Risk Rate Counterfactuals

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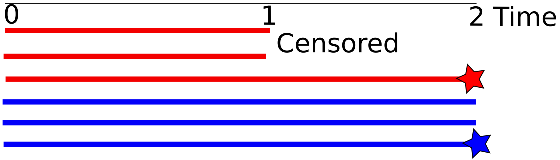
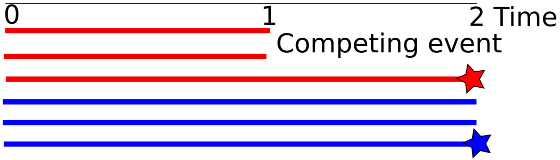
Rate and Risk



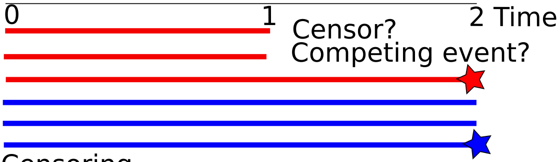
1-Kaplan meier: 0 2/3 Risk Ratio: 1/(1/3)=3
Rate: 1/4 1/6 Rate Ratio: (1/4)/(1/6)=1.5
Risk by Inverse Probability of Censoring Weighting:
(1/(1/3))*1/3=1 1*1/3=1/3 Risk ratio: (1)/(1/3)=3

Rate and Risk



Cumulative risk: 1/3*1=1/3 1*1/3=1/3 Risk ratio: 1

Rate and Risk



Censoring

1-Kaplan meier: 0 2/3 Risk Ratio: 1/(1/3)=3

Rate: 1/4 1/6 Rate Ratio: (1/4)/(1/6)=1.5

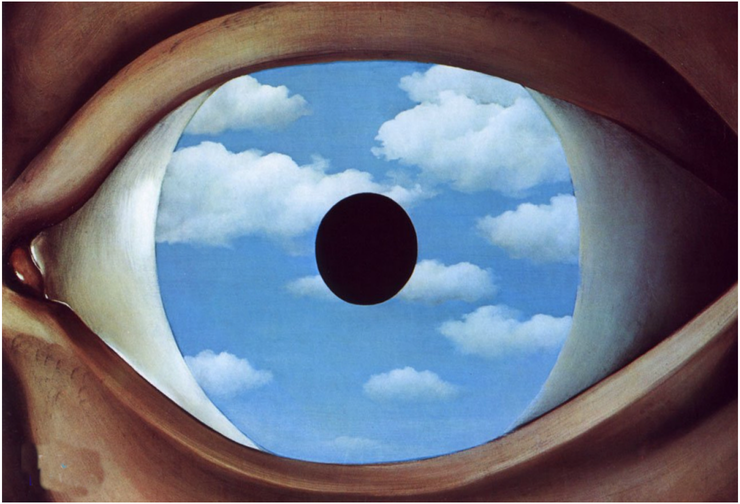
Risk by Inverse Probability of Censoring Weighting:

