Dynamic Models in Reliability and Survival Analysis

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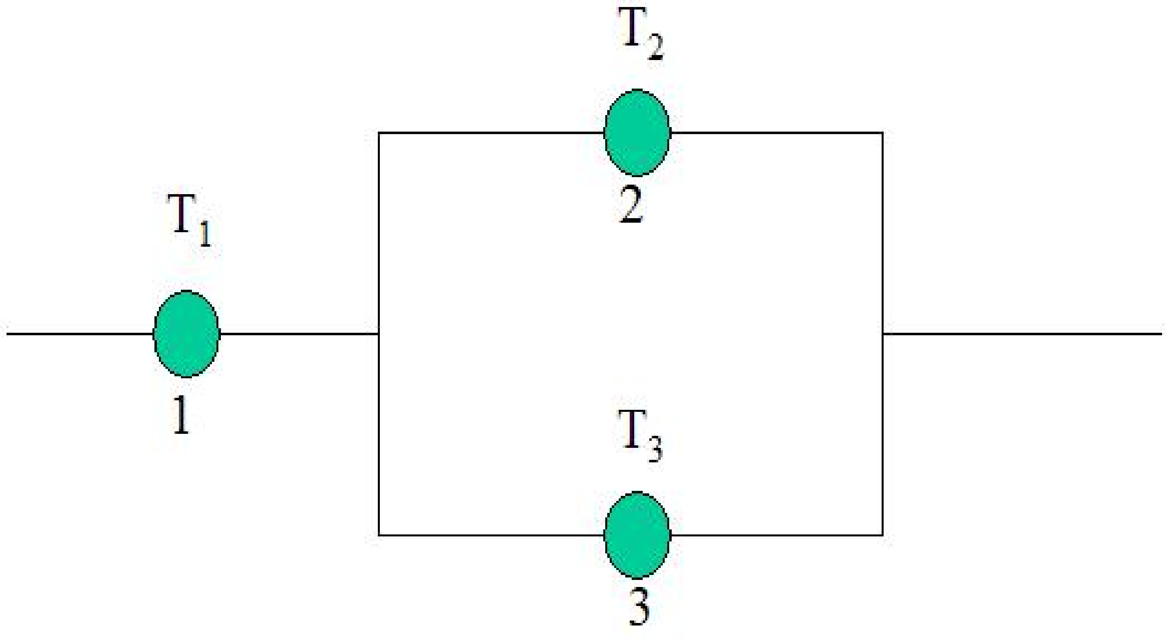
Outline of Talk

- Reliability and Recurrent Event Setting
- Static Modeling and its Limitations
- Need for Dynamic Models
- A Dynamic Model in Reliability
- A Dynamic Load-Sharing Model
- A General Model for Recurrent Events
- Inference Methods for Dynamic Models
- Properties; Applications; Some Asymptotics
- Concluding Remarks

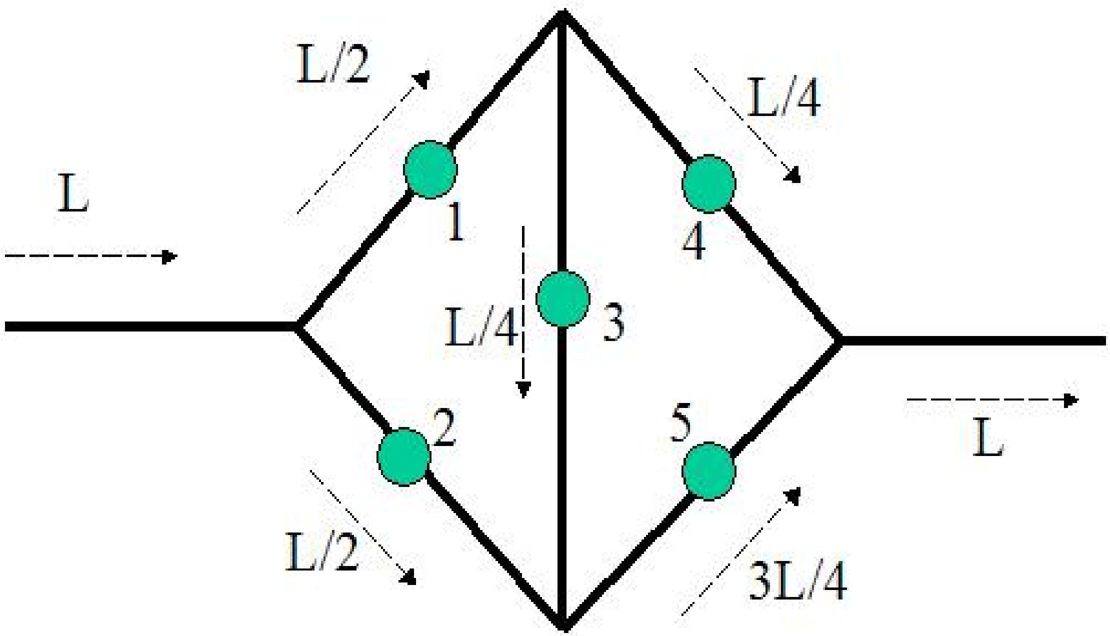
Reliability Systems

Series-Parallel: $\phi(x_1, x_2, x_3) = x_1 \vee (x_2 \wedge x_3)$



A Bridge System

$$\phi(x_1, x_2, x_3, x_4, x_5) = (x_1 x_4) \vee (x_1 x_3 x_5) \vee (x_2 x_5) \vee (x_2 x_3 x_4)$$



Reliability Notation

- Coherent system: p components
- Component and System states: $x_i \in \{0,1\}$; $\phi \in \{0,1\}$
- Structure function: $\phi = \phi(x_1, x_2, \ldots, x_p)$
- Component lifetimes: $(T_1, T_2, \ldots, T_p)$
- System lifetime: $S = h_\phi(T_1, T_2, \ldots, T_p)$
- Note: $I\{S > s\} = \phi(I\{T_1 > s\}, \ldots, I\{T_p > s\})$
- $\Pr\{S > s\} = \bar{H}_\phi(s) = E\{\phi(I\{T_1 > s\}, \ldots, I\{T_p > s\})\}$

Question: How should we specify the stochastic properties of $T_1, \ldots, T_p$, and consequently of S?

Recurrent Events

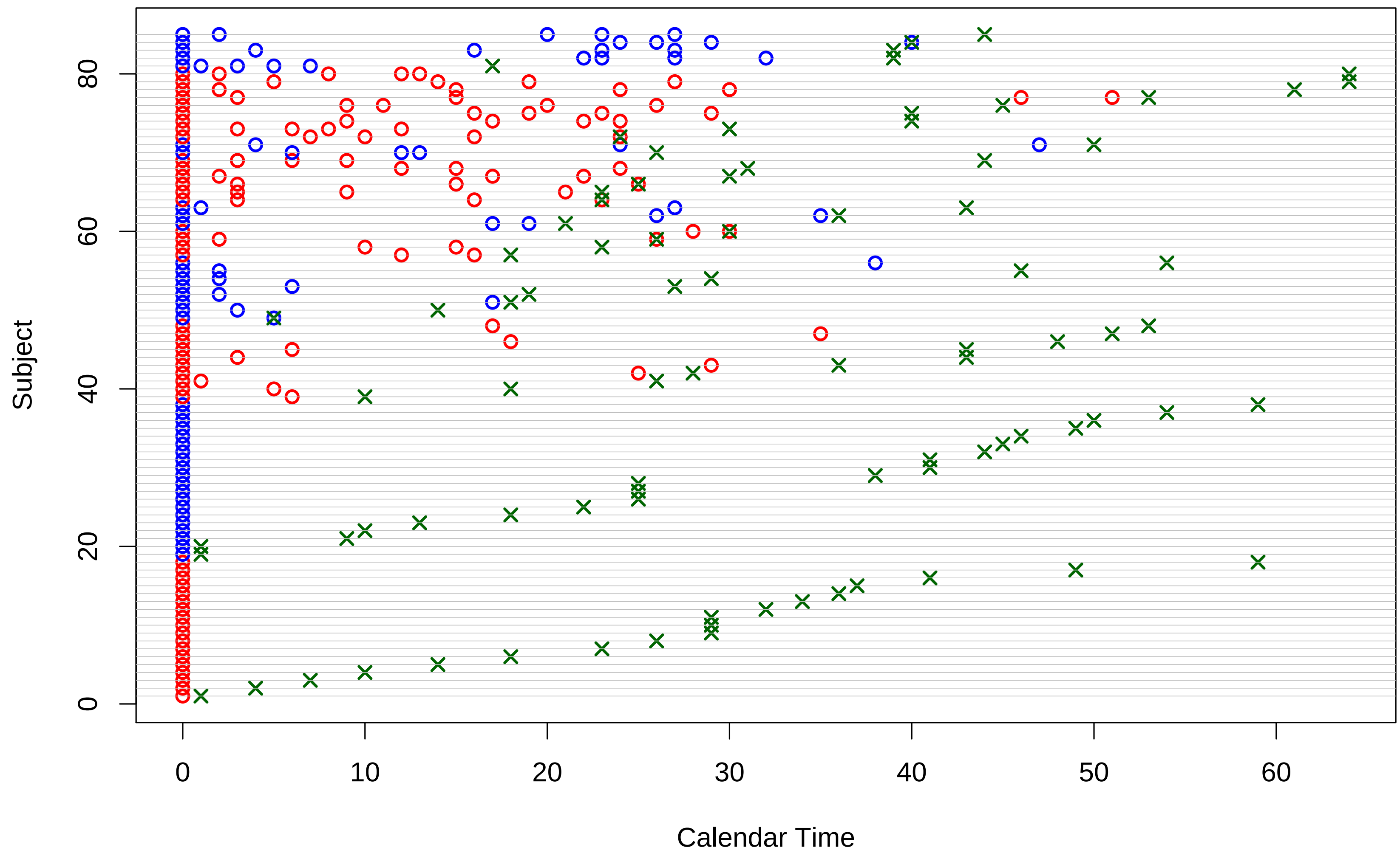
In reliability, engineering, biomedical, and other studies.

