A Deep Learning Approach for Dynamic Survival Analysis with Competing Risks in CF

THOMAS W. V. DANIELS[1], MIHAELA VAN DER SCHAAR[2,3], R. ANDRES FLOTO[4], AND CHANGHEE LEE[3]

[1] UNIVERSITY HOSPITAL SOUTHAMPTON, [2] ALAN TURING INSTITUTE, [3] UCLA, [4] DEPARTMENT OF MEDICINE, UNIVERSITY OF CAMBRIDGE & ROYAL PAPWORTH HOSPITAL, CAMBRIDGE

This work was supported by the UK Cystic Fibrosis Trust.

OBJECTIVES

Our method is a deep learning approach:

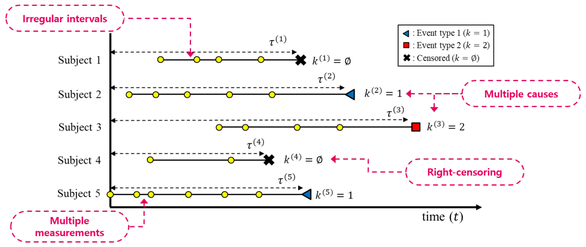
- **Predicts the cause-specific risk given** the history of observations over time.
- **Updates dynamic risk predictions** when new measurements are available.

Our method solves following challenges:

- **Competing risks**
- Longitudinal measurements with **irregular** time intervals

Longitudinal time-to-event data: $\mathcal{D} = \{(\mathcal{X}^i, \tau^i, k^i)\}$

- $\mathcal{X}$: history of longitudinal measurements
- τ: time-to-event including right-censoring
- k: event label (i.e., respiratory failure or other causes)



< Illustration of longitudinal time-to-event data >

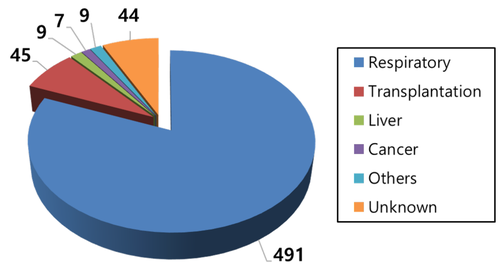
PATIENT COHORT

Inclusion criteria:

- Enrolled in the UK CF registry with annual follow-up data available from **January 1st, 2009** to **December 31st, 2015**.
- Adult patients who are over **18 years** of age.
- A total of **5,883 patients** are included.

Competing risks:

- Respiratory failure: **491 patients (8.35%)**
- Other causes: **114 patients (1.94%)**
- Right-censored: **5,278 patients (89.72%)**



< Death causes >

DISCRIMINATIVE PERFORMANCE

Time-dependent Concordance Index:

- Measure how well survival models **discriminate** the risks of patients
- The following table gives the performance given **the prediction time t age** and **the evaluation time Δt years**
  - Risk predictions are issued at the prediction time utilizing the measurements colletcted until that time.
  - Risk predictions are assessed at the evaluation time.

Algorithms		Respiratory Failure			Other Causes		
		$\Delta t = 1$	$\Delta t = 5$	$\Delta t = 10$	$\Delta t = 1$	$\Delta t = 5$	$\Delta t = 10$
$t = 30$	cs-Cox	0.748±0.10	0.748±0.09	0.748±0.09	0.604±0.13	0.602±0.13	0.602±0.13
	RSF	0.935±0.01	0.925±0.01	0.922±0.01	0.799±0.04	0.772±0.05	0.776±0.05
	JM	0.833±0.02	0.870±0.01	0.880±0.00	0.728±0.04	0.759±0.05	0.772±0.05
	Proposed	**0.954±0.00**	**0.947±0.01**	**0.948±0.01**	**0.920±0.02**	**0.914±0.02**	**0.916±0.02**
$t = 50$	cs-Cox	0.801±0.11	0.801±0.11	0.801±0.11	0.649±0.15	0.649±0.15	0.649±0.15
	RSF	0.895±0.01	0.889±0.02	0.889±0.02	0.731±0.06	0.763±0.03	0.758±0.04
	JM	0.878±0.02	0.889±0.01	0.890±0.01	0.784±0.04	0.791±0.04	0.791±0.04
	Proposed	**0.962±0.00**	**0.954±0.01**	**0.951±0.01**	**0.933±0.02**	**0.935±0.02**	**0.925±0.02**

