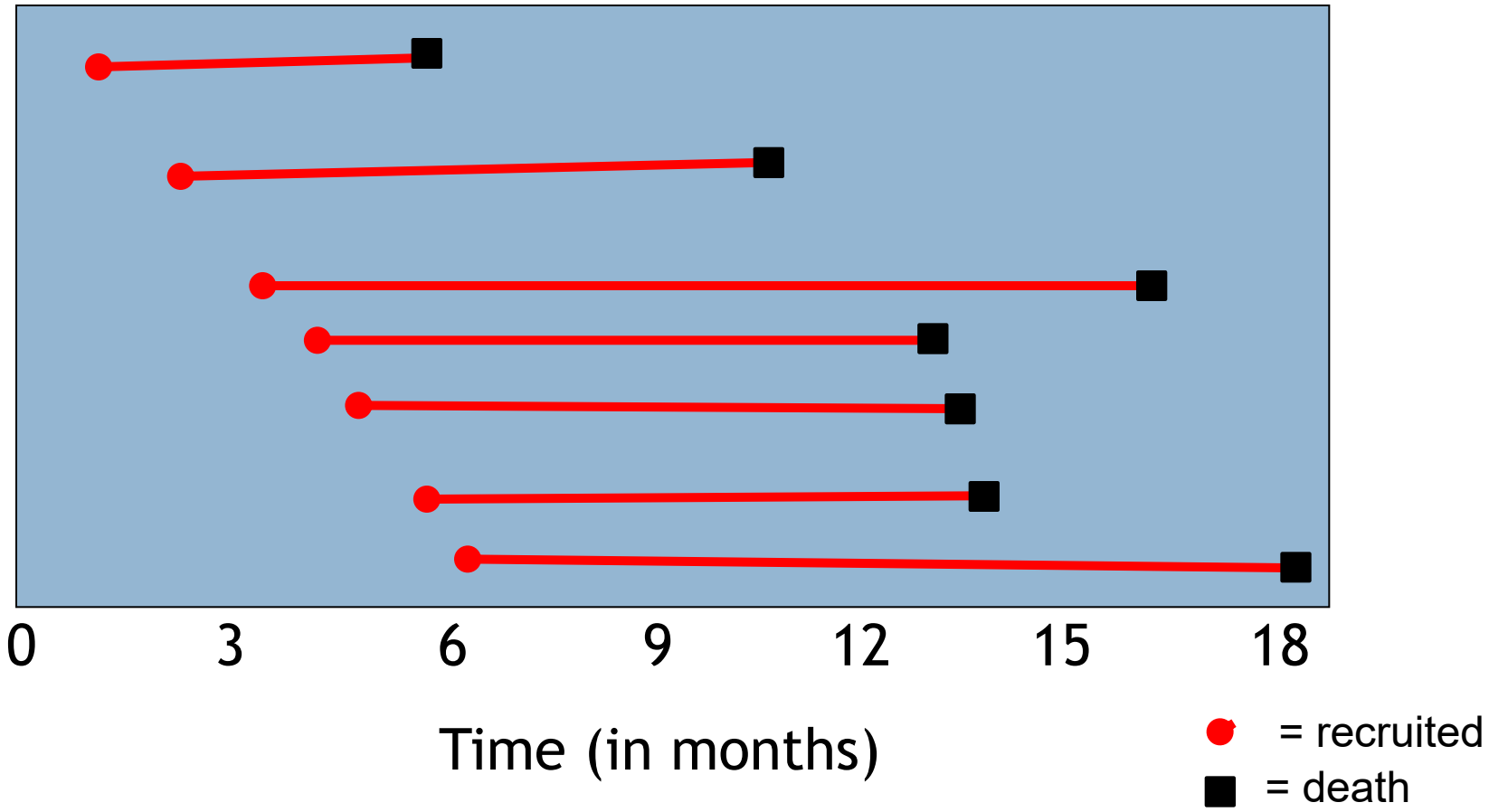
SURVIVAL ANALYSIS

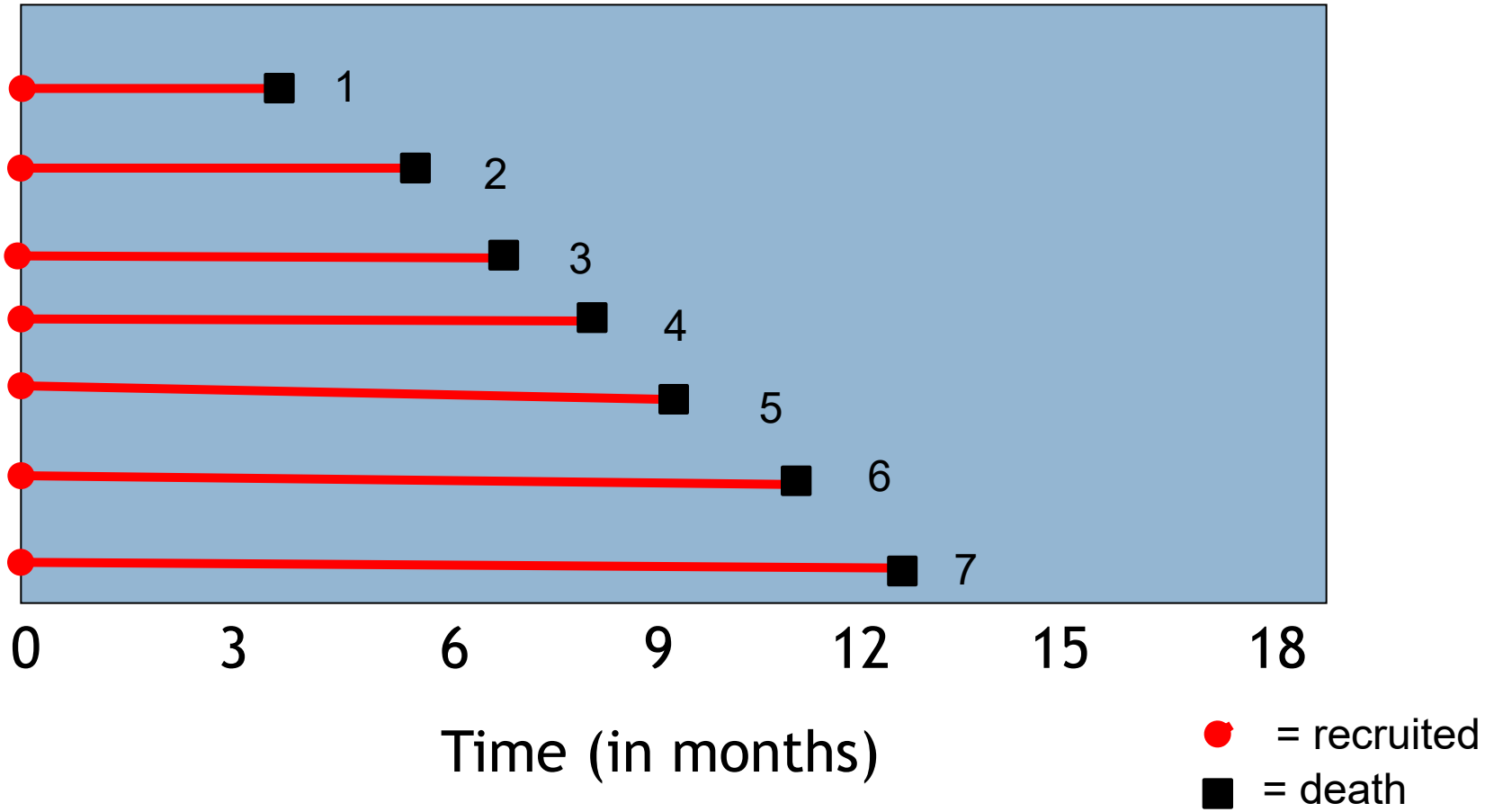
Peter Hall

Recruitment and follow-up

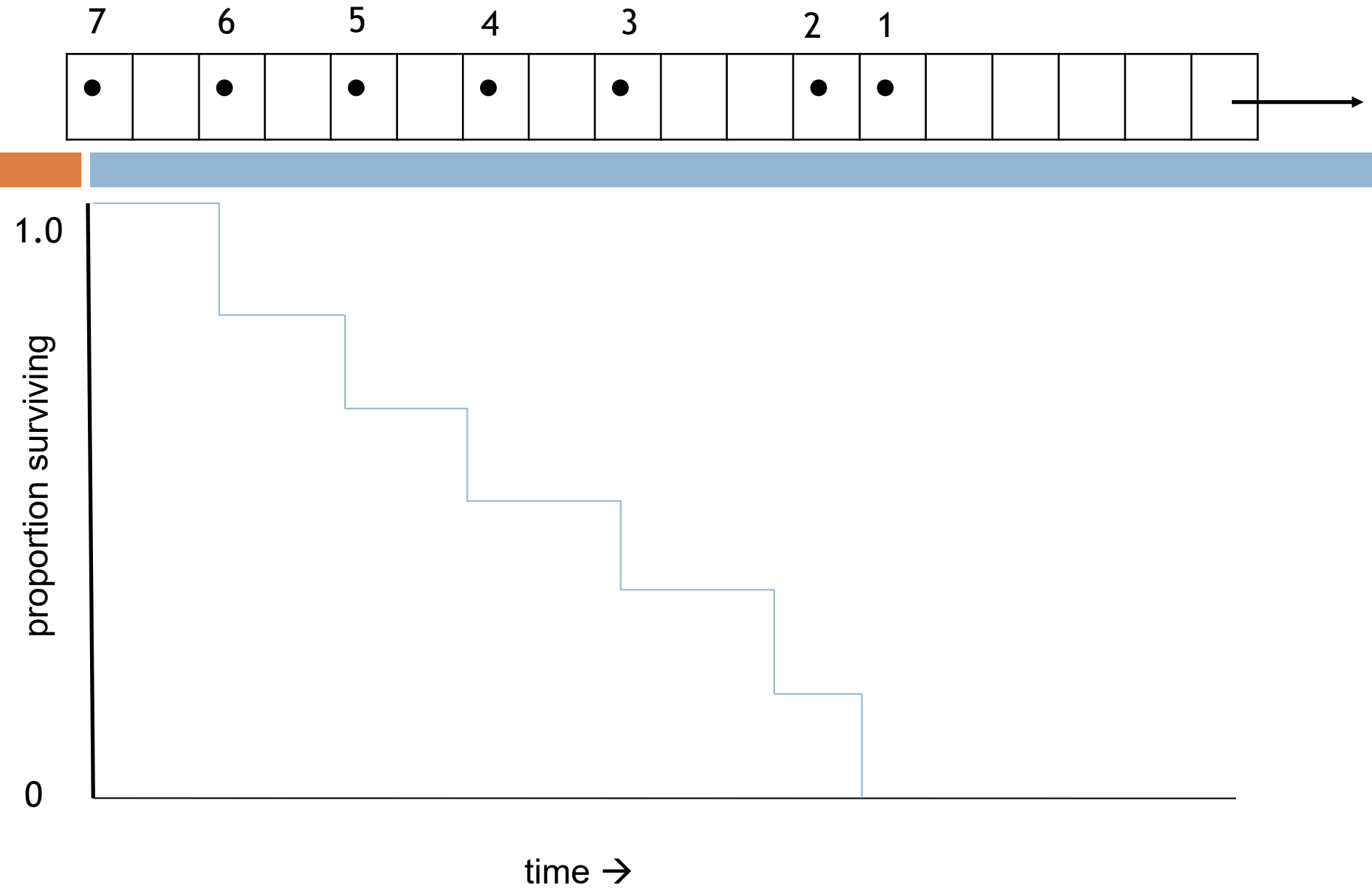


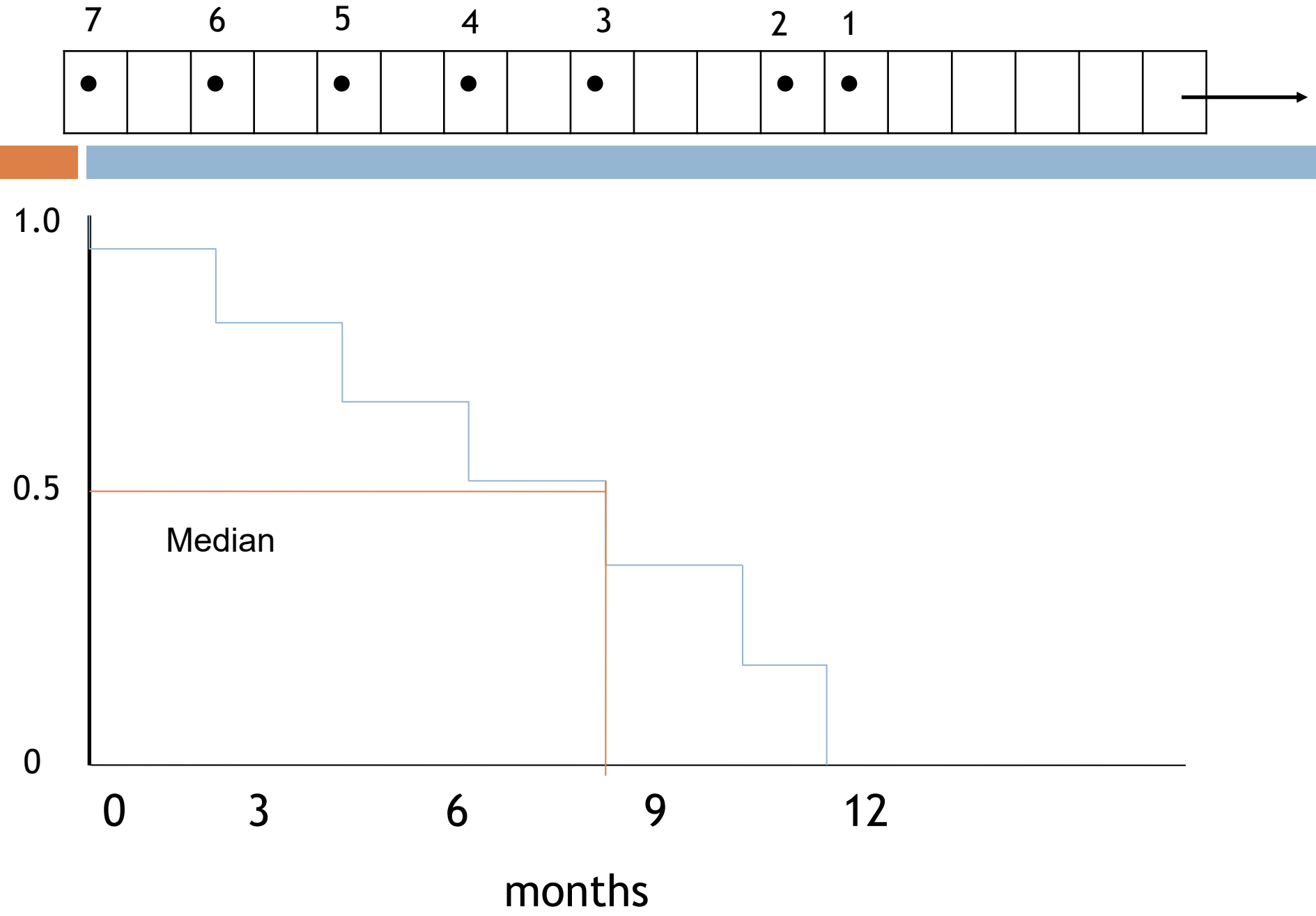
Average (mean) survival = 9 months

Recruitment and follow-up

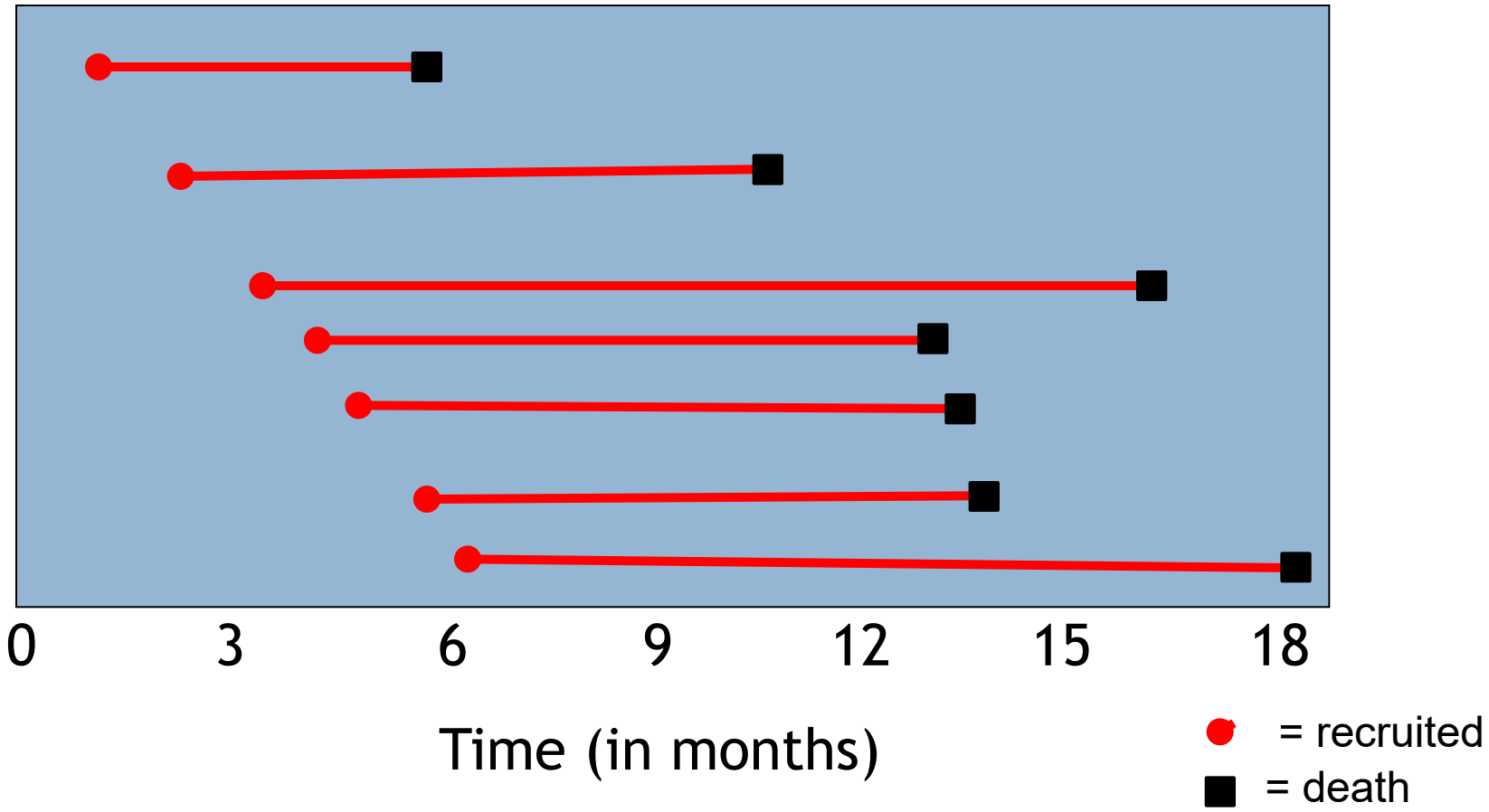


Median survival = 8 months

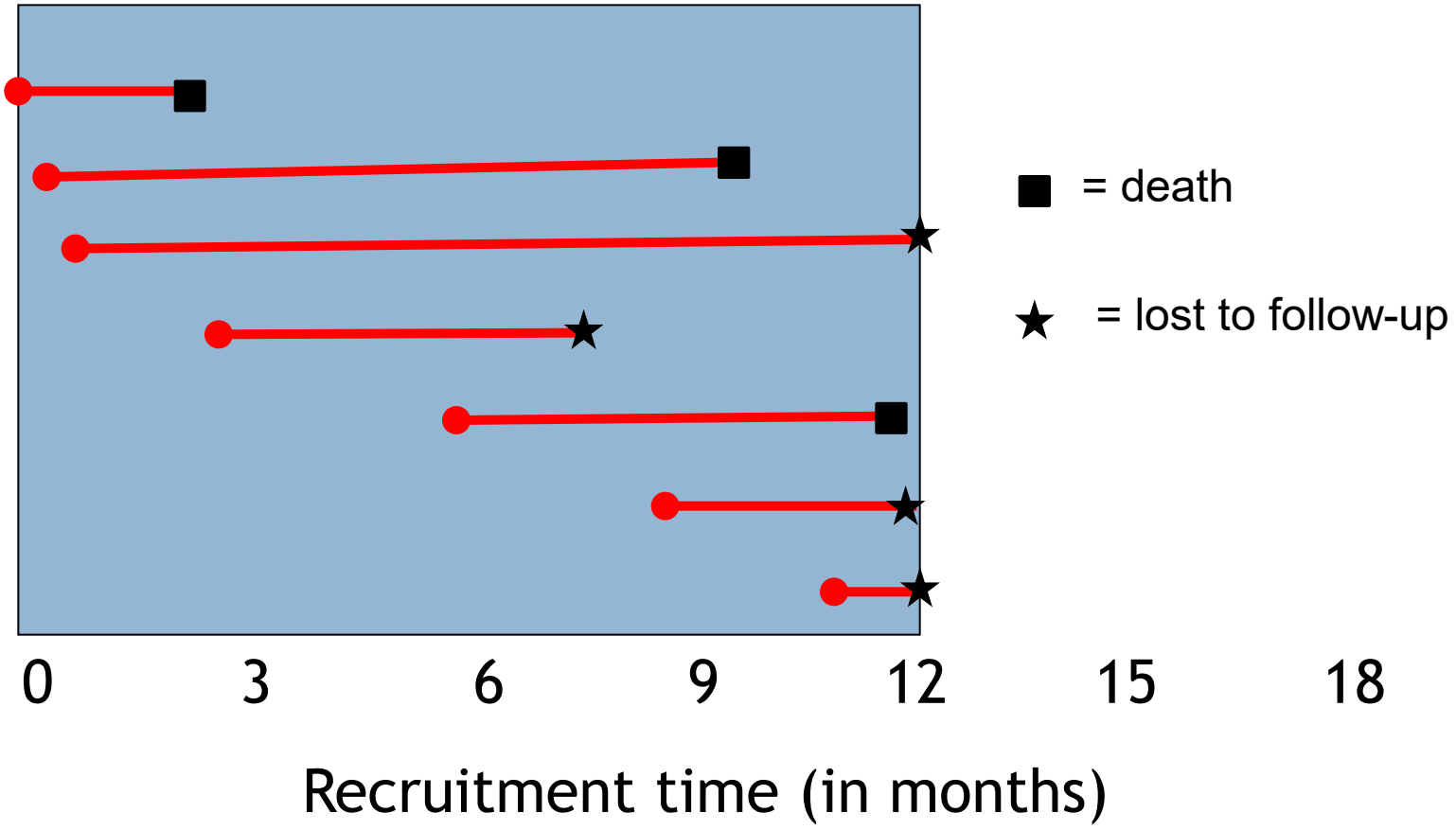

7
6
5
4
3
2
1
1.0
proportion surviving
0
time →


7
6
5
4
3
2
1
1.0
0.5
0
Median
0
3
