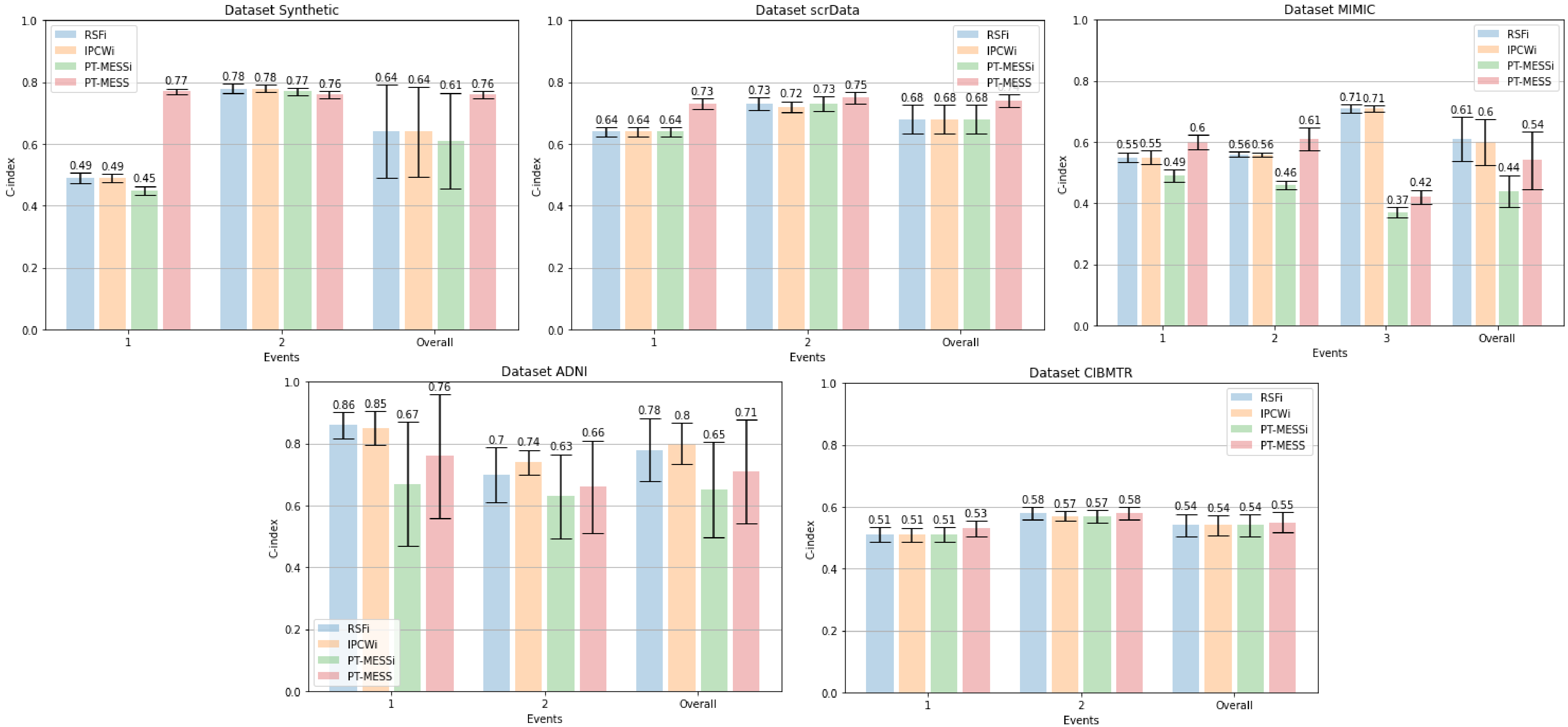
Characteristics of the datasets employed where semi-competing datasets are represented using (S) and independent as (I). The terminal event in each dataset highlighted in bold.

Evaluation metric

- Harrell’s concordance index (C-index)
  - Most used metric in SA
  - Estimates how well the predicted score ranks observations according to their true time-to-event
  - *i,l =1, …, N* pair of observations in the sample
  - r_i risk score, t_i observed time-to-event

