

Hypothesis Testing $\hat{\theta}$: unrecricted mle; $H_0 : \theta = \theta_0$ vs. $H_1 : \theta \neq \theta_0$.
Wald Test - MLE $\hat{\theta}$ under null $\theta = \theta_0$,
 $W = \frac{(\hat{\theta} - \theta_0)^2}{1/I(\hat{\theta})} \sim \chi(1)$; $W = \frac{\hat{\theta} - \theta_0}{SE(\hat{\theta})} \sim N(0, 1)$ [I($\hat{\theta}$) obs info matrix]

Score Test - Null distribution θ_0 by CLT $S(\theta) \sim N(0, I_n(\theta))$ under null
 $\frac{S(\theta_0)^2}{I(\theta_0)} \sim \chi(1)$; $\frac{S(\theta_0)}{\sqrt{I(\theta_0)}} \sim N(0, 1)$ $E[S(\theta)] = 0$ and $V(S(\theta)) = I_n(\theta)$

Res. Deviance : pf. $l(\theta_0)$ expand around $\hat{\theta}$. **Power Function**: type I:
P(reject null| null); power: p(accept null| h1); type II: 1- power

Survival Analysis

Basics $S(t) = P(\tilde{T} > t) = 1 - F(t)$ $f(t) = \frac{dF(t)}{dt} = -\frac{dS(t)}{dt}$; hazard fun.

(rate, instantaneous occurrence) $\lambda(t) = \lim_{\delta \rightarrow 0} \frac{P(t \leq \tilde{T} < t + \delta | \tilde{T} > t) = \lambda \delta}{\delta}$

lim $\frac{F(t+\delta) - F(t)}{S(t)\delta} = \frac{f(t)}{S(t)} = -\frac{dS(t)}{S(t)dt} = -\frac{d}{dt} \ln S(t) = -\frac{d}{dt} \ln 1 - F(t)$;

$\int_0^t \lambda(u)du = \int_0^t \frac{f(u)}{1-F(u)}du = -\ln(1 - F(u)) \Big|_0^t \rightarrow \Lambda(t) = -\ln S(t)$

$\rightarrow S(t) = \exp(-\Lambda(t)) = \exp(-\int_0^t \lambda(t)dt)$
likelihood(cont.) $L_n(\theta; t_i, X_i) \propto \prod_{i=1}^n [\lambda_i(t_i|x_i, \theta)^{e_i} S_i(t_i|x_i, \theta)]$

(1) uncensored $E_i = 1$ at $t \Leftrightarrow P(t \leq T_i < t + dt; E_i = 1)$

$\stackrel{A1}{=} P(C_i > t|x_i, \theta) P(t \leq \tilde{T}_i < t + dt | \tilde{T}_i > t) P(\tilde{T}_i > t|x_i, \theta) \stackrel{A2}{=}$
 $\propto \lambda_i(t|x_i, \theta) dt S_i(t|x_i, \theta)$

(2) censored ($E_i = 0$) at $t \Leftrightarrow P(t \leq T_i < t + dt; E_i = 0) \stackrel{A1}{=}$

$P(t \leq C_i < t + dt|x_i, \theta) P(\tilde{T}_i > t|x_i, \theta) \stackrel{A2}{=} \propto S_i(t_i|x_i, \theta)$

A1: indep censoring $C_i \perp \tilde{T}_i | X_i$ A2: noninfo. censor C_i not involve θ
 $\ell(\lambda) \propto \sum e_i \log(\lambda_i(t_i|x_i, \theta)) + \sum \log S_i(t_i|x_i, \theta) / \sum - \int_0^t \lambda(t; \theta) dt$
pois likelihood $D \sim \text{pois}(\lambda)$ (1) one sample:

$\ell(\lambda) = D \log(\lambda) - \lambda \sum_{i=1}^n t_i / \lambda Y$, Y: total person-year; $\hat{\lambda} = \frac{D}{Y}$,

se($\hat{\lambda}$) = $\sqrt{\frac{D}{Y^2}}$, reparam $\alpha = \log(\lambda)$ [more symmetric] ,se $\log(\hat{\lambda}) = \sqrt{\frac{1}{D}}$