6
9
12
months

Recruitment and follow-up

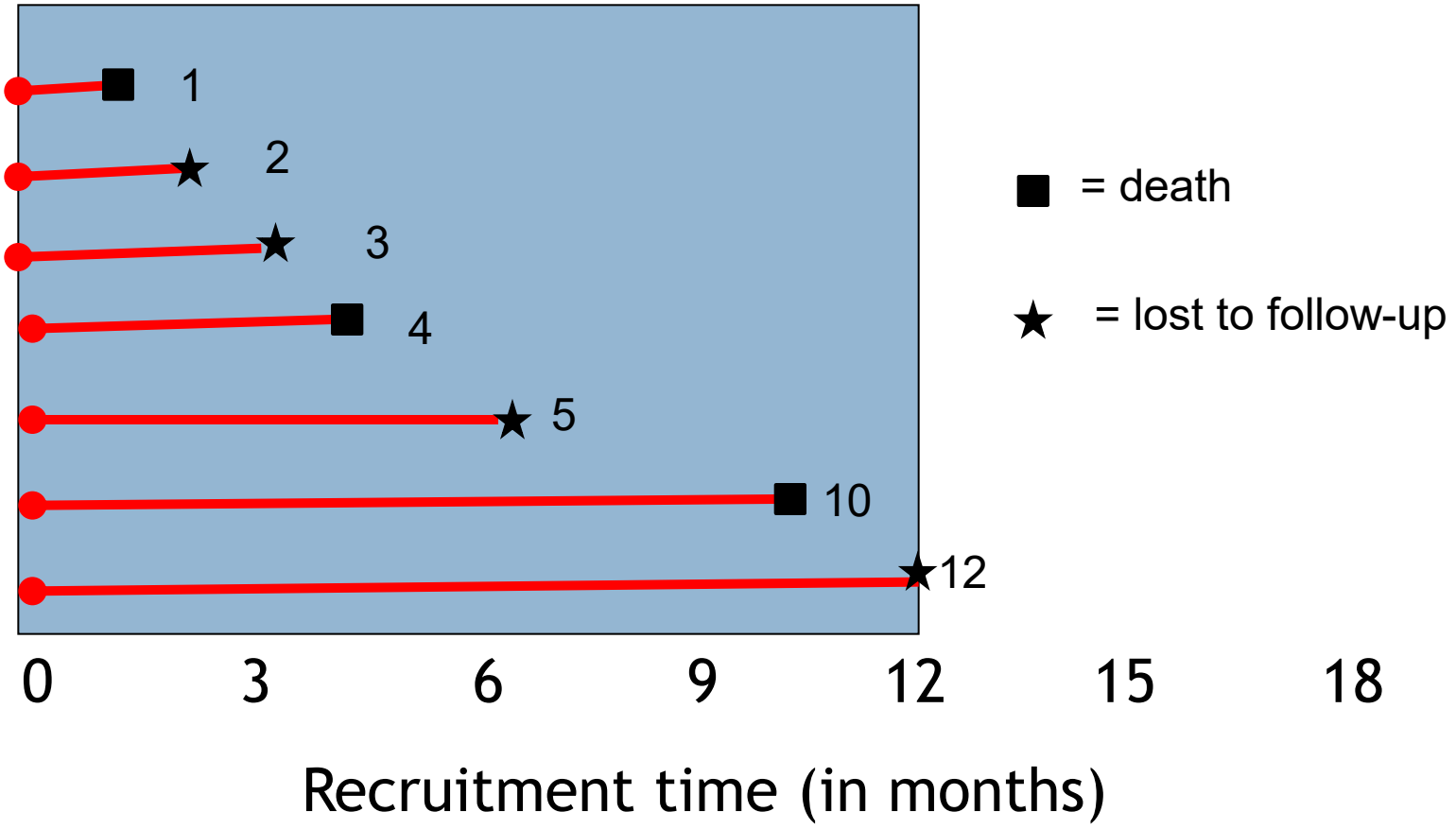


Recruitment and follow-up - reality

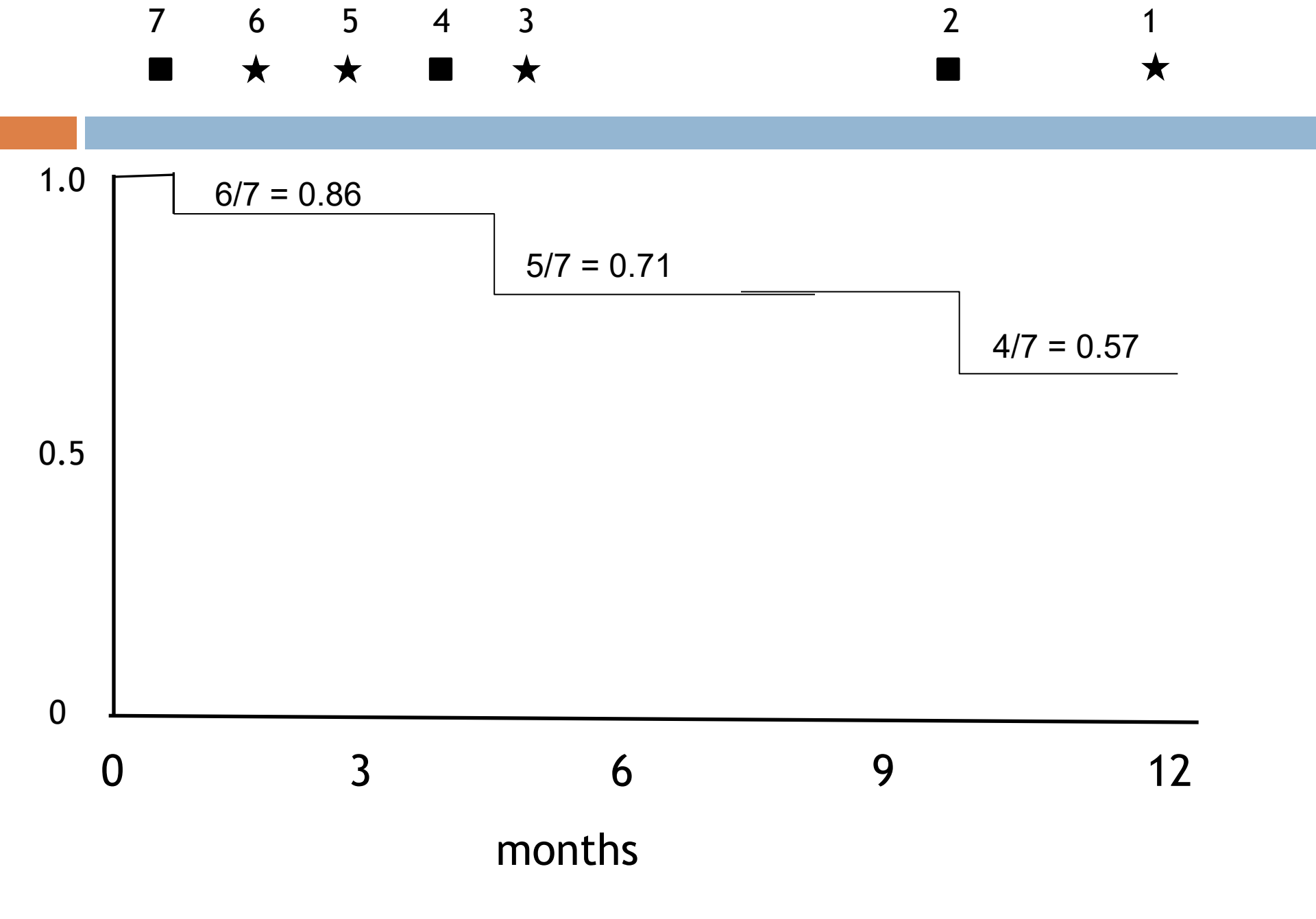


Average survival = 6 months

Analysis


1
2
3
4
5
10
12
= death
= lost to follow-up
0
3
6
9
12
15
18
Recruitment time (in months)

Option 1 – ignore patients at lost-to-follow-up



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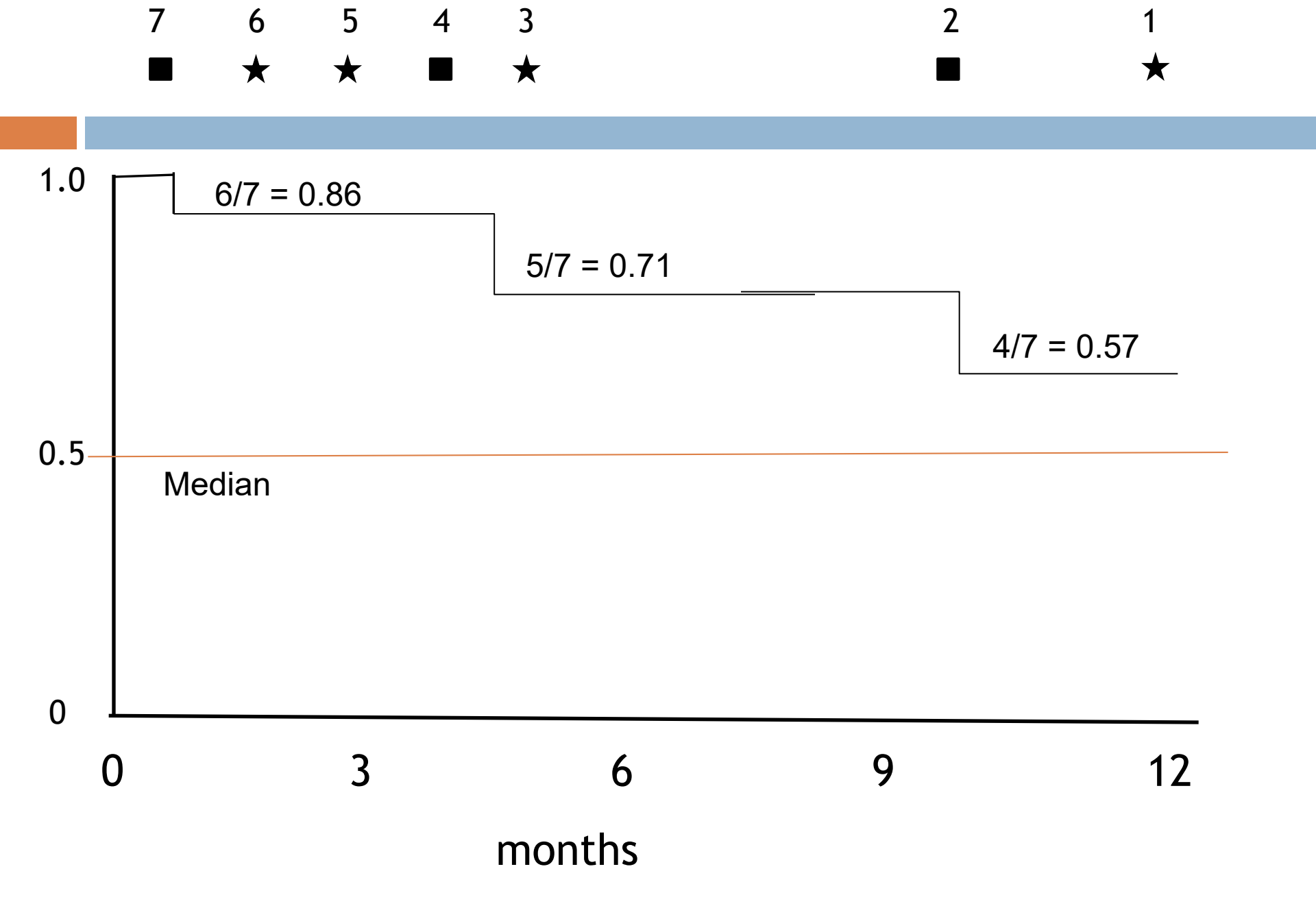
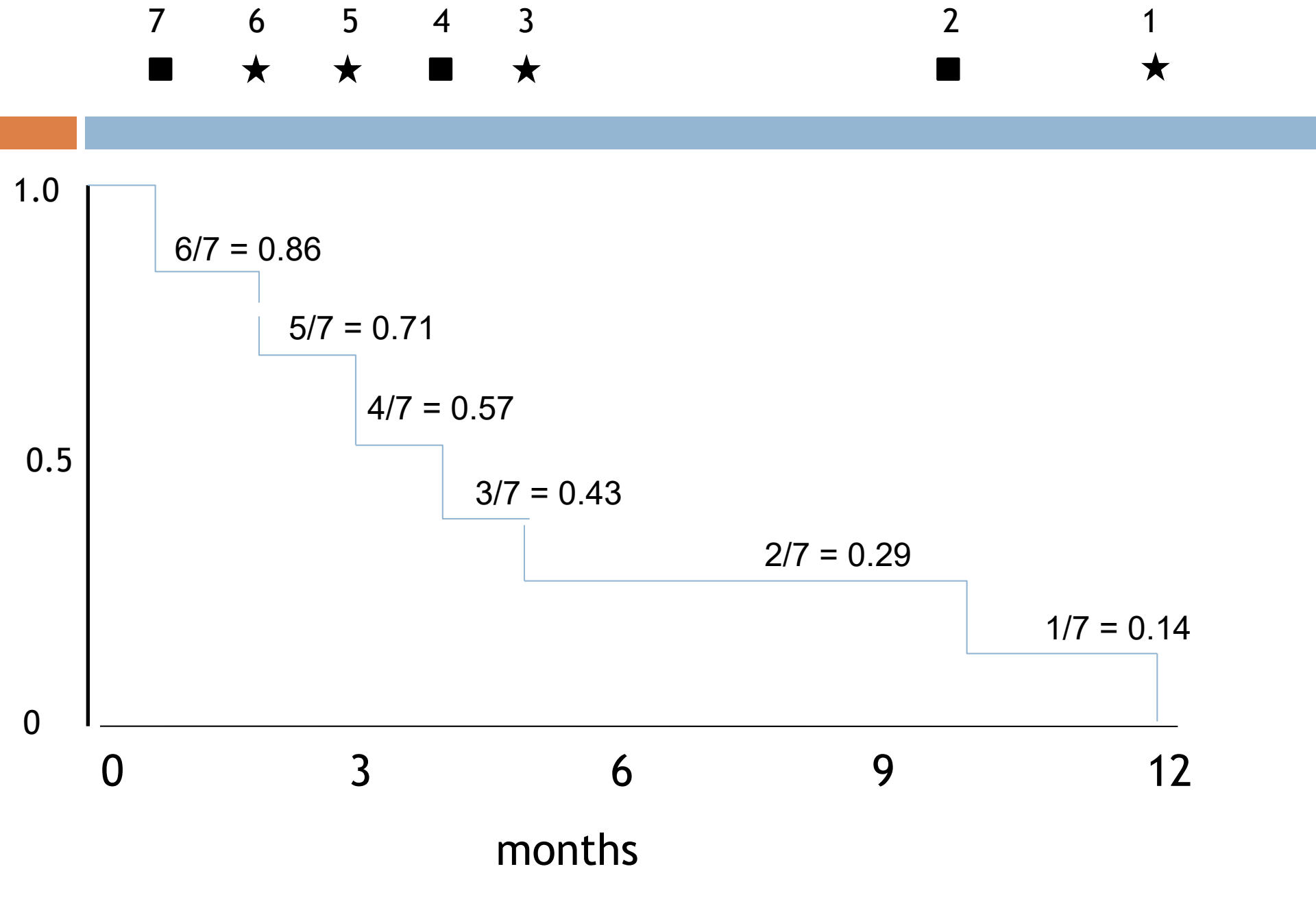