- failure of a machine, then repairs (eg., Proschan's Boeing AC data; Bus Data; Klefsjo and Kumar's LHD Data; Aalen and Husebye's MMC data)
- discovery of a computer software bug
- hospitalization due to a chronic disease
- occurrence of migraine headaches
- tumor occurrence
- onset of depression
- drop in the Dow Jones of 200 points
- terrorist attacks (V. Bier's talk)

Some Talks and Books

- H. Ascher's talk and his book.
- Z. Jin's talk.
- A. Basu's talk and his book.
- W. Nelson's book.
- T. Duchesne's talk and some of the questions.
- A. Jardine's talk
- B. Osborn's talk.
- M. Hollander's talk.
- E. Slate's talk.

Example: Bladder Cancer Data



Recurrent Event Modeling

- A probabilistic model for recurrent events specifies the stochastic properties of the times of event occurrences or the inter-event times.
- Such models would be useful for purposes of predicting future occurrences of the event, or for performing interventions or maintenance to lessen the chances of the event occurring.
- **Question:** How should the modeling of recurrent events be performed, especially in the presence of interventions?

Some Notation

- $T > 0$: a continuous failure time variable
- $f(t)$: density function
- $S(t)$ and $F(t)$: survivor and distribution functions
- $\Lambda(t) = \int_0^t dF(w)/S(w-) = -\log S(t)$: hazard function
- $\lambda(t)dt \approx \Pr\{t \le T < t + dt | T \ge t\}$: hazard rate function
- Equivalences:

$$S(t) = \exp\{-\Lambda(t)\} = \prod_{w=0}^{t} [1 - \Lambda(dw)] \,;$$

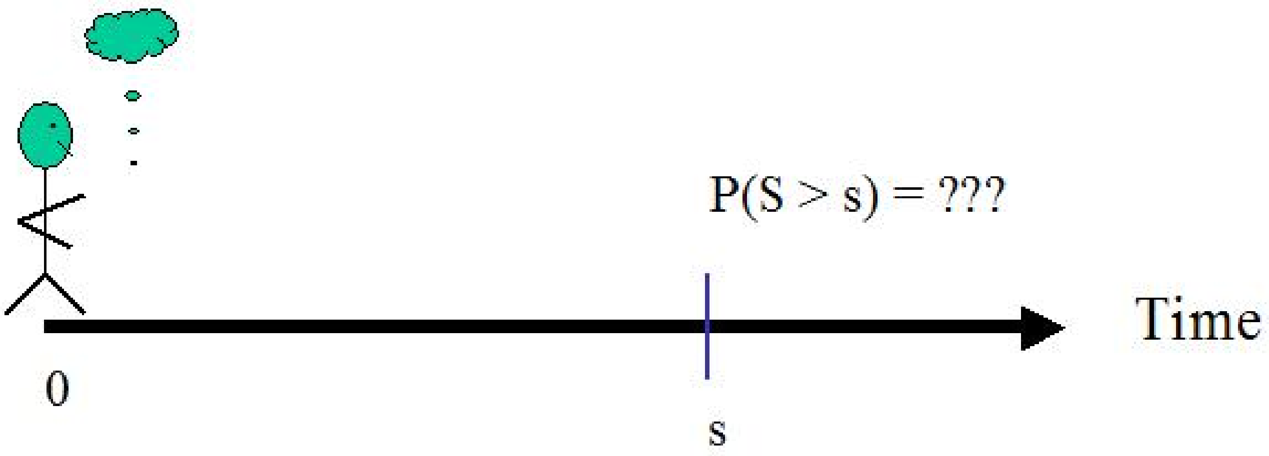
$$f(t) = \lambda(t) \exp\{-\Lambda(t)\}$$

Static Modeling Approach

- In most reliability settings, the stochastic properties of $\mathbf{T} = (T_1, T_2, \ldots, T_p)$ and of S, are done statically.
- Case, for example, in Barlow and Proschan's (1975) classic book.
- Example: In the series-parallel system, one specifies that (T_1, T_2, T_3) are IID EXP(λ). The system life distribution becomes

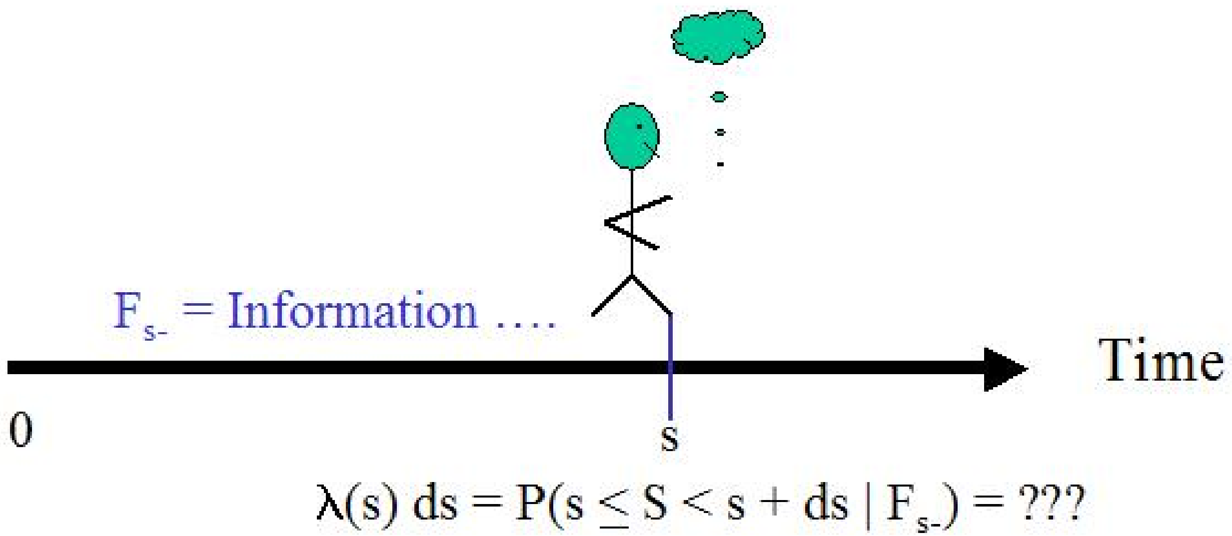
$$\Pr(S > s) = \exp(-2\lambda s)[2 - \exp(-\lambda s)].$$

Limitations of Static Approach



- Not able to account for dynamic changes.
- Specification of the model is done at the time origin, so modeling from a distance.

Essence of Dynamic Approach



$$\Pr\{S > s\} = \prod_{t=0}^{s} [1 - \lambda(t)dt]$$

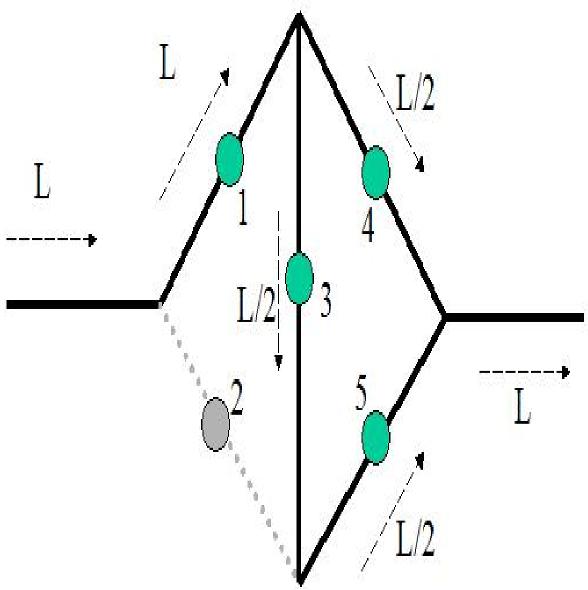
Need for Dynamic Approach

- Incorporates dynamic changes in the system or unit.
- More realistic to utilize accruing information as time evolves, and account for changing effective structure function.
- Modeling is conditional, which maybe more natural.
- Dependencies among component lifetimes could be automatically incorporated.
- Hazard or intensity-based modeling. Modern stochastic process approach as pioneered by Aalen, Gill, ABGK, etc.
- Relevant in repair/maintenance models, warranty models, and in studies with dynamic interventions.

