

# Censored Quantile Regression and Survival Models

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# Quantile Regression for Duration (Survival) Models

A wide variety of survival analysis models, following Doksum and Gasko (1990), may be written as,

$$h(T_i) = \mathbf{x}_i^T \boldsymbol{\beta} + \mathbf{u}_i$$

where  $h$  is a monotone transformation, and

- $T_i$  is an observed survival time,
- $\mathbf{x}_i$  is a vector of covariates,
- $\boldsymbol{\beta}$  is an unknown parameter vector
- $\{\mathbf{u}_i\}$  are iid with df  $F$ .

# The Cox Model

For the proportional hazard model with

$$\log \lambda(t|x) = \log \lambda_0(t) - x^\top \beta$$

the conditional survival function in terms of the integrated baseline hazard

$\Lambda_0(t) = \int_0^t \lambda_0(s) ds$  as,

$$\log(-\log(S(t|x))) = \log \Lambda_0(t) - x^\top \beta$$

so, evaluating at  $t = T_i$ , we have the model,

$$\log \Lambda_0(T) = x^\top \beta + u$$

for  $u_i$  iid with df  $F_0(u) = 1 - e^{-e^u}$ .

# The Bennett (Proportional-Odds) Model

For the proportional odds model, where the conditional odds of death  $\Gamma(t|x) = F(t|x)/(1 - F(t|x))$  are written as,

$$\log \Gamma(t|x) = \log \Gamma_0(t) - x^\top \beta,$$

we have, similarly,

$$\log \Gamma_0(T) = x^\top \beta + u$$

for  $u$  iid logistic with  $F_0(u) = (1 + e^{-u})^{-1}$ .

# Accelerated Failure Time Model

In the accelerated failure time model we have

$$\log(T_i) = \mathbf{x}_i^\top \boldsymbol{\beta} + u_i$$

so

$$\begin{aligned} P(T > t) &= P(e^u > te^{-\mathbf{x}\boldsymbol{\beta}}) \\ &= 1 - F_0(te^{-\mathbf{x}\boldsymbol{\beta}}) \end{aligned}$$

where  $F_0(\cdot)$  denotes the df of  $e^u$ , and thus,

$$\lambda(t|\mathbf{x}) = \lambda_0(te^{-\mathbf{x}\boldsymbol{\beta}})e^{-\mathbf{x}\boldsymbol{\beta}}$$

where  $\lambda_0(\cdot)$  denotes the hazard function corresponding to  $F_0$ . In effect, the covariates act to rescale time in the baseline hazard.

# Beyond the Transformation Model

The common feature of all these models is that after transformation of the observed survival times we have:

- a pure location-shift, iid-error regression model
- covariate effects shift the center of the distribution of  $h(T)$ , but
- covariates cannot affect scale, or shape of this distribution

## An Application: Longevity of Mediterranean Fruit Flies

In the early 1990's there were a series of experiments designed to study the survival distribution of lower animals. One of the most influential of these was:

CAREY, J.R., LIEDO, P., OROZCO, D. AND VAUPEL, J.W. (1992) *Slowing of mortality rates at older ages in large Medfly cohorts*, *Science*, **258**, 457-61.



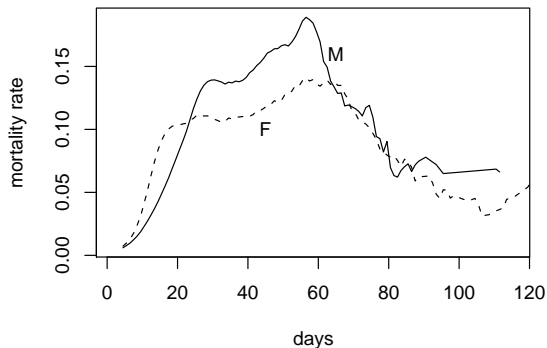
- 1,203,646 medflies survival times recorded in days
- Sex was recorded on day of death
- Pupae were initially sorted into one of five size classes
- 167 aluminum mesh cages containing roughly 7200 flies
- Adults were given a diet of sugar and water *ad libitum*

# Major Conclusions of the Medfly Experiment

- Mortality rates **declined** at the oldest observed ages. contradicting the traditional view that aging is an inevitable, monotone process of senescence.
- The right tail of the survival distribution was, at least by human standards, remarkably long.
- There was strong evidence for a crossover in gender specific mortality rates.



