University of Zurich[UZH]

Biostatistics STA490 Consulting Statistics

What are the Predictors of Long-term Work Participation in Patients with Cystic Fibrosis undergoing Lung Transplantation (LTx)

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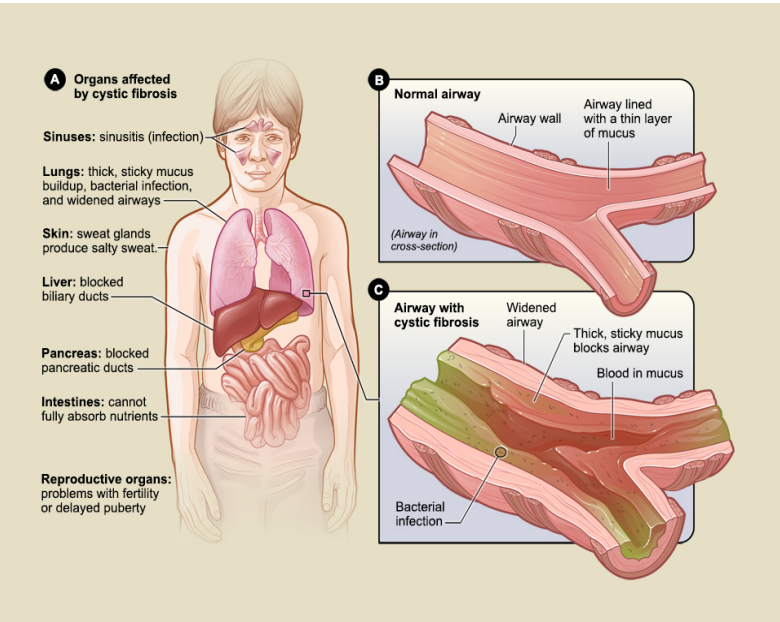
Overview

- Background
- Data Description
- Data Analysis
- Conclusion

Cystic Fibrosis

Mutations in both copies of the gene for CFTR protein



source: https://www.nhlbi.nih.gov

Complications

Cancers of the digestive tract

Diabetes

Heart failure

Kidney problems

Lung infections

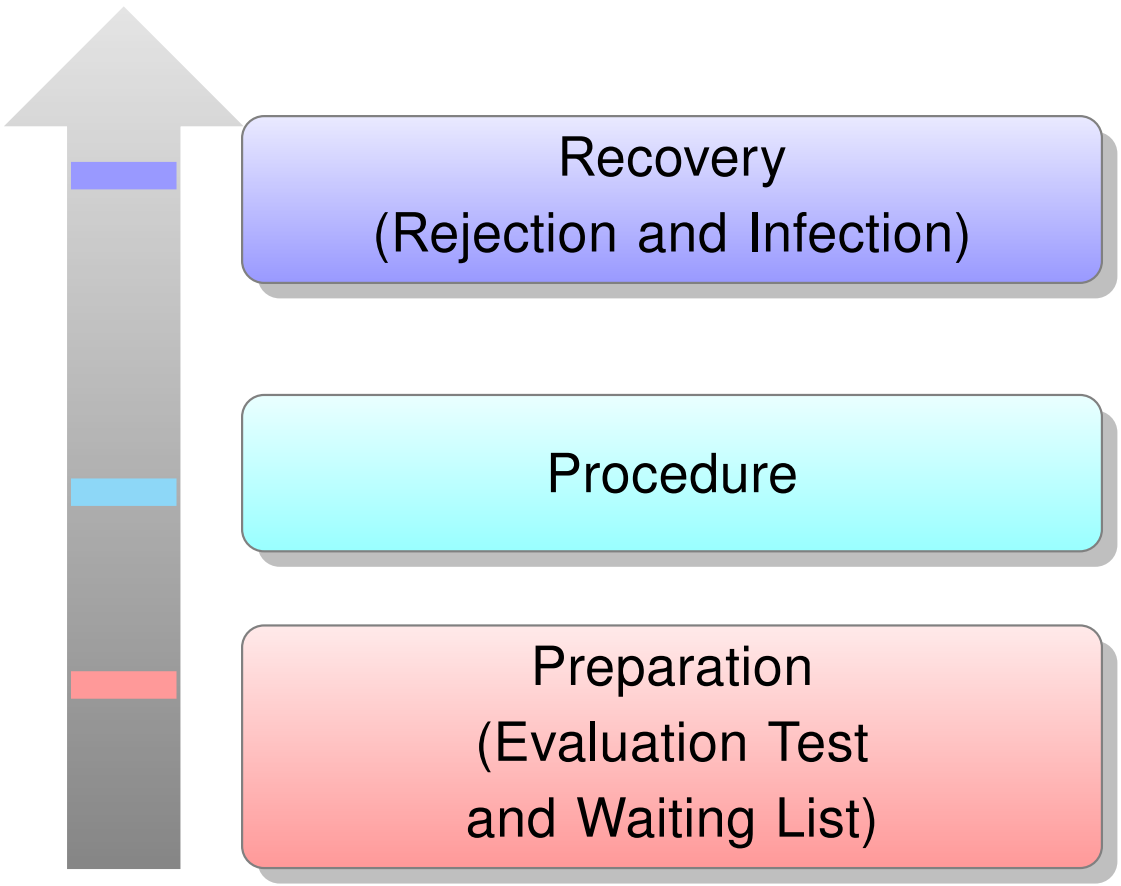
Treatments

Airway clearance techniques

Medicines

Surgery

Lung Transplantation



Study Aim

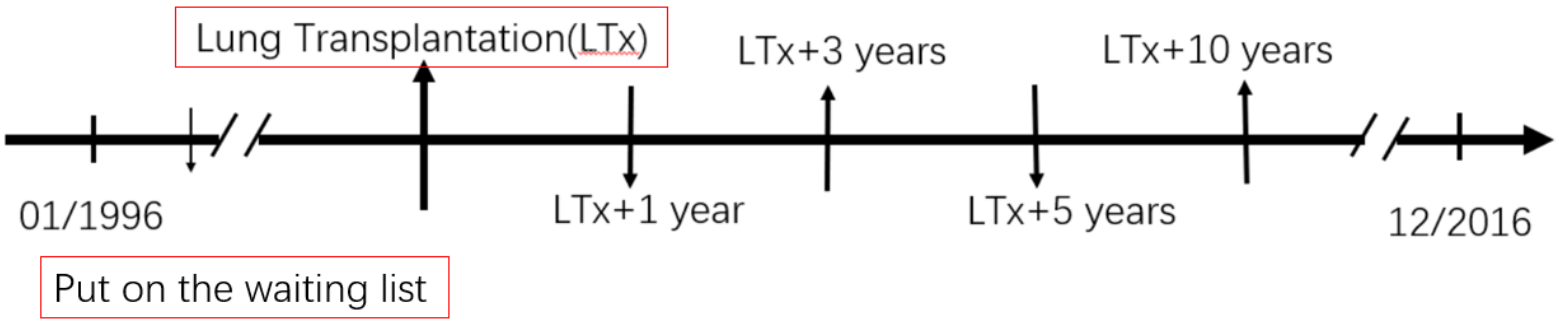
Identification of predictors

- Post-transplantation work status
- Post-transplantation work percentage

Study Design

- Design: Retrospective
- Setting: Single center study at University Hospital Zurich
- Study Population: Cystic Fibrosis patients who underwent Lung Transplantation (n=99)

Study Design



2 types of factors:
Pre-transplantation factors
Post-transplantation factors

5 time points:
One year later
Three years later
Five years later
Ten years later
End of study

2 types of outcomes:
Work status (yes or no)
Work percentage (%)

Data Description

Pre-transplantation Factors (9)

Age
Sex (Male vs. Female)
Education (Academic vs. Non-academic)
Relationship status (Single vs. Not-single)
Living status (Alone vs. Not-alone)
Pre-transplant employment (yes vs. no)