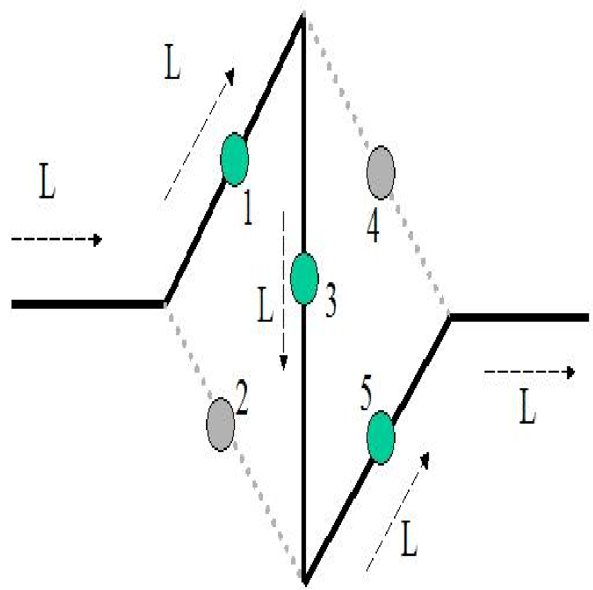
Motivating Example

Consider the bridge system and the component loads (**usage?**) as components fail.

After Component 2 Has Failed: Series-Parallel



After Components 2 and 4 Have Failed: Series



Some Terminology

- Coherent system: p components
- Structure function: ϕ
- $\mathcal{Z}_p = \{1, 2, \ldots, p\}$; $\quad \mathcal{P} =$power set of $\mathcal{Z}_p$
- Cut set: consists of indices such that failure of these components lead to system failure.
- $\mathcal{K}_\phi =$ minimal cut sets of ϕ
- $J \subseteq \mathcal{Z}_p$ is an absorbing set if $\exists K \in \mathcal{K}_\phi, K \subseteq J$
- $\mathcal{Q}_\phi =$ absorbing sets
- $\mathcal{Q}_\phi^0 = \mathcal{P} \setminus \mathcal{Q}_\phi =$ non-absorbing sets

A Dynamic Reliability Model

- $N^\dagger(s) =$ be the number component failures for the system in $[0, s]$
- $Y^\dagger(s) =$ an indicator that system is at-risk at s.
- $\mathcal{F}_s^\dagger =$ all information that accrued in $[0, s]$.
- Intensity process:

$$\alpha(s) = \lim_{h \downarrow 0} \frac{1}{h} \Pr\{N^\dagger((s+h)-) - N^\dagger(s-) \geq 1 | \mathcal{F}_{s-}^\dagger\}$$

- Each $J \in \mathcal{Q}_\phi^0$, let $\{\alpha_i[J], i \in J^c\}$ be positive reals.
- $F(s) =$ set of component indices failed at $s-$.

Intensity Specification

- For a hazard rate function $\lambda_0(\cdot)$, the intensity process of the system is

$$\alpha(s) = Y^\dagger(s) \left[\sum_{J \in \mathcal{Q}_\phi^0} I\{F(s) = J\} \sum_{j \in J^c} \alpha_j[J] \right] \lambda_0(s)$$

- Martingale property for

$$\left\{ M^\dagger(s) = N^\dagger(s) - \int_0^s \alpha(v)dv : \quad s \geq 0 \right\}.$$

System Life Distribution (HP '95)

- **Theorem:** For the special case of a parallel system, if

$$\left\{ \alpha_{\bullet}[J] = \sum_{j \in J^c} \alpha_j[J] : J \subseteq \mathcal{Z}_p \right\}$$

satisfies the condition that $|J| = k \Rightarrow \alpha_{\bullet}[J] = \alpha_k$ with $\alpha_k \neq \alpha_l$ for $k \neq l$, and if $\mathcal{C}_k = \{0, 1, \ldots, k\}$, then

$$\Pr\{S_k > s\} = \sum_{i=0}^{k-1} \left[\prod_{j \in \mathcal{C}_{k-1};\ j \neq i} \left(\frac{\alpha_j}{\alpha_j - \alpha_i} \right) \right] \exp\{-\alpha_i \Lambda_0(s)\}.$$

An Exercise and a Problem!

- Let $\zeta_1, \zeta_2, \ldots, \zeta_M$ be your M most esoteric and favorite real numbers (e.g., c = speed of light; e, Planck's constant, π, $\sqrt{2}$, number of stars, Avogadro's number, golden number, etc.).
- Prove: $\sum_{i=1}^{M} \prod_{j=1;\ j\neq i}^{M} \left[\frac{\zeta_j}{\zeta_j - \zeta_i}\right] = 1$
- **Problem:** Is there an analogous Block and Savits **IFRA Closure Theorem** in this dynamically-specified model?

A Load-Sharing Model

- Special case arises by taking a parallel system so

$$\phi(x_1, x_2, \ldots, x_n) = \max(x_1, x_2, \ldots, x_p)$$

and letting $\alpha_j[J] = \gamma_{|J|}$ where

$$\{\gamma_j = \gamma[j] : j = 0, 1, \ldots, p-1\}$$

are non-negative reals with $\gamma_0 = 1$.

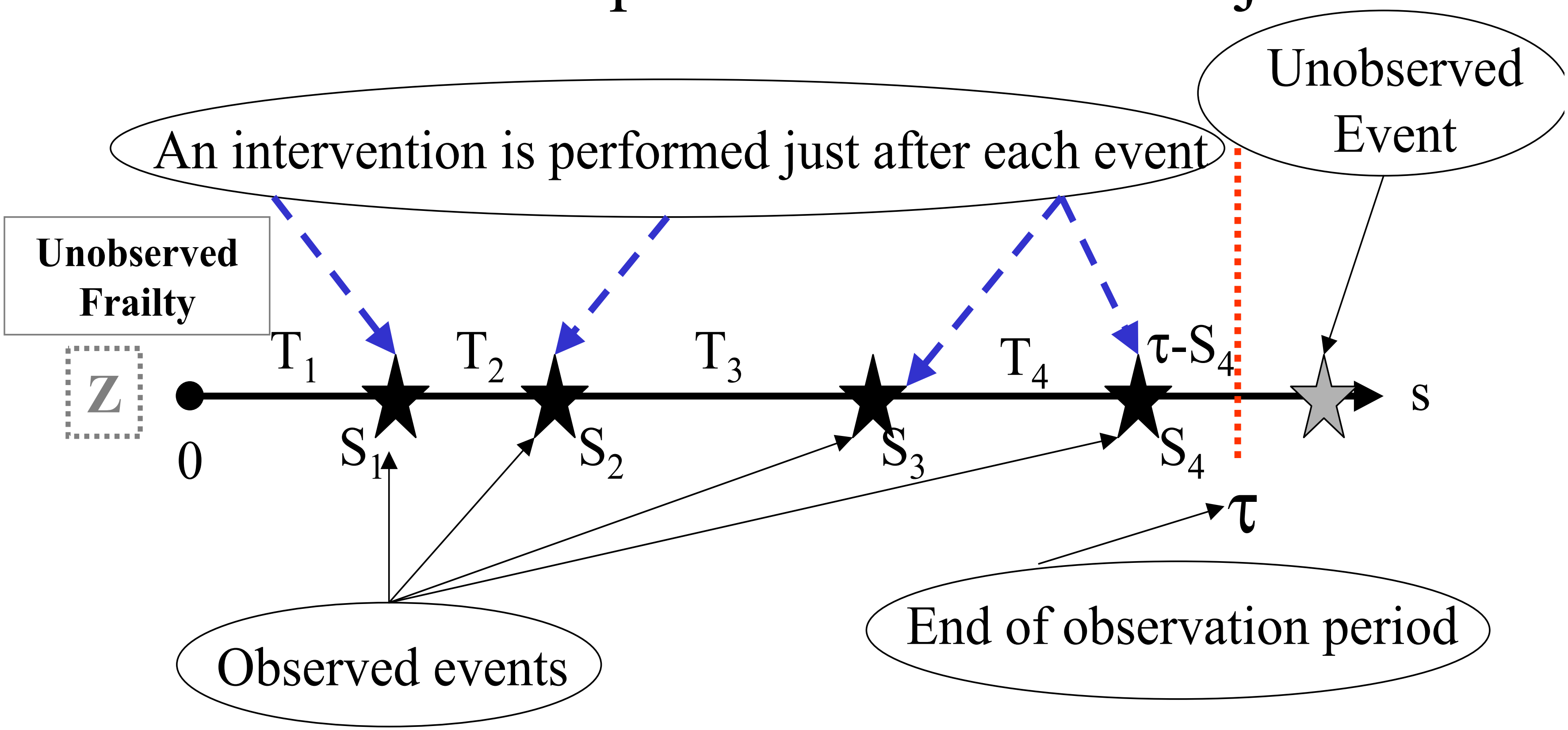
- Results in a load-sharing model with

$$\alpha(s) = Y^\dagger(s)[p - N^\dagger(s-)]\gamma[N^\dagger(s-)]\lambda_0(s).$$

- Inference issues in Kvam and Peña (2004, to appear in JASA).

