Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples

# Bootstrap Consistency for General Semiparametric M-Estimation

### Guang Cheng

## Department of Statistics, Purdue University

Statistics Seminar at University of Michigan March 12th, 2010 Joint Work with Jianhua Huang at Texas A& M University

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Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples

# Outline

### Introduction

Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

## Bootstrapping Semiparametric MLE

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

## More General Conclusions

Examples

Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data

Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

As a general data-resampling based method, the bootstrap has been applied to the semiparametric models in a wide variety of contexts, e.g. Biostatistics, Survival Analysis and Econometrics, for a long time.

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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- A long existing problem for applying bootstrap to semiparametric models is that there is no theoretical justifications !

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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- Cited from an Annals paper by Kosorok et al (2004) "Unfortunately, there is no sufficiently general theory, as far as we are aware, available for the nonparametric bootstrap in the penalized (semiparametric) maximization likelihood setting."

Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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- Cited from a JASA paper by Lee et al (2005)
   "The bootstrap is a possible solution to these problems, but theoretical justification is not available for semiparametric models."

Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

# **Major Contributions**

 We establish the theoretical validity of a broad class of bootstrap methods as an inferential tool for the general semiparametric models.

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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- Specifically, we prove that
  - the bootstrap distribution asymptotically imitates the distribution of the M-estimate, i.e., bootstrap distributional consistency;

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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Most (but not all) details of this talk can be found in a forthcoming Annals paper.

Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

## **Semiparametric Models**

▶ Random Variable  $X \sim \{P_{\theta,\eta} : \theta \in \Theta \subset \mathbb{R}^k, \eta \in \mathcal{H}\}$ 

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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  - *θ*: linear regression parameter;
  - f: nonlinear smooth function.

Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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Bootstrapping Semiparametric MLE More General Conclusions Examples Motivations Major Contributions Semiparametric Models Commonly Used Semiparametric Inference Procedures

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  - $\theta$ : linear regression parameter;
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- Example III: Generalized Estimating Equation (GEE)
  - $\beta$ : mean regression parameter;
  - $\alpha$ : finite dimensional nuisance correlation parameter.

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

# • The semiparametric MLE $(\widehat{\theta}, \widehat{\eta})$ is defined as

$$(\widehat{\theta}, \widehat{\eta}) = \arg \sup_{\theta \in \Theta, \eta \in \mathcal{H}} \sum_{i=1}^{n} \log lik(\theta, \eta)(X_i).$$

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

• The semiparametric MLE  $(\widehat{ heta}, \widehat{\eta})$  is defined as

$$(\widehat{\theta}, \widehat{\eta}) = \arg \sup_{\theta \in \Theta, \eta \in \mathcal{H}} \sum_{i=1}^{n} \log lik(\theta, \eta)(X_i).$$

► Given regularity conditions, it is proven that MLE θ is semiparametric efficient (minimal asymptotic variance) in the sense that

$$\sqrt{n}(\widehat{\theta} - \theta_0) \stackrel{d}{\longrightarrow} N(0, \widetilde{I}_0^{-1}),$$
 (1)

where  $\tilde{l}_0$  is the efficient information matrix.

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

1. The confidence set construction and asymptotic covariance estimation for  $\theta$  both involve estimating and inverting a hard-to-estimate infinite-dimensional operator.

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

- 1. The confidence set construction and asymptotic covariance estimation for  $\theta$  both involve estimating and inverting a hard-to-estimate infinite-dimensional operator.
- 2. Convergence rates for  $\theta$  and  $\eta$  may be different, i.e.,  $\theta$  has a parametric rate and  $\eta$  has a nonparametric rate. Thus, we can not treat  $(\theta, \eta)$  as a whole component.

Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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- 3. See Bickel et al (1998) and Kosorok (2008) for more details.