Six-minute walk distance test (6MWD,m)
Body Mass Index (BMI, kg/m^2)

Waiting time (weeks)

Data Description

Post-transplantation Factors (4)

Best FEV1 % predicted

Chronic lung allograft dysfunction"CLAD" (yes vs. no)

Kidney-Dialysis (yes vs. no)

Cancer (yes vs. no)

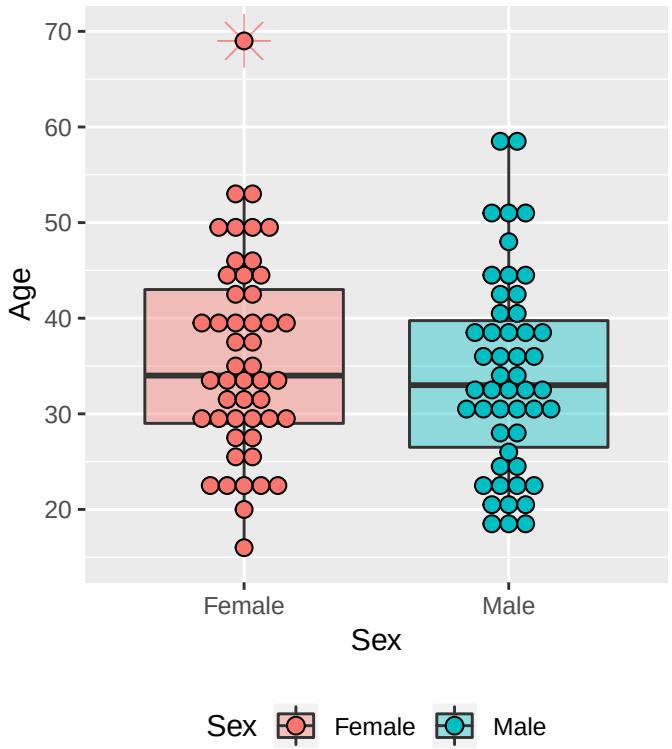
Data Description

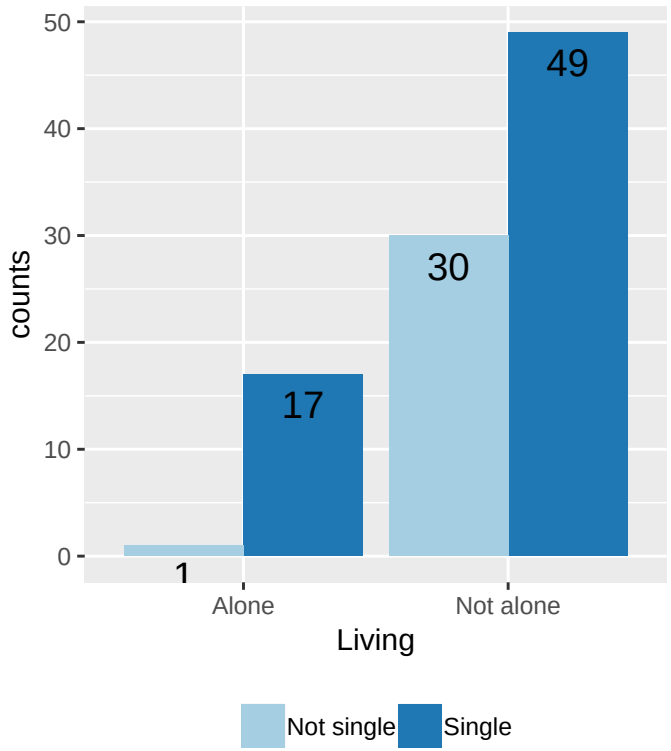
Time-independent Factors

Factors	n	Min	Mean	Max	#NA
Age	99	16.0	35.0	69.0	0
BMI (kg/m^2)	97	13.4	18.3	33.7	2
6MWD (m)	82	150.0	394.3	650.0	17
Best FEV1(%)	94	47.0	92.7	133.0	5
Waiting time (weeks)	94	0.1	41.8	177.3	5

