



Das Netzwerk für eine optimale Versorgung.



Überleben nach Rezidiv – Der Kaplan Meier Schätzer und seine Grenzen

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Die Daten – Brustkrebs: operiert & kurativ

Status	Anzahl	Prozent
Complete Cases	11169	81,1
Incomplete Cases	2605	18,9
Total	13774	100

Variable	n	Mean	sd	Median	Min	Max
age_diag	13774	60,1	13,009	60,062	18,226	100,41
TumorSize	11631	24,004	13,832	16	0	173

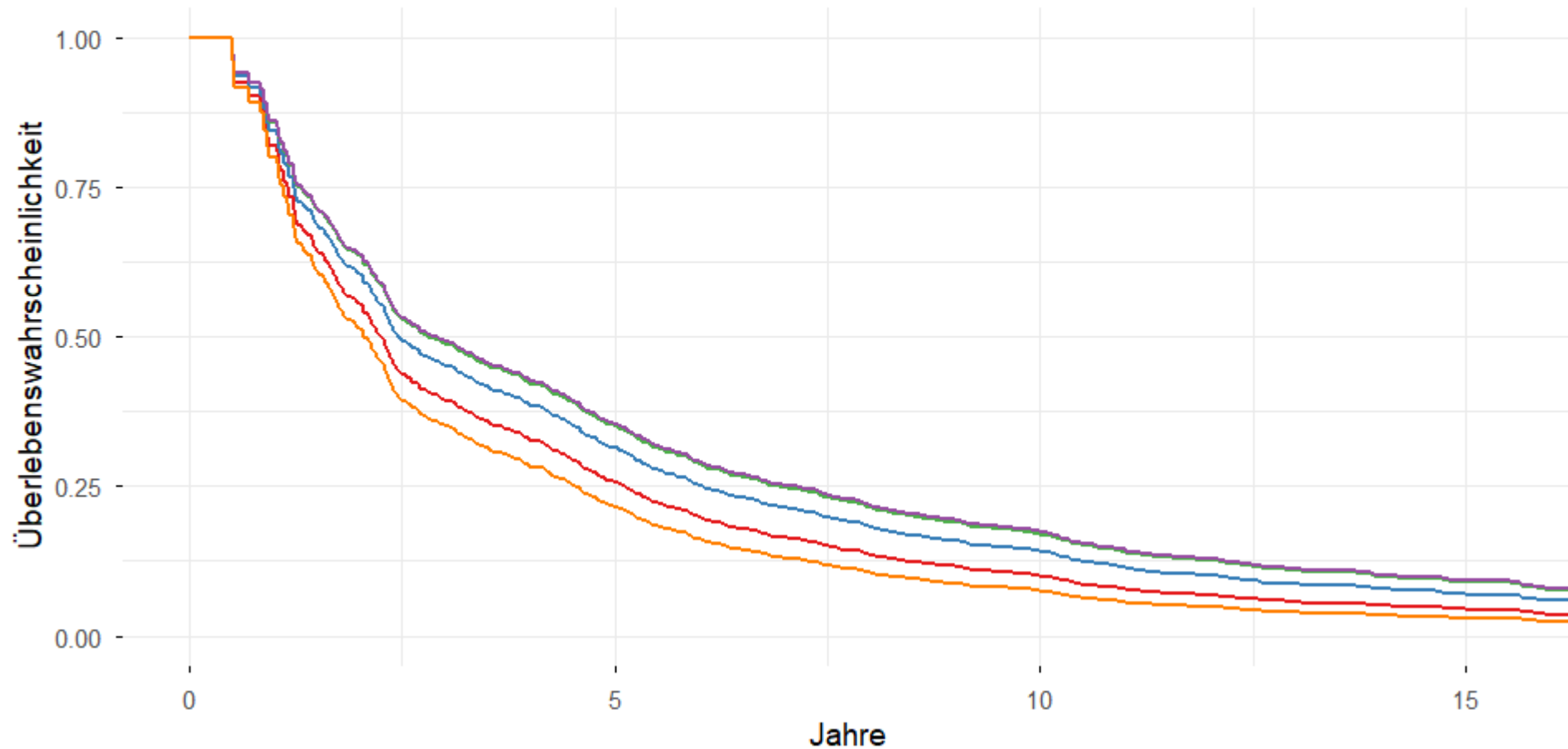
Variable	Kategorie	n	Prozent
treat	BCT	1019	7,4
treat	BCT+RT	8518	61,8
treat	MAS	1423	10,3
treat	MAS+RT	1123	8,2
treat	BCT-MAS	658	4,8
treat	BCT-MAS+RT	576	4,2
treat	NA	457	3,3
adjuvant	no	2991	21,7
adjuvant	yes	10783	78,3