[FI] (2) two sample $\ell(\lambda_0, \lambda_1) = d_0 \log(\lambda_0) - \lambda_0 \sum_{i=1}^n t_i^{\lambda_0 Y_0} +$

$d_1 \log(\lambda_1) - \lambda_1 \sum_{i=1}^n t_i^{\lambda_1 Y_1}$ mle $\hat{\lambda}_i = \frac{\lambda_i}{Y_i}$ reparam: $\log(\lambda_0) = \alpha$,

$\log(\lambda_1) = \alpha + \beta$; mle $\hat{\alpha} = \log(\frac{d_0}{Y_0})$, $\hat{\beta} = \log(\frac{d_0}{Y_0} / \frac{d_1}{Y_1})$

bern likelihood π bins each $\hat{\pi}$ Bern(π), length h (Y = Nh). $\mu = \lambda Y$
 $= N\pi \rightarrow \lambda^{constant} = \pi \frac{Y}{N} = \frac{\hat{\pi}}{\hat{\pi}} / \frac{N}{N}$ [bern/pois]. surv one bin=1- risk
 $= 1 - \pi = (1 - \lambda h)$. T-year surv: $(1 - \lambda h)^N = \exp(\log(1 - \lambda h)^N)$
 $= \exp(N \times (-\lambda h)) \approx \exp(-\lambda T)$ [T = Nh], **trick** $e^x \approx 1 + x$, $\log(1 + x) \approx x$

exp likelihood $\lambda \exp(-\lambda t)$, then $L(\lambda) = e^{-\lambda \sum_{j=1}^n U_j} \prod_{j=1}^n \lambda \exp(-\lambda u_j) =$
 $\lambda^D \exp^{-\lambda T}$, [aggre data, each interval U_j is exp dist, U_{j+1} censor at T]
(1) one sample mle $\frac{\sum y_i}{\sum u_i} \sum y_i \sim \Gamma \rightarrow \chi$ cal CI (2) two sample: HR ω

(OI), ρ hazard in group0, $LRT=2(\ell(\hat{\omega}, \hat{\rho}) - \ell(\omega_0, \hat{\rho}_{\omega_0}))$

exp model repa $\tilde{T} \sim \exp(\lambda = \lambda_0 e^{\beta X} = e^{\alpha + \beta X})$, model $\lambda = \lambda_0 e^{\beta X}$.

$S_i(t; \theta) = e^{-\int_0^t \lambda_0 e^{\beta x_i} dt} = e^{-t \lambda_0 e^{\beta x_i}} = S_0(t; \theta) e^{\beta x_i}$ [log(-logS)]

AFT $\log \tilde{T}_i = \alpha + \gamma x_i + \sigma \epsilon$, $S_i(te^{\gamma x_i}) = S_0(t)$ or $S_i(t) = S_0(te^{-\gamma x_i})$

$\lambda_0 = e^{-\alpha}$, $\beta = -\gamma$ or $(-\gamma/\sigma)$; $\sigma = 1$ or $(1/\kappa)$

Weibull $\lambda_i(t; \theta) = \lambda \kappa (\lambda t)^{\kappa-1} e^{\beta x_i}$; $S_i(t; \theta) = e^{-(\lambda t)^{\kappa} e^{\beta x_i}}$ shape param
 $\kappa > 1 \uparrow$ hazard

Discrete case $S(t_j) = P(\tilde{T} > t_j) = \frac{P(\tilde{T} > t_j)}{P(\tilde{T} > t_{j-1})} P(\tilde{T} > t_{j-1}) =$

$\frac{P(\tilde{T} > t_j)}{P(\tilde{T} > t_{j-1})} \frac{P(\tilde{T} > t_{j-1})}{S(t_{j-1})} \dots = \prod \frac{S(t_j)}{S(t_{j-1})} = \prod (1 - h(t_j))$

Discrete hazard is a condit. prob $h(t_j) = P(\tilde{T} = t_j | \tilde{T} \geq t_j)$

$= \frac{S(t_{j-1}) - S(t_j)}{S(t_{j-1})} = 1 - \frac{S(t_j)}{S(t_{j-1})} \rightarrow S(t_j) = \prod \frac{S(t_j)}{S(t_{j-1})}$