Data Description

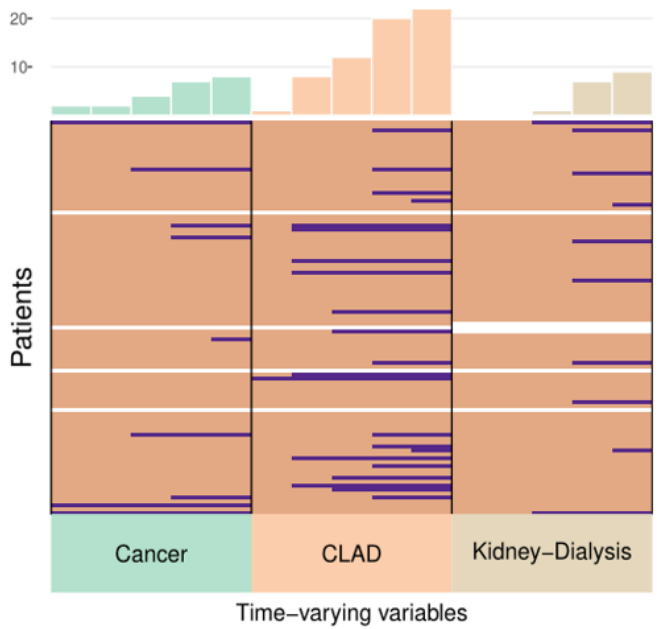
Time-independent Factors

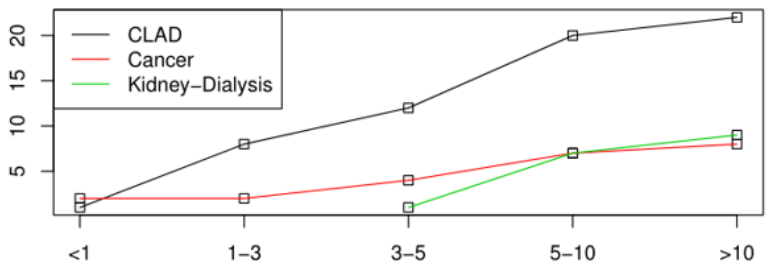




Data Description

Time-dependent Factors

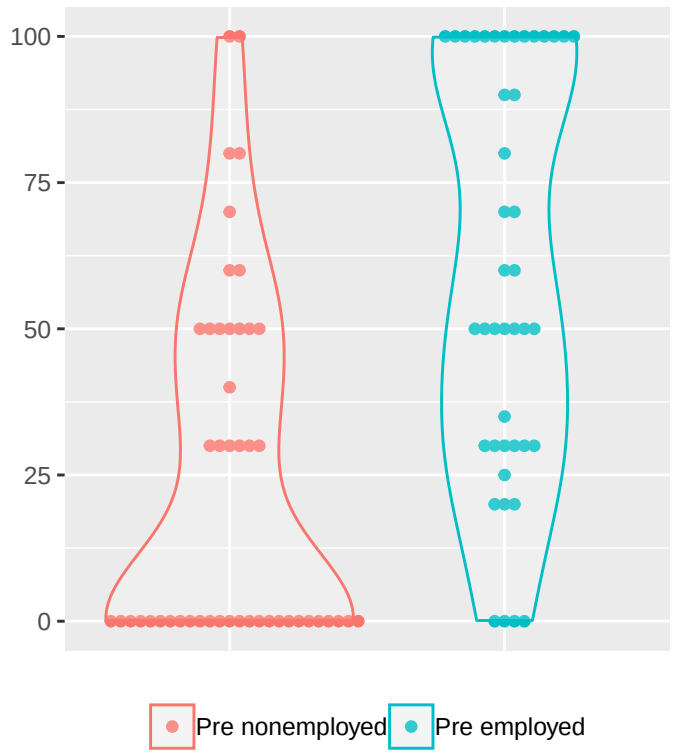


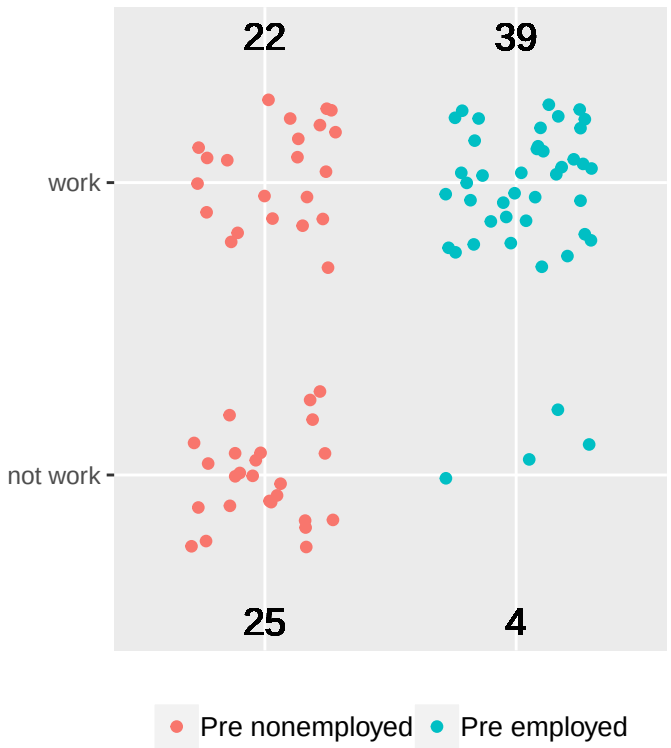


Factors (NA)	<1	1-3	3-5	5-10	>10
CLAD (4)	1	8	12	20	22
Cancer (4)	2	2	4	7	8
Kidney-Dialysis (6)	0	0	1	7	9

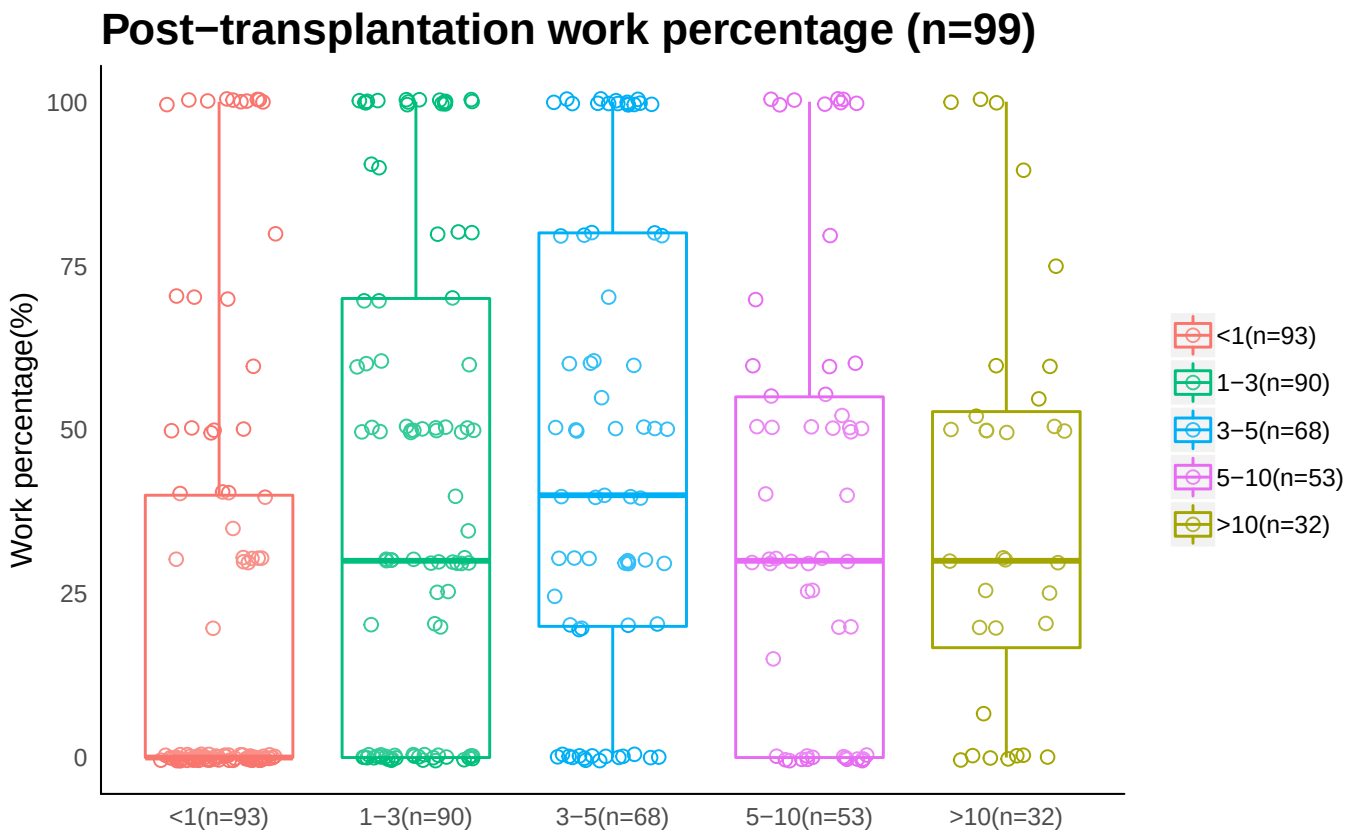
Data Description

Work percentage and work status 1-3 years after LTx





Data Description



Data Description

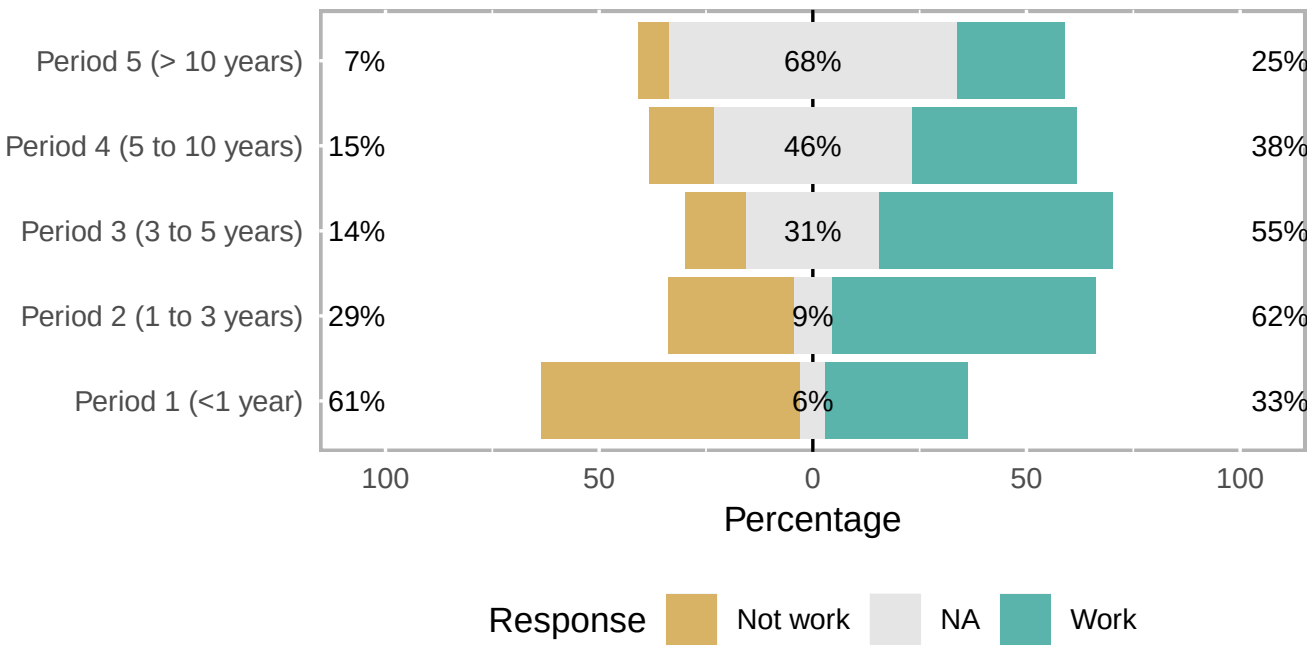


Figure: Post-transplantation work status for all the periods

Data Analysis

- Each time point:
  Logistic regression for post-transplantatiaon work status
  Linear regression for post-transplantatiaon work percentage