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 Introduction
 Motivations

 Bootstrapping Semiparametric MLE
 Major Contributions

 More General Conclusions
 Examples

 Commonly Used Semiparametric Inference Procedures

### Three semiparametric inferential tools are thus motivated:

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Introduction Motivations Bootstrapping Semiparametric MLE Major Contributions More General Conclusions Semiparametric Models Examples Commonly Used Semiparametric Inference Procedures

### Three semiparametric inferential tools are thus motivated:

1. The Profile Likelihood Approach

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

Three semiparametric inferential tools are thus motivated:

- 1. The Profile Likelihood Approach
  - Murphy and van der Vaart (2000) proved that the log-profile likelihood defined as

$$\log pl_n(\theta) = \sup_{\eta \in \mathcal{H}} \sum_{i=1}^n \log lik(\theta, \eta)(X_i)$$

asymptotically possesses the parabolic form, like a parametric likelihood, when making inferences for  $\theta.$ 

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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asymptotically possesses the parabolic form, like a parametric likelihood, when making inferences for  $\theta.$ 

► For example, we can use the second order numerical derivative (curvature) of the log  $pl_n(\theta)$  at  $\hat{\theta}$ , called *observed information*, to estimate  $-\tilde{l}_0$ .

Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

The inferences of θ are based on the sampling from the posterior of the profile likelihood.

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

- The inferences of θ are based on the sampling from the posterior of the profile likelihood.
- MCMC is used for sampling from the above posterior distribution. For example, we can use the chain mean (the inverse of chain variance) to approximate MLE θ (*l*<sub>0</sub>).

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

- The inferences of θ are based on the sampling from the posterior of the profile likelihood.
- MCMC is used for sampling from the above posterior distribution. For example, we can use the chain mean (the inverse of chain variance) to approximate MLE θ (*l*<sub>0</sub>).
- The theoretical validity of the profile sampler depends on the parabolic form of the profile likelihood proven in Murphy and van der Vaart (2000).

Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

### However,

The profile likelihood may not approximate well the desired parabolic form when the sample size is small;

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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- The profile likelihood may not approximate well the desired parabolic form when the sample size is small;
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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

- The profile likelihood may not approximate well the desired parabolic form when the sample size is small;
- The profile likelihood based procedures are not automatic:
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- MCMC convergence in the profile sampler is not well studied.

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

- The profile likelihood may not approximate well the desired parabolic form when the sample size is small;
- The profile likelihood based procedures are not automatic:
  - we need to specify a prior in the profile sampler;
  - we need to choose the step size in computing the observed information.
- ► MCMC convergence in the profile sampler is not well studied.
- It takes long time to run Markov chain to get accurate inferences for θ when η has slow convergence rate (Cheng and Kosorok, 2008a, b);

Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

Methodological Features:

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

Methodological Features:

A. A lot of well studied resampling techniques are available;

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

Methodological Features:

- A. A lot of well studied resampling techniques are available;
- B. It is conceptually simple to implement, just resampling;

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

Methodological Features:

- A. A lot of well studied resampling techniques are available;
- B. It is conceptually simple to implement, just resampling;
- C. we can make bootstrap inferences for both  $\theta$  and  $\eta$  based on the bootstrap sample;

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

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Introduction	Motivations
Bootstrapping Semiparametric MLE	Major Contributions
More General Conclusions	Semiparametric Models
Examples	Commonly Used Semiparametric Inference Procedures

Methodological Features:

- A. A lot of well studied resampling techniques are available;
- B. It is conceptually simple to implement, just resampling;
- C. we can make bootstrap inferences for both  $\theta$  and  $\eta$  based on the bootstrap sample;
- D. It is an automatic procedure, e.g., needless to specify prior;
- E. It has small sample advantages.
- ► However, there is no theoretical justifications available now.

In this talk, we consider the general class of *exchangeably weighted bootstrap*. This general resampling scheme was first proposed by Rubin (1981), i.e., Bayesian Bootstrap, and then extensively studied by Newton and Mason (1992), Praestgaard and Wellner (1993) and Bertail and Barbe (1995) in the parametric and nonparametric context.

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

The class of exchangeably weighted bootstrap includes

 Standard Nonparametric Bootstrap: Sample with replacement (sampling from the empirical distribution)

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- Double Bootstrap:

Sampling from the nonparametric bootstrap sample.

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- **Double Bootstrap**:

Sampling from the nonparametric bootstrap sample.

 Others: Multivariate Hypergeometric Bootstrap, Polya-Eggenberger Bootstrap, Bootstrap generated from deterministic weights.....