Option 2 – assume patients experience event at loss-to-follow-up



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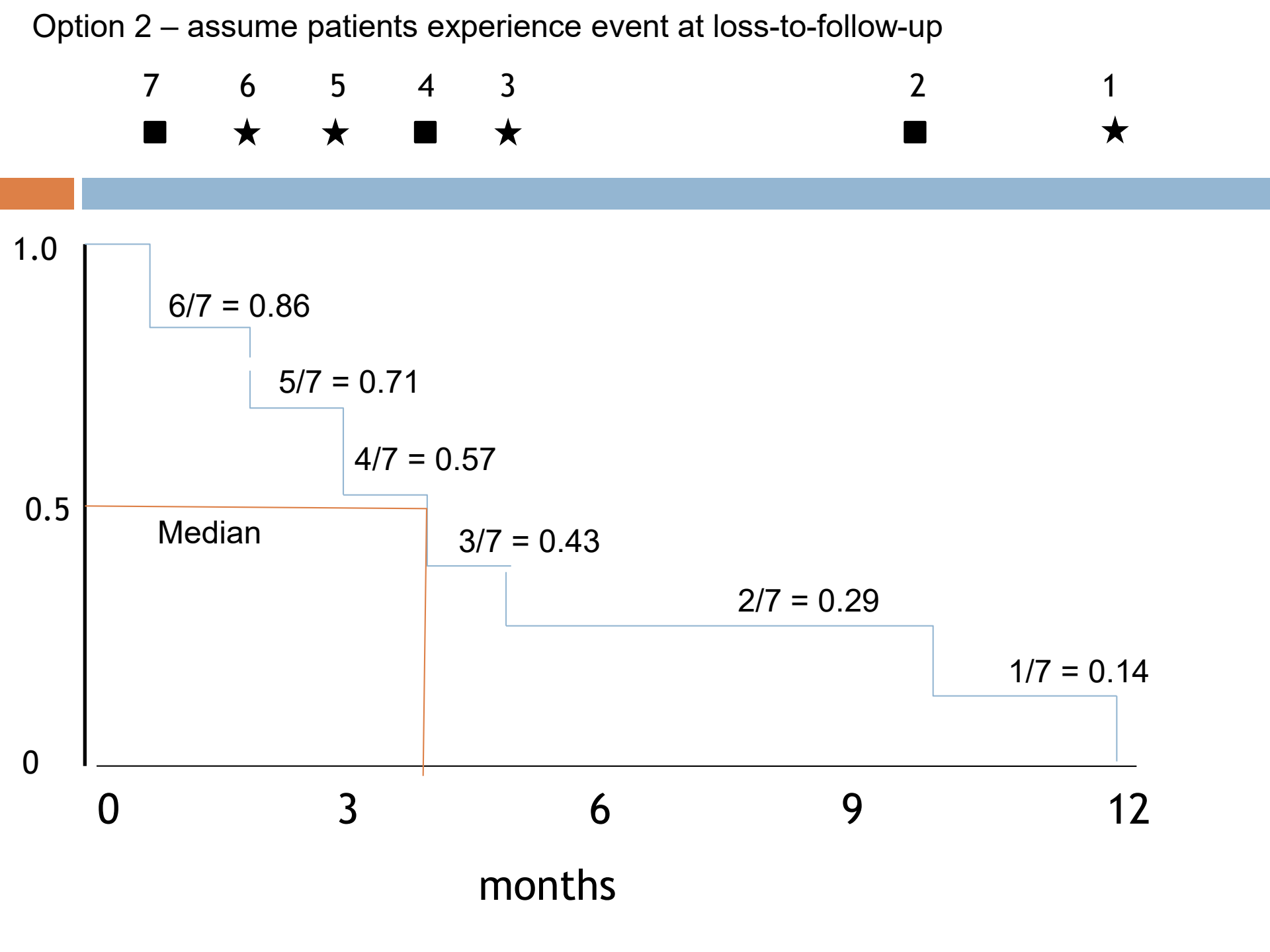
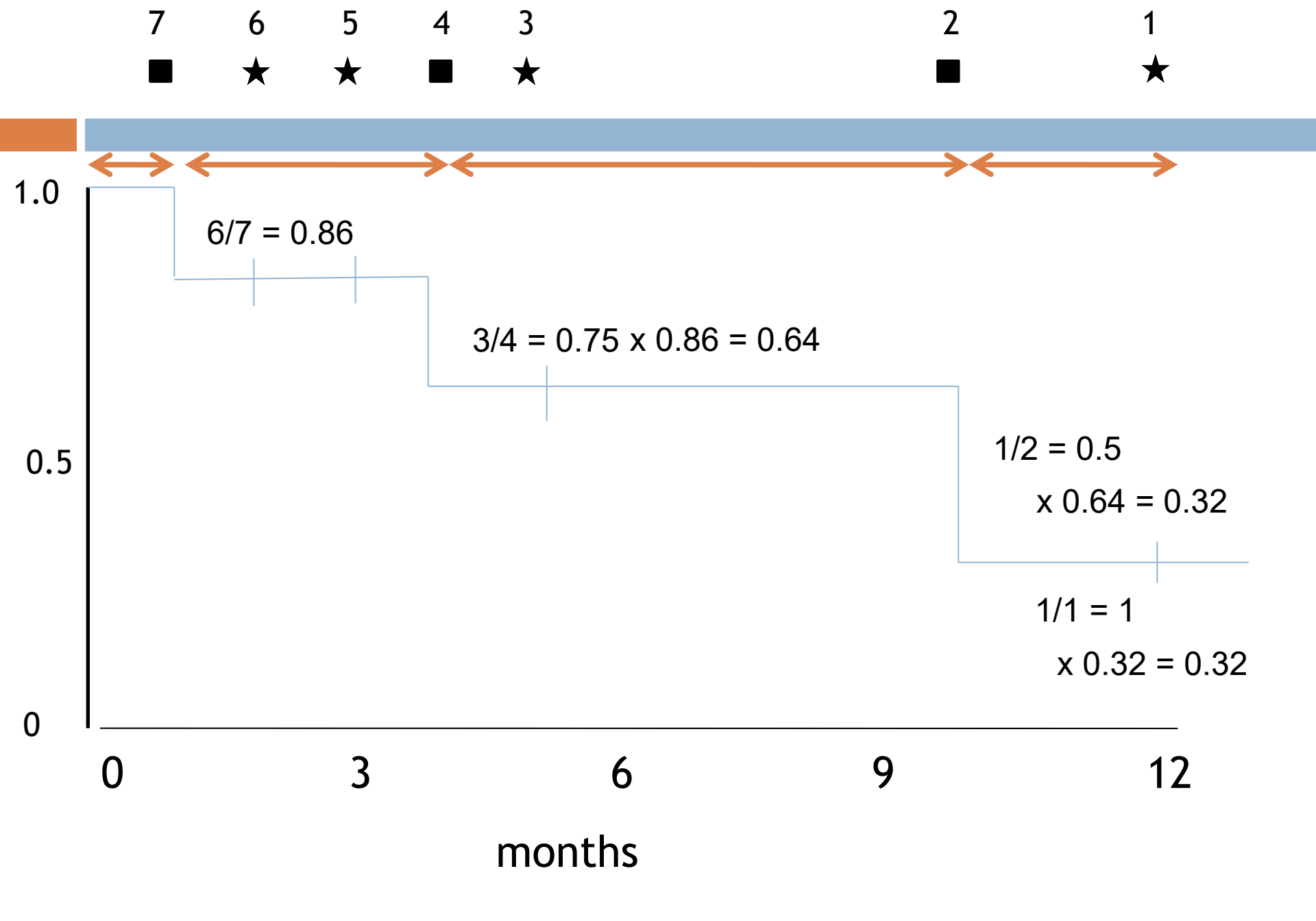


Option 3 – Kaplan-Meier estimator



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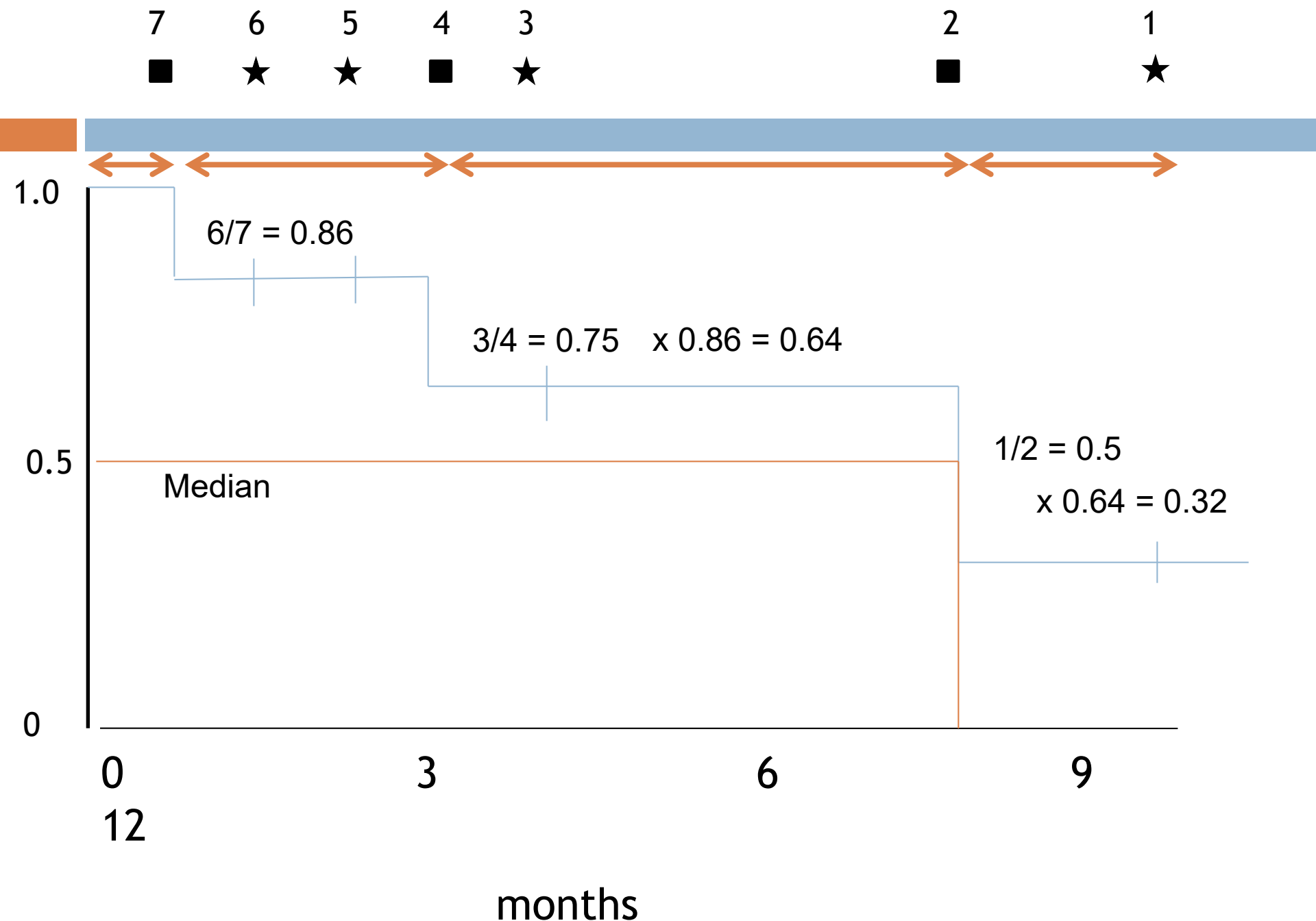
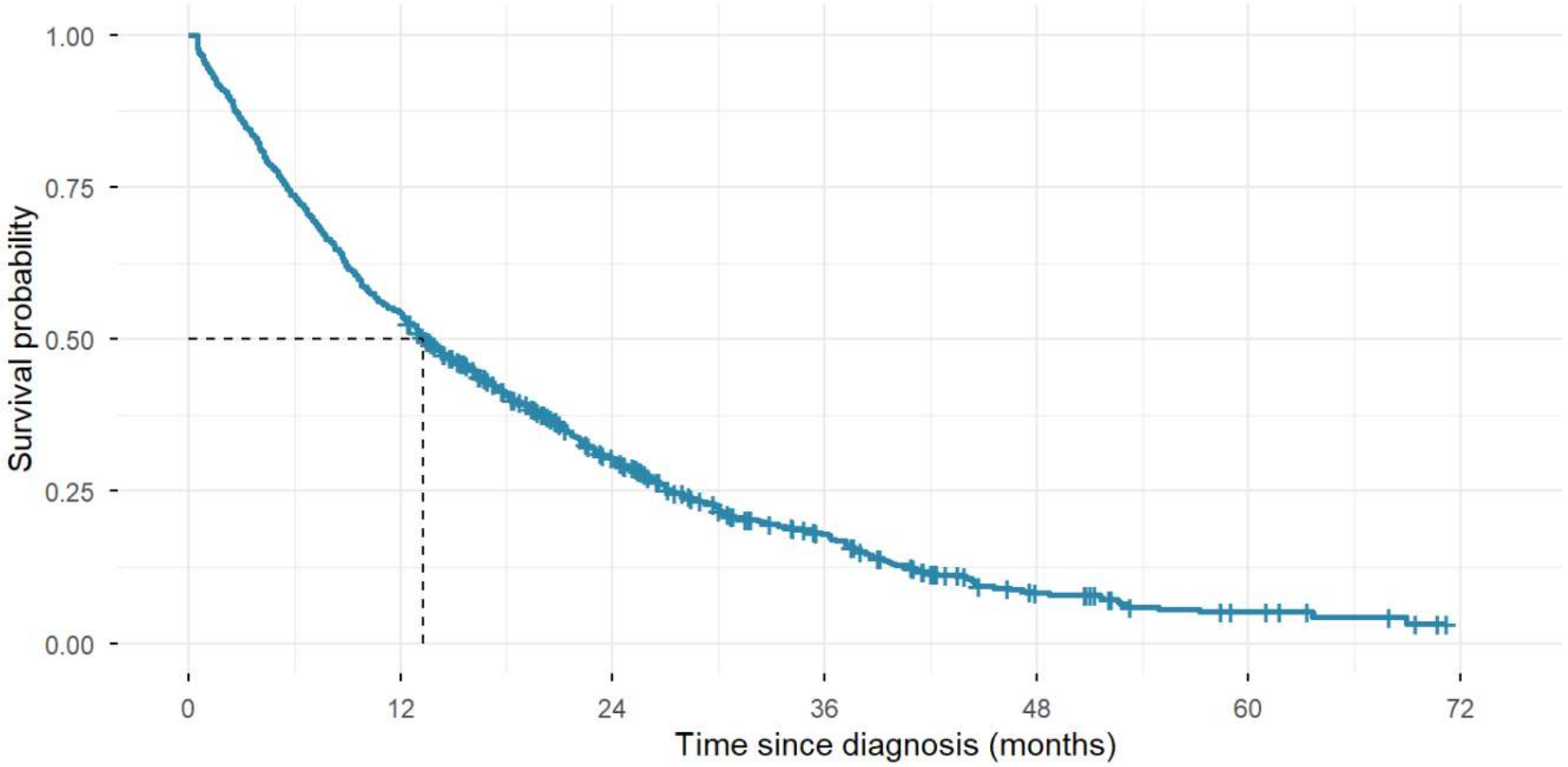