- All time points (Repeated measurements):
  Generalized linear mixed effect model (GLMM)
  Linear mixed effect model(LMM)

Logistic Regression: 1-3 years after LTx

	Odds Ratio	95%-confidence interval	p-value	AUC	BIC
Age	0.95	from 0.91 to 1.00	0.041	0.63	95.97
Best FEV1(%)	1.00	from 0.98 to 1.03	0.92	0.62	98.92
BMI	0.91	from 0.78 to 1.05	0.21	0.45	97.37
Education(Academic)	5.22	from 1.35 to 34.53	0.036	0.62	92.92
Living(Alone)	0.78	from 0.26 to 2.54	0.67	0.51	99.53
Pre-employment(Employed)	11.08	from 3.73 to 41.39	< 0.0001	0.80	72.59
Relationship(Single)	1.61	from 0.63 to 4.06	0.31	0.58	97.88
Sex(Male)	1.96	from 0.80 to 5.05	0.15	0.59	97.52
6MWD	1.00	from 1.00 to 1.00	1.00	0.54	99.52
Waiting time	1.01	from 1.00 to 1.03	0.13	0.55	98.21

Univariate Models (61 work, 29 not work)

Model	BIC
Pre-employment+Education	70.33
Pre-employment	72.59

Model Selection

	Odds Ratio	95%-confidence interval	p-value
Education(Academic)	5.34	from 1.22 to 37.82	0.045
Pre-employment(employed)	11.19	from 3.67 to 42.71	< 0.0001

Selected Model

Analogously for other time points

Logistic Regression: 3-5 years after LTx

Logistic Regression for Post-LTx work status

Model(N)	Pre-employment(Employed)	*p*-value	Education(Academic)	*p*-value
<1 year (93)	8.67 [3.33 ,25.12]	< 0.0001		
1-3 years (90)	11.19 [3.67, 42.71]	< 0.0001	5.34 [1.22 , 37.82]	0.045
5-10 years (53)	36.51 [5.84, 724.4]	0.001	11.56 [1.61, 240.46]	0.036

Table: Odds Ratio and CI for all time periods

Linear Regression: 1-3 years after LTx

	Coefficient	95%-confidence interval	p-value	BIC
Age	-1.20	from -1.91 to -0.48	0.001	732.13
Best FEV1(%)	0.00	from -0.44 to 0.45	0.99	740.81
BMI	-3.40	from -5.85 to -0.94	0.007	735.00
Education(Academic)	15.73	from -3.11 to 34.56	0.10	740.01
Living(Single)	-20.07	from -39.89 to -0.25	0.047	738.99
Pre-employment(Employed)	35.41	from 21.69 to 49.12	< 0.0001	714.92
Relationship(Single)	13.66	from -2.58 to 29.90	0.098	737.90
Sex(Male)	6.16	from -9.46 to 21.79	0.44	740.38
6MWD	0.00	from -0.08 to 0.07	0.94	741.17
Waiting time	0.13	from -0.07 to 0.32	0.20	740.02

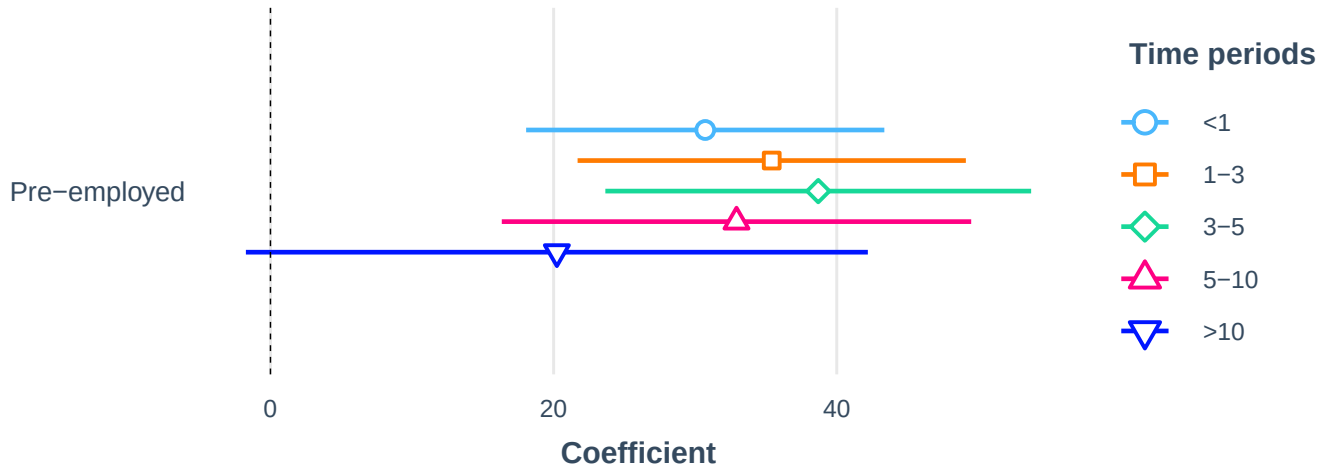
Univariate Models

	BIC
Pre-employment+Living+Education	718.44
Pre-employment+Living	715.06
Pre-employment+Education	718.51
Pre-employment	714.92

Model Selection

Analogously for other time points

Linear Regression for Post-LTx Work Percentage



Model(N)	Pre-employment(Employed)	*p*-values
<1 year (93)	30.71 [17.48, 43.94]	< 0.0001
1-3 years (90)	35.41 [21.69, 49.12]	< 0.0001
3-5 years (68)	38.69 [23.45, 53.93]	< 0.0001
5-10 years (53)	32.92 [16.02, 49.82]	0.0002
>10 years (32)	20.23 [-3.42, 43.88]	0.07

Longitudinal Data

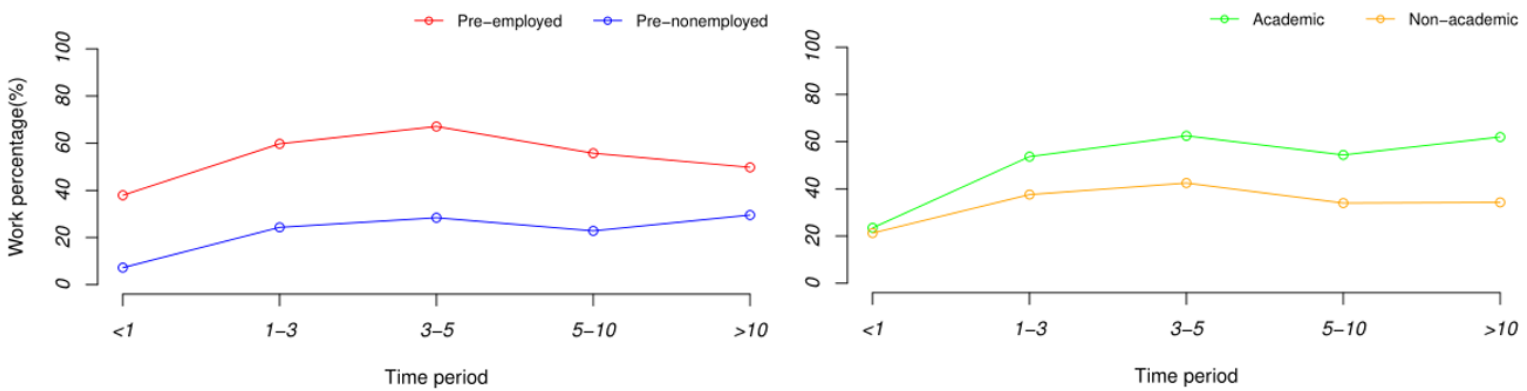


Figure: Mean of Post-LTx work percentage for all time periods

Longitudinal Data Analysis

- Use all measurements in one model (GLMM and LMM)
- Time effects
- Time-varying variables with few cases in each time point