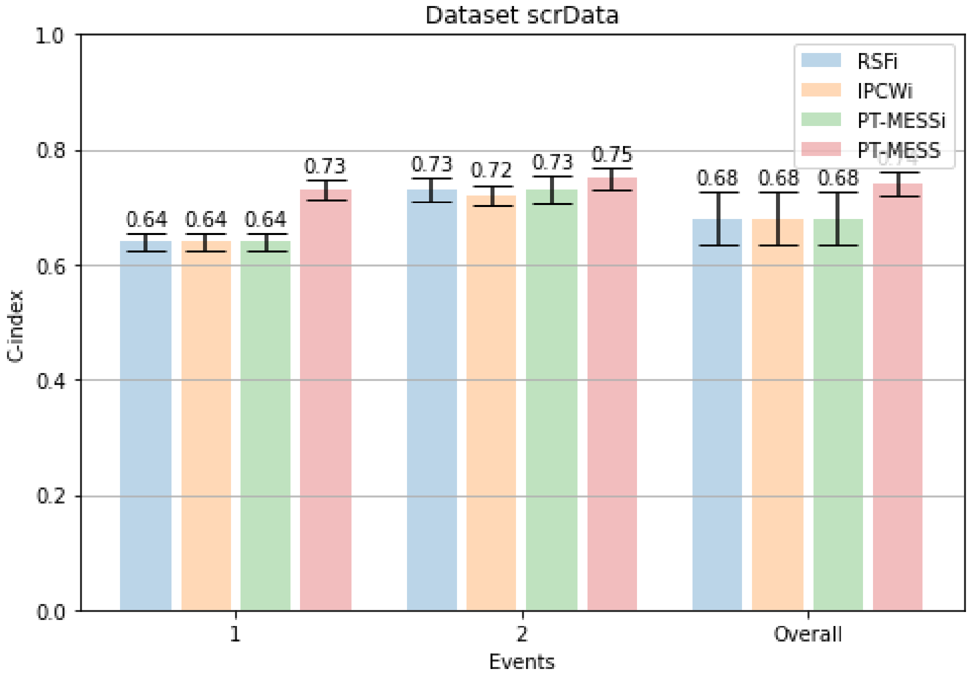
$$C = \frac{\sum_{i,l} I(T_i > T_l) \times I(r_l > r_i) \times \Delta_l}{\sum_{i,l} (T_i > T_l) \times \Delta_l}$$