(1/(1/3))*1/3=1 1*1/3=1/3 Risk ratio: (1)/(1/3)=3

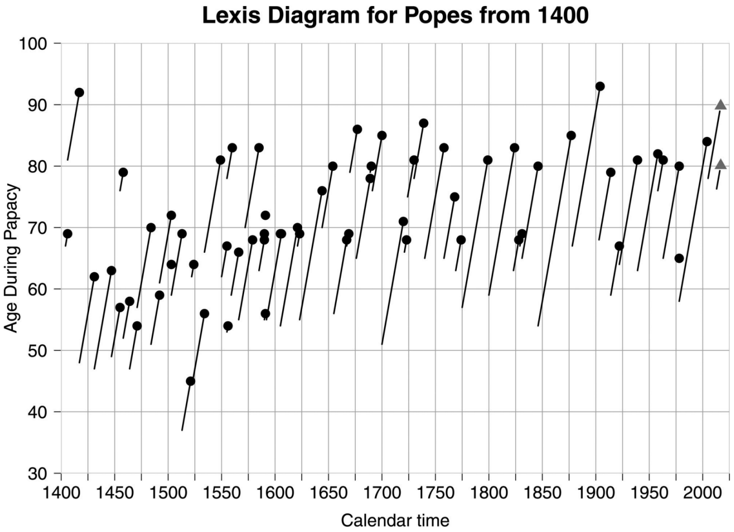
Competing risk

Cumulative risk: 1/3*1=1/3 1*1/3=1/3 Risk ratio: 1

Rate and rate ratio: unchanged

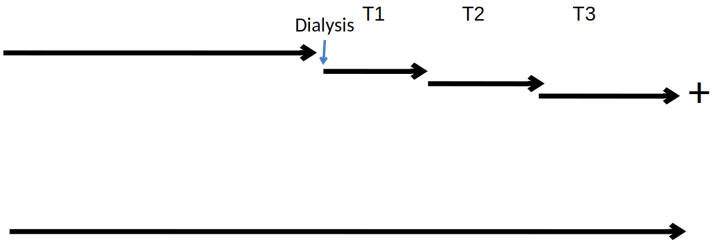


Lexis Diagram



Stander, American Statistician 2018

Splitting



Cohort Study - Time varying exposure

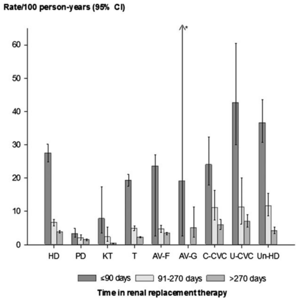
Table 1 Characteristics of study population at baseline

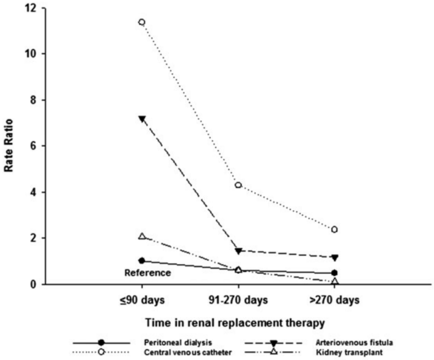
Characteristics	Hemodialysis	Peritoneal dialysis	Kidney transplant (preemptive)	Total (N%)
Total (N%)	6826 (68)	2882 (29)	289 (3)	9997 (100)
Age (years)[a]	65 ± 15	59 ± 15	41 ± 16	62.3 ± 16
	Preexisting heart valve disease			
Aortic valve	285 (4)	111 (3.6)	5 (2)	401 (4)
Mitral valve	172 (2.5)	56 (2)	6 (2)	234 (2.3)
	Comorbidity			
Myocardial infarction	621 (9)	185 (7)	4 (1.4)	810 (8)
Diabetes with complication	1924 (29)	759 (27)	47 (17)	2730 (28)
Diabetes	2133 (31)	818 (29)	48 (17)	2999 (31)
Chronic obstructive lung disease	518 (8)	120 (4)	<4	639 (7)
Peripheral vascular disease	791 (12)	189 (7)	<4	982 (10)
Liver disease	175 (2.5)	35 (1.2)	<4	212 (2.1)
Ischemic heart disease	1476 (22)	496 (18)	15 (5)	1987 (20)
Cardiac arrhythmia disorder	883 (13)	215 (8)	8 (3)	1106 (11)
Previous atrial fibrillation/flutter	746 (11)	174 (6)	5 (2)	925 (9)
Chronic heart failure	1185 (18)	316 (11)	< 4	1503 (15)
	Etiology of kidney disease			
Diabetes mellitus	1663 (24)	713 (24)	44 (15)	2420 (24)
Chronic glomerulonephritis	523 (8)	383 (13)	66 (23)	1024 (10)
Vascular and hypertensive nephropathy	855 (13)	365 (13)	15 (5)	1235 (12)
Polycystic kidney disease	386 (6)	253 (9)	46 (16)	685 (7)
Chronic tubulointerstitial nephropathy	340 (5)	115 (4)	17 (6)	472 (5)
Other	1254 (18)	369 (13)	55 (19)	1678 (17)
Unknown	1805 (26)	684 (25)	46 (16)	2535 (25)

[a]Values are given as mean, +/– SD or N (%)

Chaudry, Hemodialysis International 2019

Cohort study - Time varying Exposure





Chaudry, Hemodialysis International 2019

Note with classical time dependent analysis

- What is estimated is the rate ratio at the time of event
- Exposure is treated as a switch which is immediately on during exposure and immediately off during a break
- Variables summing cumulative exposure can be calculated, but often erroniously
- Breaks in exposure can be difficult to summarize
- LTMLE is possibly the best way to examine future studies

CHADS VASC score derivation

Table 4—*Univariate and Multivariate Predictive Power of Risk Factors for Thromboembolic Events*

	Event Rate With Risk Factor	Event Rate Without Risk Factor	Univariate *P* Value	OR[a]	Multivariate *P* Value[a]
Age > 75	11 (3.6)	14 (1.8)	.083	1.46 (0.63-3.35)	.383
Female	16 (3.6)	9 (1.4)	.017	2.53 (1.08-5.92)	.029
Stroke/TIA/TE	5 (5.9)	20 (2.0)	.023	2.22 (0.78-6.35)	.163
Hypertension	19 (2.6)	6 (1.7)	.349	1.01 (0.38-2.66)	.992
Diabetes	8 (4.3)	17 (1.9)	.048	1.79 (0.73-4.40)	.220
Heart failure	6 (2.4)	19 (2.3)	.967	0.72 (0.27-1.88)	.493
LVEF < 40	1 (0.8)	12 (2.1)	.335	0.34 (0.04-2.73)	.243
Vascular disease[b]	16 (3.6)	9 (1.5)	.022	2.27 (0.94-5.46)	.063

OR = odds ratio. See Tables 1 and 2 for expansion of other abbreviations.
[a]All results other than LVEF from model without LVEF.
[b]Coronary artery disease, peripheral vascular disease, or a previous thromboembolism other than stroke/TIA.