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

The bootstrap estimator is defined as

$$(\widehat{\theta}^*, \widehat{\eta}^*) = \arg \sup_{\theta \in \Theta, \eta \in \mathcal{H}} \sum_{i=1}^n \log lik(\theta, \eta)(X_i^*),$$
(2)

where  $(X_1^*, \ldots, X_n^*)$  is the bootstrap sample.

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**Exchangeably Weighted Bootstrap** Bootstrap Distributional Consistency **Bootstrap Confidence Set** 

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(2)

where  $(X_1^*, \ldots, X_n^*)$  is the bootstrap sample.

• In the exchangeably weighted bootstrap sampling,  $(\hat{\theta}^*, \hat{\eta}^*)$  can be reformulated as

$$(\widehat{\theta}^*, \widehat{\eta}^*) = \arg \sup_{\theta \in \Theta, \eta \in \mathcal{H}} \sum_{i=1}^n W_{ni} \log lik(\theta, \eta)(X_i), \quad (3)$$

where  $W_n \equiv (W_{n1}, \ldots, W_{nn})$  is the bootstrap weight.

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

Different bootstrap sampling schemes correspond to different bootstrap weights  $W_n$ , e.g.,

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► Standard Nonparametric Bootstrap: W<sub>n</sub> ~ Multinomial (n, (n<sup>-1</sup>,..., n<sup>-1</sup>)).

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- ► Standard Nonparametric Bootstrap: W<sub>n</sub> ~ Multinomial (n, (n<sup>-1</sup>,..., n<sup>-1</sup>)).
- Multiplier Bootstrap:

 $W_{nj} = \alpha_j / \bar{\alpha}$ , where  $(\alpha_1, \dots, \alpha_n) \stackrel{\text{id}}{\sim}$  nonnegative continuous r.v.s. For example,  $\alpha_j \sim \text{Exp}(1)$  in Bayesian Bootstrap.

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Double Bootstrap:

 $W_n \sim Multinomial(n, (M_{n1}/n, \ldots, M_{nn}/n))$  $(M_{n1}, \ldots, M_{nn}) \sim Multinomial(n, (n^{-1}, \ldots, n^{-1})).$ 

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Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

### Bootstrap Consistency Assumptions

► Regularity conditions (those in guaranteeing the asymptotic normality of MLE \(\heta\)).

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### Bootstrap Consistency Assumptions

- ► Regularity conditions (those in guaranteeing the asymptotic normality of MLE \(\heta\)).
- Bootstrap weights satisfy:
  - 1. The vector  $W_n = (W_{n1}, \ldots, W_{nn})'$  is exchangeable;
  - 2.  $W_{ni} \ge 0$  and  $\sum_{i=1}^{n} W_{ni} = n$ ;
  - 3.  $(1/n)\sum_{i=1}^{n}(W_{ni}-1)^2 \xrightarrow{P_W} c^2 > 0$ ;
  - 4. Some lower moment conditions for  $W_{ni}$ .

## Bootstrap Consistency Assumptions

- ► Regularity conditions (those in guaranteeing the asymptotic normality of MLE \(\heta\)).
- Bootstrap weights satisfy:
  - 1. The vector  $W_n = (W_{n1}, \ldots, W_{nn})'$  is exchangeable;

2. 
$$W_{ni} \ge 0$$
 and  $\sum_{i=1}^{n} W_{ni} = n;$ 

- 3.  $(1/n) \sum_{i=1}^{n} (W_{ni} 1)^2 \xrightarrow{P_W} c^2 > 0$ ;
- 4. Some lower moment conditions for  $W_{ni}$ .
- Some measurability conditions (so that the Fubini's Theorem can be used freely), envelop conditions and empirical processes conditions (the entropy number of some function class is manageable).

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Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

# Bootstrap Consistency Theorem (Theorem I):

Assuming the above conditions, we have

1.  $\sqrt{n}$  consistency of  $\hat{\theta}^*$ :

$$\|\widehat{ heta}^* - heta_0\| = O_{P_W}(n^{-1/2})$$
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Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

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2. Asymptotic Normality for  $\hat{\theta}^*$ :

$$(\sqrt{n}/c)(\widehat{\theta}^* - \widehat{\theta}) \Longrightarrow N(0, \widetilde{l}_0^{-1}) \quad \text{ in } P_X - \text{probability},$$

where  $\implies$  denotes *conditional weak convergence*.