- cs-Cox: Landmarking with cause-specific Cox model
- RSF: Landmarking with random survival forest
- JM: Joint models with linear mixture effect & Cox model

INFLUENTIAL COVARIATES

Influence of each covariate on the predicted risks:

- Different ranking of influential covariates are found for different causes.
- Well-known risk factors, e.g., **lung function scores** and **nutritional status**, are found to be influential.

Rank	Death Causes	
	Resp. Failure	Other Causes
1	IV ABX Days Hosp. (+1.65)	Colonic Stricture (+0.89)
2	**FEV1% Predicted (-0.85)**	IV ABX Days Hosp. (+0.79)
3	GI Bleed (non-var.) (-0.69)	Cancer (+0.44)
4	Gram-Negative (-0.68)	**FEV1% Predicted (-0.43)**
5	HD iBuprofen (-0.66)	Gram-Negative (-0.40)
6	O2 Continuous (+0.65)	GI Bleed (var.) (+0.39)
7	**BMI (-0.54)**	O2 Continuous (+0.38)
8	**Weight (-0.49)**	HD iBuprofen (-0.32)
9	GI Bleed (var.) (+0.46)	**BMI (-0.28)**
10	Oral Hypo. Agents (-0.44)	Pancreatitis (-0.27)

ABX: antibiotics

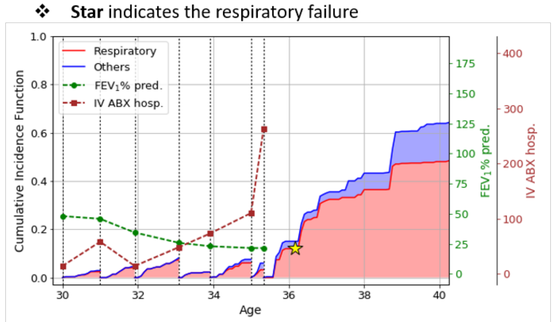
DYNAMIC SURVIVAL ANALYSIS

Our method is flexible:

- **Updates** the risk predictions **whenever new measurements are available**.

Patient died of respiratory failure

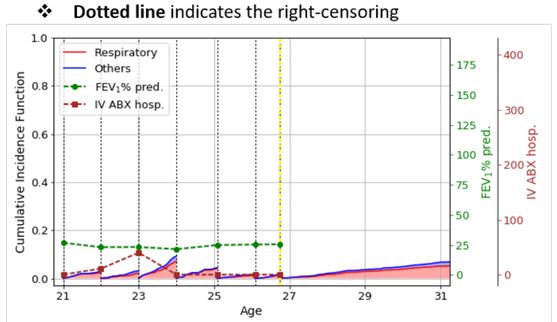
Star indicates the respiratory failure



- Increasing IV antibiotic days in hospital + decreasing FEV1% predicted
  → **relatively high risks**
- Sudden increase of IV antibiotic days (around age 35)
  → **steep increase in predicted risks**

Censored patient

Dotted line indicates the right-censoring



- Low IV antibiotic days in hospital + low but steady FEV1% predicted
  → **relatively low risks**

CONCLUSIONS

- Our results indicate that our approach for dynamic survival analysis with competing risks (on the basis of longitudinal data) signficantly improves discriminative performance.
- Different covariates that are influential when making risk predictions are found for different causes.
- Our method provides dynamic survival analysis that flexibly updates the risk predictions when new mearurements are collected.

We believe that:

- Our approach has the potential to provide clinicians and people with CF with individually tailored risk predictions that may replace the current score-based methods.
- These results need validation in other cohorts but could play a role in day-to-day clinical consultations.