# Lifetable Hazard Estimates by Gender



Smoothed mortality rates for males and females.

## Medfly Survival Prospects

Lifespan (in days)	Percentage Surviving	Number Surviving
40	5	60,000
50	1	12,000
86	.01	120
146	.001	12

Initial Population of 1,203,646

## Medfly Survival Prospects

Lifespan (in days)	Percentage Surviving	Number Surviving
40	5	60,000
50	1	12,000
86	.01	120
146	.001	12
Initial Population of 1,203,646		

## Human Survival Prospects\*

Lifespan (in years)	Percentage Surviving	Number Surviving
50	98	591,000
75	69	413,000
85	33	200,000
95	5	30,000
105	.08	526
115	.0001	1

\* Estimated Thatcher (1999) Model

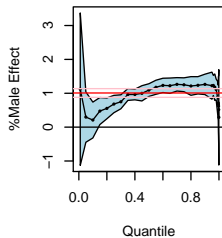
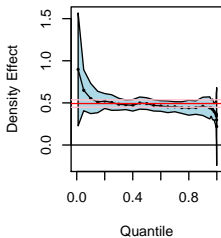
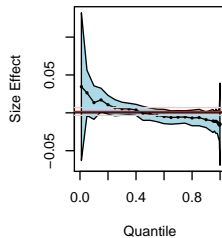
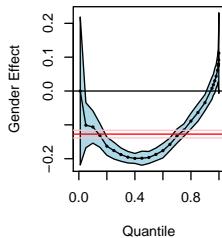
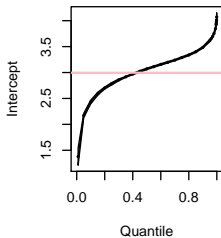
# Quantile Regression Model (Geling and K (JASA,2001))

Criticism of the Carey et al paper revolved around whether declining hazard rates were a result of confounding factors of cage density and initial pupal size. Our basic QR model included the following covariates:

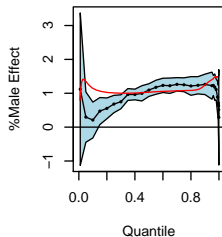
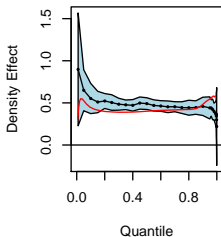
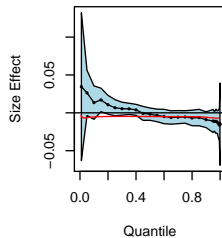
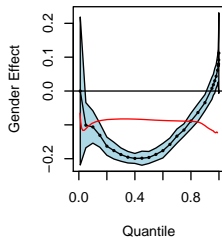
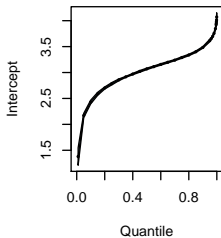
$$Q_{\log(T_i)}(\tau|x_i) = \beta_0(\tau) + \beta_1(\tau)\text{SEX} + \beta_2(\tau)\text{SIZE} \\ + \beta_3(\tau)\text{DENSITY} + \beta_4(\tau)\% \text{MALE}$$

- SEX      Gender
- SIZE     Pupal Size in mm
- DENSITY    Initial Density of Cage
- %MALE    Initial Proportion of Males

# Base Model Results with AFT Fit



# Base Model Results with Cox PH Fit



# What About Censoring?

There are currently 3 approaches to handling censored survival data within the quantile regression framework:

- Powell (1986) Fixed Censoring
- Portnoy (2003) Random Censoring, Kaplan-Meier Analogue
- Peng/Huang (2008) Random Censoring, Nelson-Aalen Analogue

Available for R in the package `quantreg`.

# Powell's Approach for Fixed Censoring

**Rationale** *Quantiles are equivariant to monotone transformation:*

$$Q_{h(Y)}(\tau) = h(Q_Y(\tau)) \text{ for } h \nearrow$$

**Model**  $Y_i = T_i \wedge C_i \equiv \min\{T_i, C_i\}$

$$Q_{Y_i|x_i}(\tau|x_i) = x_i^\top \beta(\tau) \wedge C_i$$

**Data** *Censoring times are known for **all** observations*

$$\{Y_i, C_i, x_i : i = 1, \dots, n\}$$

**Estimator** *Conditional quantile functions are nonlinear in parameters:*

$$\hat{\beta}(\tau) = \operatorname{argmin} \sum \rho_\tau(Y_i - x_i^\top \beta \wedge C_i)$$