Number at risk

No. at risk	850	463	207	94	27	9	0
Events	0	12	24	36	48	60	72

Time since diagnosis (months)

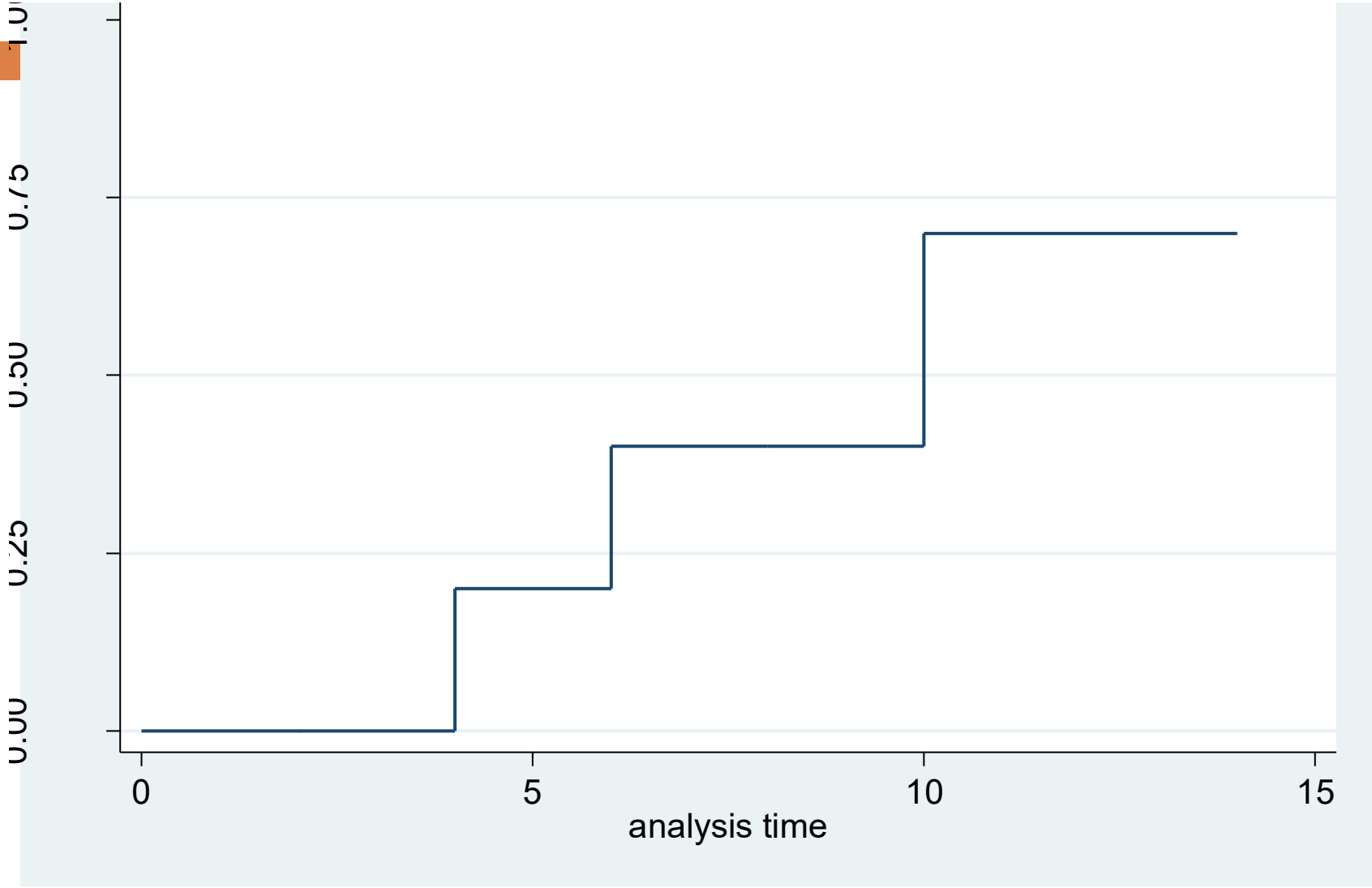
Tabulated K-M function

Interval (Start-End)	# At Risk at Start of Interval	# Censored During Interval	# At Risk at End of Interval	# Who Died at End of Interval	Proportion Surviving This Interval	Cumulative Survival at End of Interval
0-1	7	0	7	1	6/7 = 0.86	**0.86**
1-4	6	2	4	1	3/4 = 0.75	0.86 * 0.75 = **0.64**
4-10	3	1	2	1	1/2 = 0.5	0.86 * 0.75 * 0.5 = **0.31**
10-12	1	0	1	0	1/1 = 1.0	0.86 * 0.75 * 0.5 * 1.0 = **0.31**

Life table

Time	Survival
0	1.0000
1	0.86
2	0.86
3	0.86
4	0.64
5	0.64
10	0.32
12	0.32

Cumulative incidence



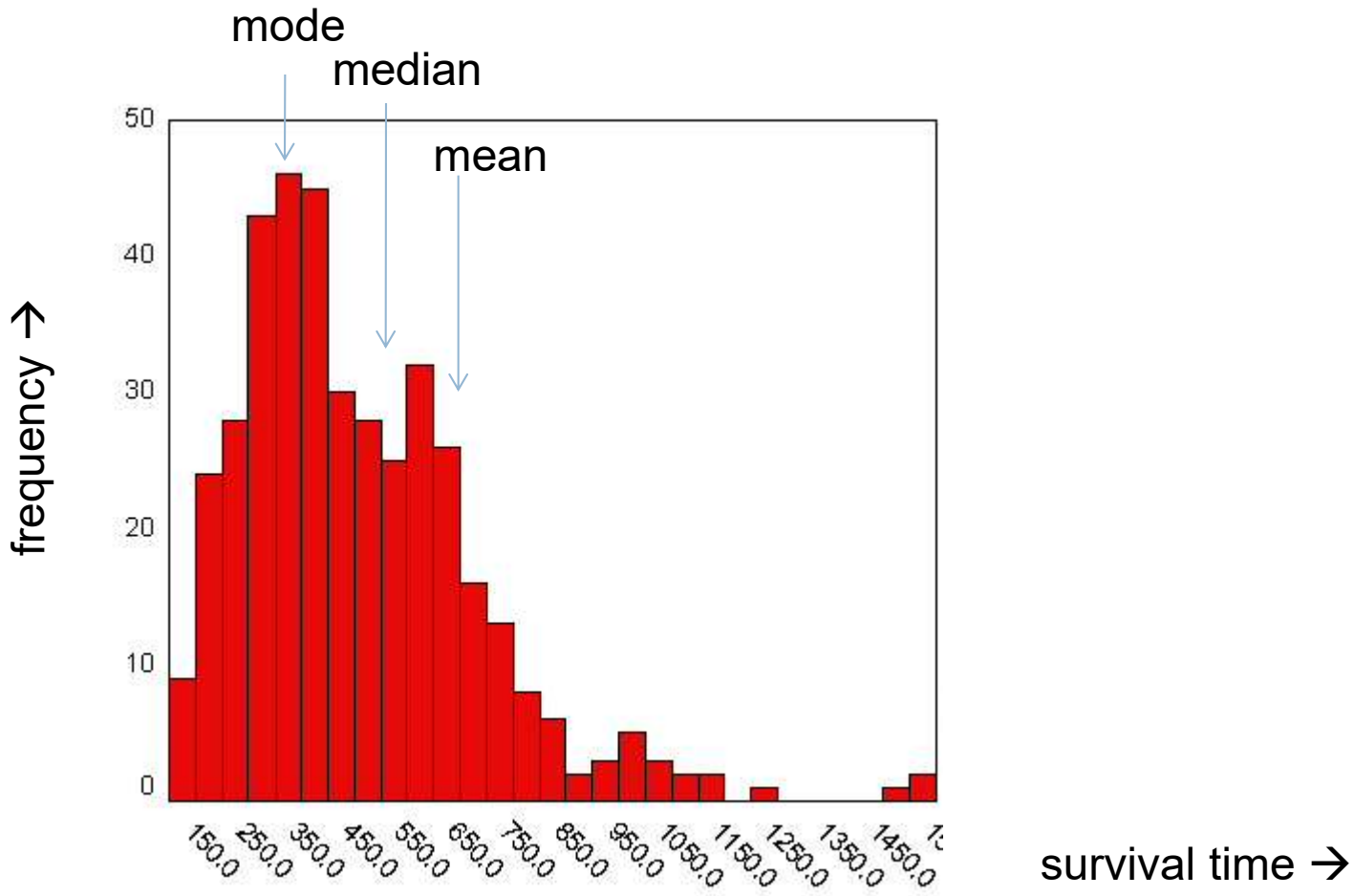
Terminology

- survival analysis,
- survival modeling,
- survival data analysis,
- actuarial analysis,
- lifetable,
- life-history analysis,
- life data analysis,
- life-testing,
- failure-time data,
- event-history analysis,
- censored data analysis
- product limit estimator

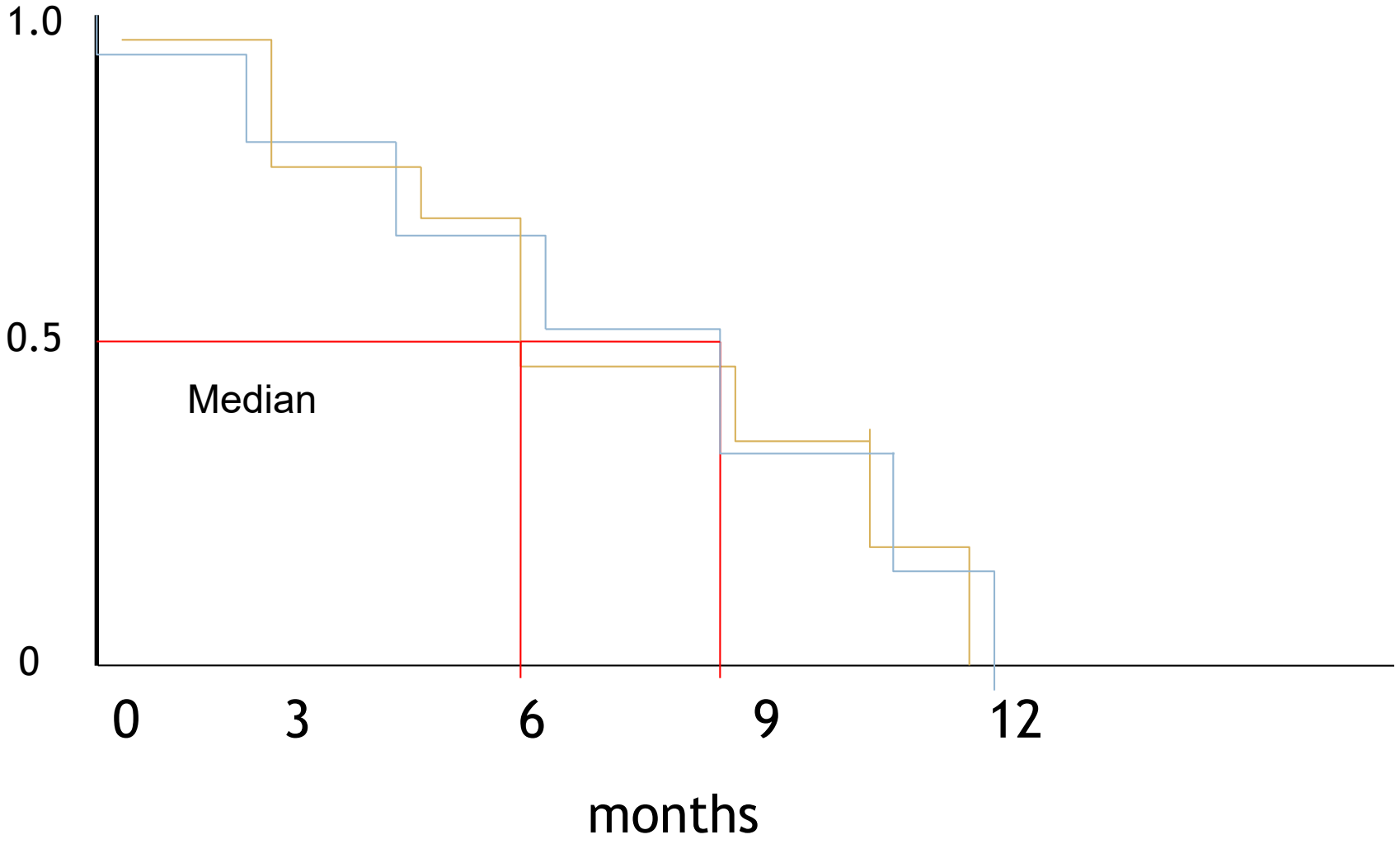
= all the same thing

Summary measures

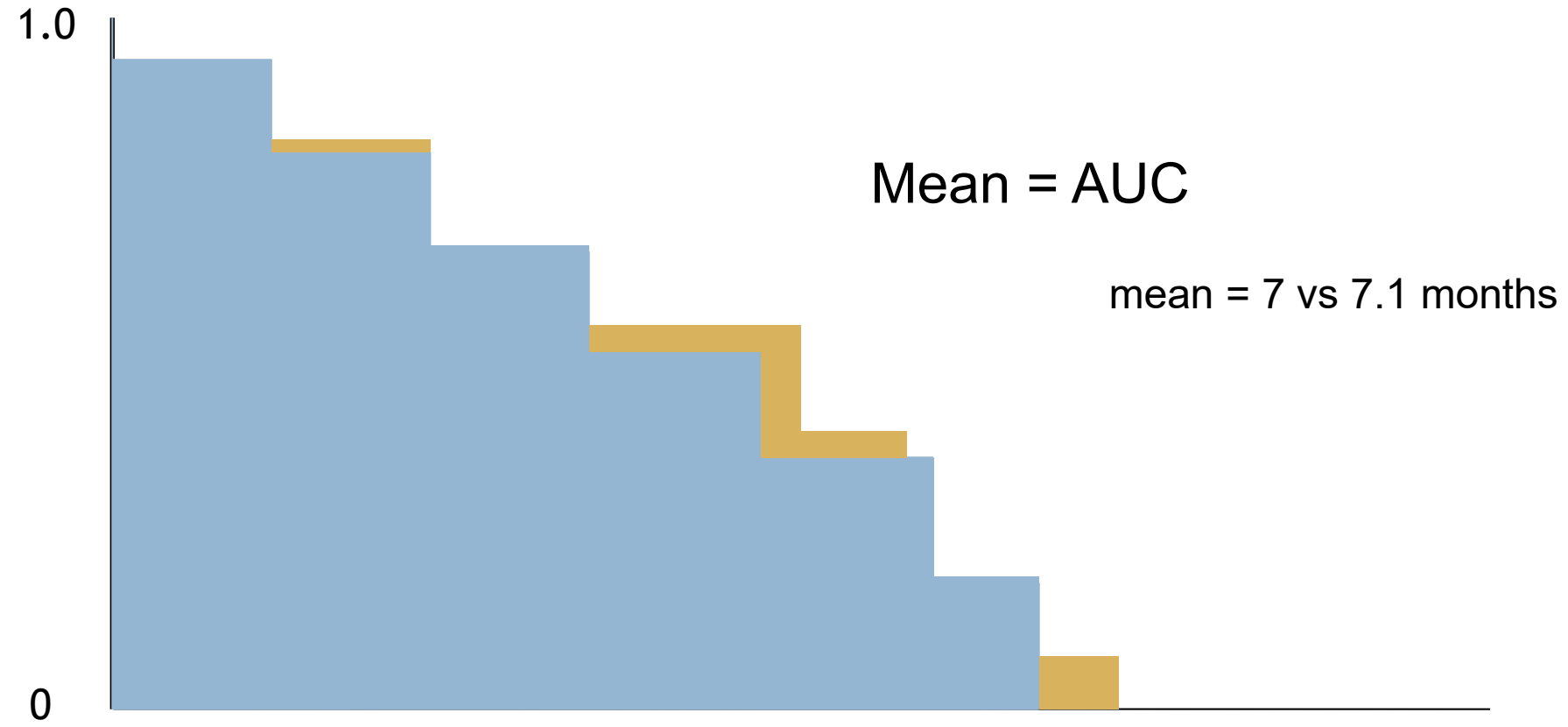
- Median or mean or mode?