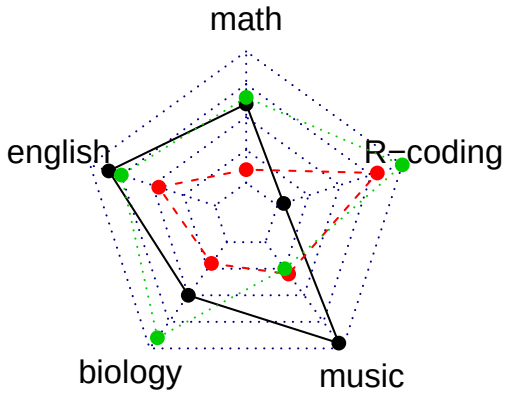
Time Transformation

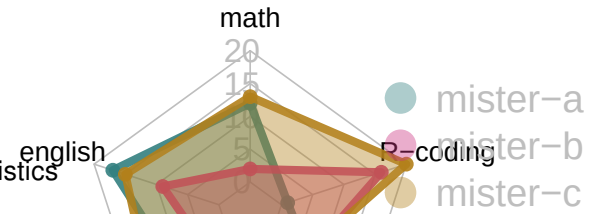
Table: Model selection for Post-LTx Work Status

	Pre-employment	Education + Pre-employmet
$\log(Time)$	352.90	342.66
$Time$	371.31	361.66
$(Time)^2$	382.26	372.56

Table: Model selection for Post-LTx work percentage

	Pre-employment	Education + Pre-employmet
$\log(Time)$	3293.67	3290.57
$Time$	3303.93	3300.93
$(Time)^2$	3307.96	3304.99


math
english
R−coding
biology
music


math
20
15
10
5
0
english
R−coding
mister−a
mister−b
mister−c

Selection of Time-dependent Factors

CLAD	Cancer	KD	BIC
1	0	0	332.85
0	0	1	333.30
1	0	1	335.77
0	1	0	336.33
1	1	0	338.53
0	1	1	339.03
1	1	1	341.47

Table: For work status

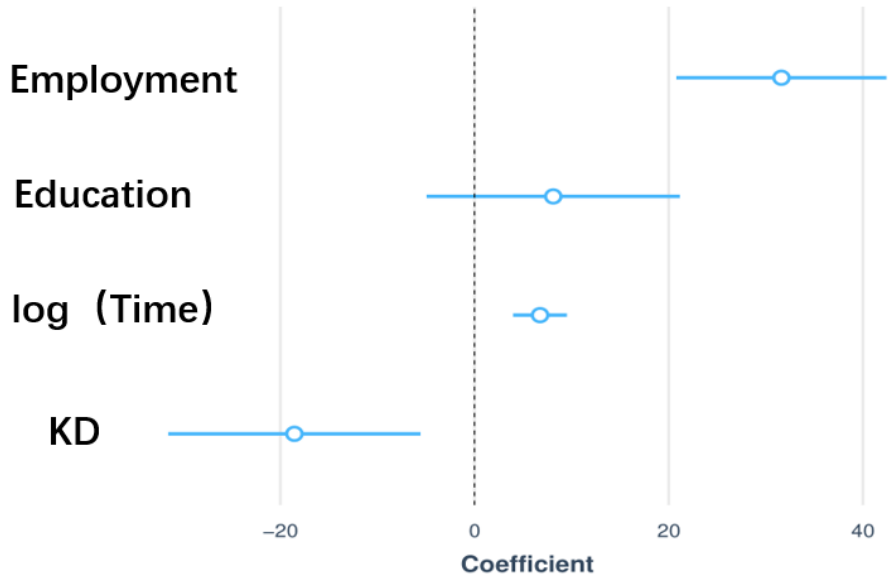
CLAD	Cancer	KD	BIC
0	0	1	3195.54
1	0	0	3198.16
0	1	0	3198.60
1	0	1	3199.81
0	1	1	3200.26
1	1	0	3202.93
1	1	1	3204.64

Table: For work percentage

GLMM for Post-transplantation Work Status

	Odds Ratio	95%-confidence interval	*p*-values
Pre-employment(Employed)	40.84	[8.70, 191.68]	< 0.0001
Education(Academic)	5.57	[1.21, 25.70]	0.028
log(Time)	6.69	[3.41, 13.10]	< 0.0001
CLAD	0.21	[0.05, 0.97]	0.039

LMM for Post-LTx Work Percentage



	Coefficient	CI	*p*-values
Employment	31.60	[20.78, 42.42]	< 0.0001
Education	8.10	[-4.94, 21.14]	0.028
log(Time)	6.75	[3.98, 9.51]	< 0.0001
KD	-18.56	[-31.55, -5.56]	0.039

Conclusion

Post-LTx work status $\sim$
Pre-employment + Education + CLAD +log(Time)

Post-LTx work percentage $\sim$
Pre-employment + Education + Kidney-Dialysis + log(Time)

References

Krivchenia, K., Hayes Jr, D., Tobias, J. D., and Tumin, D. (2016). Long-term work participation among cystic fibrosis patients undergoing lung transplantation. *Journal of Cystic Fibrosis*, 15(6):846–849.

Vieux, L., Simcox, A. A., Mediouni, Z., Wild, P., Koller, M., Studer, R. K., Danuser, B., et al. (2018). Predictors of return to work 12 months after solid organ transplantation: Results from the swiss transplant cohort study. *Journal of occupational rehabilitation*, pages 1–10.

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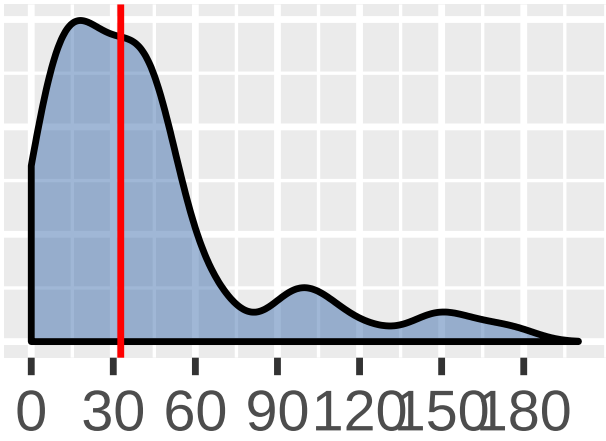
Epidemiology, Biostatistics and Prevention Institute,
University of Zurich

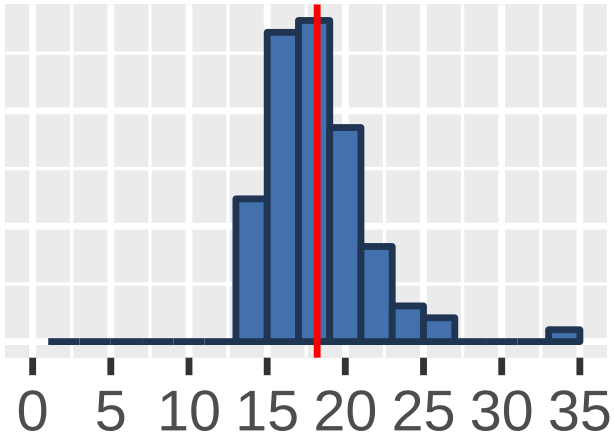
Post-LTx work status

	<1	1-3	3-5	5-10	>10
Work	33	61	54	38	25
Not Work	60	29	14	15	7
NA	6	9	31	46	67
Total	93	90	68	53	32
Woking patients(%)	0.35	0.68	0.79	0.72	0.78