Recurrent Events Accrual

A Pictorial Representation: One Subject



An observable covariate vector: $\mathbf{X}(s) = (X_1(s), X_2(s), \ldots, X_q(s))^t$

On Recurrent Event Modeling

- Intervention effects after each event occurrence.
- Effects of accumulating event occurrences. Could be weakening or strengthening effect.
- Effects of covariates.
- Associations of event occurrences per subject.
- Random observation monitoring period.
- Number of events observed informative about stochastic mechanism generating events.
- Informative and dependent right-censoring mechanism arising because of the sum-quota accrual scheme.

Random Entities: One Subject

- $\mathbf{X}(s) =$ covariate vector, possibly time-dependent
- $T_1, T_2, T_3, \ldots =$ inter-event or gap times
- $S_1, S_2, S_3, \ldots =$ calendar times of event occurrences
- $\tau =$ end of observation period
- $\mathbf{F}^\dagger = \{\mathcal{F}_s^\dagger : s \geq 0\} =$ filtration (information that includes interventions, covariates, etc.)
- $Z =$ unobserved frailty variable
- $N^\dagger(s) =$ number of events in $[0, s]$
- $Y^\dagger(s) =$ at-risk indicator at time s

Some Modeling Approaches

- J. Lawless and co-workers; Pepe and co-workers: modeled mean # of occurrences, $\mu(t) \equiv E\{N^\dagger(s)\}$.
- Time-to-first event: ignores information hence inefficient.
- Wei, Lin Weissfeld (WLW) marginal model: event number is used as a stratification variable; separate model per stratum.
- Prentice, Williams and Peterson (PWP) conditional method: ‘at-risk process’ for jth event only becomes 1 after the $(j-1)$th event.
- Andersen and Gill (AG) method: ‘at-risk process’ remains at 1 until unit is censored.

General Class of Models

- Class of models in Peña and Hollander (2004).
- $\{A^{\dagger}(s|Z) : s \geq 0\}$ is a predictable, nondecreasing process such that given Z and wrt $\mathbf{F}^{\dagger}$:

$$\{M^{\dagger}(s|Z) = N^{\dagger}(s) - A^{\dagger}(s|Z) : \ s \geq 0\}$$

  is a square-integrable zero-mean local martingale.
- Multiplicative form:

$$A^{\dagger}(s|Z) = \int_0^s Y^{\dagger}(w)\lambda(w|Z)dw.$$

Intensity Process

- Specify, possibly dynamically, a predictable, observable process $\{\mathcal{E}(s) : \ 0 \le s \le \tau\}$ called the *effective age process*, satisfying
  - $\mathcal{E}(0) = e_0 \ge 0$;
  - $\mathcal{E}(s) \ge 0$ for every s;
  - On $[S_{k-1}, S_k)$, $\mathcal{E}(s)$ is monotone and differentiable with $\mathcal{E}'(s) \ge 0$.

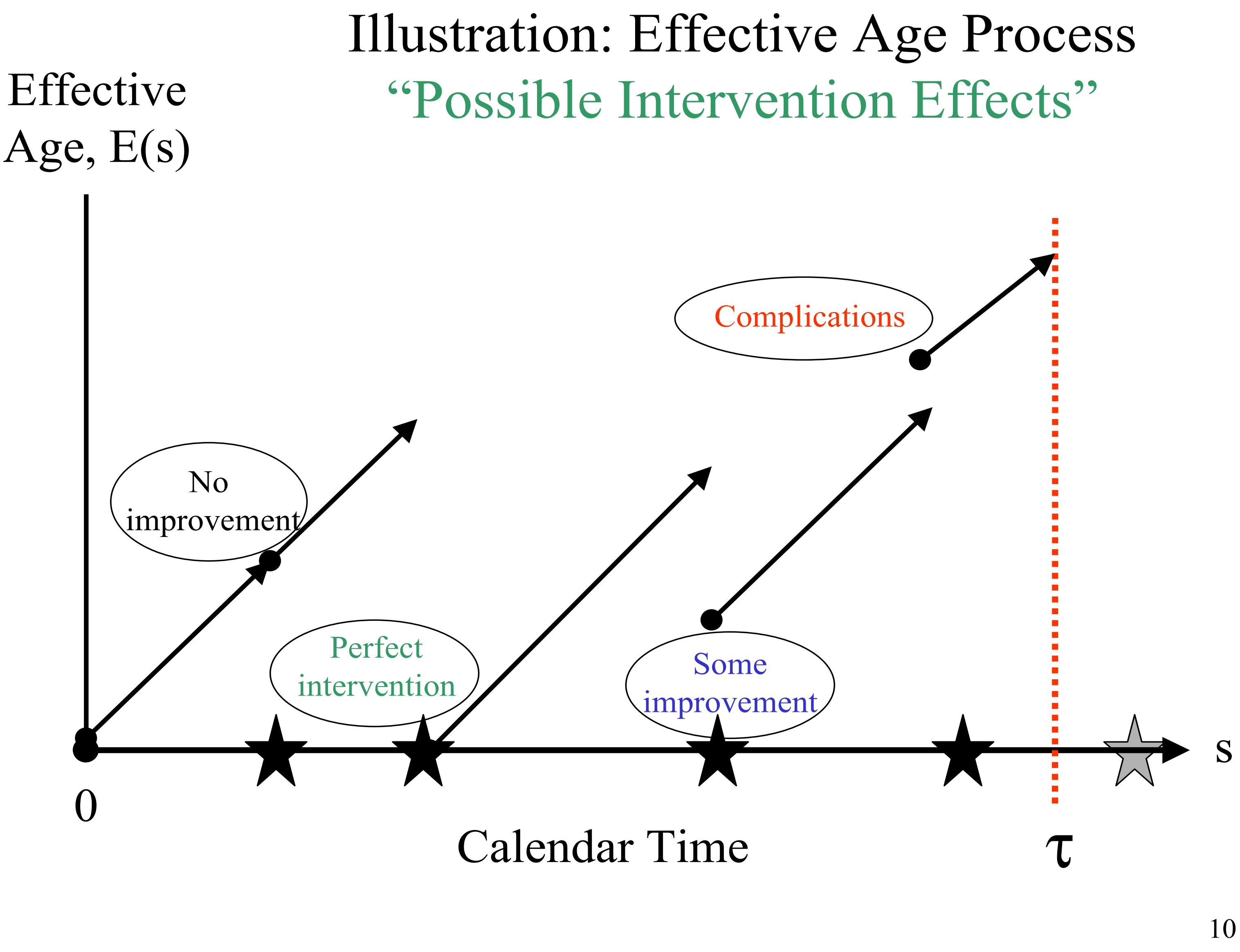
- Intensity Specification:

$$\lambda(s|Z) = Z\, \lambda_0[\mathcal{E}(s)]\, \rho[N^\dagger(s-); \alpha]\, \psi[\beta^{\mathsf{t}} X(s)]$$

Model Components

- $\lambda_0(\cdot) =$ unknown baseline hazard rate function.
- $\mathcal{E}(s) =$ effective age at calendar time s.
- **Rationale:** intervention changes effective age acting on baseline hazard.
- $\rho(\cdot;\alpha) =$ a positive function on $\mathcal{Z}_+$; known form; $\rho(0;\alpha) = 1$; unknown α. Encodes effect of accumulating events.
- $\psi(\cdot) =$ positive link function containing the effect of subject covariates. β is unknown.
- $Z =$ unobservable frailty variable. (E.g., unobserved environmental factors, genetic traits, or unknown defects.)

Effective Age Process



Some Special Cases

- IID renewal model with and without frailties: $\mathcal{E}(s) = s - S_{N^\dagger(s-)}$, $\rho(k) = 1$, $\psi(x) = 1$. In PSH (*JASA*, 2001); Wang and Chang (*JASA*, 1999).
- Extended Cox (1972) PH model; Prentice, Williams and Peterson (1981) model; Lawless (1987):

$$\mathcal{E}(s) = s, \rho(k) = 1, \psi(x) = \exp(x)$$

- Gail, Santner and Brown (1980) carcinogenesis model and Jelinski and Moranda (1972) software reliability model.