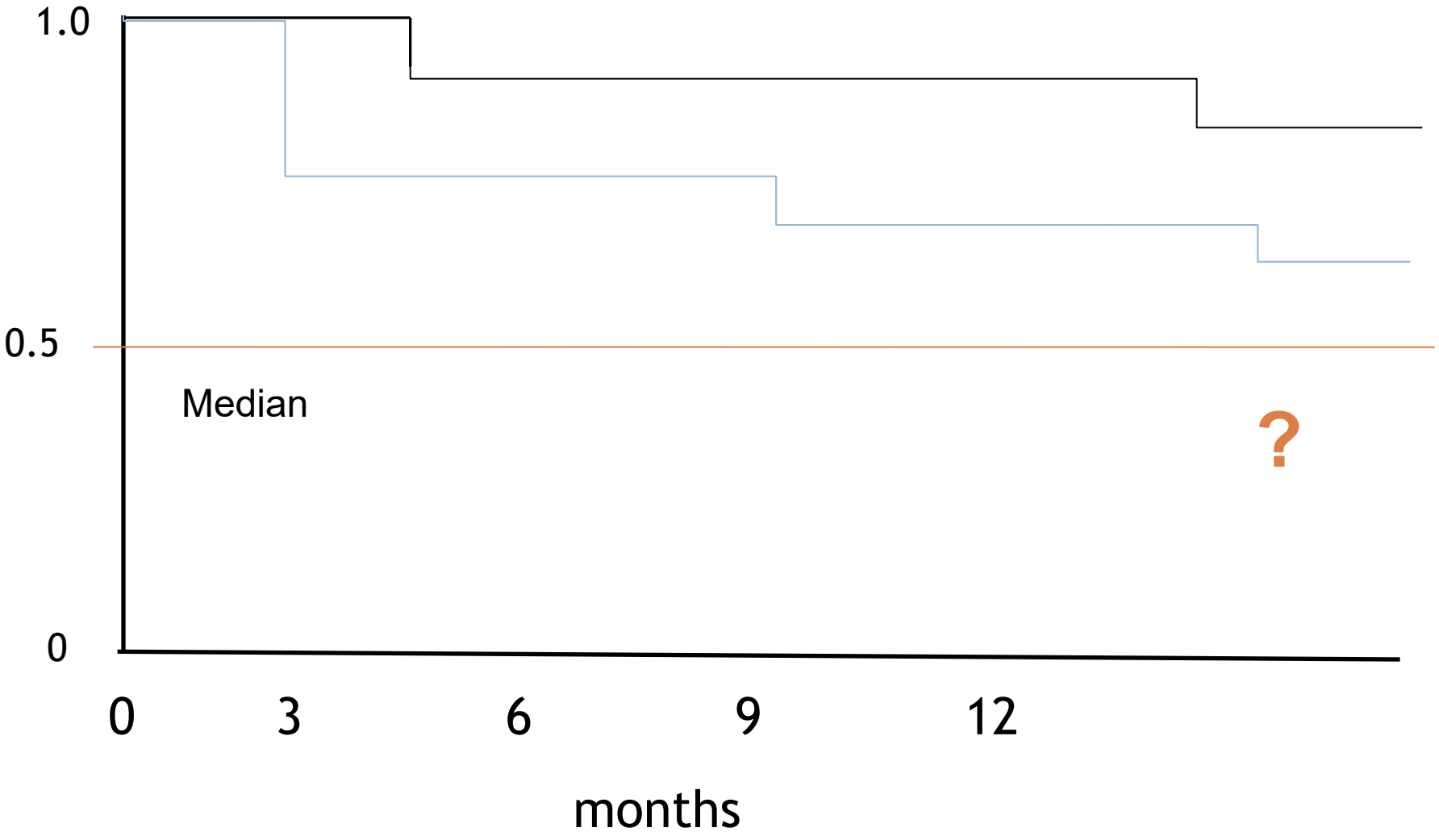
Summary measures



Summary measures



Summary measures



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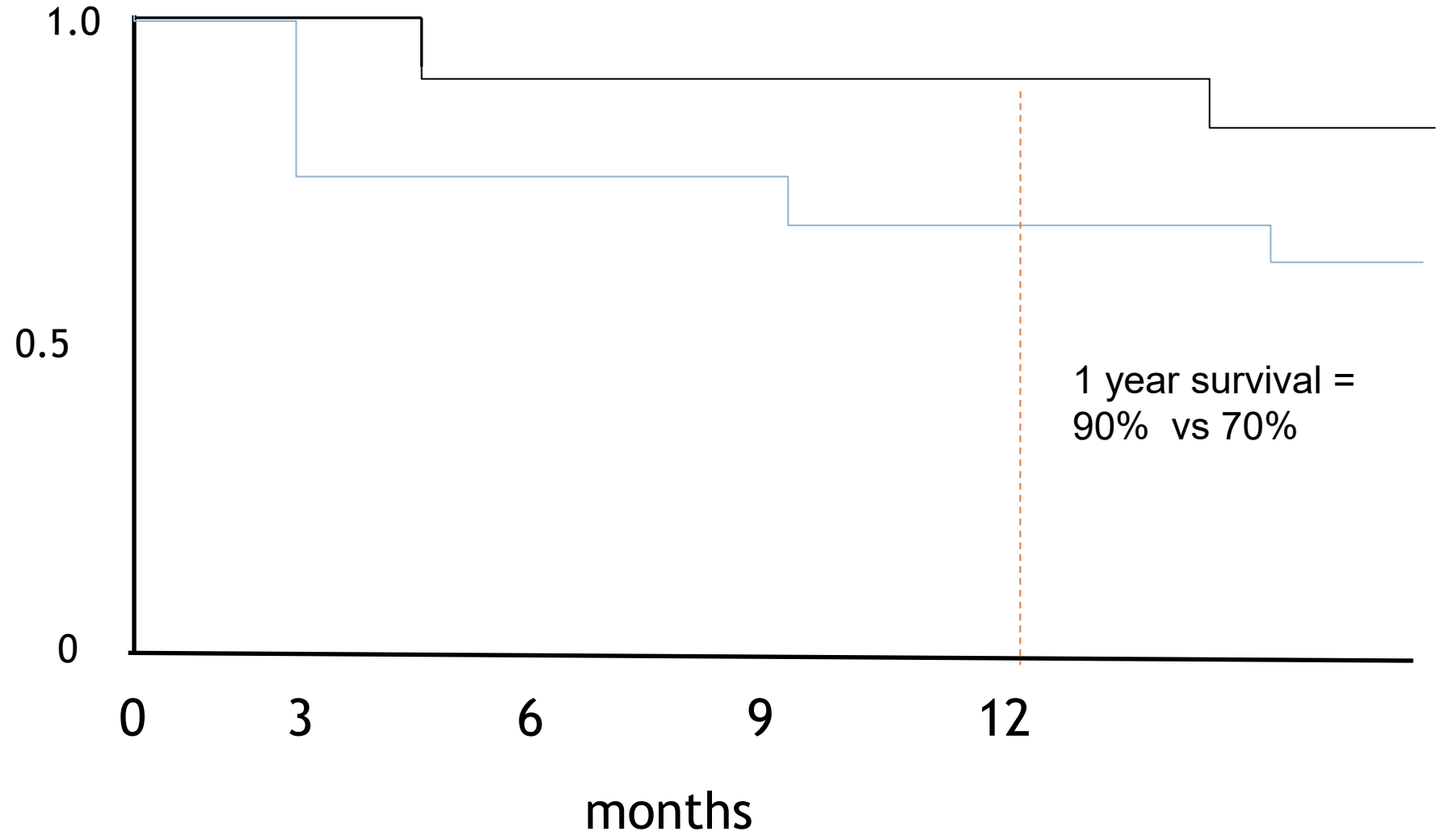
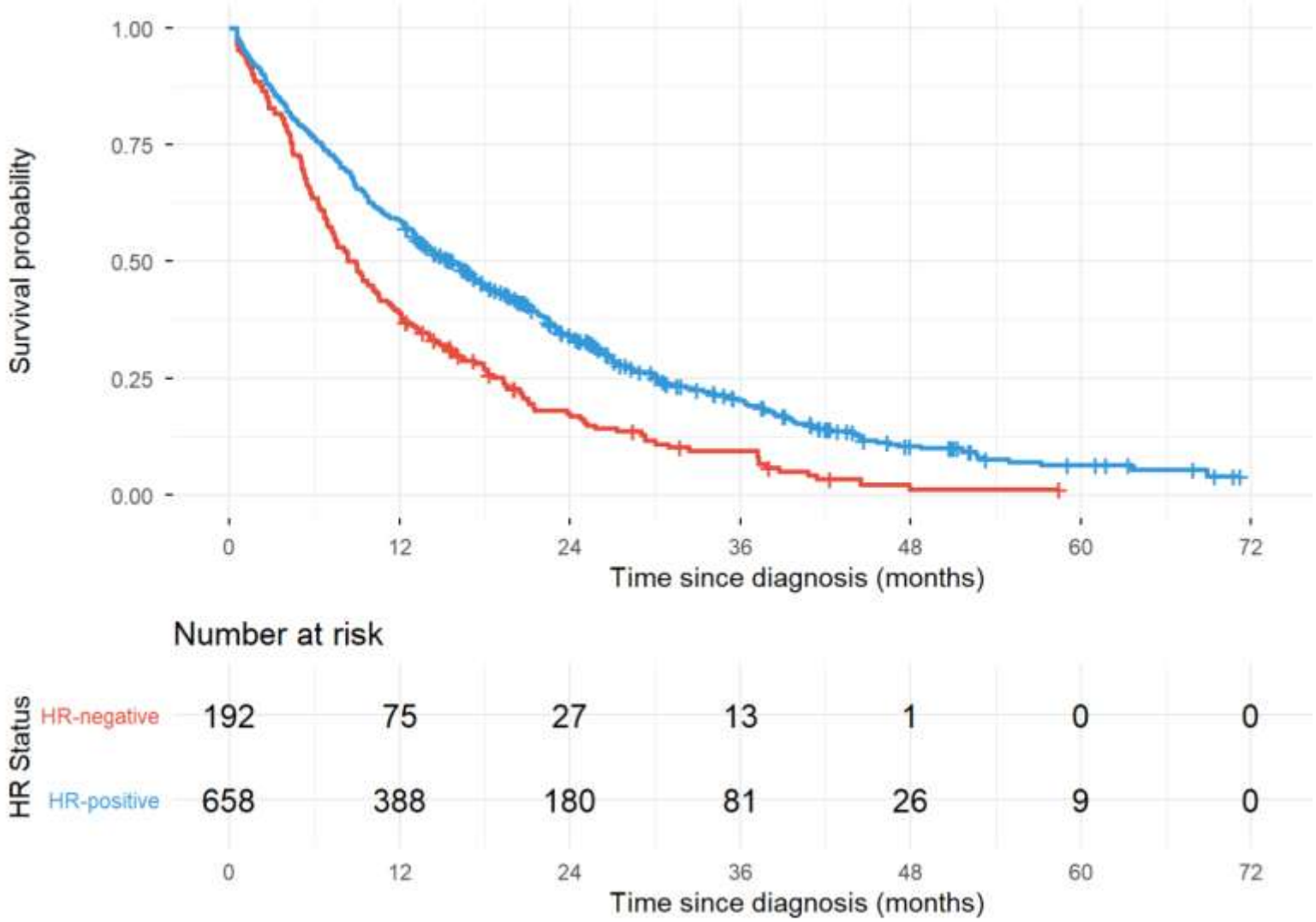


Comparing survival

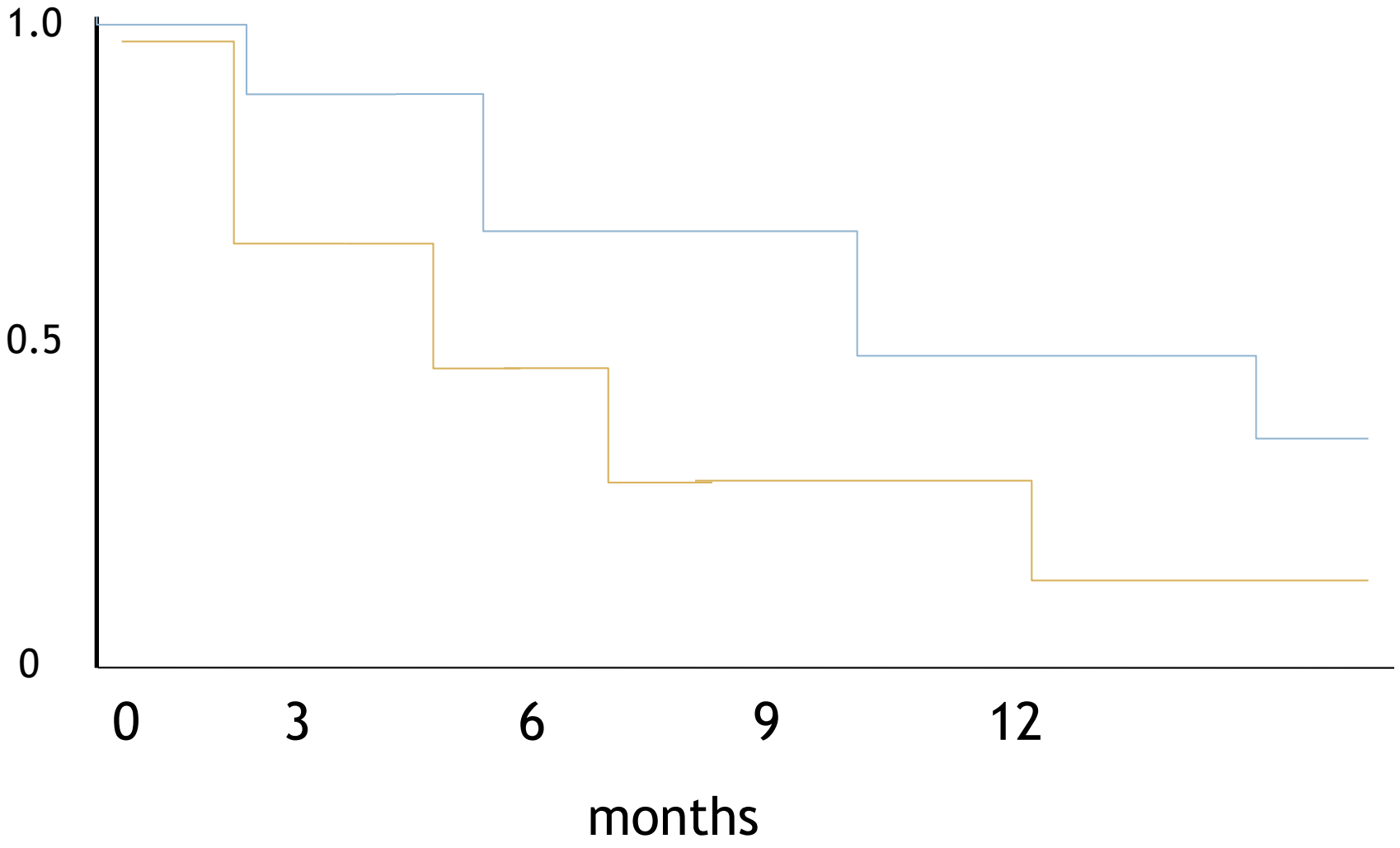


Comparing survival

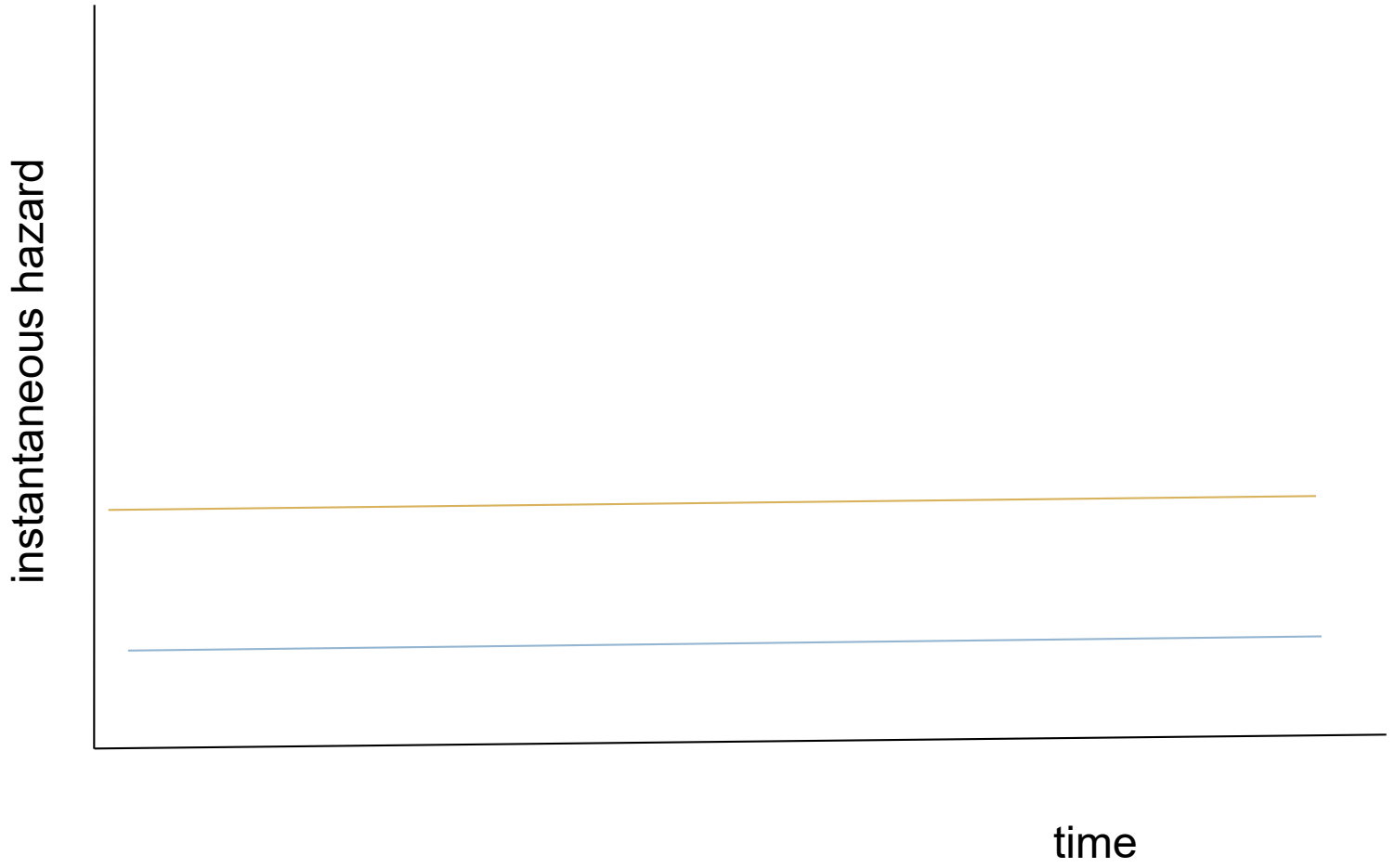
- Significant difference?
- Logrank test
  - gives a p-value
  - tests equality of survival function
- Stratified log-rank test
- Relies on proportional hazards

Sums the observed-minus-expected differences across all event times, then standardizes by the variance. If no difference, this follows a chi-squared distribution.

