PARAMETER ESTIMATION: TRANSITION PROBABILITIES

PHD 3998 DECISION ANALYSIS IN PUBLIC HEALTH /SPRING 2021

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OBJECTIVE

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HOW TO EXTRACT DATA TO DERIVE MODEL TRANSITION PROBABILITIES FROM THE PUBLISHED LITERATURE

OVERVIEW

- RATES VS PROBABILITIES
- OTHER PUBLISHED EVIDENCE TO PROBABILITIES
- LIFE TABLE FOR BACKGROUND MORTALITY
- TIME-DEPENDENT PROBABILITIES FROM SURVIVAL ANALYSIS
- SUGGESTED HIERARCHY OF EVIDENCE
- REFERENCES

RATES VS PROBABILITIES

	RATE	PROBABILITY (RISK)
Concept	Instantaneous potential for change in one variable per unit change in another variable	Probability that a person will experience a change in health state within a specified time period. 0-1
Range	0 to ∞	0 to 1
Definition	$\frac{\text{\# of events that occurred in a time period}}{\text{Total time period experienced by all subjects followed}}$	$\frac{\text{\# of events that occurred in a time period}}{\text{\# of people followed for that time period}}$
Relationship to time	Inferred from measurement on a population taken over time.	Requires period referent of time which transitions occur (the period referent .
Practical aspects	Usually measured as events/person-time Estimation must be based on group data, not individual outcomes.	Usually measured as persons experiencing a transition per total population at risk over the relevant time period. Estimates may be based on individual outcomes (e.g., Kaplan-Meier)

RATES VS PROBABILITIES

Terms in the Medical Literature

RATE	PROBABILITY (RISK)
HAZARD RATE	LIKELIHOOD
POTENTIAL	CUMULATIVE INCIDENCE
PERSON-TIME INCIDENCE RATE	KAPLAN-MEIER (PRODUCT-LIMIT)
INCIDENCE DENSITY	
FORCE OF MORBIDITY	
INTANTANEOUS RISK	

RATES VS PROBABILITIES

- Distinguishing example

A cohort of 1000 people is followed for 3 year. During the 3 follow-up years, 12 patients experienced a hip fracture. Let's assume 6 of them occurred after 1 year and 6 of them occurred after 2 years.

Probability (3-year probability)= ?

Rate= ?

RATES VS PROBABILITIES

- Distinguishing example

A cohort of 1000 people is followed for 3 year. During the 3 follow-up years, 12 patients experienced a hip fracture. Let's assume 6 of them occurred after 1 year and 6 of them occurred after 2 years.

Probability (**3-year probability** or cumulative incidence)= 12/1000 = 0.012

Rate= 12/2982 = 0.004 per person-time

Denominator: Sum of the total amount of person-time of no-fracture, 988*3, and Sum of total amount of P-T of fractures, (6*1)+(6*2) => 2982

RATES VS PROBABILITIES

If an event occurs at a constant rate r per time unit t,

- Converting Rate (r) to Probability (P)

$$P = 1 - \exp(-rt)$$

- Converting Probability (P) to Rate (r)

$$r = \frac{-\ln(1 - P)}{t}$$

- Converting Probability for model's cycle length (Ex. n-year P into annual P)

$$r_1 = -\frac{1}{n}\ln(1 - P_n) \quad \Rightarrow \quad P_1 = 1 - \exp(-r_1)$$

RATES VS PROBABILITIES

- Exercise:

Assume 100 well patients are followed for 3 years. Over the 3-year period, 70 patients experienced an event (EX. death)

Calculate the **annual** probability p of the event.

RATES VS PROBABILITIES

- Answer:

First, convert 3-year probability to annual rate.

- $r_1 = -\frac{1}{3}\ln(1 - \mathbf{0.7}) = 0.4013$

Then, convert annual rate to annual probability.