$= \prod_{t_j \leq t} (1 - h(t_j))$ [S(t) multiplication of previous survivals]

Discrete likelihood $\ell(\tilde{h})$ $= \sum_{j=1}^T d_j \log(h_j) + \sum_{j=1}^T (r_j - d_j) \log(1 - h_j)$

Kaplan-Meier from liklhd, $\hat{h}_j = \frac{d_j}{r_j}$, so $\hat{S}(t) = \prod_{j:t_j \leq t} [1 - \frac{d_j}{r_j}]$

$= \prod_{u \leq t} [1 - \frac{1\{Y(u) > 0\}}{Y(u)} dN(u)]$ term2: $(1 - \lambda(t)dt)$ [d_j death at j; r_j risk

at j]; , var(\hat{h}_j) = var($1 - \hat{h}_j$) = $\frac{\hat{h}_j(1 - \hat{h}_j)}{r_j}$ [OFI inverse]. curve [5,14]

Greenwood $V(\hat{S}(t))$ $V(\log \hat{S}(t)) = \sum_{j:t_j \leq t} V(\log(1 - \frac{d_j}{r_j}))$

$g = \log(1 - h) \approx \sum_{j:t_j \leq t} [1/(1 - d_j/n_j)^2] V(\frac{d_j}{r_j}) = \sum \frac{d_j}{r_j(r_j - d_j)}$;

$V(\hat{S}(t)) = \hat{S}(t)^2 \sum_{j:t_j \leq t} \frac{d_j}{n_j(n_j - d_j)} = \hat{S}(t)^2 \int_0^t \frac{dN(u)}{Y(u)[Y(u) - dN(u)]}$

[delta2:g = exp(x) $x = \log S(t)$]; twice delta method. Problem: CI not bounded in (0,1).

Nelson-Aalen unbiased cum. hazard $\hat{\Lambda}_{NA}(t) = \sum_{j:t_j \leq t} \frac{d_j}{r_j}$,

$= \int_0^t \frac{1\{Y(u) > 0\}}{Y(u)} dN(u)$ $\hat{S}_{KM}(t) \approx \exp[-\hat{\Lambda}_{NA}(t)]$,

$CI = \Lambda(t) \pm z_{1-\frac{\alpha}{2}} \times S.E.[\hat{\Lambda}(t)]$, var($\hat{\Lambda}(t)$) = var(log($S(t)$)) as

$\hat{\Lambda}(t) = -\log(S(t))$ see greenwood; KM var : $V(\hat{H}(t)) = \sum_{j:t_j \leq t} \frac{d_j}{r_j^2}$

COX reg partial likelihood model $\lambda_i(t; Z_i) = \lambda_0(t) \exp(\beta' Z_i(t))$

$z_i(t) = 1_{\{v_i < t\}}$, $\prod_{i=1}^n \left(\frac{\exp(\beta' z_i(t_i))}{\sum_{l=1}^n Y_l(t_i) \exp(\beta' z_l(t_i))} \right)^{e_i}$, i and j with $v_i < t$

and $v_j > t$ $\frac{\lambda_i(t)}{\lambda_j(t)} = \exp(\beta)$ [time-varying cov/immortal]

log-rank $d_{kj} \sim \text{Bin}(r_{kj}, \lambda_j h)$ & $d_{kj} | d_j \sim \text{hyp}(r_{kj}, r_j, d_j)$, r_{kj} is the number at risk for group k at time t_j , d_{kj} is event count for group k at time t_j , n_j is total count. $E_j(0) = \frac{d_j r_{1j}}{r_j}$ $V_j(0) = \frac{d_j r_{0j} r_{1j} (r_j - d_j)}{r_j^2 (r_j - 1)}$

$U(0)^2 / I(0) = \left(\sum_{j=1}^g d_{1j} - \sum_{j=1}^g E_j \right)^2 / \sum_{j=1}^g V_j \sim \chi^2(1)$