Lip, Chest 2010

Counterfactual

Causal Inference

- Display causal consequences in observational studies
- Display observtional studies similar to randomised studies

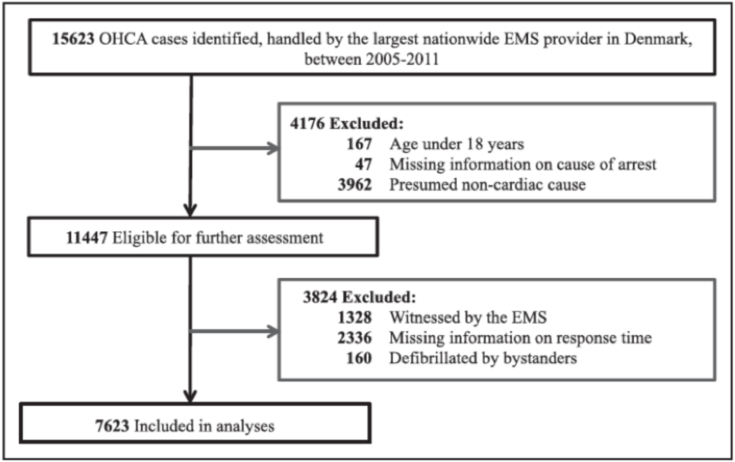
Causal assumptions

- Exchangeability
- Consistency
- Positivity

Practical options

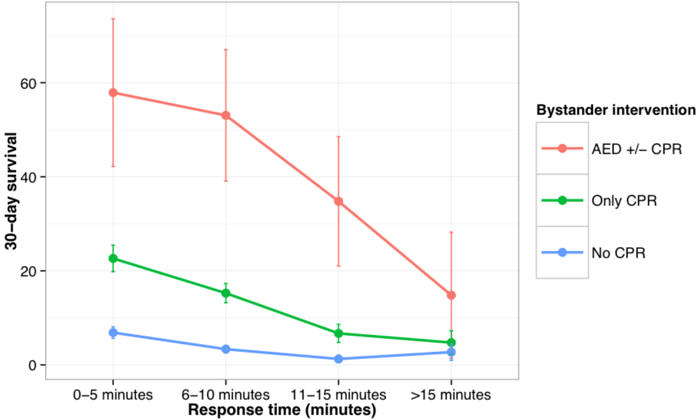
- g-model
- Propensity matching
- Inverse Probability Weighting
- Double Robust Methods

Is CPR important in cardiac arrest

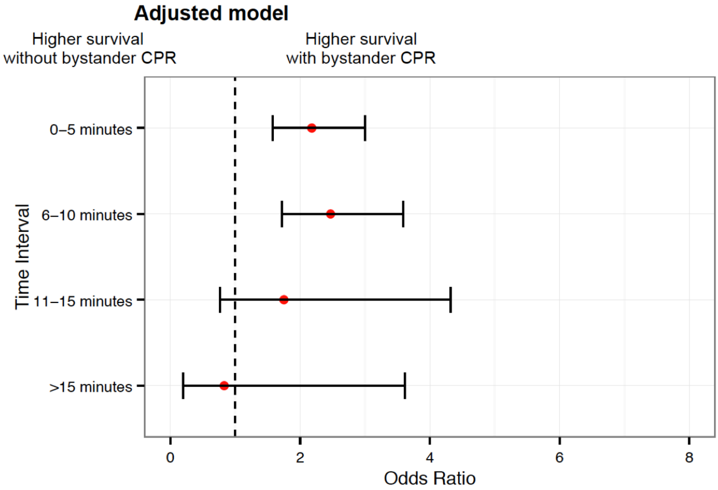


Rajan, Circulation 2016

Crude survival by time



Adjusted logistic regression

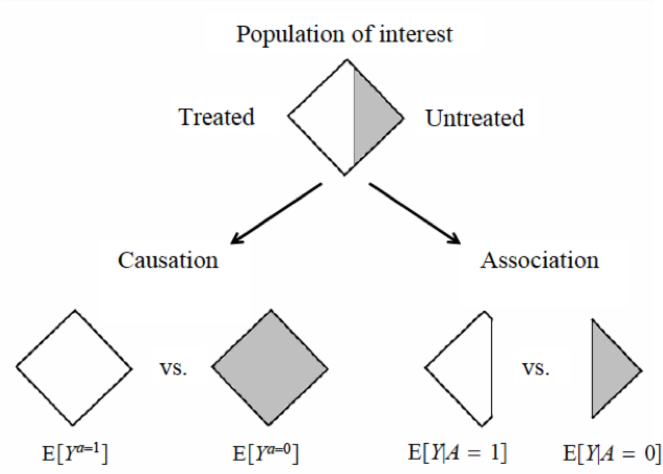


The model!