- $P_1 = 1 - \exp(-0.4013) = 0.3306$

OTHER PUBLISHED EVIDENCE TO PROBABILITIES

Statistic	Definition	Range
Relative Risk (RR)	$\frac{\text{Probability of outcome in exposed}}{\text{Probability of outcome in unexposed}}$	0 to ∞
Odds	$\frac{\text{Probability of outcome}}{1 - \text{Probability of outcome}}$	0 to ∞
Odds Ratio (OR)	$\frac{\text{Odds of outcome in exposed}}{\text{Odds of outcome in unexposed}}$	0 to ∞

OTHER PUBLISHED EVIDENCE TO PROBABILITIES

- Using RR to derive transition probabilities for the treated group

  RR=$\frac{p_1}{p_0}$, p_1 = RR $* \, p_0$

- Using OR to derive transition probabilities for the treated group

  Derive RR from OR : RR = $\frac{\mathbf{OR}}{(1-p_0+(p_0 * \mathbf{OR}))}$

LIFE TABLE FOR BACKGROUND MORTALITY

- Many decision models use life tables of all-cause mortality to approximate background mortality.
- Use competing mortality risks in simulation models: other-cause mortality (background mortality) with disease-specific mortality.
- For example, in a cancer model,

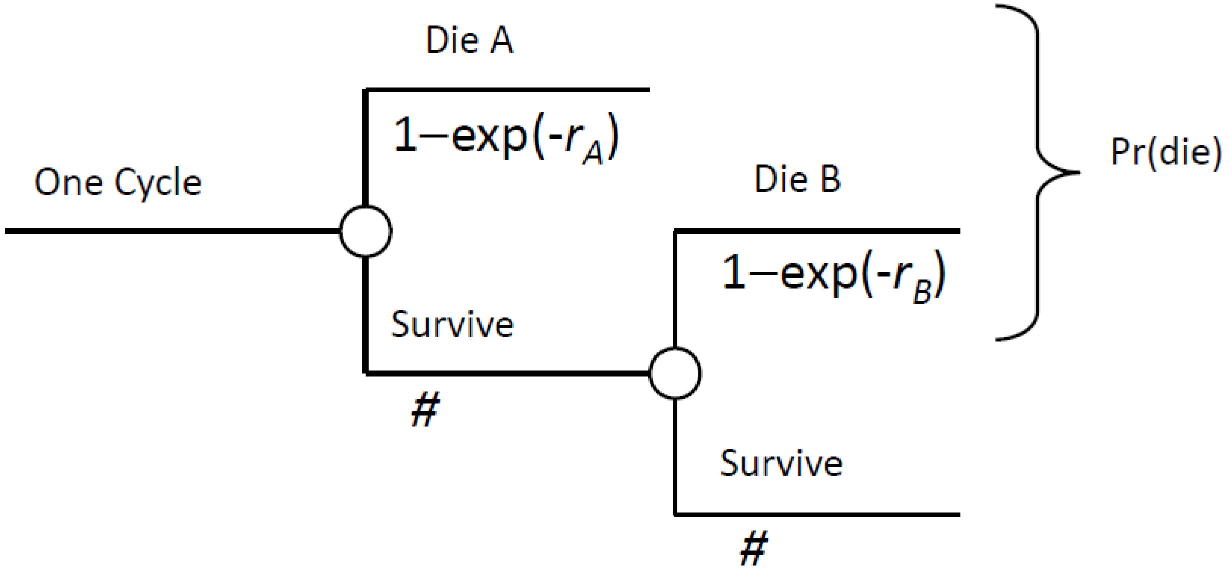
  r_c = the annual rate of dying from cancer