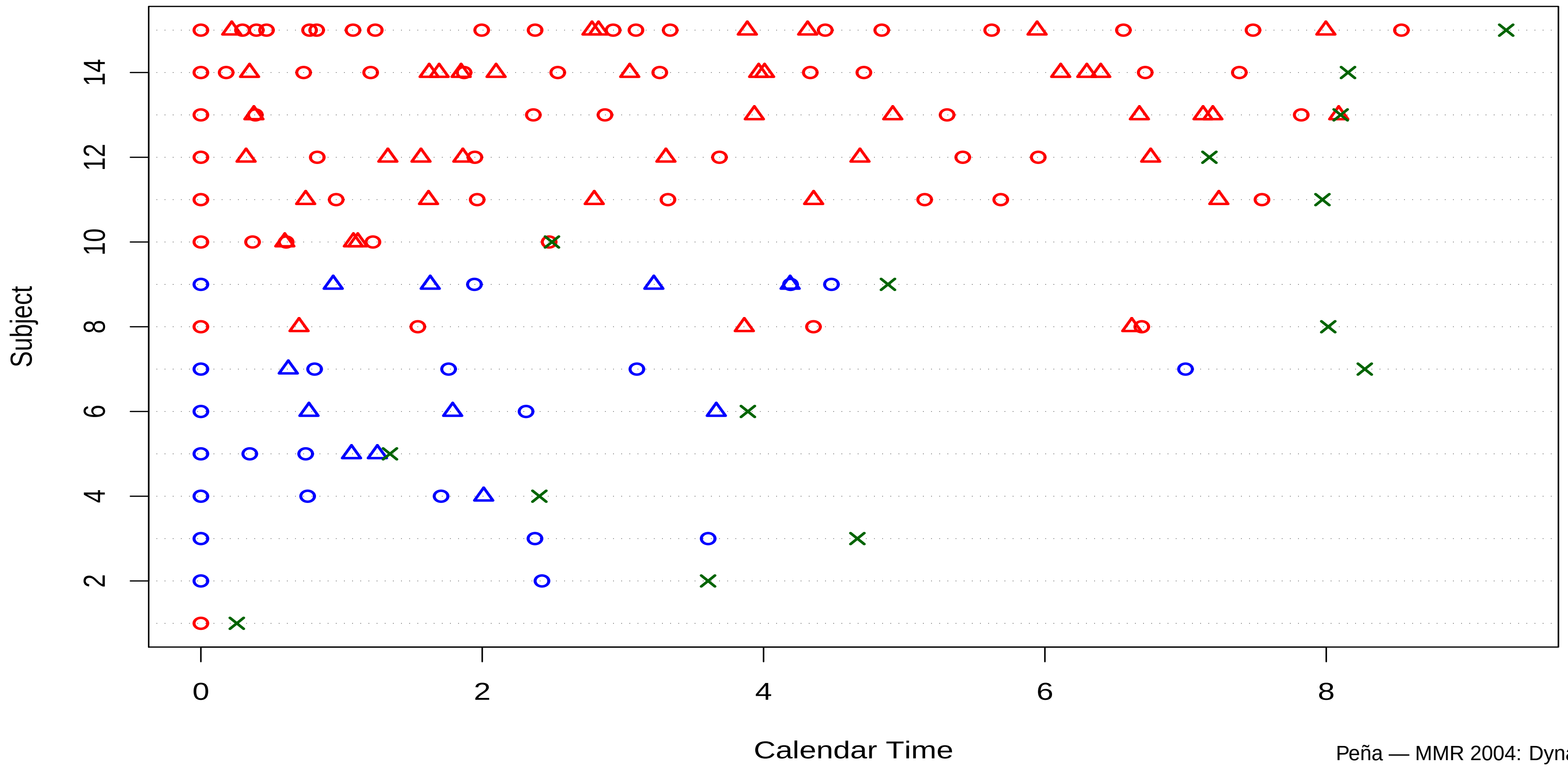
$$\rho(k;\alpha) = \max(0, \alpha - k + 1)$$

Minimal Repair Models

- Dorado, Hollander and Sethuraman (1997) general repair model; Kijima (1989); load-share model in Kvam and Peña (2004); others.
- Brown and Proschan (1983) minimal repair model and Block, Borges and Savits (1985):
- Let $I_1, I_2, \ldots$ IID Ber(p), p be the 'perfect repair or intervention' probability.
  - $\Gamma_k = \min\{j > \Gamma_{k-1} : \ I_j = 1\}$: index kth perfect repair
  - $\eta(s) = \sum_{i=1}^{N^\dagger(s)} I_i$: # of perfect repairs till s
  - $\mathcal{E}(s) = s - S_{\Gamma_{\eta(s-)}}$: length since last perfect repair

A Simulated Data from Model

True Model Parameters: $n = 15$; $\alpha = 0.90$; $\beta = (1.0, -1.0)$; $X_1 \sim Ber(.5)$; $X_2 \sim N(0,1)$; $\tau \sim U(0,10)$; Minimal Repair with 0.6 prob; Baseline $\lambda_0(\cdot)$: Weibull(2,1); Frailty: Gamma$(2,2)$



Statistical Inference

- Dynamic models lead to complicated inference procedures. Price paid for a more realistic modeling scheme.
- Inference methods usually rely on a stochastic process formulation.
- Use of counting processes, martingales, stochastic integration, and empirical processes.
- Reliability models: parametric; whereas, biomedical models: semiparametric.
- Peña, Slate and Gonzalez (2004): considered estimation for the general model when $\lambda_0(\cdot)$ is non-parametric.

For Model Without Frailties

Processes for n units or subjects:

$$\{(\mathbf{X}_i(s), N_i^\dagger(s), Y_i^\dagger(s), \mathcal{E}_i(s)) :\ 0 \leq s \leq s^*\}, i = 1, \ldots, n$$

$$N_i^\dagger(s) = \text{\# of events in } [0, s]$$

$$Y_i^\dagger(s) = \text{at-risk indicator at } s$$

$$A_i^\dagger(s) = \int_0^s Y_i^\dagger(v)\, \lambda_0[\mathcal{E}_i(v)]\, \rho[N_i^\dagger(v-); \alpha]\, \psi[\beta^{\mathtt{t}} \mathbf{X}_i(v)]\, dv$$

$$\mathbf{M}^\dagger = \mathbf{N}^\dagger - \mathbf{A}^\dagger = (N_1^\dagger - A_1^\dagger, \ldots, N_n^\dagger - A_n^\dagger)$$

Calendar/Gap Time Processes

Idea: From Sellke (1988) and Gill (1981).

$$Z_i(s,t) = I\{\mathcal{E}_i(s) \le t\},\ i = 1,\ldots,n$$

$$N_i(s,t) = \int_0^s Z_i(v,t) N_i^{\dagger}(dv)$$

$$A_i(s,t) = \int_0^s Z_i(v,t) A_i^{\dagger}(dv)$$

$$M_i(s,t) = N_i(s,t) - A_i(s,t) = \int_0^s Z_i(v,t) M_i^{\dagger}(dv)$$

Remark: $M_i(\cdot,t)$ is a martingale, but not $M(s,\cdot)$.

Notational Reductions

$$\mathcal{E}_{ij-1}(v) \equiv \mathcal{E}_i(v) I_{(S_{ij-1}, S_{ij}]}(v) I\{Y_i^\dagger(v) > 0\}$$

$$\varphi_{ij-1}(w|\alpha,\beta) \equiv \frac{\rho(j-1;\alpha)\psi\{\beta^{\mathsf{t}}\mathbf{X}_i[\mathcal{E}_{ij-1}^{-1}(w)]\}}{\mathcal{E}'_{ij-1}[\mathcal{E}_{ij-1}^{-1}(w)]}$$

Generalized At-Risk Process:

$$Y_i(s,w|\alpha,\beta) \equiv \sum_{j=1}^{N_i^\dagger(s-)} I_{(\mathcal{E}_{ij-1}(S_{ij-1}),\ \mathcal{E}_{ij-1}(S_{ij})]}(w)\, \varphi_{ij-1}(w|\alpha,\beta)$$

$$+\ I_{(\mathcal{E}_{iN_i^\dagger(s-)}(S_{iN_i^\dagger(s-)}),\ \mathcal{E}_{iN_i^\dagger(s-)}(\min(s,\tau_i))]}(w)\, \varphi_{iN_i^\dagger(s-)}(w|\alpha,\beta)$$

G-Nelson-Aalen 'Estimator'

$$A_i(s,t|\alpha,\beta) = \int_0^t Y_i(s,w|\alpha,\beta)\Lambda_0(dw)$$

$$S_0(s,t|\alpha,\beta) = \sum_{i=1}^{n} Y_i(s,t|\alpha,\beta)$$

$$\hat{\Lambda}_0(s,t|\alpha,\beta) = \int_0^t \left\{\frac{I\{S_0(s,w|\alpha,\beta) > 0\}}{S_0(s,w|\alpha,\beta)}\right\} \left\{\sum_{i=1}^{n} N_i(s,dw)\right\}$$

Note: But, α and β need to be estimated.