Variable	Kat.	n	%
sex	weiblich	13774	100
Center	A	4122	29,9
Center	B	3221	23,4
Center	C	3147	22,8
Center	D	2053	14,9
Center	X	1231	8,9
Grading	G1	1424	10,3
Grading	G2	8135	59,1
Grading	G3	3866	28,1
Grading	NA	349	2,5
NodalStatus	0	9511	69,1
NodalStatus	1	3979	28,9
NodalStatus	NA	284	2,1
Chemo	no	8320	60,4
Chemo	yes	5454	39,6

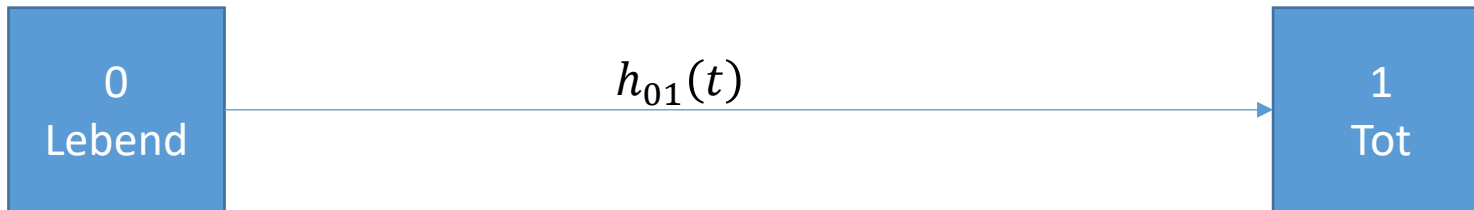
“Kaplan - Meier“ Schätzung

Adjustierte Überlebenskurven nach Center

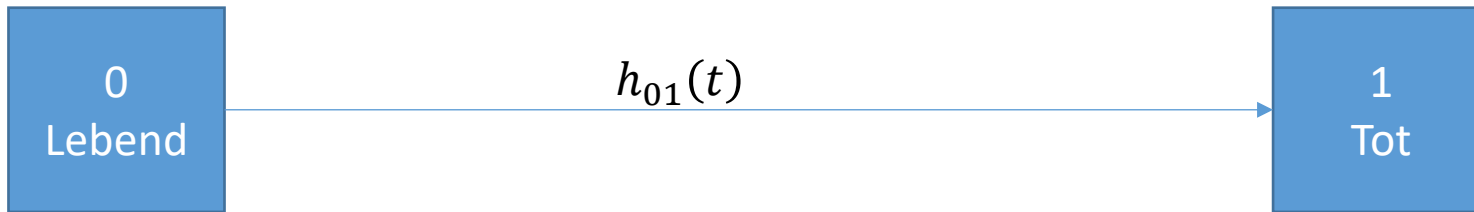
Center — A — B — C — D — X



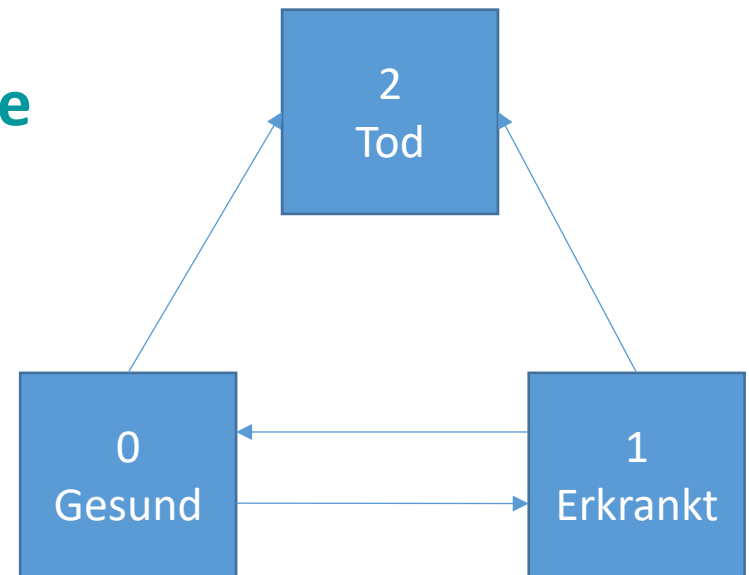
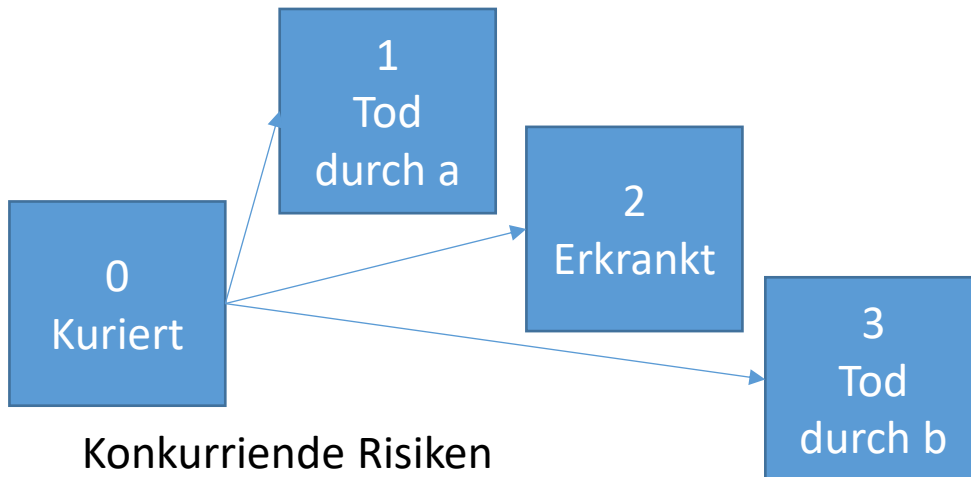
Hazard basierte Überlebenszeitanalyse