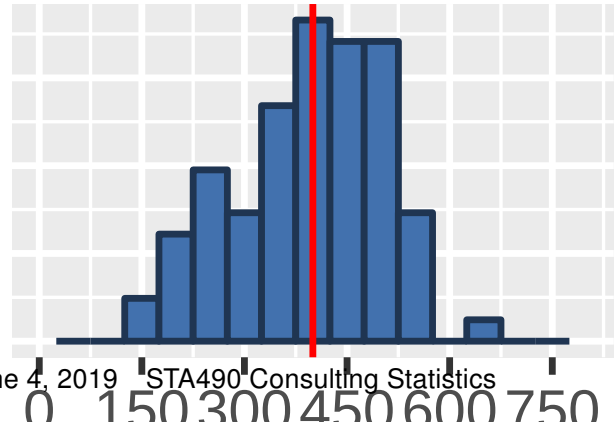
Basic characterristics

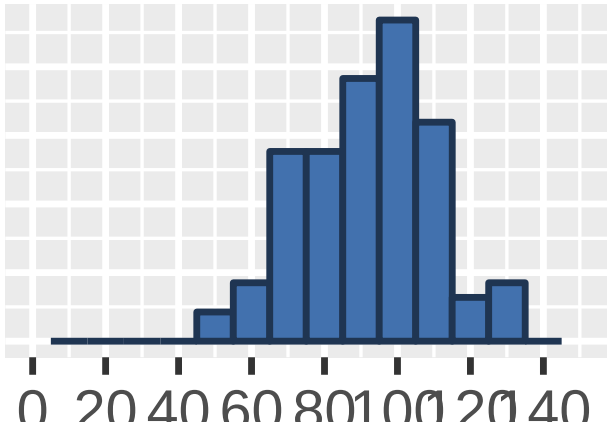


Waiting time in weeks



BMI

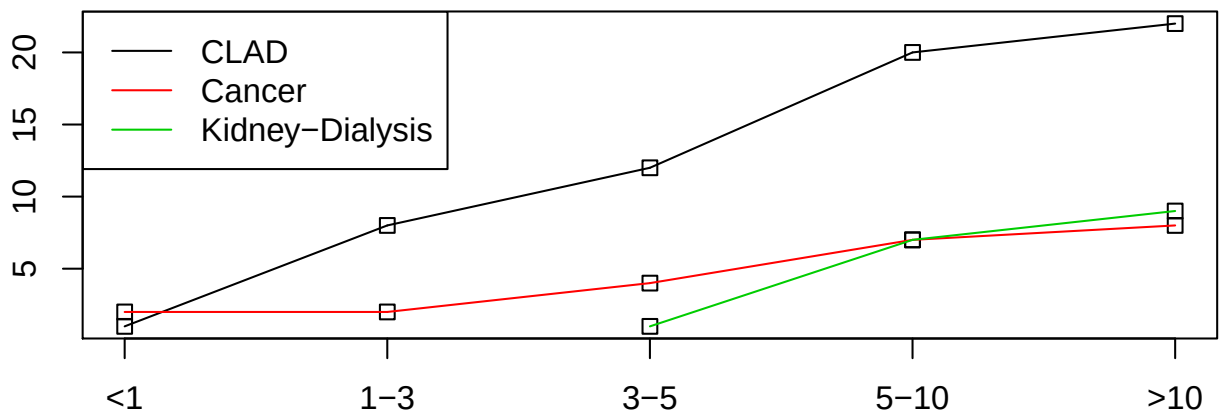




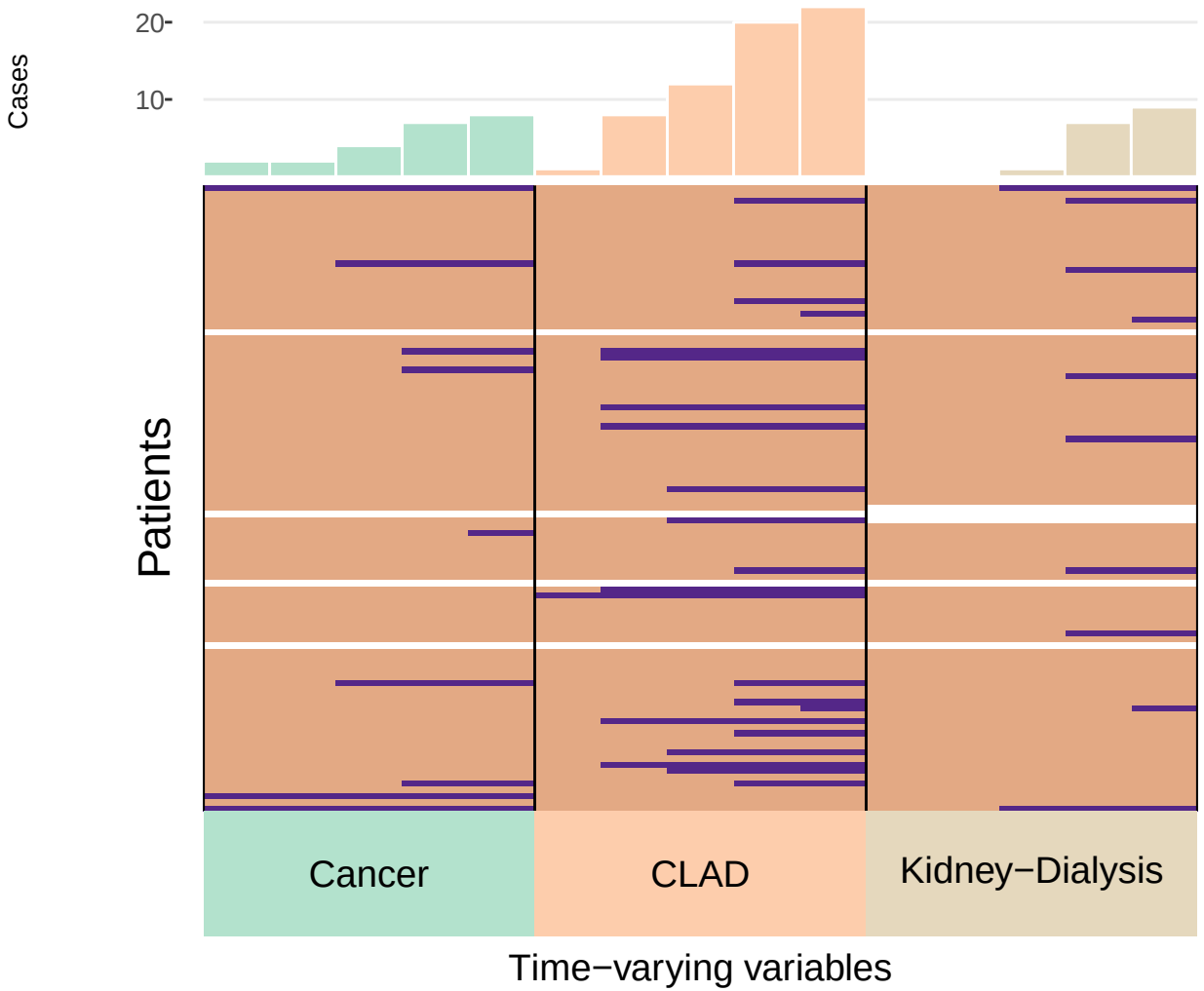
Data Description

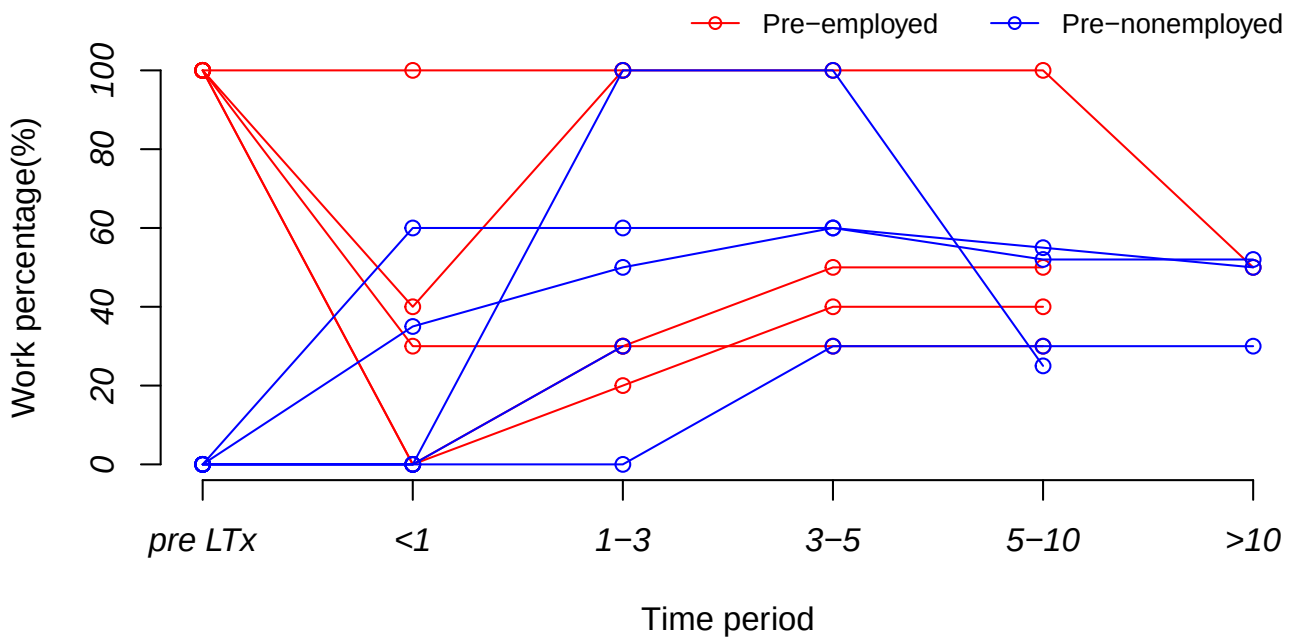
Factors	level	Proportion
Sex	female	50 (50.5)
	male	49 (49.5)
Education	Academic	21 (21.2)
	Non-academic	78 (78.8)
Relationship status	Not single	31 (32.0)
	Single	66 (68.0)
Living status	Alone	18 (18.6)
	Not alone	79 (81.4)
Pre-employment	Employed	47 (47.5)
	Not employed	52 (52.5)