Breslow Estimator $\hat{\Lambda}_0(t)$ $S_i(t) = e^{-\Lambda_0(t) \exp(\beta' X)}$ [Model-based survival

probability], $\hat{\Lambda}_0(t_i) = \sum_{j:t_j \leq t} \left(\frac{d_j}{\sum_l^n Y_l \exp(\beta' X_l)} \right)$ where $Y_i(t) = 1_{T_i \geq t}$

at-risk. $\hat{\Lambda}(t) = \hat{\Lambda}_0(t) e^{\beta' X}$

s-year risk $\pi_i(s)$ $= 1 - S_i(s) = 1 - e^{-\Lambda_0(s) \exp(\beta' X)}$

Diagnostic (1) martingale resi fun form cont var (2) cum hazard vs cox-snell resi (model fit linear) (3) score resi outlier/influential (4) schoenfeld resi PH assum (5) dfbeta(s) influential obs $\frac{2}{\sqrt{n}}$ threshold
Assess PH assmp. (1) Schoenfeld residuals, (2) log(-log(S(t))) plots - parallel lines, (3) covariate-time interaction.

homogeneous pois process: (1) $N(t) - N(s) \sim \text{poi}(\lambda(t - s))$ (2)

interarrival time U_j idep $\exp(1/\lambda)$ (3) num event in non-overlap tiem

intervals \perp

Counting process: (1) $\tilde{N}_i(t) = 1_{\{\tilde{T}_i \leq t_i\}}$; At-risk $Y_i(t) = 1_{\{\tilde{T}_i \geq t_i\}}$;

(2) jump: $d\tilde{N}_i(t) = \tilde{N}_i(t^- + dt) - \tilde{N}_i(t^-)$; (3) $P(d\tilde{N}_i(t) = 1 | \tilde{N}_i(t) = 0)$

$= \lambda(t) dt$. (4) $N(t) = \sum N_i(t)$ (cum case); $dN(t)$: jump/cases at t;

$Y(t) = \sum Y_i(t)$ (5) $P(dN_i(t) = 1 | F_{t-}) = E(dN_i(t) | F_{t-}) = Y_i(t) \lambda_i(t) dt$

intensity process $Y_i(t) \lambda_i(t)$ define diff $dM_i(t) = dN_i(t) - Y_i(t) \lambda_i(t) dt$ (O-E), take **E**, $E[dM_i(t) | \mathcal{F}_{t-}] = E[dN_i(t) | \mathcal{F}_{t-}] = 0$

martingale ϵ $M_i(t) = N_i(t) - \int_0^t Y_i(u) \lambda_i(u) du$; $M_i = \delta_i - e^{\beta T} z_i \hat{H}_0(t_i)$;

$E[M_i(t) | \mathcal{F}_s] = M_i(s)$, $E[M(t) - M(s) | \mathcal{F}_s] = 0$

competing risk 1 - p(transplant) : die before trans or surv not trans.

cause-speci hazard $\lambda_j(t) \equiv \lim P(t \leq \tilde{T}_i < t + h, \tilde{E}_i = j | \tilde{T}_i \geq t) / h$;

$f_j(t) dt = \lambda_j(t) dt \exp \left\{ - \int_0^t \sum_{k=1}^J \lambda_k(u) du \right\}$ no event occ, $\sum f_j = 1$;

cox-type: $\lambda_{ij}(t) = \lambda_{0j}(t) \exp\{\beta_j' x_i\}$; cum incidence: $\hat{\pi}_{ij}(s) =$

$\sum_k d\hat{\Lambda}_{ij}(t_k) \exp \left\{ - \sum_{j=1}^J \hat{\Lambda}_{ij}(t_{k-1}) \right\}$, $\Lambda_{ij}(t) = \Lambda_{0j}(t) \exp\{\beta_j' x_i\}$ cum

base from breslow; non-param: nelson+KM, Aalen.Johansen

$\hat{\pi}_j(s) = \sum_{k:t_k \leq s} \frac{d_k}{r_k} \hat{S}_{KM}(t_{k-1})$, $\hat{S} = \prod_{k:t_k \leq t} \left(1 - \frac{\sum_{j=1}^J d_{jk}}{r_k} \right)$

subdist hazard at risk or devlp other event $\psi_{ij}(t) = \psi_{0j}(t) \exp\{\gamma_j' x_i\}$
 $\psi_j(t) \equiv \lim P(t \leq \tilde{T}_i < t + h, \tilde{E}_i = j | \tilde{T}_i \geq t \text{ or } (\tilde{T}_i < t \text{ and } \tilde{E}_i \neq j))$,