$$\log(\frac{p}{1-p}) = \beta_0 + \beta_1 sex + \beta_2 * age + \beta_3 * CPR + RCS(\beta_4 * time)$$

$$p = \frac{e^{\beta_0 + \beta_1 sex + \beta_2 * age + \beta_3 * CPR + RCS(\beta_4 * time)}}{1 + e^{\beta_0 + \beta_1 sex + \beta_2 * age + \beta_3 * CPR + RCS(\beta_4 * time})}$$

G-model versus association



Herman Robins: Causal Inference

Modelling

$$\log(\frac{p}{1-p}) = \beta_0 + \beta_1 sex + \beta_2 * age + \beta_3 * CPR + RCS(\beta_4 * time)$$

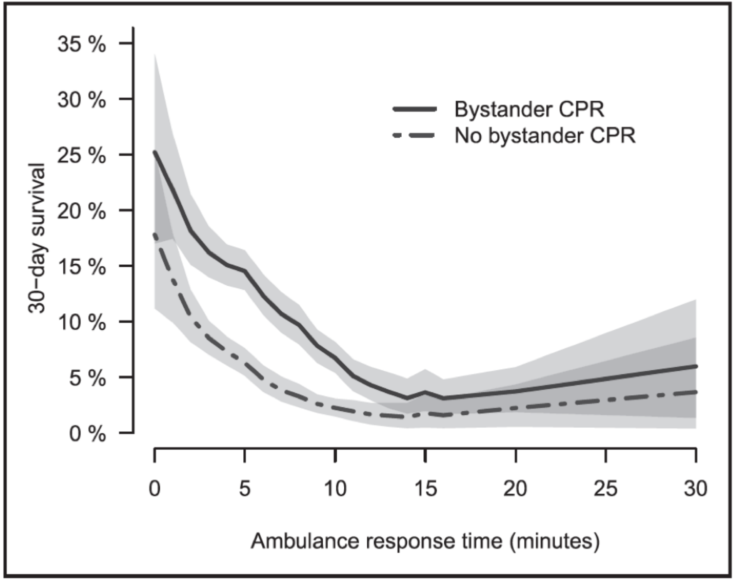
$$p = \frac{e^{\beta_0+\beta_1 sex+\beta_2*age+\beta_3*CPR+\beta_4*time}}{1+e^{\beta_0+\beta_1 sex+\beta_2*age+\beta_3*CPR+\beta_4*time}}$$

```
fit <- glm(Surv30~sex+age+CPR+RCS(time),data=data,
    family=binomial(link=logit))
pred <- predictStatusProb(fit,newdata=data)
```

G-model

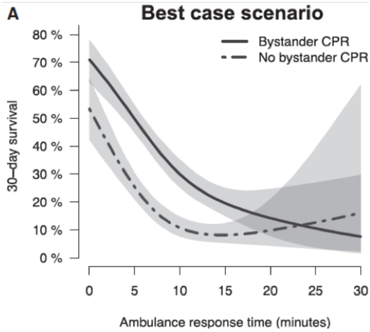
- Make 2 copies of the data
- Set CPR to 0 in one and 1 in the other
- Make predictions for each dataset
- Plot means for each dataset and each time
- Make 1000 bootstraps of the original dataset
- Repeat prediction as above
- find 5/95 percentiles from bootstraps

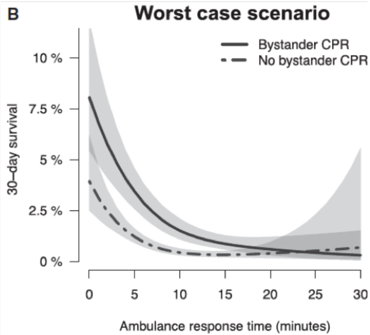
G-model



Bystander CPR
No bystander CPR
30–day survival
35 %
30 %
25 %
20 %
15 %
10 %
5 %
0 %
0
5
10
15
20
25
30
Ambulance response time (minutes)

Extreme cases





Age<65, no comorbidity

Age $\leq$ 65, $\geq$ 1 comorbidity