  r_o = the annual rate of dying from other causes

  The annual probability of overall death is: $P = 1 – \exp(-(r_c + r_o))$

LIFE TABLE FOR BACKGROUND MORTALITY

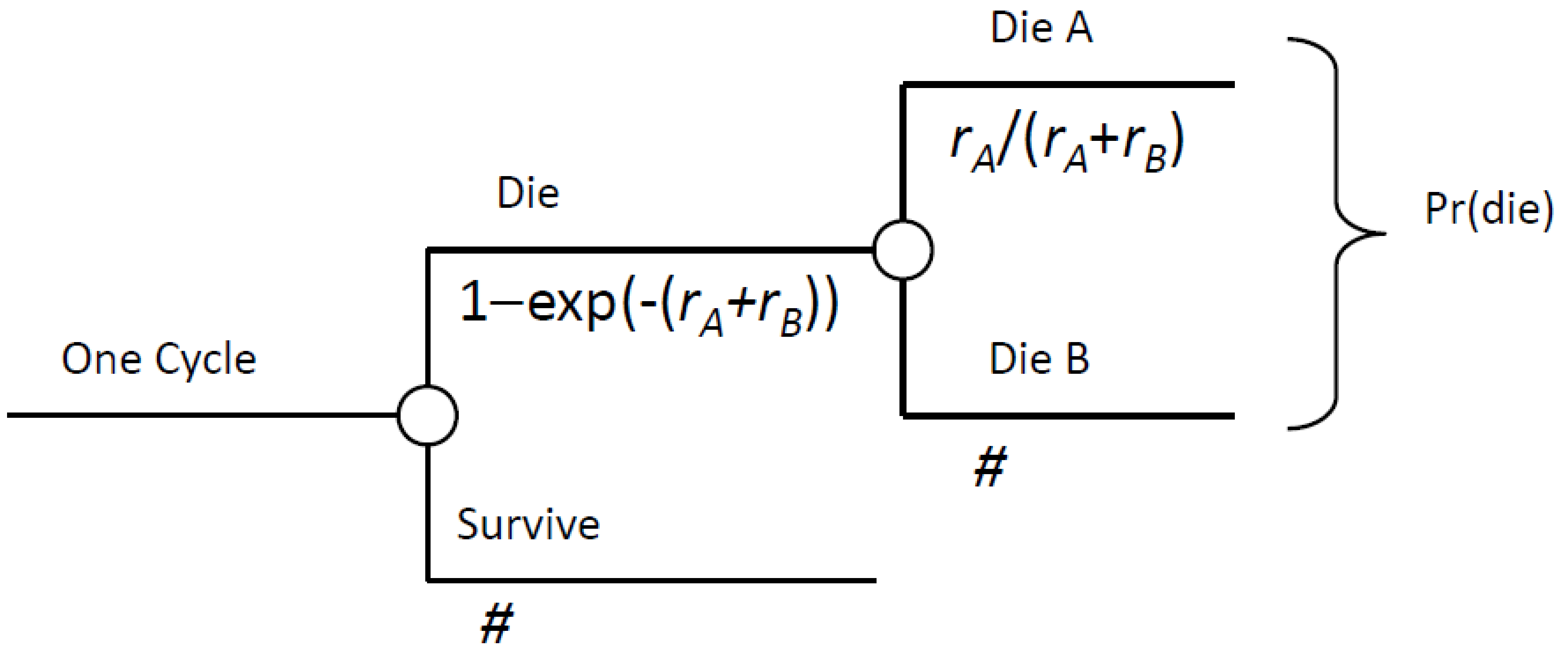
- Competing mortality in the model (as sequential events)



$$\Pr(\text{die}) = 1 - \exp(-r_A) + \exp(-r_A)\left[1 - \exp(-r_B)\right]$$
$$= 1 - \exp\left[-(r_A + r_B)\right]$$