Einfache Mehrstadienmodelle



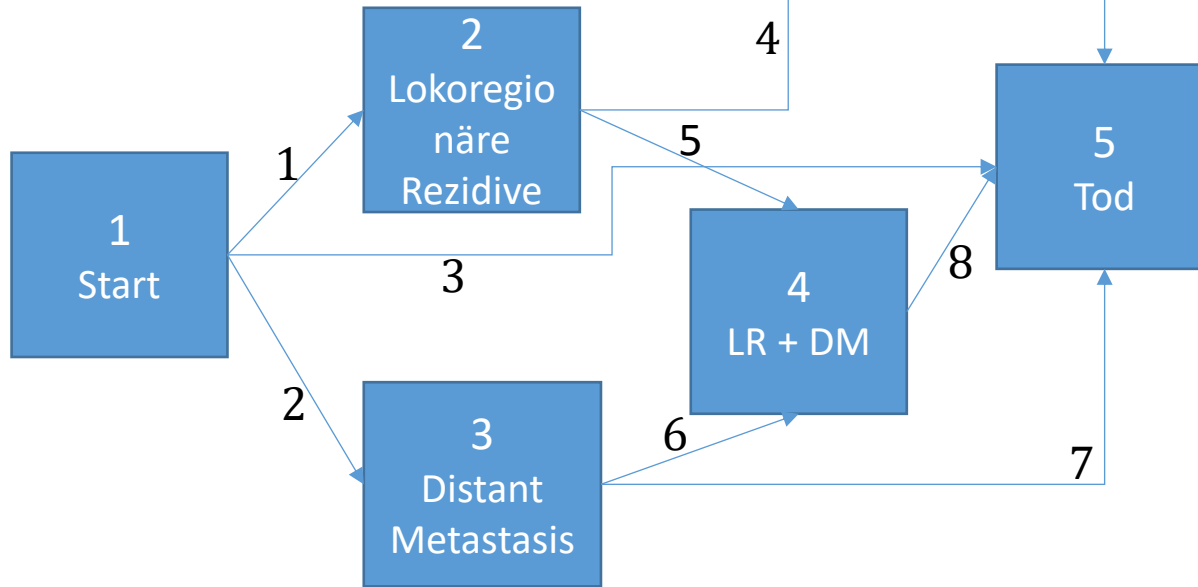
Multistatamodelle



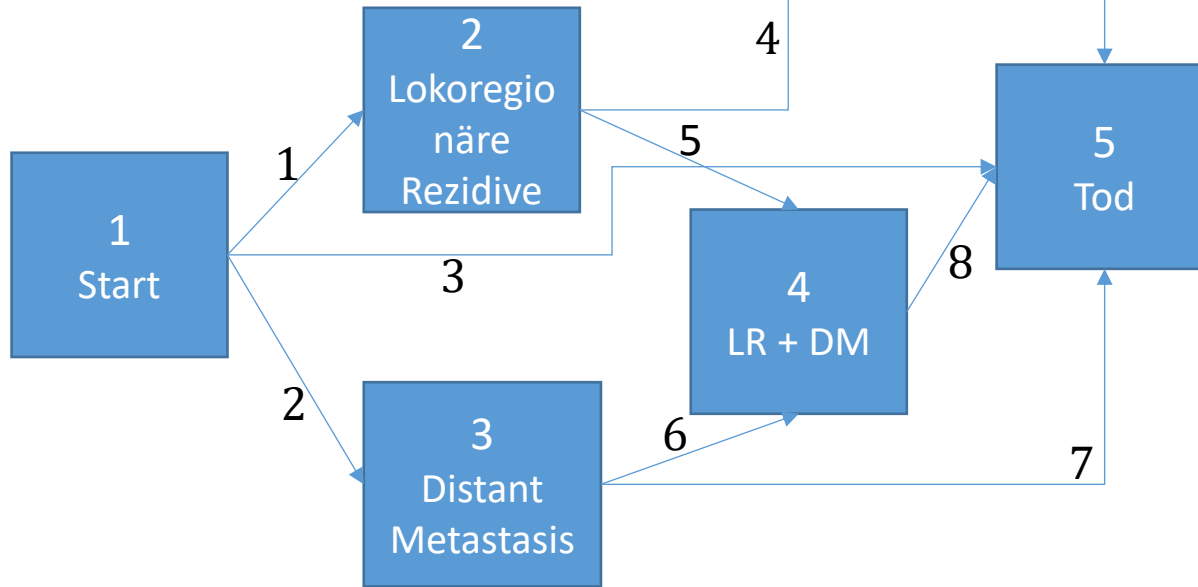
Recurrent-Events Modell

Und viele weitere

Mehrstadienmodell für Rezidivanalyse



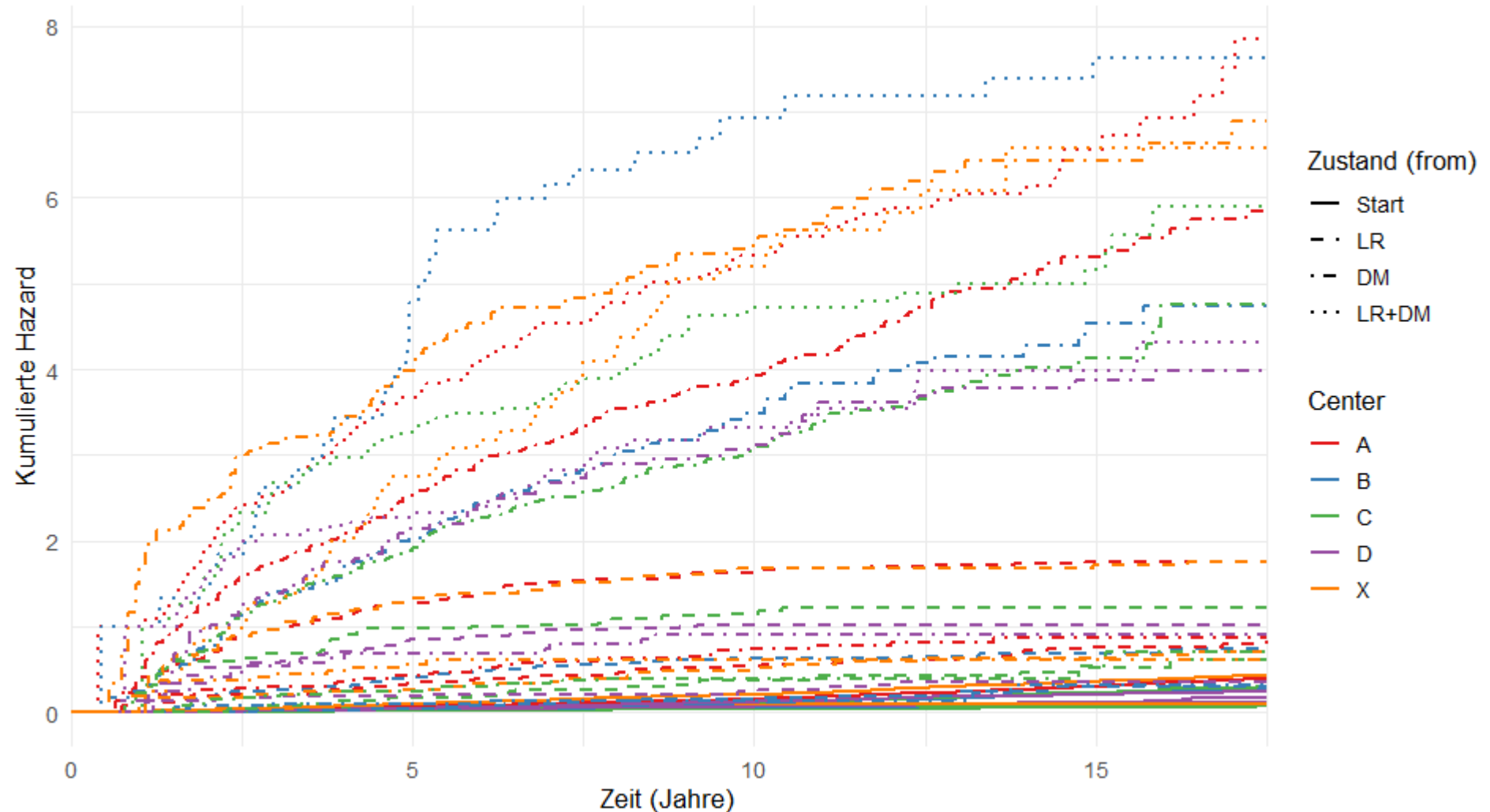
Mehrstadienmodell für Rezidivanalyse



from/to	LR	DM	LR+DM	Tod	no event	total entering
Start	696 (5.1%)	888 (6.4%)	0 (0%)	1946 (14.1%)	10244 (74.4%)	13774
LR	0 (0%)	0 (0%)	197 (28.3%)	98 (14.1%)	401 (57.6%)	696
DM	0 (0%)	0 (0%)	83 (9.3%)	645 (72.6%)	160 (18%)	888
LR+DM	0 (0%)	0 (0%)	0 (0%)	288 (78%)	81 (22%)	369
Tod	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2977 (100%)	2977