$\hat{\pi}_{ij}(s) = 1 - \exp \left\{ - \hat{\Psi}_{0j}(s) \exp \left\{ \hat{\gamma}_j' x_i \right\} \right\}$ connect cox-type-finegray

$\pi_j(t) = 1 - \exp \left\{ - \Psi_j(t) \right\}$

Piecewise hazard: $\prod_{i=1}^n \prod_{k=1}^K \lambda_{ikl}^{d_{ikl}} \exp(-y_{ikl} \lambda_{kl} dt)$ where

$\sum_i^n d_{ikl} \sim \text{pois}(\lambda_{kl})$, $\sum_i^n y_{ikl}$, model $\log(\lambda_{ikl}) = \alpha_k + \beta_l + \gamma' X_i$

$L(\beta) = \prod_{i=1}^n \prod_{k=1}^K [(\lambda_{0k} \exp(\beta' x_i))^{d_{ik}} \exp(-y_{ik} \lambda_{0k} \exp(\beta' x_i))]$,

$\hat{\lambda}_{0k}(\beta) = d_k / \left\{ \sum_i^n y_{ik} \exp(\beta' x_i) \right\}$

Diagnostics (1) Sen/TP = $P(\hat{\pi}_i(s) > \pi^* | \tilde{N}_i(s) = 1)$ and

$PPV = P(\tilde{N}_i(s) = 1 | \hat{\pi}_i(s) > \pi^*)$. (2) Spe/TN = $P(\hat{\pi}_i(s) < \pi^* | N_i(s) = 0)$ and NPV = $P(N_i(s) = 0 | \hat{\pi}_i(s) < \pi^*)$

AUC sen vs 1-spe $P(\hat{\pi}_i(s) > \hat{\pi}_j(s) | N_i(s) = 1, N_j(s) = 0)$, w/o censoring,

estimate as prop. of concordant pairs: $P(\hat{\pi}_i(s) > \hat{\pi}_j(s) | T_i < T_j)$ when

censor, use C-index: $(T_{\text{censor}} > T_{\text{non-censor}})$.

Estimate sen/spe w/ censoring: use bayes & KM est.

Sen = $\frac{(1 - P(N_i(s) = 0 | \hat{\pi}_i(s) \geq \pi^*)) (1 - P(\hat{\pi}_i(s) < \pi^*))}{1 - P(N_i(s) = 0)}$.

Spe = $\frac{P(N_i(s) = 0 | \hat{\pi}_i(s) < \pi^*) P(\hat{\pi}_i(s) \leq \pi^*) [\text{empirical prop}]}{P(N_i(s) = 0) \cdot \text{s-year survival KM}}$,

Calibration Hosmer-Lemeshow $\sum_{k=1}^K \frac{(O_k - E_k)^2}{N_k \hat{\pi}_k (1 - \hat{\pi}_k)} \sim \chi_{k-2}^2$, $E_k = N_k \hat{\pi}_k$;

$\hat{\pi}_k$ avg risk in grp k, w/ censor $O_k = N_k (1 - S_k(s))$ from KM. **Brier**

score $(1/n) \sum_{i=1}^n \left(\tilde{N}_i(s) - \hat{\pi}_i(s) \right)^2$

Eliminate nuisance param: (1) data $y = (v, w)$,
 $P(v, w | \theta, \psi) = P(w | v, \theta) P(v | \theta, \psi)$ if v3 is ancillary. (2) Profile

$\prod_{i=1}^n \prod_{k=1}^K [\lambda_{0k} \exp(\beta' x)]^{d_{ik}} \exp(-y_{ik} \lambda_{ik} \exp(\beta' x_i))$ (person i , int k).

MLE BaseHaz $\hat{\lambda}_{0k} = \frac{d_k}{\sum_{i=1}^n y_{ik} \exp(\beta x_i)}$ to get

$\prod_{i=1}^n \prod_{k=1}^K \left(\frac{\exp(\beta x_i)}{\sum_{l=1}^n y_l(t_i) \exp(\beta x_l)} \right)^{d_{ik}}$ where i =individual, k =interval.