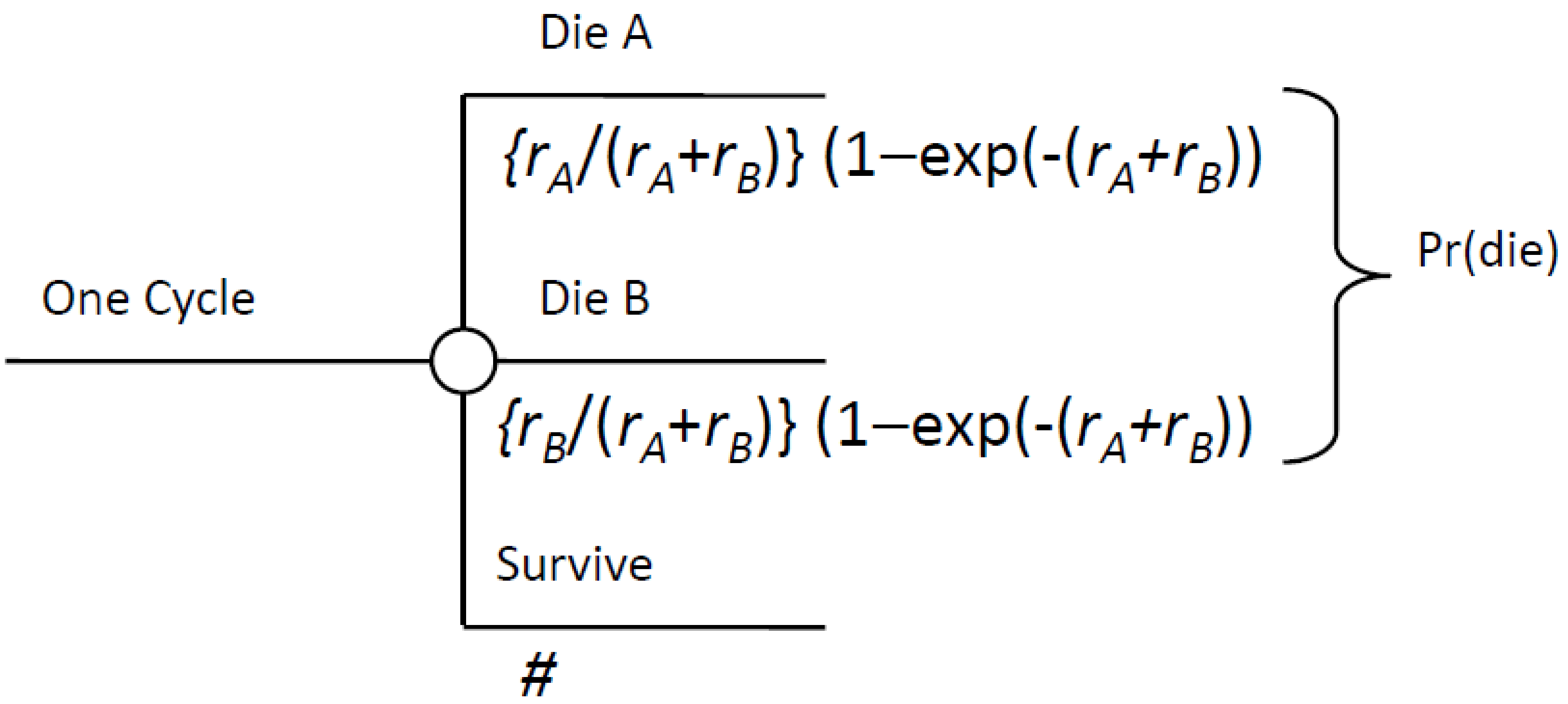
LIFE TABLE FOR BACKGROUND MORTALITY

- Competing mortality in the model (another possible structure)



LIFE TABLE FOR BACKGROUND MORTALITY

- Competing mortality in the model (as exclusive events)



LIFE TABLE FOR BACKGROUND MORTALITY

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Age (x)	Q_x	l_x	d_x	L_x	T_x	e_x
0	0.005683	100000	568	99602	2439752	76.52
1	0.000406	99432	40	99412	2340150	75.95
2	0.000249	99391	25	99379	2240738	74.98
3	0.000207	99367	21	99356	2141360	74.00
4	0.000139	99346	14	99339	2042003	73.02
5	0.000119	99332	12	99326	1942664	72.03
6	0.000134	99320	13	99314	1843338	71.04
7~96 omitted						
97	0.313100	2067	647	1743	4195	2.03
98	0.336227	1420	477	1181	2452	1.73
99	0.349848	942	330	777	1271	1.35
100	0.389974	613	239	493	493	0.80

LIFE TABLE FOR BACKGROUND MORTALITY

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- Limitation: Certain diseases of interest can be substantial contributors to all-cause mortality.
- Example: For an average 60-year-old adult in the US, cancers of the lung, breast, and colorectum are responsible for approximately 13%, 7% (in women), and 3 % of mortality, respectively. –> Double-counting
- For accurate other-cause mortality, the process to remove such disease-specific mortality from all-cause cohort life tables is needed.

TIME-DEPENDENT PROBABILITIES FROM SURVIVAL ANALYSIS

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- When we cannot assume the rate is constant over time, we need time-dependent transition probabilities.
- One way is to extrapolate RCTs survival analysis results.
- There are several different methodologies for extrapolating survival analysis results for transition probabilities.

TIME-DEPENDENT PROBABILITIES FROM SURVIVAL ANALYSIS

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- **Step 1**: Fit the extracted data from survival analysis to parametric survival models.
- **Step 2**: Find the statistically best fitted parametric survival distribution based on the goodness-of-fit metrics (e.g., Akaike information criterion (AIC), Bayesian information criteria (BIC))
- **Step 3**: Convert the fitted survival distribution to the transition probabilities for each model cycle.

$$m(t) = \frac{p(t \le T < t+1)}{p(t \le T)} = \frac{S(t+1) - S(t)}{S(t)}$$

SUGGESTED HIERARCHY OF EVIDENCE

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1. Systematic review of primary studies
   - Identifies all relevant primary research, undertake standardized appraisal of study quality, and summarize the studies of acceptable quality.
   - Meta-analysis: A special type of systematic review that entails a quantitative synthesis of evidence.
2. Best single study
   - Choose the largest study that meets some quality criteria.
3. Subjective estimates
   - e.g., expert opinion

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