Mehrstadienmodelle verstehen

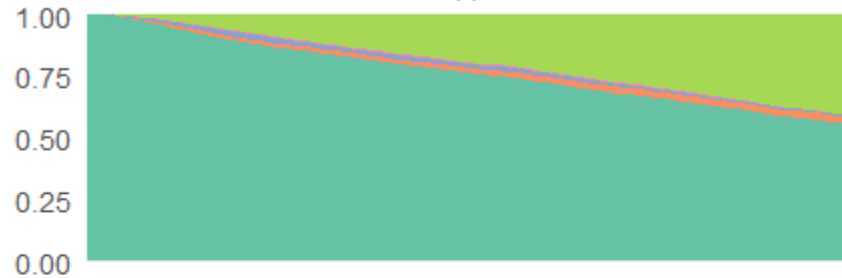
Kumulative Hazards – alle Transitionen



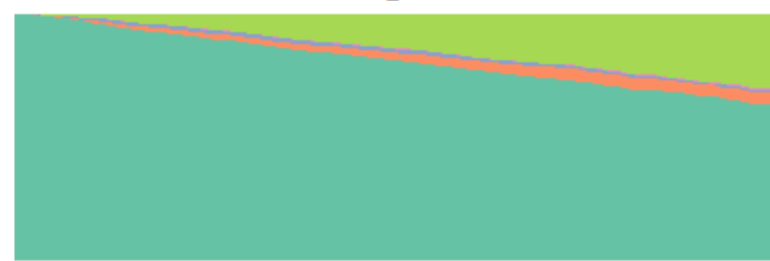
Zustandswahrscheinlichkeiten

State-Occupancy (Aalen–Johansen) – je Center

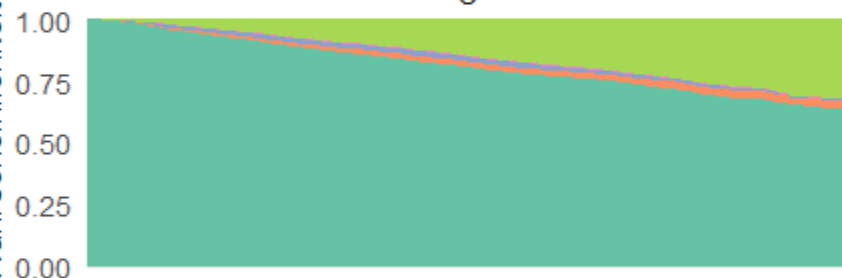
A



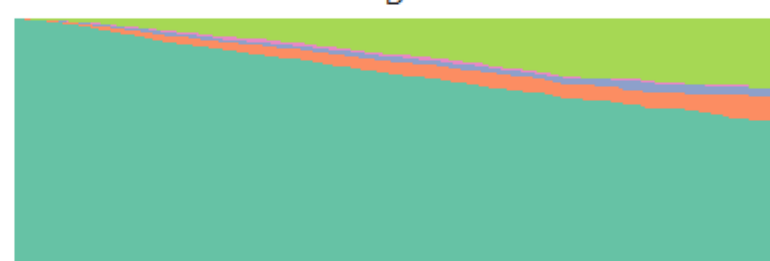
B



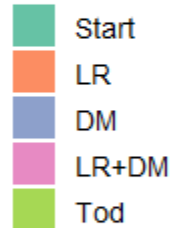
C



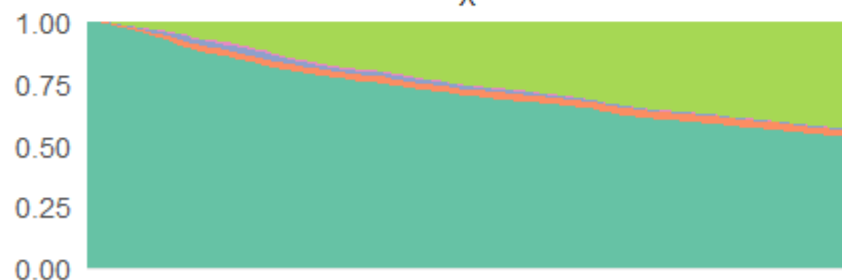
D



Zustand



X



0 5 10 15
Zeit (Jahre)

- Kaplan Meier Schätzungen unterliegen häufig Annahmefehlern
- Ob der KM Schätzer valide ist, hängt auch von der *konkreten Fragestellung* ab
Bspw.: Für die Analyse von Diagnose zu Rezidiv ggf nicht angemessen (**competing risk**)
- Auch bei korrekter Anwendung des KM-Schätzers erzielen Multistate Modelle ein tieferes Verständnis und ermöglicht Zusammenhänge zwischen mehreren Stadien besser zu erkennen
- Multistate Modelle erlauben auch gezieltere Prognosen und die Möglichkeit die Aufenthaltsdauer in einem Status mit aufzunehmen
(bei Lockerung der Markov Eigenschaft)
- Haben Sie Mut, sich auch an komplexeren Modellen zu versuchen!