# Portnoy's Approach for Random Censoring I

**Rationale** Efron's (1967) interpretation of Kaplan-Meier as *shifting mass* of censored observations *to the right*:

**Algorithm** Until we "encounter" a censored observation KM quantiles can be computed by solving, starting at  $\tau = 0$ ,

$$\hat{\xi}(\tau) = \operatorname{argmin}_{\xi} \sum_{i=1}^n \rho_{\tau}(Y_i - \xi)$$

Once we "encounter" a censored observation, i.e. when  $\hat{\xi}(\tau_i) = y_i$  for some  $y_i$  with  $\delta_i = 0$ , we split  $y_i$  into two parts:

- ▶  $y_i^{(1)} = y_i$  with weight  $w_i = (\tau - \tau_i)/(1 - \tau_i)$
- ▶  $y_i^{(2)} = y_{\infty} = \infty$  with weight  $1 - w_i$ .

Then denoting the index set of censored observations "encountered" up to  $\tau$  by  $K(\tau)$  we can solve

$$\min \sum_{i \notin K(\tau)} \rho_{\tau}(Y_i - \xi) + \sum_{i \in K(\tau)} [w_i(\tau) \rho_{\tau}(Y_i - \xi) + (1 - w_i(\tau)) \rho_{\tau}(y_{\infty} - \xi)].$$

## Portnoy's Approach for Random Censoring II

When we have covariates we can replace  $\xi$  by the inner product  $x_i^\top \beta$  and solve:

$$\min \sum_{i \notin K(\tau)} \rho_\tau(Y_i - x_i^\top \beta) + \sum_{i \in K(\tau)} [w_i(\tau) \rho_\tau(Y_i - x_i^\top \beta) + (1 - w_i(\tau)) \rho_\tau(y_\infty - x_i^\top \beta)].$$

At each  $\tau$  this is a simple, weighted linear quantile regression problem.

## Portnoy's Approach for Random Censoring II

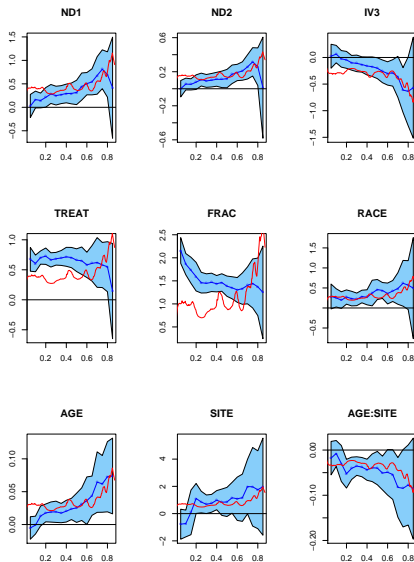
When we have covariates we can replace  $\xi$  by the inner product  $x_i^\top \beta$  and solve:

$$\min \sum_{i \notin K(\tau)} \rho_\tau(Y_i - x_i^\top \beta) + \sum_{i \in K(\tau)} [w_i(\tau) \rho_\tau(Y_i - x_i^\top \beta) + (1 - w_i(\tau)) \rho_\tau(y_\infty - x_i^\top \beta)].$$

At each  $\tau$  this is a simple, weighted linear quantile regression problem. The following R code fragment replicates an analysis in Portnoy (2003):

```
require(quantreg)
data(uis)
fit <- crq(Surv(log(TIME), CENSOR) ~ ND1 + ND2 + IV3 +
           TREAT + FRAC + RACE + AGE * SITE, data = uis, method = "Por")
Sfit <- summary(fit, 1:19/20)
PHit <- coxph(Surv(TIME, CENSOR) ~ ND1 + ND2 + IV3 +
             TREAT + FRAC + RACE + AGE * SITE, data = uis)
plot(Sfit, CoxPHit = PHit)
```

# Reanalysis of the Hosmer-Lemeshow Drug Relapse Data



# Peng and Huang's Approach for Random Censoring I

**Rationale** *Extend the martingale representation of the Nelson-Aalen estimator of the cumulative hazard function to produce an “estimating equation” for conditional quantiles.*