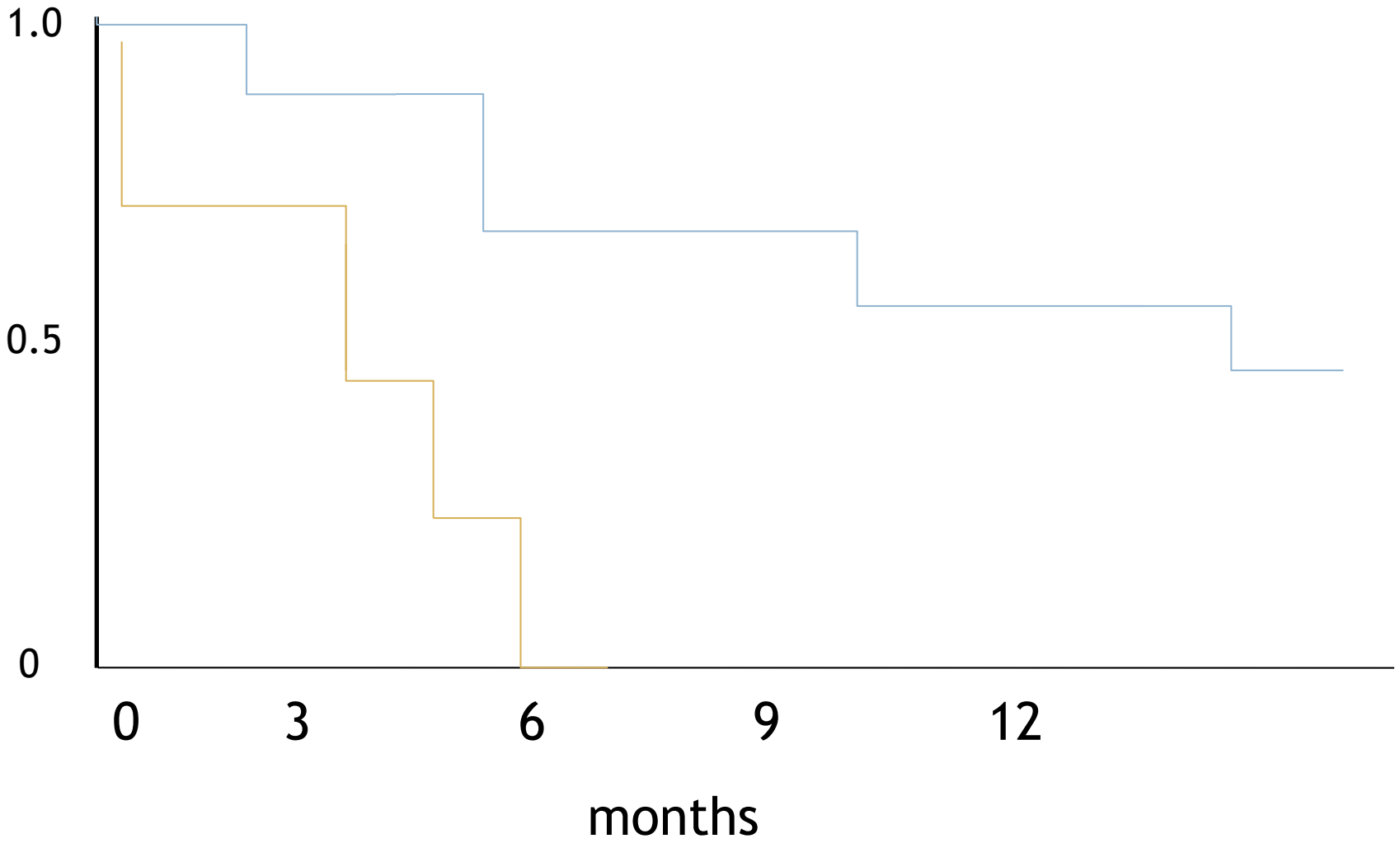
Proportional Hazards?



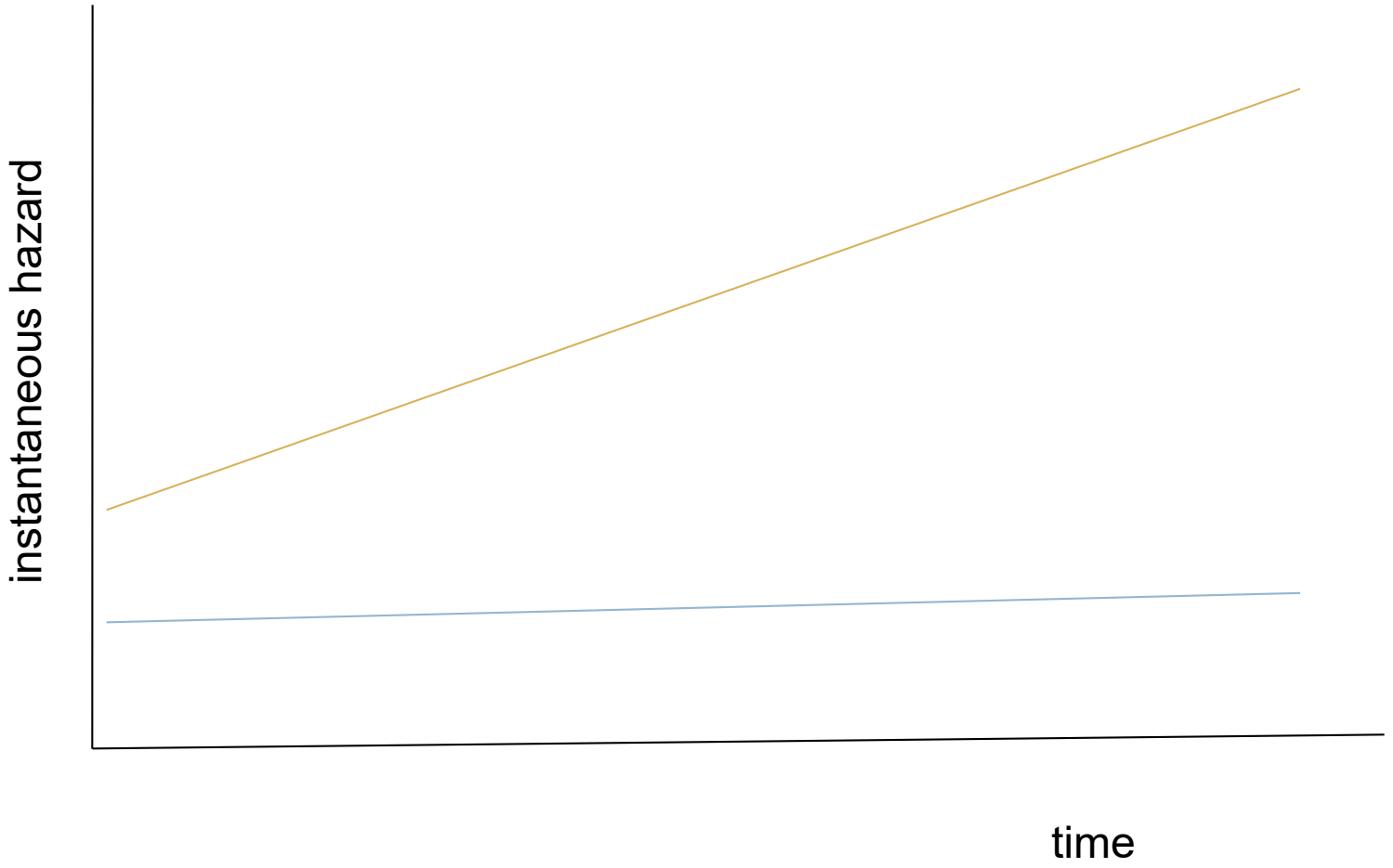
Proportional Hazards?



Summary measures



Proportional hazards?



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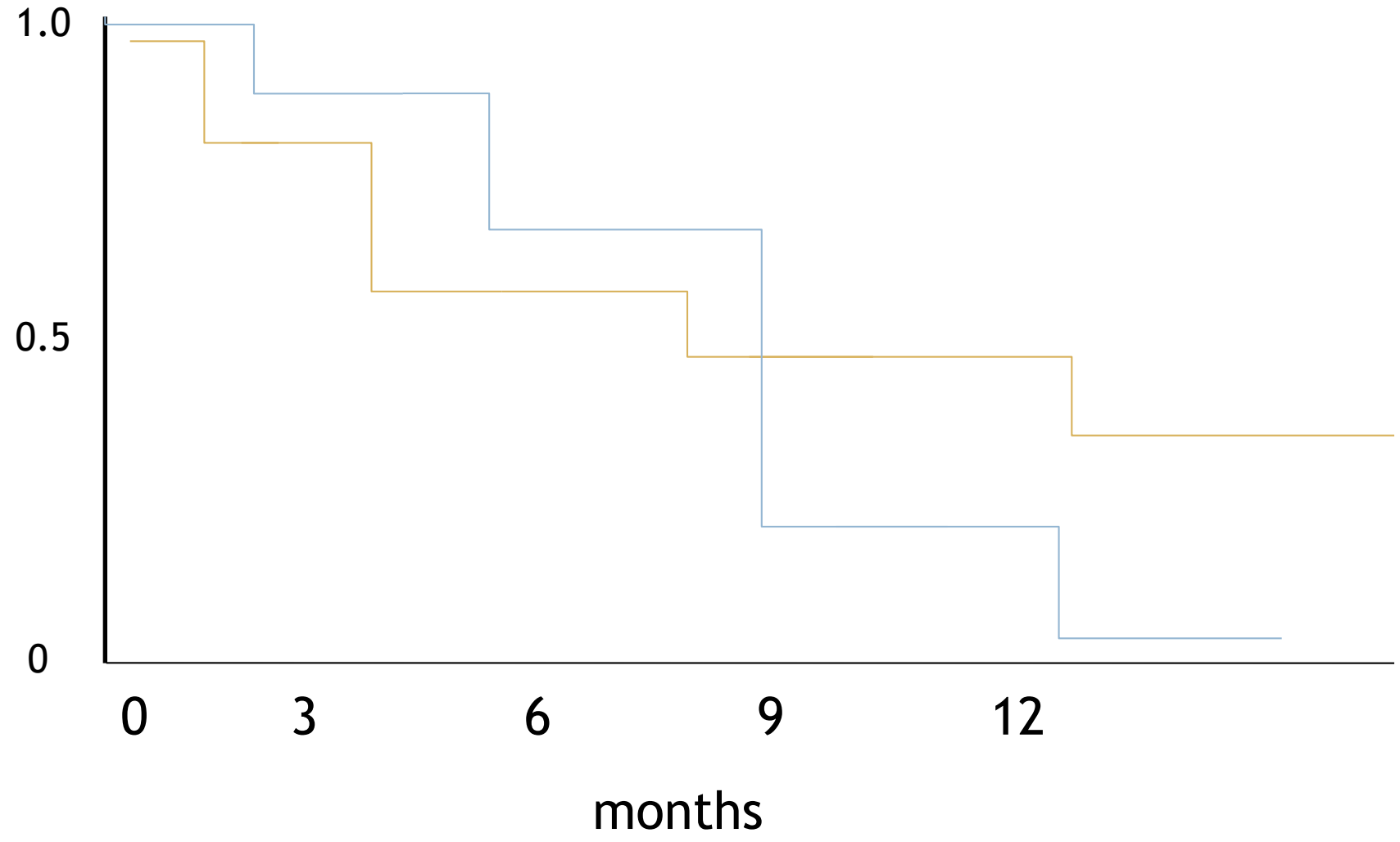

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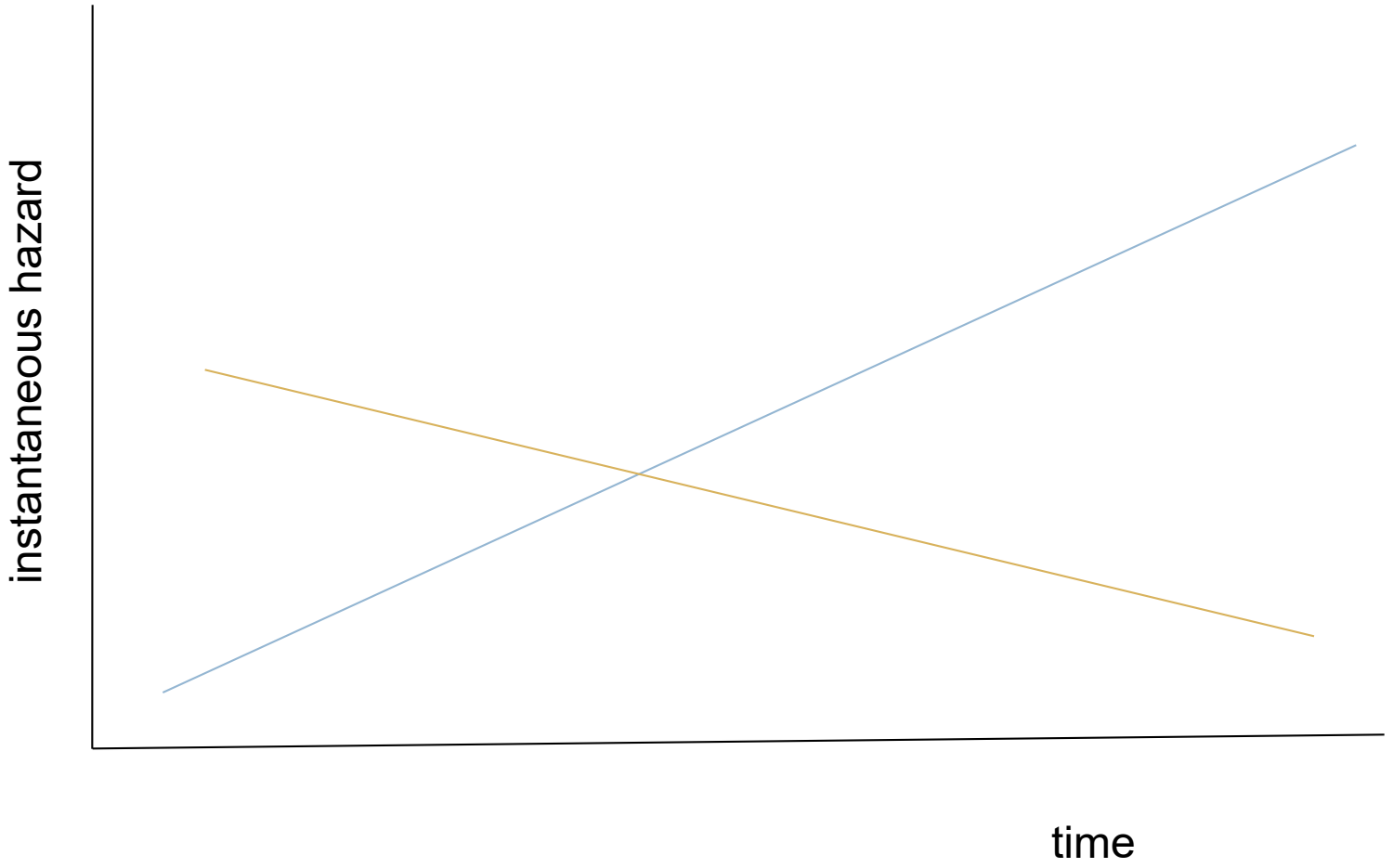

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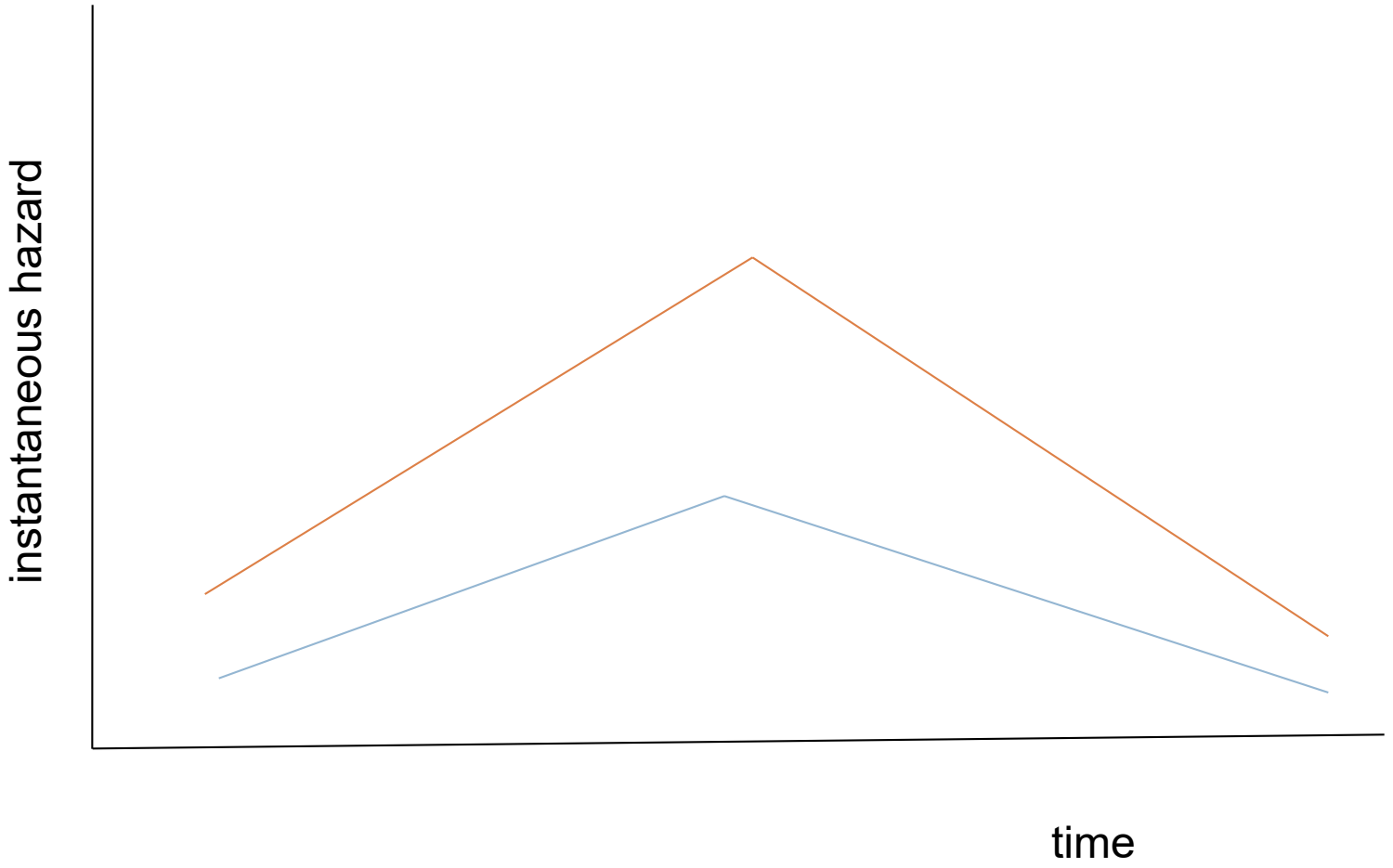