Multivariates Mehrstadien Cox Modell

variable	Coef (SE)	p.value
age_diag.1	0.008 (0.004)	0,038
TumorSize.1	-0.01 (0.003)	0,00167
GradingG2.1	0.547 (0.235)	0,0165
GradingG3.1	1.26 (0.241)	1,07E-07
NodalStatus.1	-0.73 (0.107)	5,3E-10
Chemoyes.1	0.156 (0.107)	0,159
CenterB.1	0.037 (0.128)	0,757
CenterC.1	-0.054 (0.127)	0,671
CenterD.1	0.47 (0.129)	0,000248
CenterX.1	0.319 (0.147)	0,0317
treatBCT.RT.1	-1.089 (0.264)	0,00405
treatMAS.1	-0.477 (0.249)	0,0551
treatMAS.RT.1	1.037 (0.274)	0,00798
treatBCT.MA S.1	0.314 (0.244)	0,213
treatBCT.MA S.RT.1	2.295 (0.257)	3,58E-10
adjuvantyes.1	-0.011 (0.214)	0,974

variable	Coef (SE)	p.value
age_diag.2	0.017 (0.003)	2,82E-07
TumorSize.2	0.02 (0.003)	1,44E-13
GradingG2.2	0.899 (0.258)	0,000459
GradingG3.2	1.135 (0.263)	0,0000153
NodalStatus.2	0.749 (0.089)	1,7E-15
Chemoyes.2	0.752 (0.102)	1,48E-12
CenterB.2	-0.112 (0.109)	0,307
CenterC.2	-0.143 (0.1)	0,162
CenterD.2	-0.236 (0.125)	0,0602
CenterX.2	0.012 (0.138)	0,93
treatBCT.RT.2	1.718 (0.29)	7,61E-08
treatMAS.2	0.443 (0.277)	0,116
treatMAS.RT.2	2.339 (0.291)	2,63E-13
treatBCT.MA S.2	-0.205 (0.378)	0,589
treatBCT.MA S.RT.2	1.927 (0.309)	7,98E-09
adjuvantyes.2	-1.396 (0.161)	2,78E-14

variable	Coef (SE)	p.value
age_diag.3	0.091 (0.003)	2,53E-178
TumorSize.3	0.013 (0.002)	1,55E-08
GradingG2.3	0.039 (0.09)	0,682
GradingG3.3	0.161 (0.104)	0,139
NodalStatus.3	0.392 (0.062)	2,7E-10
Chemoyes.3	-0.281 (0.073)	0,000152
CenterB.3	-0.007 (0.075)	0,921
CenterC.3	-0.216 (0.069)	0,00159
CenterD.3	-0.024 (0.095)	0,796
CenterX.3	0.077 (0.084)	0,376
treatBCT.RT.3	-0.729 (0.127)	3,61E-08
treatMAS.3	0.019 (0.102)	0,862
treatMAS.RT.3	-0.591 (0.153)	0,000188
treatBCT.MA S.3	-0.452 (0.149)	0,0047
treatBCT.MA S.RT.3	-1.146 (0.227)	2,15E-07
adjuvantyes.3	0.169 (0.111)	0,138

variable	Coef (SE)	p.value
age_diag.4	0.007 (0.006)	0,351
TumorSize.4	0.016 (0.006)	0,00932
GradingG2.4	11.484 (159.049)	5,87E-173
GradingG3.4	12.048 (159.049)	2,36E-183
NodalStatus.4	0.658 (0.173)	0,000381
Chemoyes.4	0.688 (0.219)	0,00435
CenterB.4	-1.147 (0.258)	0,0000109
CenterC.4	-0.791 (0.25)	0,00341
CenterD.4	-0.584 (0.245)	0,0277
CenterX.4	-0.179 (0.238)	0,448
treatBCT.RT.4	-0.023 (0.432)	0,962
treatMAS.4	-0.307 (0.515)	0,525
treatMAS.RT.4	0.375 (0.418)	0,391
treatBCT.MA S.4	-1.248 (0.591)	0,0189
treatBCT.MA S.RT.4	-0.235 (0.43)	0,617
adjuvantyes.4	-0.579 (0.23)	0,0261