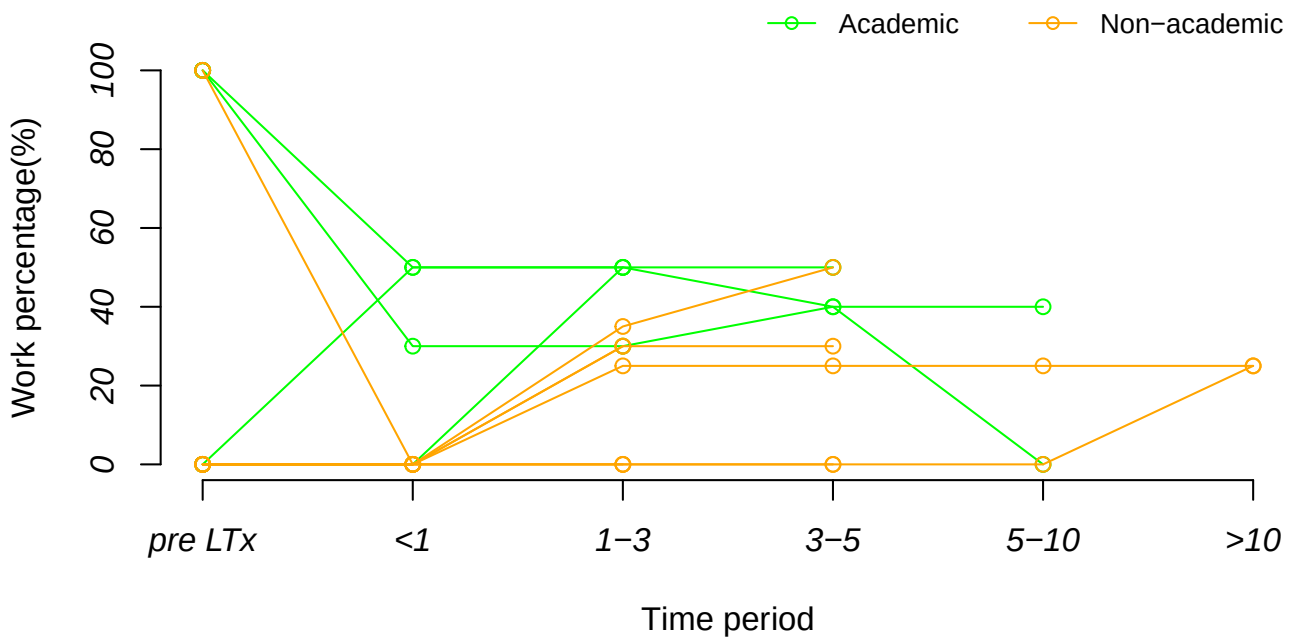
Time-dependent factors

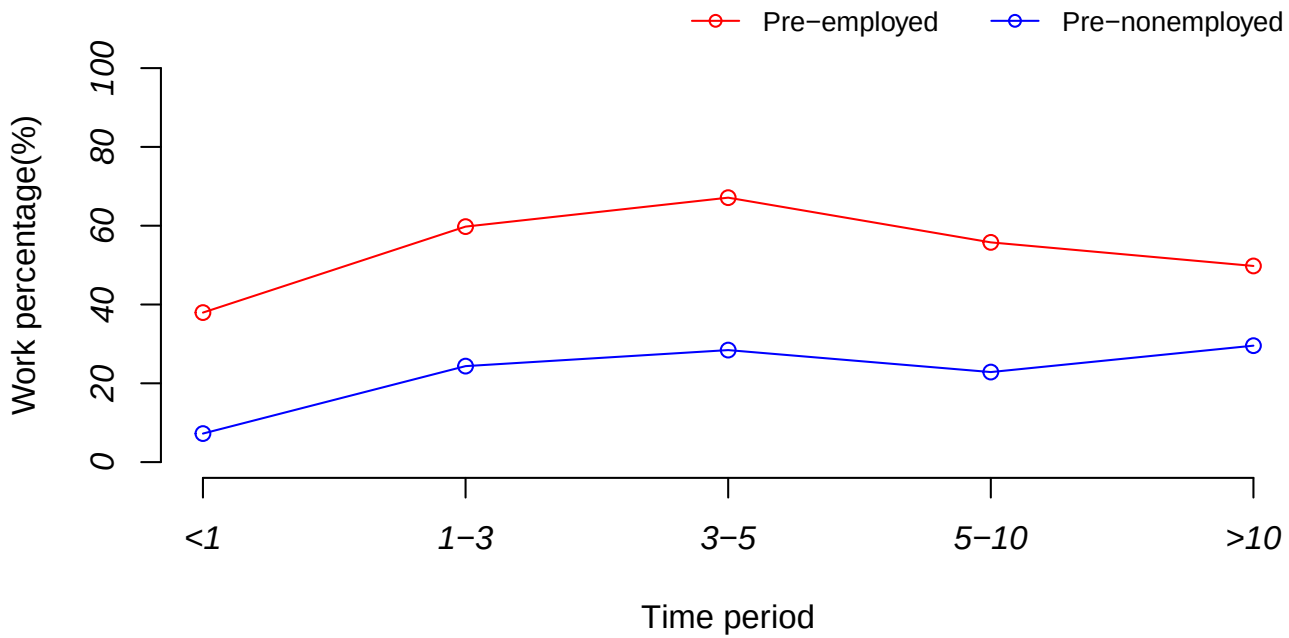


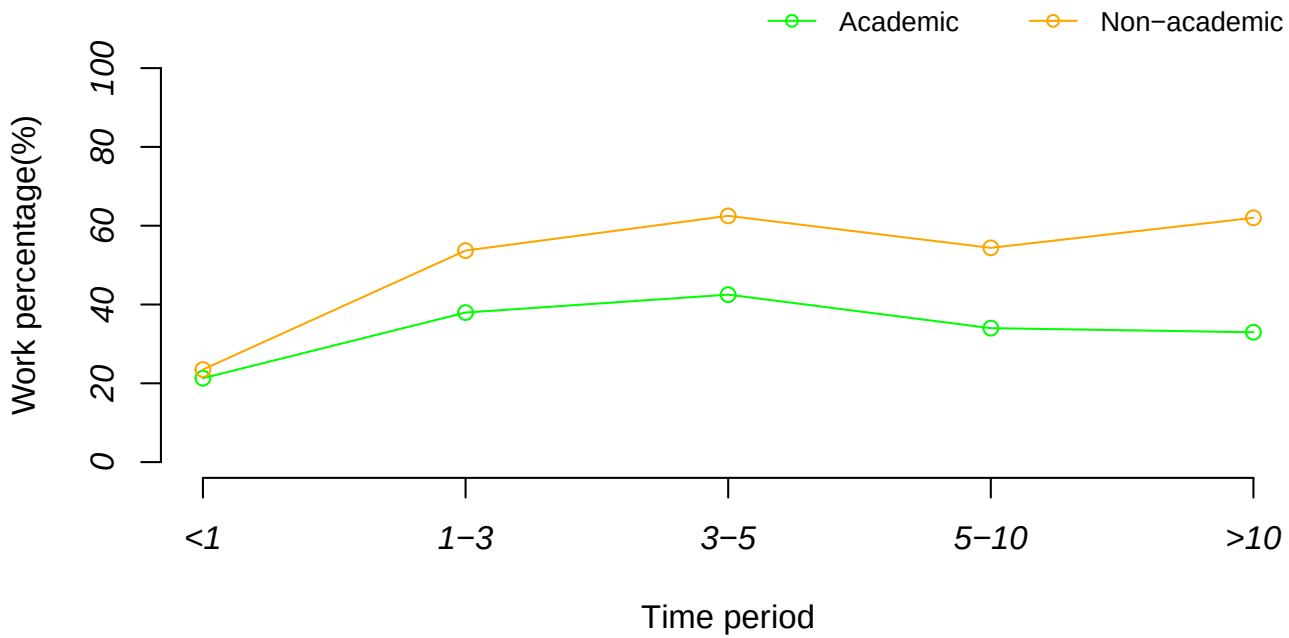
Factors (NA)	<1	1-3	3-5	5-10	>10
CLAD (4)	1	8	12	20	22
Cancer (4)	2	2	4	7	8
Kidney-Dialysis (6)	0	0	1	7	9


Cases
20
10
Patients
Cancer
CLAD
Kidney−Dialysis
Time−varying variables


Pre−employed
Pre−nonemployed
Work percentage(%)
0
20
40
60
80
100
pre LTx
<1
1−3
3−5
5−10
>10
Time period

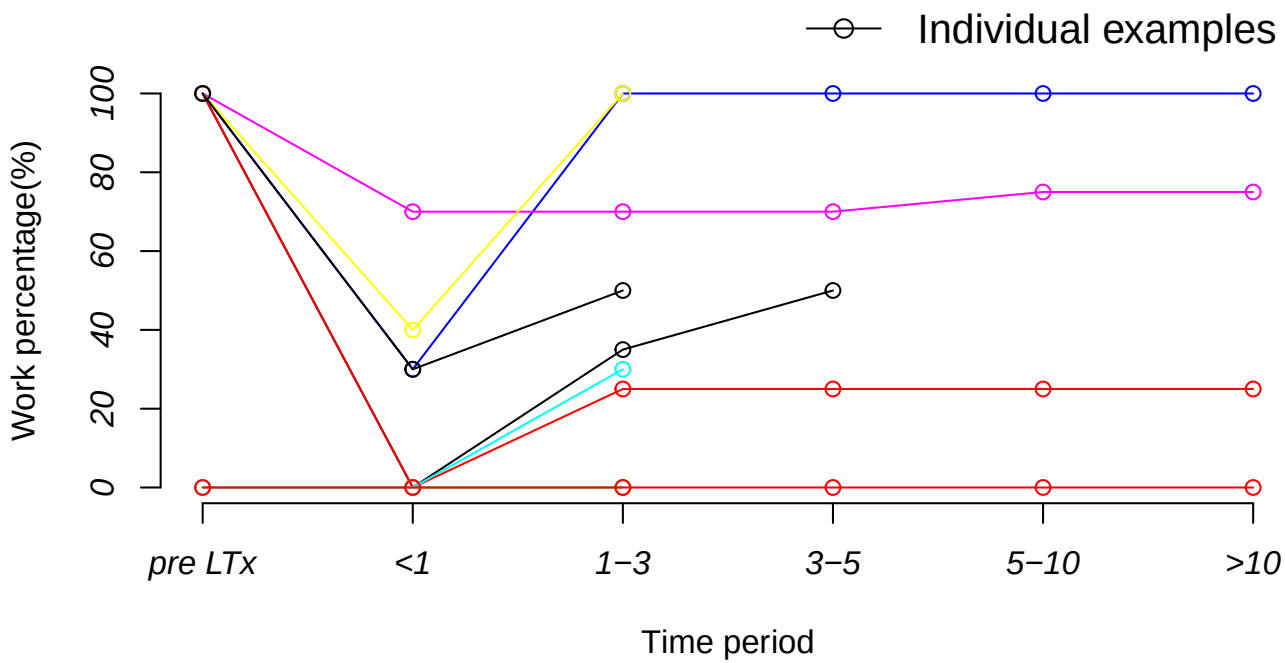

Academic
Non−academic
Work percentage(%)
0
20
40
60
80
100
pre LTx
<1
1−3
3−5
5−10
>10
Time period


Pre−employed
Pre−nonemployed
Work percentage(%)
0
20
40
60
80
100
<1
1−3
3−5
5−10
>10
Time period


Academic
Non−academic
Work percentage(%)
0
20
40
60
80
100
<1
1−3
3−5
5−10
>10
Time period

Data Description

Time plots of trends (n=10)



Model selection for GLMM

CLAD	Cancer	Kidney-Dialysis	BIC