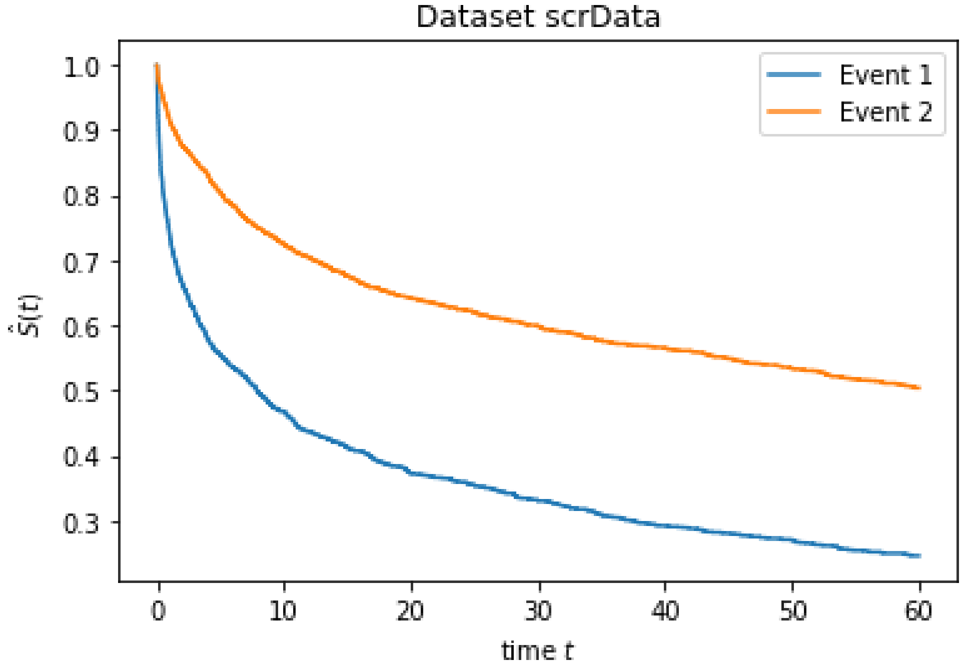
Results



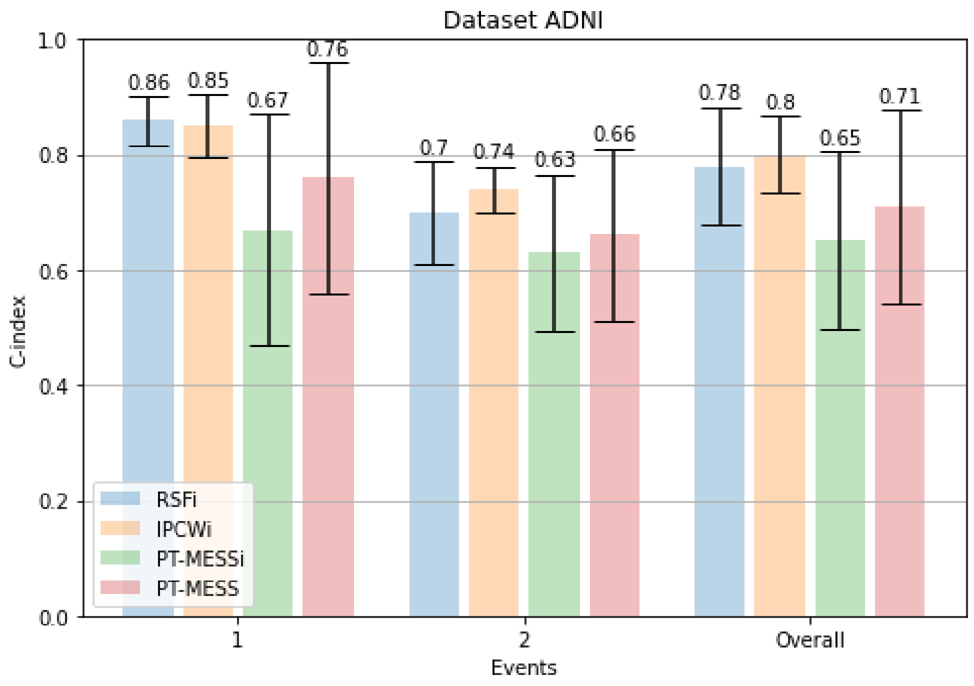
Dataset Synthetic
RSFi
IPCWi
PT-MESSi
PT-MESS
C-index
Events
1
2
Overall
0.49 0.49 0.45 0.77
0.78 0.78 0.77 0.76
0.64 0.64 0.61 0.76
Dataset scrData
0.64 0.64 0.64 0.73
0.73 0.72 0.73 0.75
0.68 0.68 0.68
Dataset MIMIC
3
0.55 0.55 0.49 0.6
0.56 0.56 0.46 0.61
0.71 0.71 0.37 0.42
0.61 0.6 0.44 0.54
Dataset ADNI
0.86 0.85 0.67 0.76
0.7 0.74 0.63 0.66
0.78 0.8 0.65 0.71
Dataset CIBMTR
0.51 0.51 0.51 0.53
0.58 0.57 0.57 0.58
0.54 0.54 0.54 0.55

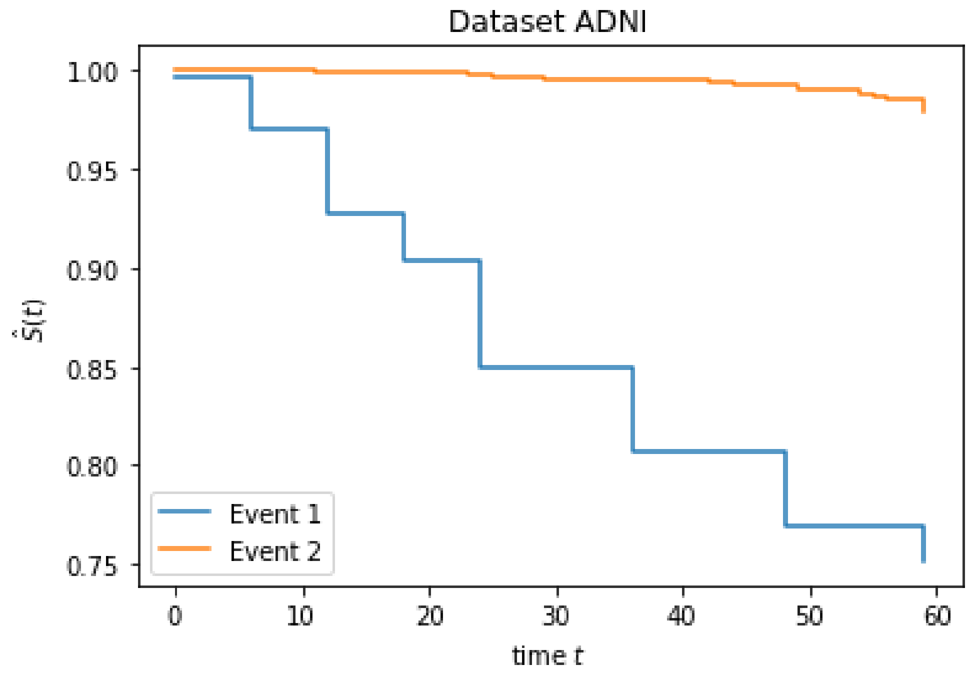
Events time distribution





Events time distribution





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Conclusions & future work

- New problem transformation approach to address multi-event survival analysis, where data scarcity is present as right-censored outcomes
- Decent results, especially when events are correlated according to Kaplan-meier
- Future work
  - Mathematical formulation instead of visual cues
  - Hybrid approaches, where global and local methods may be used in cooperation

Questions?