**Model** *AFT form of the quantile regression model:*

$$\text{Prob}(\log T_i \leq x_i^\top \beta(\tau)) = \tau$$

**Data**  $\{(Y_i, \delta_i) : i = 1, \dots, n\}$   $Y_i = T_i \wedge C_i$ ,  $\delta_i = I(T_i < C_i)$

**Martingale** *We have  $EM_i(t) = 0$  for  $t \geq 0$ , where:*

$$M_i(t) = N_i(t) - \Lambda_i(t \wedge Y_i | x_i)$$

$$N_i(t) = I(\{Y_i \leq t\}, \{\delta_i = 1\})$$

$$\Lambda_i(t) = -\log(1 - F_i(t|x_i))$$

$$F_i(t) = \text{Prob}(T_i \leq t|x_i)$$

## Peng and Huang's Approach for Random Censoring II

The estimating equation becomes,

$$E n^{-1/2} \sum \mathbf{x}_i [N_i(\exp(\mathbf{x}_i^\top \boldsymbol{\beta}(\tau))) - \int_0^\tau I(Y_i \geq \exp(\mathbf{x}_i^\top \boldsymbol{\beta}(\mathbf{u}))) dH(\mathbf{u})] = 0.$$

where  $H(\mathbf{u}) = -\log(1 - \mathbf{u})$  for  $\mathbf{u} \in [0, 1]$ , after rewriting:

$$\begin{aligned} \Lambda_i(\exp(\mathbf{x}_i^\top \boldsymbol{\beta}(\tau)) \wedge Y_i | \mathbf{x}_i) &= H(\tau) \wedge H(F_i(Y_i | \mathbf{x}_i)) \\ &= \int_0^\tau I(Y_i \geq \exp(\mathbf{x}_i^\top \boldsymbol{\beta}(\mathbf{u}))) dH(\mathbf{u}), \end{aligned}$$

## Peng and Huang's Approach for Random Censoring III

Approximating the integral on a grid,  $0 = \tau_0 < \tau_1 < \dots < \tau_J < 1$  yields a simple linear programming formulation to be solved at the gridpoints,

$$\alpha_i(\tau_j) = \sum_{k=0}^{j-1} I(Y_i \geq \exp(x_i^\top \hat{\beta}(\tau_k))) (H(\tau_{k+1}) - H(\tau_k)),$$

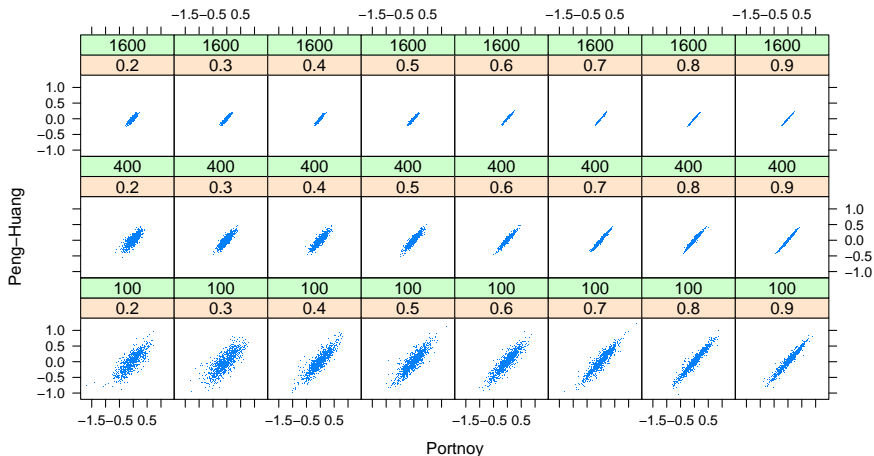
yielding Peng and Huang's final estimating equation,

$$n^{-1/2} \sum x_i [N_i(\exp(x_i^\top \beta(\tau))) - \alpha_i(\tau)] = 0.$$

Setting  $r_i(\mathbf{b}) = \log(Y_i) - x_i^\top \mathbf{b}$ , this convex function for the Peng and Huang problem takes the form

$$R(\mathbf{b}, \tau_j) = \sum_{i=1}^n r_i(\mathbf{b}) (\alpha_i(\tau_j) - I(r_i(\mathbf{b}) < 0) \delta_i) = \min!$$