Estimating α and β

- Partial Likelihood (PL) Process:

$$L_P(s^*|\alpha,\beta) = \prod_{i=1}^{n} \prod_{j=1}^{N_i^\dagger(s^*)} \left[\frac{\rho(j-1;\alpha)\psi[\beta^{\mathtt{t}}\mathbf{X}_i(S_{ij})]}{S_0[s^*,\mathcal{E}_i(S_{ij})|\alpha,\beta]}\right]^{\Delta N_i^\dagger(S_{ij})}$$

- PL-MLE: $\hat{\alpha}$ and $\hat{\beta}$ are maximizers of

$$(\alpha,\beta) \mapsto L_P(s^*|\alpha,\beta)$$

- Iterative procedures (Newton-Raphson, `optim` routine in R) may be used.

G-PLE of $\bar{F}_0$

- G-NAE of $\Lambda_0(\cdot)$: $\hat{\Lambda}_0(s^*, t) \equiv \hat{\Lambda}_0(s^*, t | \hat{\alpha}, \hat{\beta})$
- G-PLE of $\bar{F}_0(t)$:

$$
\begin{aligned}
\hat{\bar{F}}_0(s^*, t) &= \prod_{w=0}^{t} \left[1 - \hat{\Lambda}_0(s^*, dw)\right] \\
&= \prod_{w=0}^{t} \left[1 - \frac{\sum_{i=1}^{n} N_i(s^*, dw)}{S_0(s^*, w | \hat{\alpha}, \hat{\beta})}\right]
\end{aligned}
$$

- Remark: When $\mathcal{E}_i(s) = s - S_{iN_i^\dagger(s-)}$, $\rho(k; \alpha) = 1$, and $\psi(w) = 1$, estimator of $\bar{F}_0$ in PSH (2001, JASA) for the IID renewal model obtains.

For Model With Frailty

- Recall the intensity process:

$$\lambda_i(s|Z_i, \mathbf{X}_i) = Z_i\, \lambda_0[\mathcal{E}_i(s)]\, \rho[N_i^{\dagger}(s-); \alpha]\, \psi(\beta^{\mathtt{t}} \mathbf{X}_i(s))$$

- Frailties $Z_1, Z_2, \ldots, Z_n$ are unobserved and assumed IID Gamma(ξ, ξ)
- Unknown parameters: $(\xi, \alpha, \beta, \lambda_0(\cdot))$
- Use of EM algorithm (Dempster, et al; Nielsen, et al), with frailties as missing observations.
- Estimator of baseline hazard function under no-frailty model plays an important role.

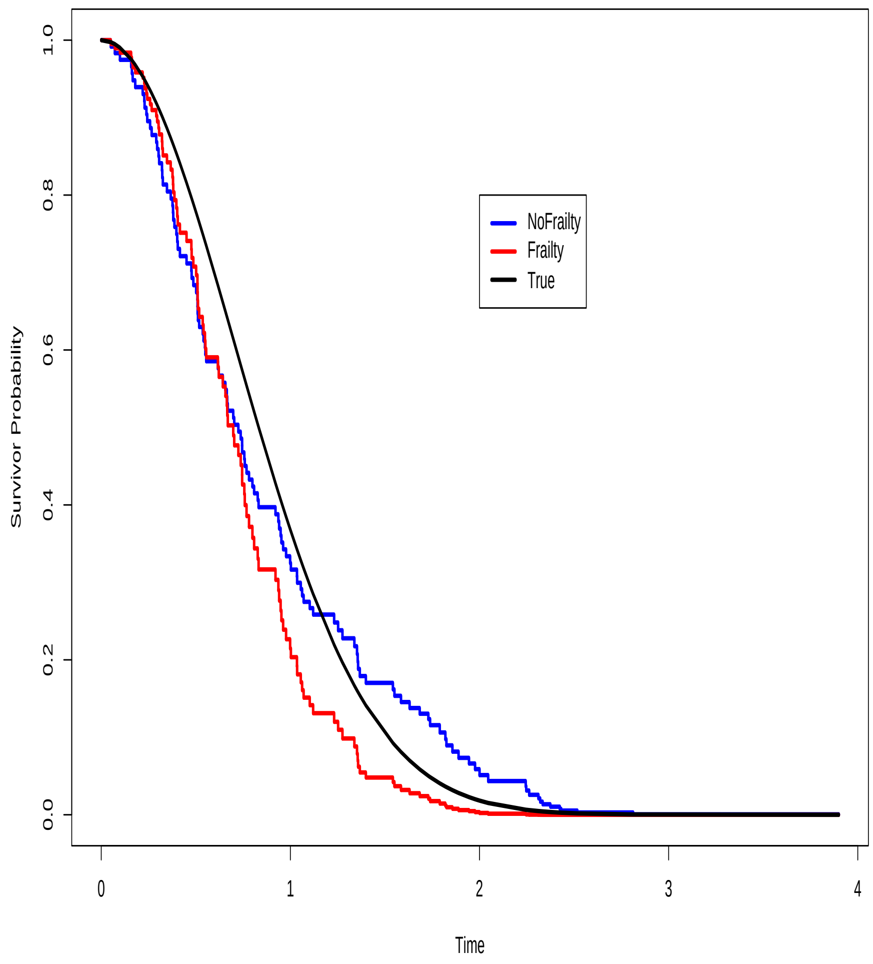
Algorithm

- Step 0: (Initialization) Seed values $\hat{\xi}, \hat{\alpha}, \hat{\beta}$; no-frailty estimator $\hat{\Lambda}_0$.
- Step 1: (E-step) Compute $\hat{Z}_i = E(Z_i|\text{data}, \hat{\xi}, \hat{\alpha}, \hat{\beta}, \hat{\Lambda}_0)$.
- Step 2: (M-step 1) New estimate of $\Lambda_0(\cdot)$. Form: analogous to the no-frailty case with $\hat{Z}_i$'s.
- Step 3: (M-step 2) New estimates of α and β.
- Step 4: (M-step 3) New estimate of ξ; maximize marginal likelihood for ξ.
- Step 5: Check for convergence.

Implemented in an R package called ‘gcmrec’ (Gonzalez, Slate, Peña).

Estimates for Simulated Data

- **With Frailty Fit**
  - 102 iterations in EM
  - $\hat{\alpha} = .8748$
  - $\hat{\beta} = (1.099, -1.3986)$
  - $\hat{\xi} = 2.1831$
- **Without Frailty Fit**
  - $\hat{\alpha} = .963$
  - $\hat{\beta} = (0.590, -0.571)$



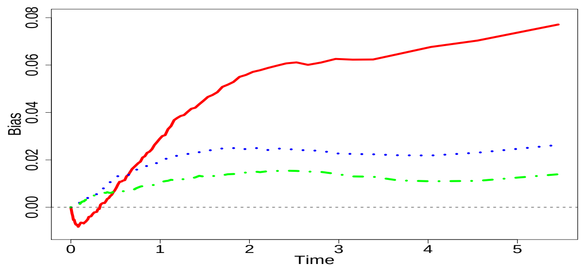
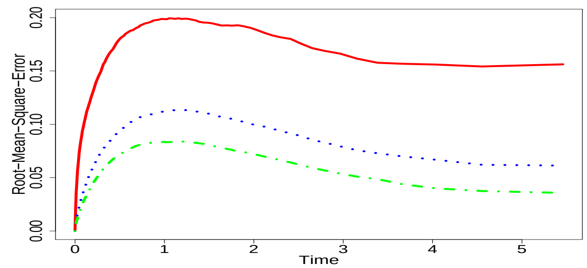
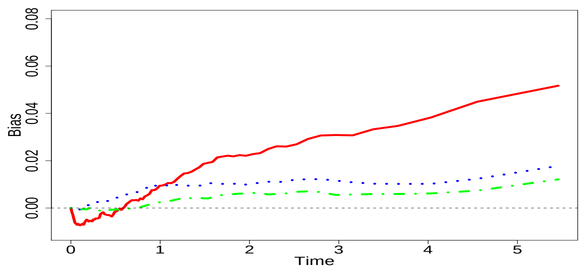
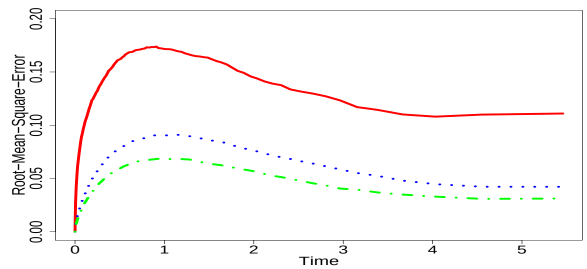
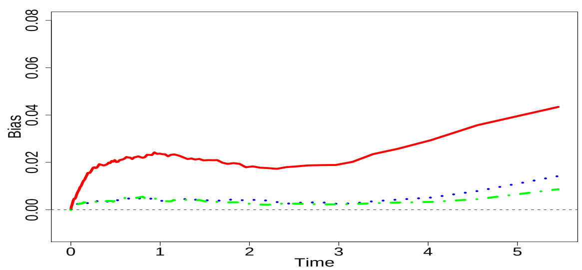
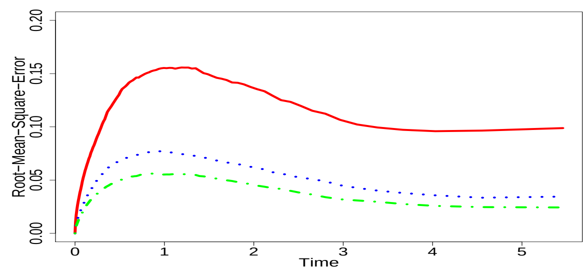
Properties: Simulated