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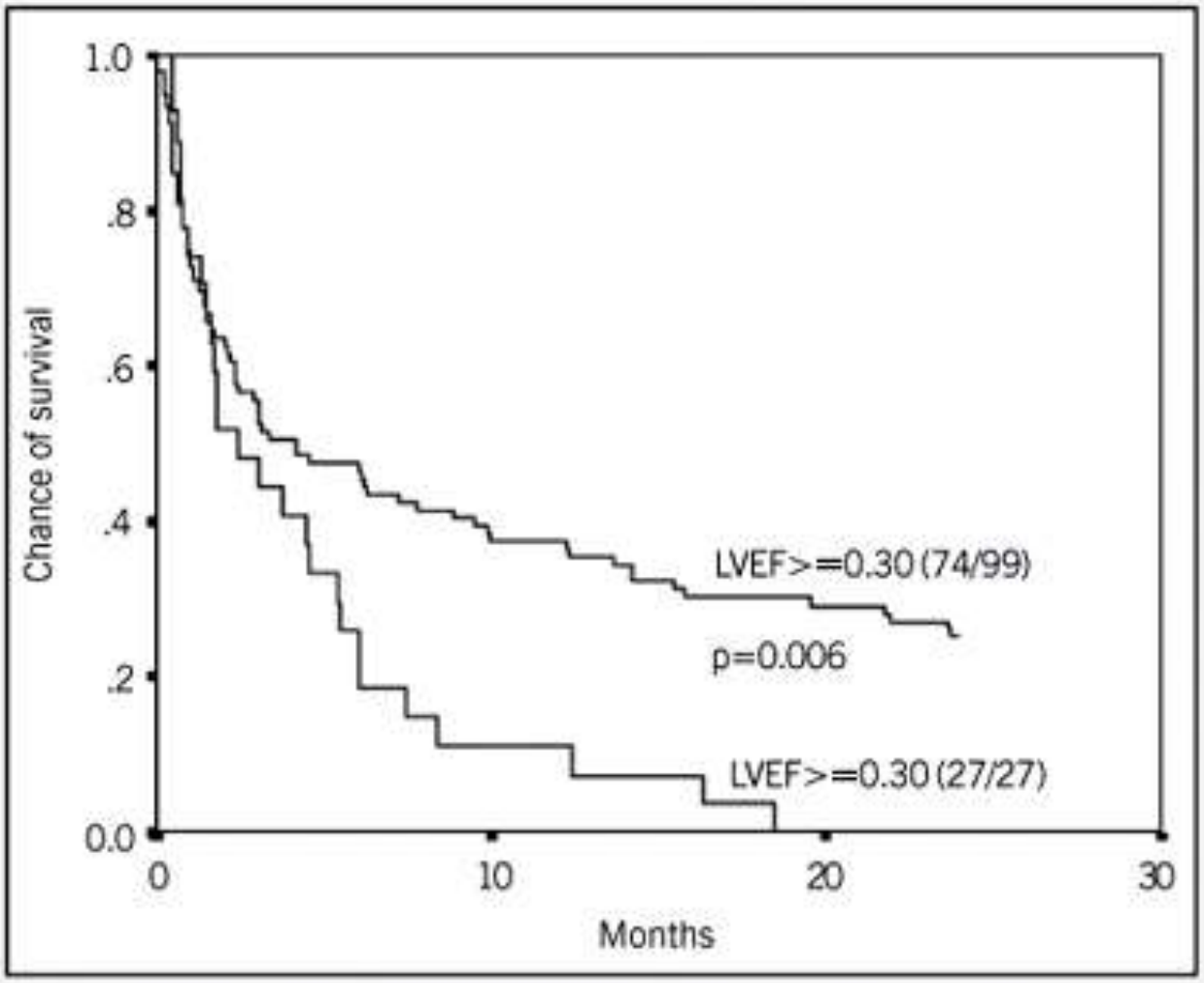
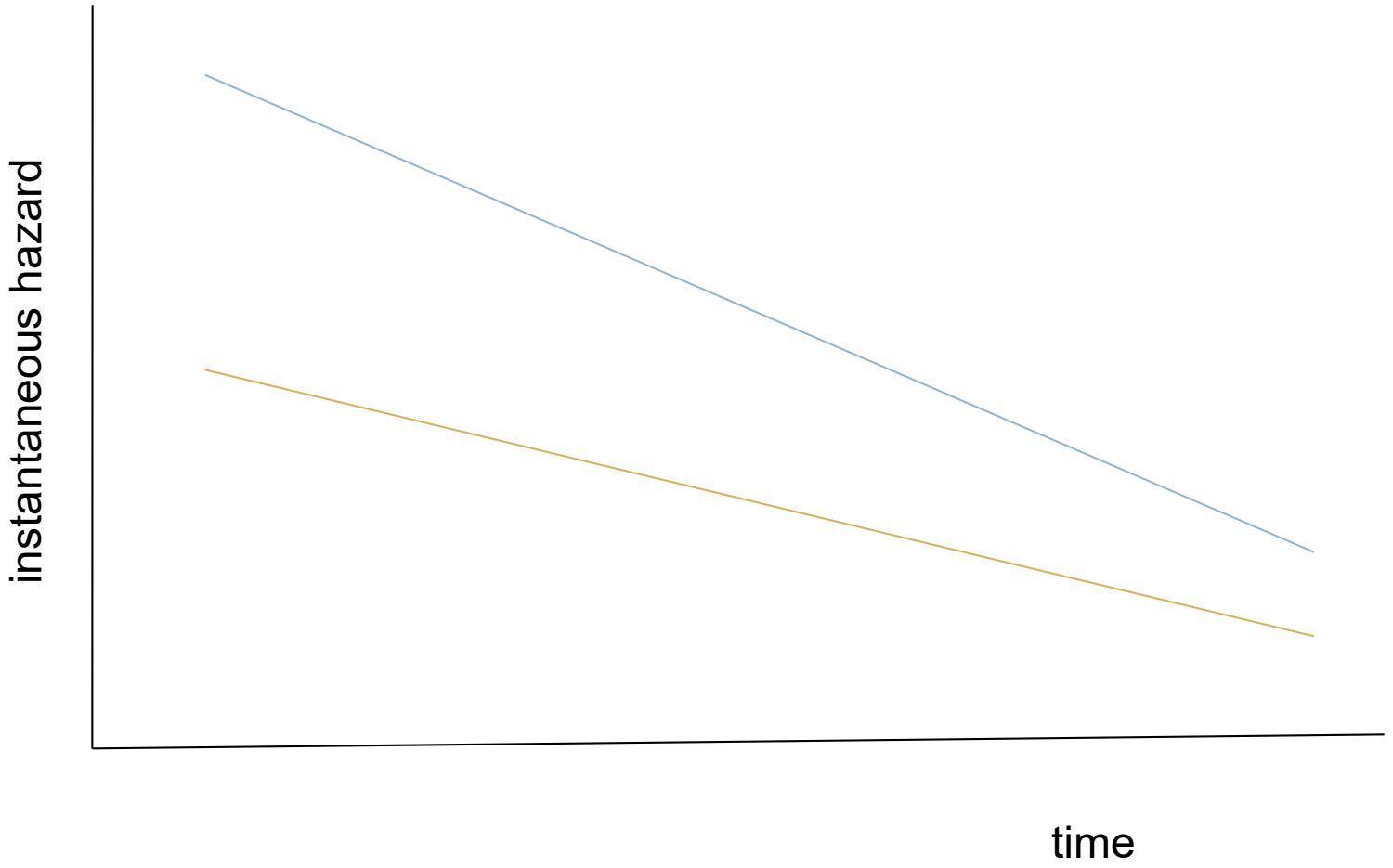


Fig. 3 - Survival curve for ejection fraction greater or lower than 0.30.

Proportional hazards?



Proportional hazards?

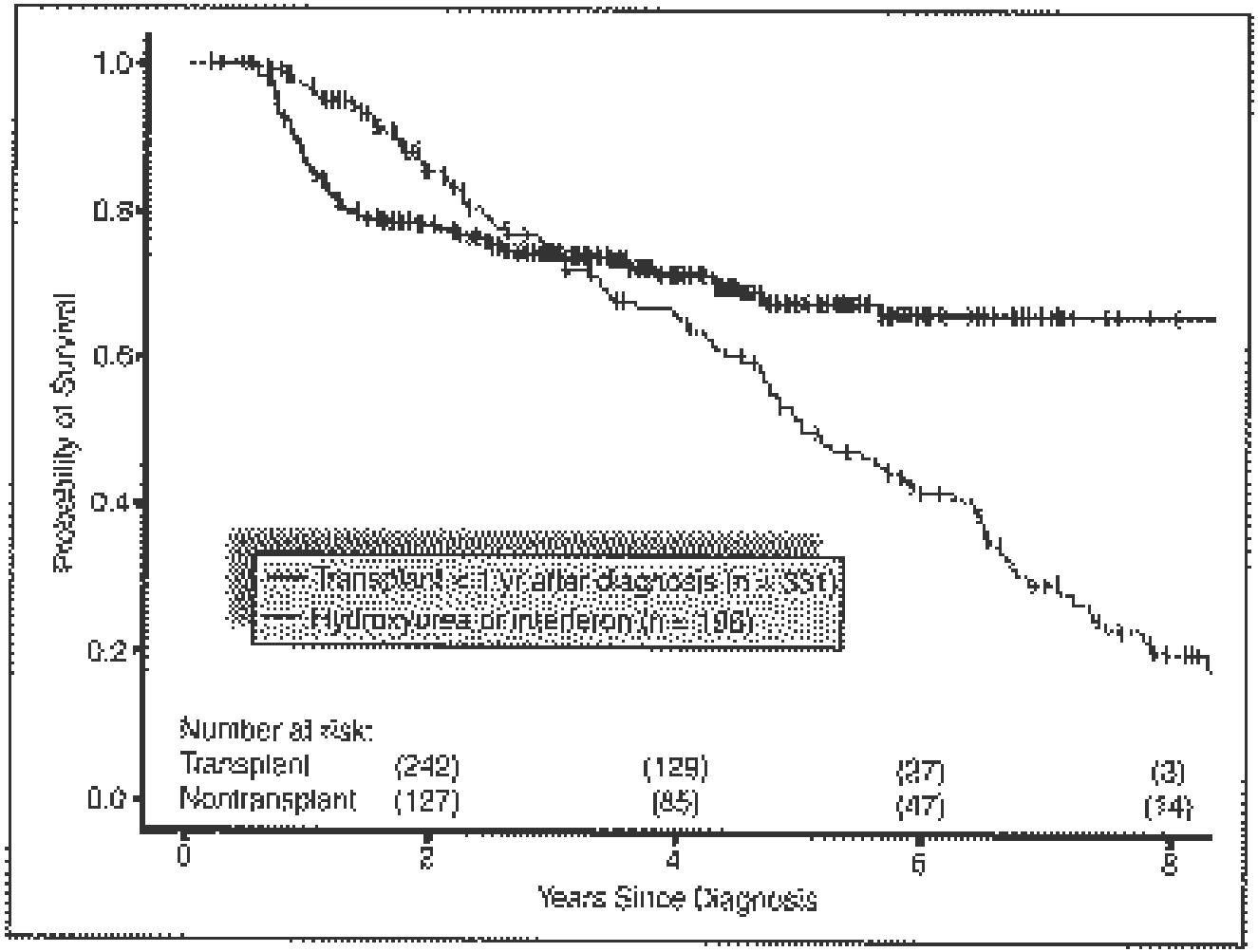
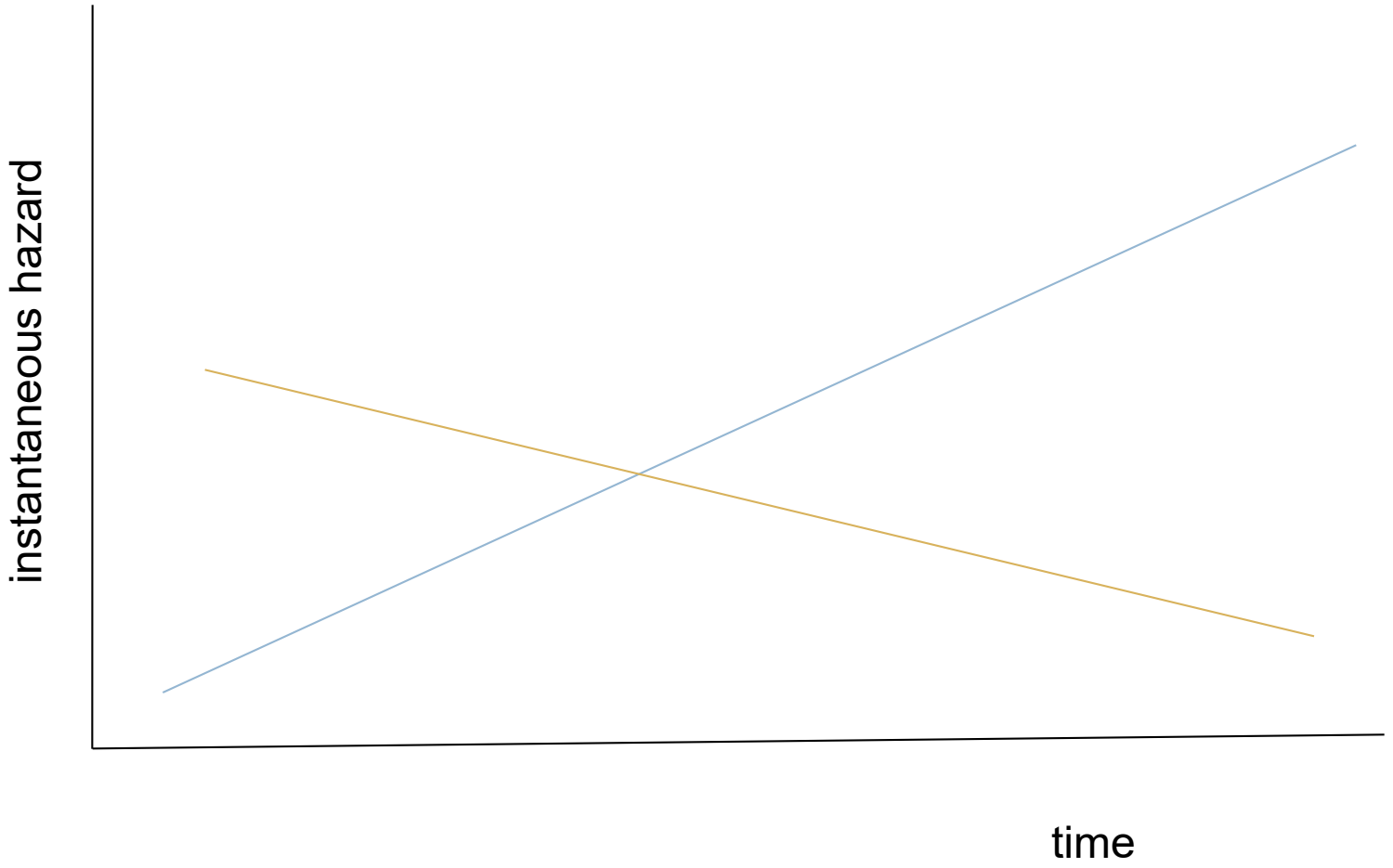
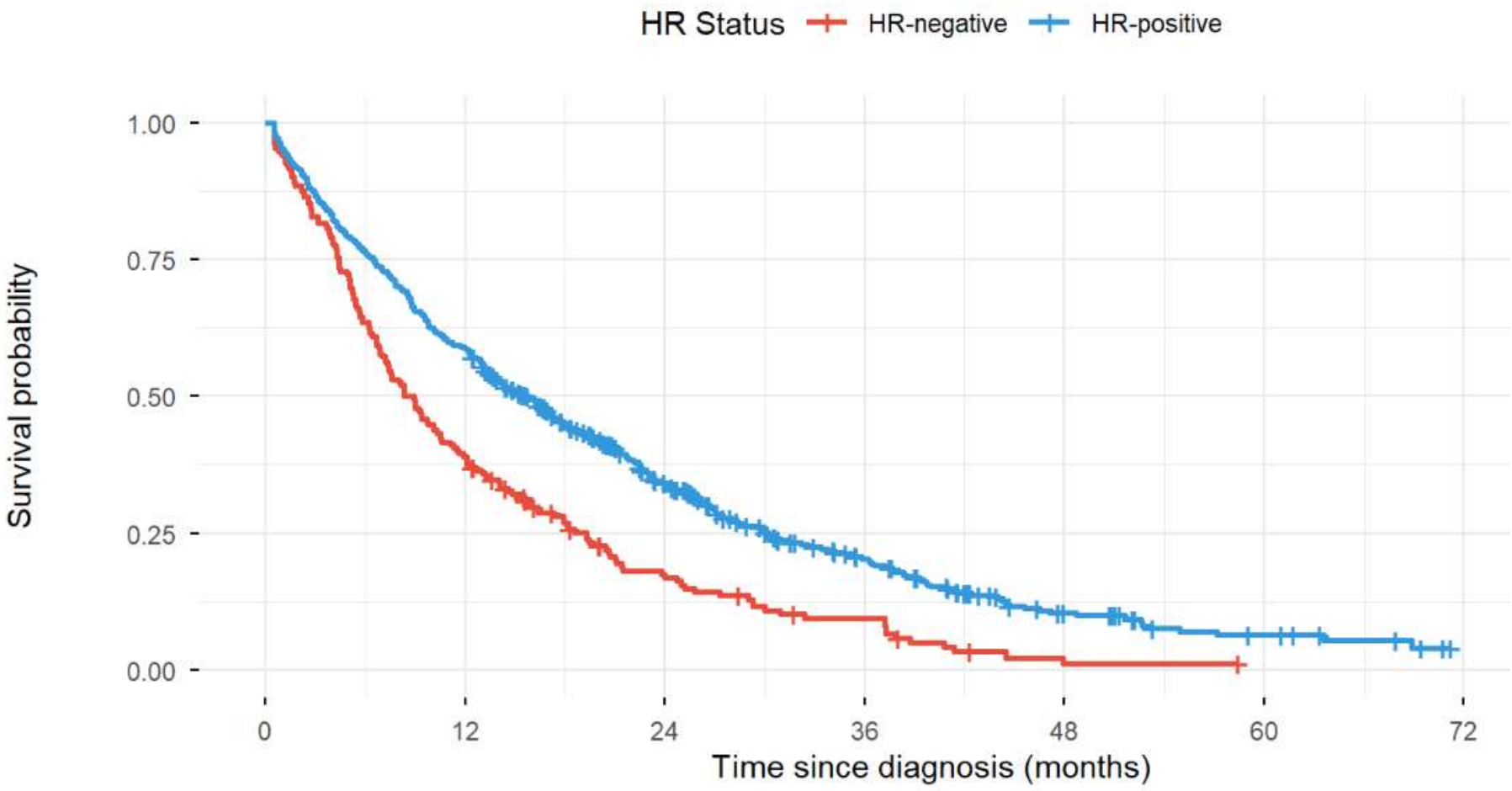


Figure 2: Effect of Therapy on Survival in Chronic Myelogenous Leukemia—Hydroxyurea or interferon-alpha vs related-donor transplantation. Adapted, with permission, from Gale et al [29].