# Portnoy vs. Peng-Huang





## Some One Sample Asymptotics

Suppose that we have a random sample of pairs,  $\{(T_i, C_i) : i = 1, \dots, n\}$  with  $T_i \sim F$ ,  $C_i \sim G$ , and  $T_i$  and  $C_i$  independent. Let  $Y_i = \min\{T_i, C_i\}$ , as usual, and  $\delta_i = I(T_i < C_i)$ . In this setting the Powell estimator of  $\theta = F^{-1}(\tau)$ ,

$$\hat{\theta}_P = \operatorname{argmin}_{\theta} \sum_{i=1}^n \rho_{\tau}(Y_i - \min\{\theta, C_i\}).$$

is asymptotically normal,

$$\sqrt{n}(\hat{\theta}_P - \theta) \rightsquigarrow \mathcal{N}(0, \tau(1 - \tau)/(f^2(\theta)(1 - G(\theta)))).$$

# One Sample Asymptotics

In contrast, the asymptotic theory of the quantiles of the Kaplan-Meier estimator is slightly more complicated. Using the  $\delta$ -method one can show,

$$\sqrt{n}(\hat{\theta}_{\text{KM}} - \theta) \rightsquigarrow \mathcal{N}(0, \text{Avar}(\hat{S}(\theta))/f^2(\theta))$$

where, see e.g. Anderson et al,

$$\text{Avar}(\hat{S}(t)) = S^2(t) \int_0^t (1 - H(u))^{-2} d\tilde{F}(u)$$

and  $1 - H(u) = (1 - F(u))(1 - G(u))$  and  $\tilde{F}(u) = \int_0^t (1 - G(u)) dF(u)$ . Since the Powell estimator makes use of more sample information than does the Kaplan Meier estimator it might be thought that it would be more efficient. But this isn't true.

# Kaplan Meier vs Powell

## Proposition

$$\text{Avar}(\hat{\theta}_{KM}) \leq \text{Avar}(\hat{\theta}_P).$$

### Proof:

$$\begin{aligned} f^2(\theta)\text{Avar}(\hat{\theta}_{KM}) &= S(\theta)^2 \int_0^\theta (1 - H(s))^{-2} d\tilde{F}(s) \\ &= S(\theta)^2 \int_0^\theta (1 - G(s))^{-1} (1 - F(s))^{-2} dF(s) \\ &\leq \frac{S(\theta)^2}{1 - G(\theta)} \int_0^\theta (1 - F(s))^{-2} dF(s) \\ &= \frac{S(\theta)^2}{1 - G(\theta)} \cdot \frac{1}{1 - F(s)} \Big|_0^\theta \\ &= \frac{S(\theta)^2}{1 - G(\theta)} \cdot \frac{F(\theta)}{1 - F(\theta)} \\ &= \frac{F(\theta)(1 - F(\theta))}{(1 - G(\theta))} \\ &= \frac{\tau(1 - \tau)}{(1 - G(\theta))}. \end{aligned}$$

## Alice in Asymptopia

Leurgans (1987) considered the weighted estimator of the censored survival function,

$$\hat{S}_L(t) = \frac{\sum I(Y_i > t)I(C_i > t)}{\sum I(C_i > t)},$$

that uses all the  $C_i$ 's. Conditioning on the  $C_i$ 's, it can be shown that  $\mathbb{E}(\hat{S}_L(t)|C) = S(t)$ , and that the conditional variance is

$$\text{Var}(\hat{S}_L(t)|C) = \frac{F(t)(1 - F(t))}{1 - \hat{G}(t)}.$$

Averaging this expression gives the unconditional variance which converges to

$$\text{Avar}(\hat{S}_L(t)|C) = \frac{F(t)(1 - F(t))}{1 - G(t)},$$

and consequently quantiles based on Leurgan's estimator behave (asymptotically) just like those produced by the Powell estimator.

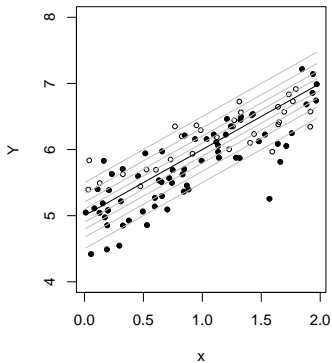
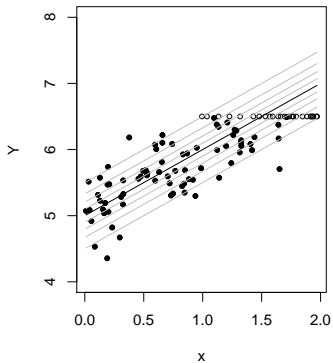
## Alice in Asymptopia