- $\rho(k; \alpha) = \alpha^k$; $\alpha \in \{.9, 1.0, 1.05\}$
- $\psi(u) = \exp(u)$; $\beta = (1, -1)$; $X_1 \sim$ Ber$(.5)$; $X_2 \sim$ N$(0, 1)$
- Weibull baseline with shape $\gamma = .9$ (DFR) and $\gamma = 2$ (IFR)
- Gamma frailty parameter $\xi \in \{2, 6, \infty\}$
- Effective Age: Minimal repair model with $p = .6$
- Sample Size $n \in \{10, 30, 50\}$
- Censoring $\tau \sim$ Unif$(0, B)$ (approx 10 events/unit)
- 1000 replications per simulation combination

Finite-Dimensional Parameters

TableA	α	γ	ξ	η	n	$\hat{\mu}_{Ev}$	$\hat{\alpha}$	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\eta}$
A2.me	0.9	0.9	2	0.67	30	4.1	0.898	1.01	-1.01	0.734
A2.sd							0.031	0.379	0.24	0.124
A3.me	0.9	0.9	2	0.67	50	5.2	0.899	1.02	-1	0.705
A3.sd							0.021	0.287	0.165	0.091
A5.me	0.9	0.9	6	0.86	30	4.3	0.9	0.988	-1.01	0.904
A5.sd							0.030	0.3	0.175	0.085
A6.me	0.9	0.9	6	0.86	50	5.3	0.899	0.998	-1	0.884
A6.sd							0.021	0.221	0.136	0.071
A8.me	0.9	0.9	∞	1	30	4.8	0.893	1.03	-1.03	
A8.sd							0.0247	0.222	0.135	
A9.me	0.9	0.9	∞	1	50	4.4	0.895	1.02	-1.02	
A9.sd							0.018	0.158	0.104	

Baseline Survivor Function

<table>
<tr><th>ξ</th><th>Bias</th><th>RMSE</th></tr>
<tr><td>2</td><td></td><td></td></tr>
<tr><td>6</td><td></td><td></td></tr>
<tr><td>∞</td><td></td><td></td></tr>
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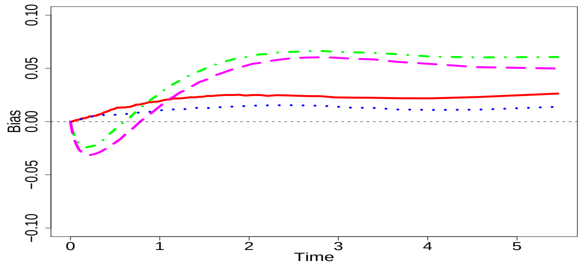
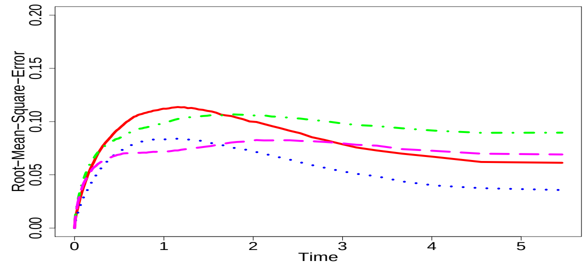
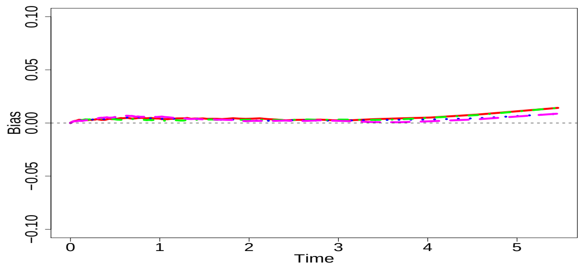
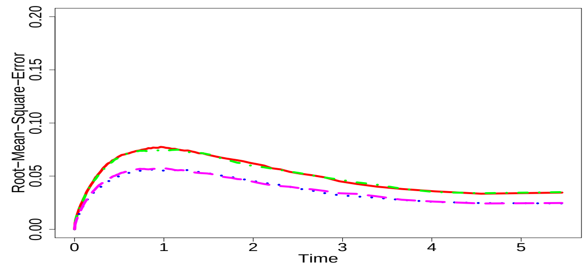
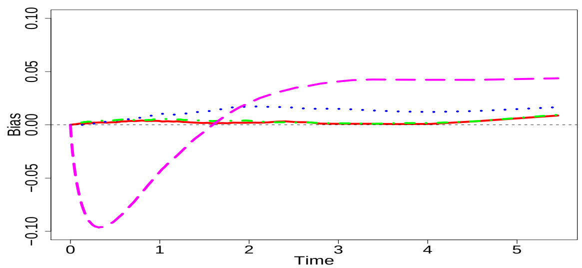
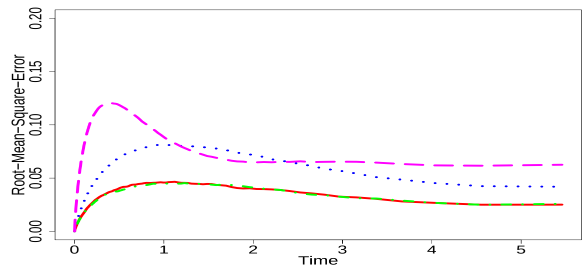
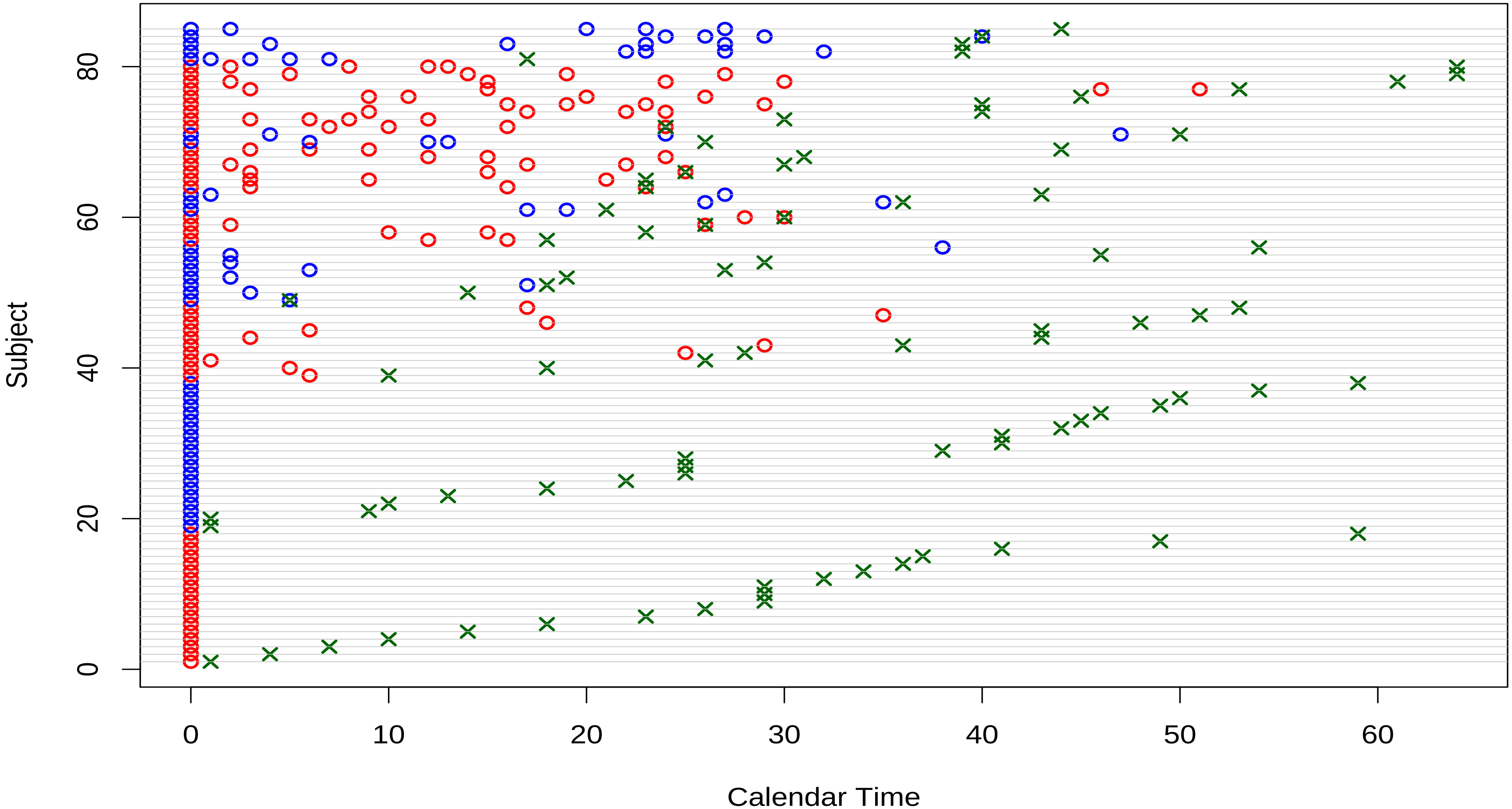
On Mis-specified Models

Type	Bias	RMSE
Under		
Over		
Comb.		

