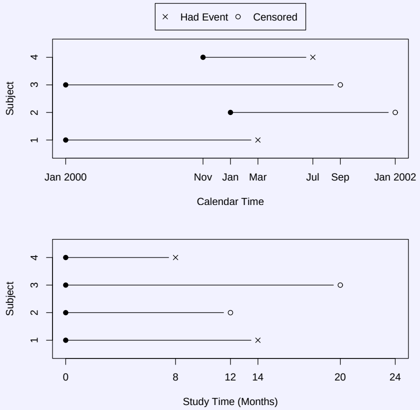
Survival Analysis

- Analysis of time to event data



- Survival time: Time from randomization to event
- Censored: Incomplete observation of survival time
  - Loss to followup, competing event, end of study
  - Informative up to time censored

Kaplan Meier Survival Estimate

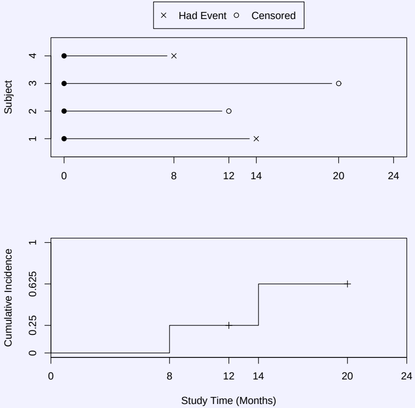
- $S(t)$ = Prob of surviving longer than time t
- Events at 8, 14; Censored at 12,20
- Interval specific survival probabilities $= \frac{\text{\# surviving}}{\text{\# at risk}}$

$$\frac{[0,8)}{\frac{4}{4}} \quad \frac{[8,12)}{\frac{3}{4}} \quad \frac{[12,14)}{\frac{3}{3}} \quad \frac{[14,20)}{\frac{1}{2}}$$

- Kaplan Meier Estimate: $S(t)$ calculated using the product of conditional probabilities
  - $S(8) = \frac{4}{4} * \frac{3}{4} = 0.75$
  - $S(14) = \frac{4}{4} * \frac{3}{4} * \frac{3}{3} * \frac{1}{2} = 0.375$

Cumulative Incidence Plot

- Cumulative Incidence $= 1 - S(t)$



- Vertical axis represents the probability of incidence in hypothetical cohort, not the observed incidence

Risk Estimates: Hazard Ratio

- T: Time that event occurs (random variable)
- Hazard rate: Prob of having an event in next interval $(t + \Delta t)$ given that you are event-free up to time t
  - $\lambda(t) = \mathrm{Pr}(t \leq T \leq t + \Delta t | T > t) \div \Delta t$
- Hazard Ratio $= \frac{\lambda_{\mathrm{treat}}(t)}{\lambda_{\mathrm{control}}(t)}$
  - Multiplicative Effect: "Subjects on aspirin are 0.95 (95% CI: [0.79,1,31]) *times* as likely to have VTE as subjects on control"
- Cox (proportional hazards) model
  - $\lambda(t; x) = \lambda_0 \exp(\beta * x); x = 0, 1$
  - Proportional Hazards assumption: Hazard Ratio is constant at all times t
  - Hazard Ratio approximates Relative Risk

Risk Estimates: Multiplicative

- Relative Risk
  - $\text{RR} = \frac{\Pr(\text{Disease in Exposed/Treated})}{\Pr(\text{Disease in Non-Exposed/Control})} = \frac{\Pr(D^+|E^+)}{\Pr(D^+|E^-)}$
  - Most interesting risk measure
- Odds Ratio
  - $\text{OR} = \frac{\text{Odds}(\text{Disease in Exposed/Treated})}{\text{Odds}(\text{Disease in Non-Exposed/Control})} = \frac{\text{Odds}(D^+|E^+)}{\text{Odds}(D^+|E^-)}$
  - $\text{Odds}(D^+|E^+) = \frac{\Pr(D^+|E^+)}{1-\Pr(D^+|E^+)}$
  - Approximates RR for rare diseases
- Hazard Ratio
  - $\text{HR} = \frac{\lambda_{\text{treat}}(t)}{\lambda_{\text{control}}(t)}$
  - Approximates RR when $\Delta t \to 0$
- Interpretation: Exposure multiplies risk

Risk Estimates: Additive

- Rate difference $= \text{rate}_{\text{treat}}(t) - \text{rate}_{\text{control}}(t)$
  - Additive Effect: "VTE events per 1000 person years are 0.06 lower in subjects taking aspirin compared to subjects on control"
  - Much less common than multiplicative model for survival data
- Interpretation: Exposure adds to risk