It might be thought that the Powell estimator would be more efficient than the Portnoy and Peng-Huang estimators given that it imposes more stringent data requirements. Comparing asymptotic behavior and finite sample performance in the simplest one-sample setting indicates otherwise.

	median	Kaplan-Meier	Nelson-Aalen	Powell	Leurgans $\hat{G}$	Leurgans $G$
n= 50	1.602	1.972	2.040	2.037	2.234	2.945
n= 200	1.581	1.924	1.930	2.110	2.136	2.507
n= 500	1.666	2.016	2.023	2.187	2.215	2.742
n= 1000	1.556	1.813	1.816	2.001	2.018	2.569
n= $\infty$	1.571	1.839	1.839	2.017	2.017	2.463

Scaled MSE for Several Estimators of the Median: Mean squared error estimates are scaled by sample size to conform to asymptotic variance computations. Here,  $T_i$  is standard lognormal, and  $C_i$  is exponential with rate parameter .25, so the proportion of censored observations is roughly 30 percent. 1000 replications.

# Simulation Settings I



# Simulations I-A

	Intercept			Slope		
	Bias	MAE	RMSE	Bias	MAE	RMSE
<b>Portnoy</b>						
n = 100	-0.0032	0.0638	0.0988	0.0025	0.0702	0.1063
n = 400	-0.0066	0.0406	0.0578	0.0036	0.0391	0.0588
n = 1000	-0.0022	0.0219	0.0321	0.0006	0.0228	0.0344
<b>Peng-Huang</b>						
n = 100	0.0005	0.0631	0.0986	0.0092	0.0727	0.1073
n = 400	-0.0007	0.0393	0.0575	0.0074	0.0389	0.0598
n = 1000	0.0014	0.0215	0.0324	0.0019	0.0226	0.0347
<b>Powell</b>						
n = 100	-0.0014	0.0694	0.1039	0.0068	0.0827	0.1252
n = 400	-0.0066	0.0429	0.0622	0.0098	0.0475	0.0734
n = 1000	-0.0008	0.0224	0.0339	0.0013	0.0264	0.0396
<b>GMLE</b>						
n = 100	0.0013	0.0528	0.0784	-0.0001	0.0517	0.0780
n = 400	-0.0039	0.0307	0.0442	0.0031	0.0264	0.0417
n = 1000	0.0003	0.0172	0.0248	-0.0001	0.0165	0.0242

Comparison of Performance for the iid Error, Constant Censoring Configuration

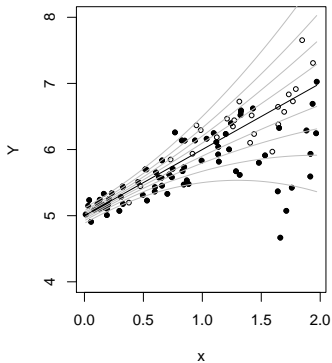
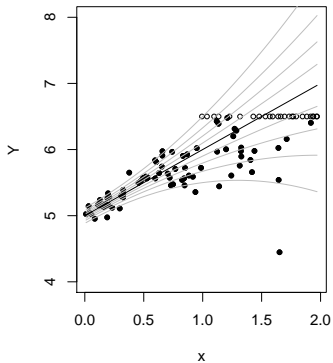
# Simulations I-B

	Intercept			Slope		
	Bias	MAE	RMSE	Bias	MAE	RMSE
<b>Portnoy</b>						
n = 100	-0.0042	0.0646	0.0942	0.0024	0.0586	0.0874
n = 400	-0.0025	0.0373	0.0542	-0.0009	0.0322	0.0471
n = 1000	-0.0025	0.0208	0.0311	0.0006	0.0191	0.0283
<b>Peng-Huang</b>						
n = 100	0.0026	0.0639	0.0944	0.0045	0.0607	0.0888
n = 400	0.0056	0.0389	0.0547	-0.0002	0.0320	0.0476
n = 1000	0.0019	0.0212	0.0311	0.0009	0.0187	0.0283
<b>Powell</b>						
n = 100	-0.0025	0.0669	0.1017	0.0083	0.0656	0.1012
n = 400	0.0014	0.0398	0.0581	-0.0006	0.0364	0.0531
n = 1000	-0.0013	0.0210	0.0319	0.0016	0.0203	0.0304
<b>GMLE</b>						
n = 100	0.0007	0.0540	0.0781	0.0009	0.0470	0.0721
n = 400	0.0008	0.0285	0.0444	-0.0008	0.0253	0.0383
n = 1000	-0.0004	0.0169	0.0248	0.0002	0.0150	0.0224