Only i individuals with events contribute, Cox PH simplifies to

$\prod_{i=1}^n \left(\frac{\exp(\beta' x_i)}{\sum_l^n Y_l(t_i) \exp(\beta' x_l)} \right)^{e_i}$ where $Y_i(t_i) = 1_{\{T_i \geq t_i\}}$ and

$e_i = 1_{\{T_i \leq C_i\}}$. **Partial lkhd for 1-1 match** :

$P(D_{i1} = 1 | D_{i1} + D_{i2} = 1, z_{i1}, x_{i1}, z_{i2}, x_{i2}; \theta) =$

$P(dN_i(t) = 1 | dN_{i1}(t) + dN_{i2}(t) = 1, F_{t-}, \theta) =$

$\frac{\exp(\alpha_i + \beta' Z_{i1} + \gamma' X_{i1})}{\exp(\alpha_i + \beta' Z_{i1} + \gamma' X_{i1}) + \exp(\beta' Z_{i2} + \gamma' X_{i2})}$. Partial LKHD becomes

$\prod_{i=1}^n \frac{\exp(\beta' Z_{i1} + \gamma' X_{i1})}{\exp(\beta' Z_{i1} + \gamma' X_{i1}) + \exp(\beta' Z_{i2} + \gamma' X_{i2})}$ where $\theta = (\alpha, \beta, \gamma)$.

Counting Process: (1) $N(0) = 0$, (2) $N(t) \in \{\dots, -1, 0, 1, \dots\}$, (3 & 4)

$s < t \Rightarrow N(s) < N(t)$ and $N(t) - N(s) = \#$ events in interval $(s, t]$.

$N(s + t) - N(s) \sim \text{Poisson}(\lambda t)$ **Properties:** (1) Memoryless

$P(X > s + t | X > t) = P(X > s) \forall s, t \geq 0$. depends only on the length

(2) Independent non-overlapping increments: $N(s + t) - N(s) \perp N(t)$.

(3) Poisson-Gamma Duality: $N(t) \sim \text{Pois}(\lambda t)$, $S_n \sim \text{Gamma}(n, \lambda) \Rightarrow$

$P(N(t) \geq n) = P(S_n \leq t)$, $N(t) = \sum N_i(t) \sim \text{Pois}(\sum \lambda_k)$ **Interarrival**

Times $\{T_n, n \geq 1\} \sim \exp(\lambda) =$ time between $(n - 1)^{\text{th}}$ and n^{th} event.

$P(T_1 > t) = P(N(t) = 0)$. $P(T_2 > t) = E[P(T_2 > t | T_1)] =$

$\int_s^\infty P(N(t + s) = 0 | N(s) = 1) ds \stackrel{!}{=} e^{-\lambda t}$

Waiting Times $S_n = \sum_{i=1}^n T_i \sim \text{Gamma}(n, \lambda)$,

Order stat: $P(T_1 < s_1, T_2 < s_1 + s_2, \dots, T_n < s_1 + \dots + s_n | N(t) = n) =$

$n! \prod_{i=1}^n \frac{s_i}{t} \mathbb{1}(0 < \dots < s_{(n)} < t) \Rightarrow U(0, t)$ Ran. Samp. Order S.

Cond. Dist: $T_1 | N(t) = 1 \sim U(0, t)$, $N(s) | N(t) = n \sim \text{Bin}(n, \frac{s}{t})$

$T_i \sim \exp(\lambda_i) \Rightarrow P(X_1 < X_2) = \int_0^\infty P(X_1 < X_2 | X_1 = x) P(X_1 = x) dx =$
 $\int_0^\infty P(x < X_2) \lambda_1 \exp(-\lambda_1 x) dx = \frac{\lambda_1}{\lambda_1 + \lambda_2}$

MC: at time n, dist of $X_n = \vec{S}_{1 \times M}$ (m states) \rightarrow dist of $X_{n+1} = \vec{S}Q$ as:
 $p(x_{n+1} = j) = \sum_i P(x_{n+1} = j | x_n = i)^{p_{ij}} P(x_n = i)^{s_i} = \sum_i s_i p_{ij}$