✓			332.85
		✓	333.30
✓		✓	335.77
	✓		336.33
✓	✓		338.53
	✓	✓	339.03
✓	✓	✓	341.47

Table: BIC under 3 Time-dependent factors

Model selection for LMM

CLAD	Cancer	Kidney-Dialysis	BIC
		✓	3195.54
✓			3198.16
	✓		3198.60
✓		✓	3199.82
	✓	✓	3200.26
✓	✓		3202.93
✓	✓	✓	3204.64

Table: BIC under 3 time-varying variables

Table: Result for Generalised Linear Mixed-effects Model for Post-LTx Work Status

	Odds Ratio	95%-confidence interval	*p*-value
Pre-employemnt	40.84	[10.73, 286.00]	< 0.0001
Education	5.57	[1.23, 30.24]	0.028
log(Time)	6.55	[3.60, 14.02]	< 0.0001
CLAD	0.21	[0.04, 0.90]	0.039

Table: Result for Linear Mixed-effects Model for Post-LTx Work percentages

	Coefficients	95%-confidence interval	*p*-value
Pre-employemnt	31.60	[20.85, 42.34]	< 0.0001
Education	6.75	[4.00, 9.55]	< 0.0001
log(Time)	8.10	[-4.87, 21.04]	0.23
KD	-18.56	[-31.51, -5.57]	0.005