Multivariates Mehrstadien Cox Modell

variable	Coef (SE)	p.value
age_diag.5	0.053 (0.01)	0,00000214
TumorSize.5	0.012 (0.009)	0,104
GradingG2.5	0.984 (0.739)	0,148
GradingG3.5	0.976 (0.752)	0,158
NodalStatus.5	0.455 (0.257)	0,0746
Chemoyes.5	0.21 (0.271)	0,432
CenterB.5	-0.67 (0.365)	0,0582
CenterC.5	-0.448 (0.326)	0,141
CenterD.5	-0.723 (0.388)	0,0471
CenterX.5	0.145 (0.333)	0,66
treatBCT.RT.5	-0.129 (0.51)	0,792
treatMAS.5	-0.684 (0.581)	0,199
treatMAS.RT.5	-0.463 (0.536)	0,34
treatBCT.MAS.5	-0.286 (0.491)	0,473
treatBCT.MAS.RT.5	-1.116 (0.527)	0,025
adjuvantyes.5	-0.085 (0.341)	0,799

variable	Coef (SE)	p.value
age_diag.6	-0.008 (0.01)	0,458
TumorSize.6	-0.001 (0.011)	0,949
GradingG2.6	-0.689 (0.836)	0,462
GradingG3.6	-0.295 (0.852)	0,745
NodalStatus.6	0.771 (0.299)	0,0177
Chemoyes.6	-0.406 (0.367)	0,275
CenterB.6	-1.022 (0.462)	0,0245
CenterC.6	-0.385 (0.306)	0,222
CenterD.6	0.16 (0.371)	0,692
CenterX.6	-0.721 (0.545)	0,171
treatBCT.RT.6	-0.079 (0.808)	0,929
treatMAS.6	0.699 (0.815)	0,428
treatMAS.RT.6	0.09 (0.815)	0,922
treatBCT.MAS.6	-0.712 (1.303)	0,645
treatBCT.MAS.RT.6	0.9 (0.822)	0,311
adjuvantyes.6	-0.165 (0.414)	0,712

variable	Coef (SE)	p.value
age_diag.7	0.01 (0.004)	0,0182
TumorSize.7	0.012 (0.004)	0,00686
GradingG2.7	-0.166 (0.36)	0,629
GradingG3.7	0.148 (0.366)	0,677
NodalStatus.7	0.404 (0.102)	0,000401
Chemoyes.7	-0.281 (0.12)	0,0409
CenterB.7	-0.159 (0.135)	0,306
CenterC.7	-0.26 (0.117)	0,0376
CenterD.7	-0.271 (0.166)	0,159
CenterX.7	0.119 (0.153)	0,517
treatBCT.RT.7	0.22 (0.336)	0,589
treatMAS.7	0.624 (0.343)	0,132
treatMAS.RT.7	0.047 (0.339)	0,909
treatBCT.MAS.7	-0.266 (0.54)	0,646
treatBCT.MAS.RT.7	-0.032 (0.364)	0,94
adjuvantyes.7	0.164 (0.169)	0,318

variable	Coef (SE)	p.value
age_diag.8	0.017 (0.005)	0,000944
TumorSize.8	0.007 (0.006)	0,138
GradingG2.8	-0.124 (0.536)	0,828
GradingG3.8	0.259 (0.541)	0,654
NodalStatus.8	0.219 (0.155)	0,143
Chemoyes.8	0.261 (0.191)	0,157
CenterB.8	-0.286 (0.238)	0,239
CenterC.8	-0.351 (0.193)	0,0562
CenterD.8	-0.75 (0.212)	0,000657
CenterX.8	0.198 (0.224)	0,394
treatBCT.RT.8	-0.628 (0.365)	0,176
treatMAS.8	-0.608 (0.408)	0,271
treatMAS.RT.8	-0.903 (0.356)	0,0546
treatBCT.MAS.8	-1.083 (0.499)	0,067
treatBCT.MAS.RT.8	-0.983 (0.36)	0,0379
adjuvantyes.8	0.015 (0.208)	0,944

Adjustierte Überlebenskurven nach Center

Center — A — B — C — D — X