Application: Bladder Data

Bladder cancer data pertaining to times to recurrence for $n = 85$ subjects studied in Wei, Lin and Weissfeld ('89).

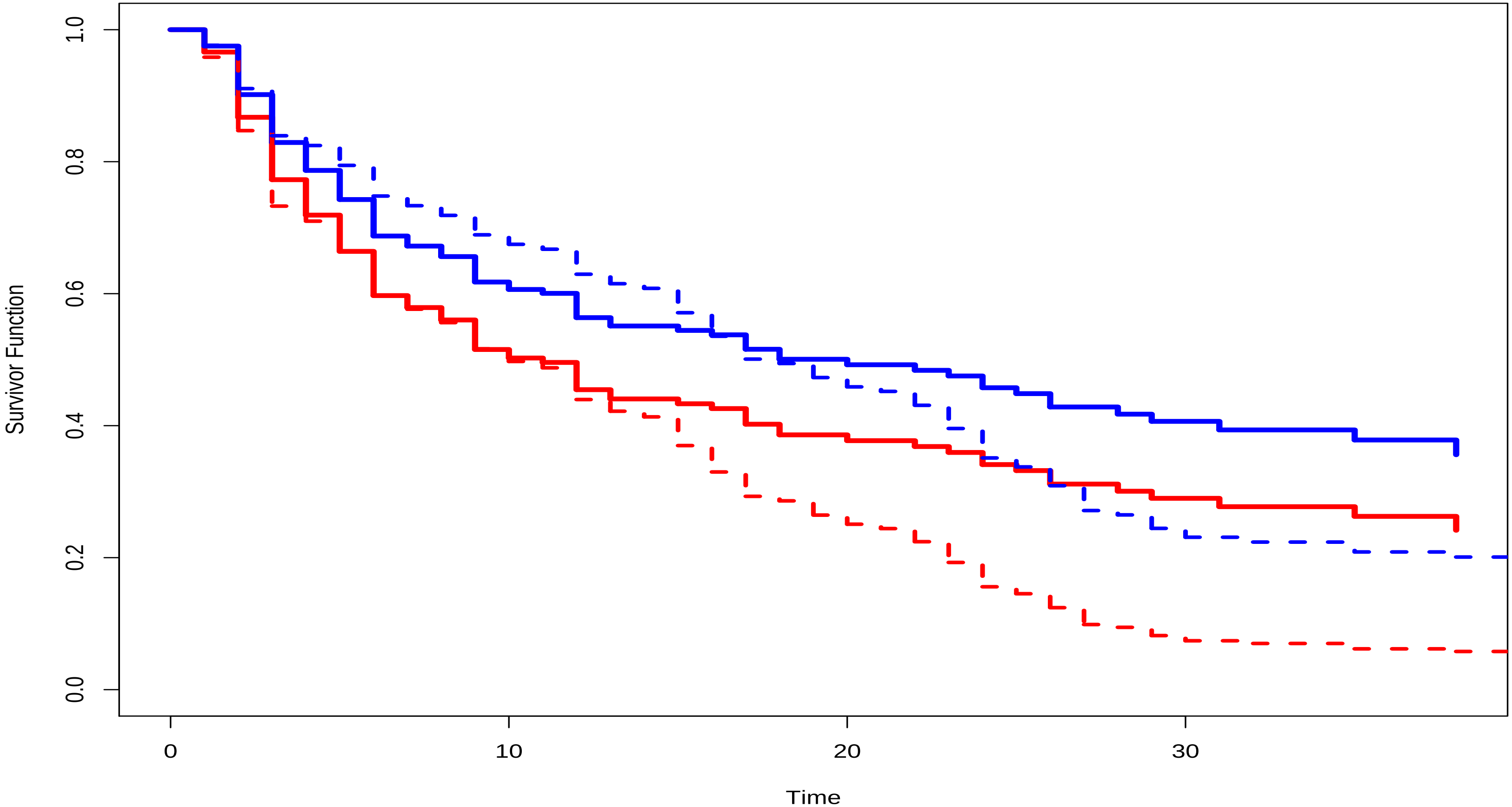


Estimates of Parameters

- X_1: (1 = placebo; 2 = thiotepa)
- X_2: size (cm) of largest initial tumor
- X_3: # of initial tumors
- Effective age: backward recurrence time (perfect repair) [also fitted with 'minimal' repair].
- Fitting model *without* frailties and 'perfect' repair:
  - $\hat{\alpha} = 0.98\ (s.e. = 0.07)$;
  - $(\hat{\beta}_1, \hat{\beta}_2, \hat{\beta}_3) = (-0.32, -0.02, 0.14)$;
  - s.e.s of $\hat{\beta} = (0.21, 0.07, 0.05)$.
- Fitting model *with* gamma frailties: 13 iterations in EM led to $\hat{\xi} = 5432999$ indicating absence of frailties.

Estimates of SFs for Two Groups

Blue: Thiotepa Group	Red: Placebo Group
Solid: Perfect Repair	Dashed: Minimal Repair



Comparisons

Estimates from Different Methods for Bladder Data

Cova	Para	AG	WLW	PWP	General Model	
			Marginal	Cond*nal	Perfect[a]	Minimal[b]
$\log N(t-)$	α	-	-	-	.98 (.07)	.79 (.13)
Frailty	ξ	-	-	-	∞	.97
rx	β_1	-.47 (.20)	-.58 (.20)	-.33 (.21)	-.32 (.21)	-.57 (.36)
Size	β_2	-.04 (.07)	-.05 (.07)	-.01 (.07)	-.02 (.07)	-.03 (.10)
Number	β_3	.18 (.05)	.21 (.05)	.12 (.05)	.14 (.05)	.22 (.10)

[a] Effective Age is backward recurrence time ($\mathcal{E}(s) = s - S_{N^\dagger(s-)}$).

[b] Effective Age is calendar time ($\mathcal{E}(s) = s$).

Remark: Example demonstrates the crucial role of the effective age process in reconciling methods!

Asymptotics: IID Renewal Model

$$\hat{\bar{F}}_0(t) \sim AN\left(\bar{F}_0(t), \frac{1}{n}\sigma^2(t)\right)$$

$$\sigma^2(t) = \bar{F}_0(t)^2 \int_0^t \frac{d\Lambda_0(w)}{y(w)}$$

$$y(w) = \bar{F}_0(w)\bar{G}(w-)\left[1 + \frac{1}{\bar{G}(w-)}\int_w^\infty \rho_0(v-w)dG(v)\right]$$

$$\rho_0(v) = \sum_{k=1}^\infty F_0^{(k)}(v) = \text{renewal function}$$

Some Remarks

- Note that the renewal function

$$\rho_0(s) = \sum_{k=1}^{\infty} F_0^{(k)}(s)$$

  plays crucial role in the limiting variance function. This is owing to the sum-quota accrual scheme, and the effect of this is oftentimes not recognized.
- Load-share model: asymptotic properties of estimators for $\Lambda_0(\cdot)$, $S_0(\cdot)$ and the load-share parameters γ_js given in Kvam and Peña (2004).
- R. Stocker: Case of $\lambda_0(\cdot)$ parametric.

Concluding Remarks

- Dynamic models appropriate and realistic in reliability and survival analysis.
- Current deficiency: Need to incorporate in the data-gathering the effective age. Calls for a paradigm-shift, but perhaps within reach!
- Open problems: Asymptotic properties of estimators for model with frailties.
- Testing hypotheses; goodness-of-fit; and model validation procedures needed.
- Use of dynamic models in issues of preventive maintenance, and finally, more interaction among those who deal with real data and academicians.