Proportional hazards?



Proportional hazards?



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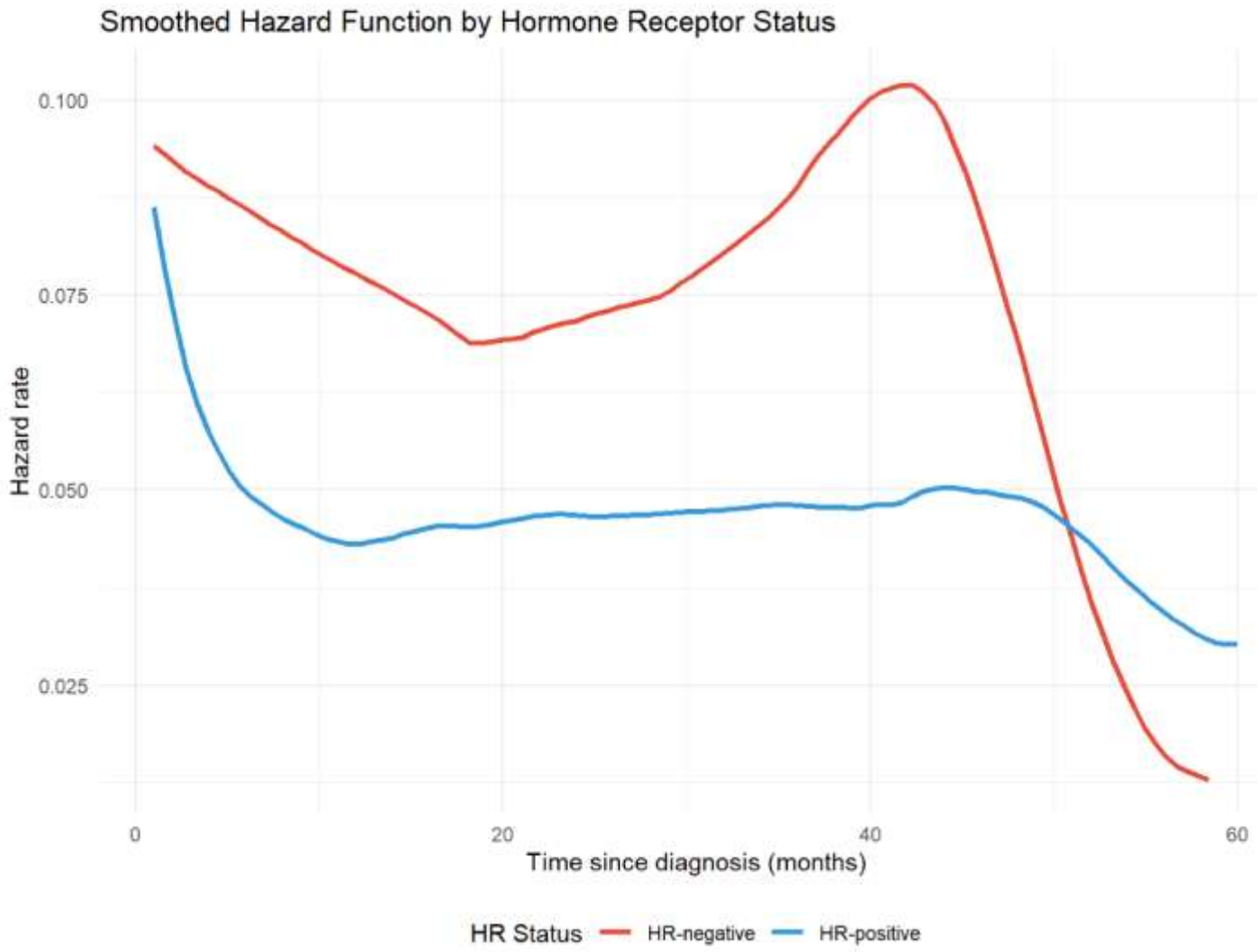

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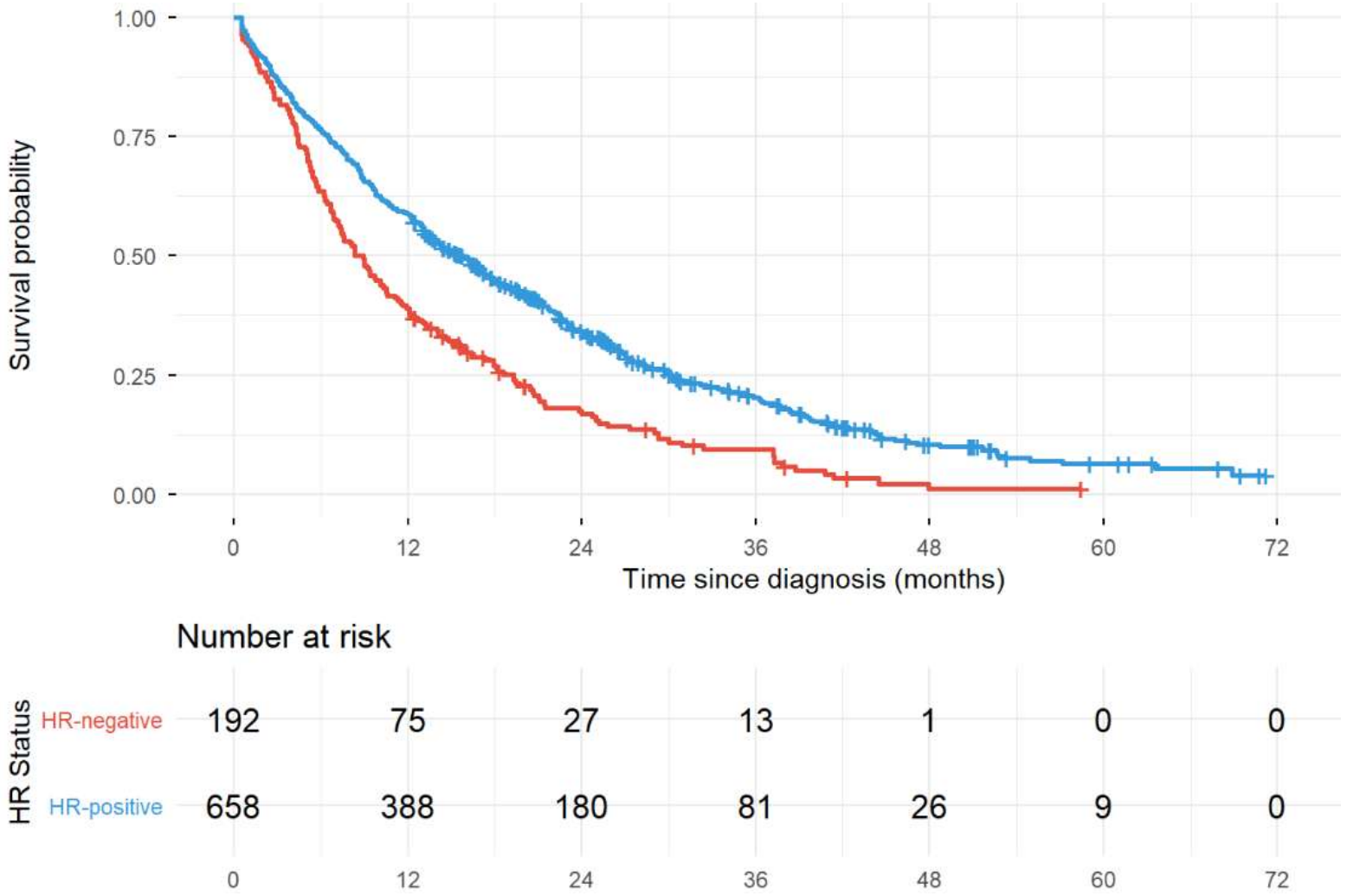
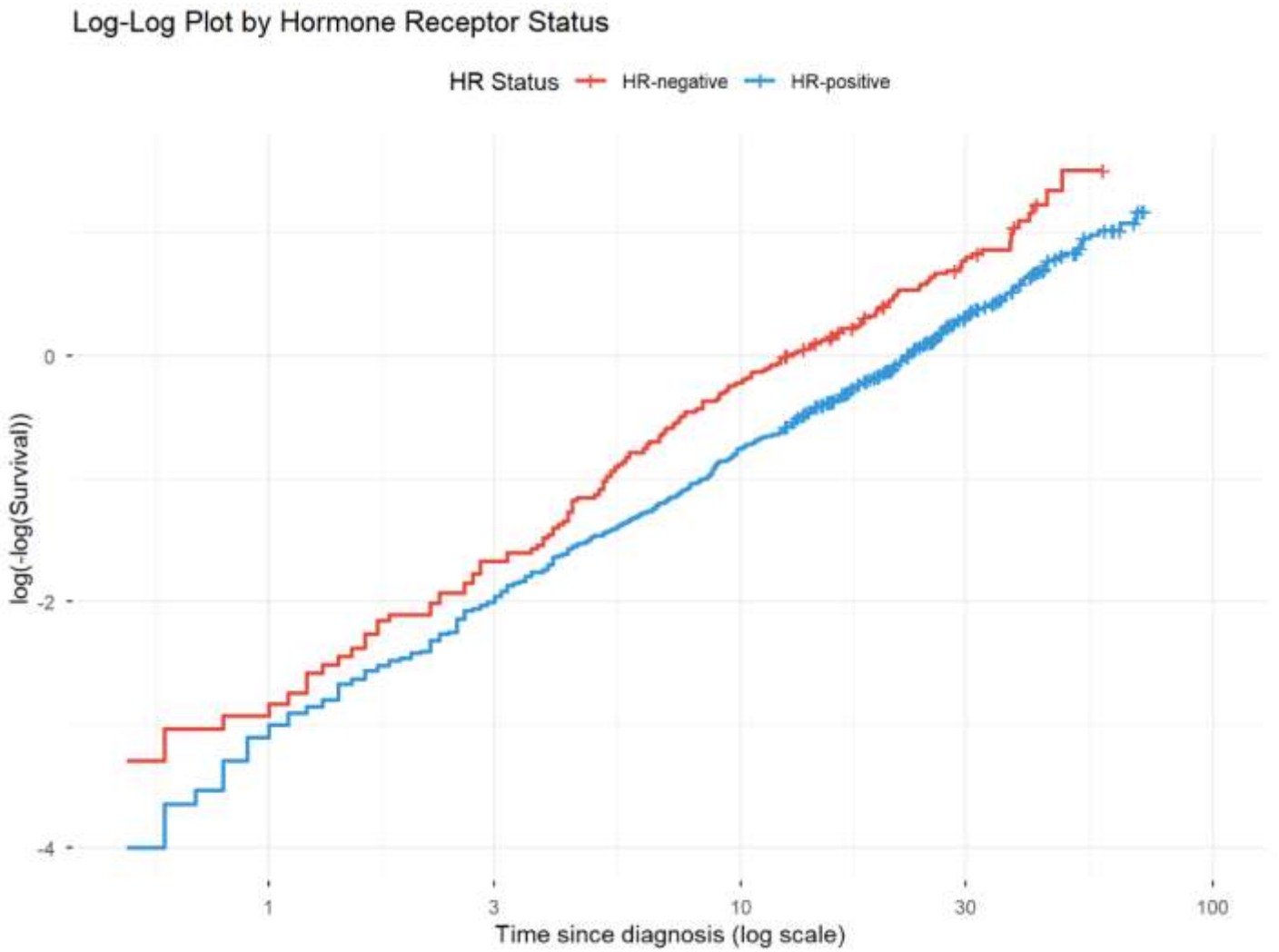


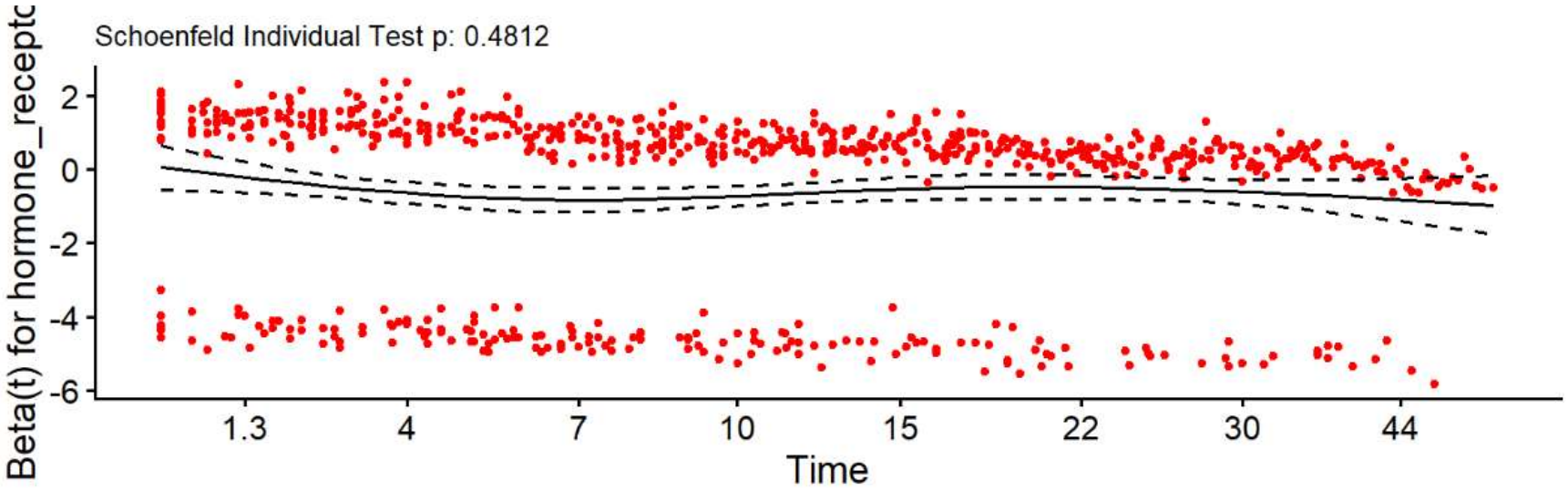
Proportional hazards?



Proportional hazards?

- Schoenfeld residuals

	chisq	df	p
age_at_diagnosis	0.140	1	0.708
ecog_ps	2.605	3	0.457
hormone_receptor	0.496	1	0.481
her2_status	4.851	1	0.028
n_metastatic_sites	2.461	1	0.117
liver_mets	3.673	1	0.055
brain_mets	1.496	1	0.221
GLOBAL	14.928	9	0.093



Size of difference?

- Cox-proportional hazards model
  - gives hazard ratio (= relative risk)
  - semi-parametric
  - doesn't specify underlying hazards but does assume proportionality
  - multivariable regression

Cox-regression

Subgroup	No. of Patients	Hazard Ratio	No. of Events (Trastuzumab vs. Observation)	Hazard Ratio (95% CI)
Region of the world				
Western and Northern Europe, Canada, South Africa, Australia, N.Z.	2430		98 vs. 159	0.58 (0.45–0.75)
Asia Pacific, Japan	405		12 vs.26	0.42 (0.21–0.84)
Eastern Europe	364		10 vs. 27	0.31 (0.15–0.65)
Central and South America	188		7 vs. 8	0.90 (0.33–2.48)
Age at randomization				
<35 yr	251		12 vs. 23	0.47 (0.23–0.94)
35–49 yr	1490		55 vs. 95	0.52 (0.37–0.72)
50–59 yr	1091		39 vs. 73	0.53 (0.36–0.79)
≥60 yr	549		21 vs. 29	0.70 (0.40–1.23)
All patients	3387		127 vs. 220	0.54 (0.43–0.67)