Comparison of Performance for the iid Error, Variable Censoring Configuration



# Simulation Settings II



## Simulations II-A

	Intercept			Slope		
	Bias	MAE	RMSE	Bias	MAE	RMSE
<b>Portnoy L</b>						
n = 100	0.0084	0.0316	0.0396	-0.0251	0.0763	0.0964
n = 400	0.0076	0.0194	0.0243	-0.0247	0.0429	0.0533
n = 1000	0.0081	0.0121	0.0149	-0.0241	0.0309	0.0376
<b>Portnoy Q</b>						
n = 100	0.0018	0.0418	0.0527	0.0144	0.1576	0.2093
n = 400	-0.0010	0.0228	0.0290	0.0047	0.0708	0.0909
n = 1000	-0.0006	0.0122	0.0154	-0.0027	0.0463	0.0587
<b>Peng-Huang L</b>						
n = 100	0.0077	0.0313	0.0392	-0.0145	0.0749	0.0949
n = 400	0.0064	0.0193	0.0240	-0.0125	0.0392	0.0493
n = 1000	0.0077	0.0120	0.0147	-0.0181	0.0279	0.0342
<b>Peng-Huang Q</b>						
n = 100	0.0078	0.0425	0.0538	0.0483	0.1707	0.2328
n = 400	0.0035	0.0228	0.0291	0.0302	0.0775	0.1008
n = 1000	0.0015	0.0123	0.0155	0.0101	0.0483	0.0611
<b>Powell</b>						
n = 100	0.0021	0.0304	0.0385	-0.0034	0.0790	0.0993
n = 400	-0.0017	0.0191	0.0239	0.0028	0.0431	0.0544
n = 1000	-0.0001	0.0099	0.0125	0.0003	0.0257	0.0316
<b>GMLE</b>						
n = 100	0.1080	0.1082	0.1201	-0.2040	0.2042	0.2210
n = 400	0.1209	0.1209	0.1241	-0.2134	0.2134	0.2173
n = 1000	0.1118	0.1118	0.1130	-0.2075	0.2075	0.2091

Comparison of Performance for the Constant Censoring, Heteroscedastic Configuration

## Simulations II-B

	Intercept			Slope		
	Bias	MAE	RMSE	Bias	MAE	RMSE
<b>Portnoy L</b>						
n = 100	0.0024	0.0278	0.0417	-0.0067	0.0690	0.1007
n = 400	0.0019	0.0145	0.0213	-0.0080	0.0333	0.0493
n = 1000	0.0016	0.0097	0.0139	-0.0062	0.0210	0.0312
<b>Portnoy Q</b>						
n = 100	0.0011	0.0352	0.0540	0.0094	0.1121	0.1902
n = 400	0.0002	0.0185	0.0270	-0.0012	0.0510	0.0774
n = 1000	-0.0005	0.0116	0.0169	-0.0011	0.0337	0.0511
<b>Peng-Huang L</b>						
n = 100	0.0018	0.0281	0.0417	0.0041	0.0694	0.1017
n = 400	0.0013	0.0142	0.0212	0.0035	0.0333	0.0490
n = 1000	0.0012	0.0096	0.0139	0.0002	0.0208	0.0310
<b>Peng-Huang Q</b>						
n = 100	0.0044	0.0364	0.0550	0.0322	0.1183	0.2105
n = 400	0.0026	0.0188	0.0275	0.0154	0.0504	0.0813
n = 1000	0.0007	0.0113	0.0169	0.0077	0.0333	0.0520
<b>Powell</b>						
n = 100	-0.0001	0.0288	0.0430	0.0055	0.0733	0.1105
n = 400	0.0000	0.0147	0.0226	0.0001	0.0379	0.0561
n = 1000	-0.0008	0.0095	0.0146	0.0013	0.0237	0.0350
<b>GMLE</b>						
n = 100	0.1078	0.1038	0.1272	-0.1576	0.1582	0.1862
n = 400	0.1123	0.1116	0.1168	-0.1581	0.1578	0.1647
n = 1000	0.1153	0.1138	0.1174	-0.1609	0.1601	0.1639

Comparison of Performance for the Variable Censoring, Heteroscedastic Configuration

# Conclusions

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- Quantile regression provides a flexible complement to classical survival analysis methods, and is now well equipped to handle censoring.