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

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3. Bootstrap distribution consistency for  $\theta$ 

$$\sup_{x\in R^d} \left| P_{W|\mathcal{X}_n}((\sqrt{n}/c)(\widehat{\theta}^* - \widehat{\theta}) \leq x) - P_X(\sqrt{n}(\widehat{\theta} - \theta_0) \leq x) \right| \xrightarrow{P_X} 0.$$

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

## Remark 1:

• c = 1 for the *nonparametric bootstrap* in which  $W_n \sim \text{Multinomial } (n, (n^{-1}, \dots, n^{-1})).$ 

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

## Remark 1:

- c = 1 for the *nonparametric bootstrap* in which  $W_n \sim \text{Multinomial } (n, (n^{-1}, \dots, n^{-1})).$
- $c = \sigma(\alpha_1)/E(\alpha_1)$  for the *multiplier bootstrap* in which  $W_{nj} = \alpha_j/\bar{\alpha}$ . [c = 1 for the bayesian bootstrap]

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

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- $c = \sqrt{2}$  for the *double bootstrap* in which  $W_n \sim \text{Multinomial}(n, (M_{n1}/n, \dots, M_{nn}/n))$  $(M_{n1}, \dots, M_{nn}) \sim \text{Multinomial}(n, (n^{-1}, \dots, n^{-1}))$

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

# Remark 2:

The bootstrap consistency assumptions are only slightly stronger than those (regularity conditions) needed in showing the asymptotic normality of  $\hat{\theta}$ . Therefore, we can conclude that the bootstrap consistency for  $\hat{\theta}^*$  is almost automatically guaranteed.

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Definition for *conditional weak convergence*  $\implies$  is as follows

 $\widehat{X}_n^* \Longrightarrow X$  conditional on data  $\mathcal{X}_n$ 

$$\text{if } \sup_{h\in BL_1(B)} |E_{|\mathcal{X}_n}h(\widehat{X}_n^*) - Eh(X)| = o_{P_X}(1),$$

where  $BL_1(B)$  is a collection of all Lipschitz continuous functions  $h: B \mapsto R$  bounded by 1 and having Lipschitz constant 1 (Hoffmann-Jorgensen, 1984).

Technical tools used in proving Bootstrap Consistency Theorem include

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Technical tools used in proving Bootstrap Consistency Theorem include

- Bootstrapped Empirical Processes (Gine and Zinn, 1990);
- Multiplier Inequality (Wellner and Zhan, 1996);
- Hoffmann-Jorgensen Inequality (van der Vaart and Wellner, 1996).
Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

# **Bootstrap Confidence Set**

 Advantages: Replace the tedious theoretical derivations in semiparametric inferences with routine simulations of bootstrap samples.

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Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

# **Bootstrap Confidence Set**

- Advantages: Replace the tedious theoretical derivations in semiparametric inferences with routine simulations of bootstrap samples.
- The bootstrap distributional consistency Theorem implies the consistency of bootstrap confidence sets of the following types:
  - percentile type
  - hybrid type
  - t type

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 Let P<sub>W|X<sub>n</sub></sub> denote the conditional distribution given observations X<sub>n</sub>. We define τ<sup>\*</sup><sub>nα</sub> satisfying

$$\mathsf{P}_{W|\mathcal{X}_n}\left(\widehat{\theta}^* \leq \tau_{n\alpha}^*\right) = \alpha.$$

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$$\mathsf{P}_{W|\mathcal{X}_n}\left(\widehat{\theta}^* \leq \tau_{n\alpha}^*\right) = \alpha.$$

▶ Based on the bootstrap distributional consistency Theorem, we can approximate the  $\alpha$ -th quantile of the distribution of  $(\hat{\theta} - \theta_0)$  by  $(\tau_{n\alpha}^* - \hat{\theta})/c$ . Thus we construct the  $(1 - \alpha)$  percentile-type bootstrap confidence set as

$$BC_{p}(\alpha) = \left[\widehat{\theta} + \frac{\tau_{n(\alpha/2)}^{*} - \widehat{\theta}}{c}, \widehat{\theta} + \frac{\tau_{n(1-\alpha/2)}^{*} - \widehat{\theta}}{c}\right]$$

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

• We define  $\kappa_{n\alpha}^*$  satisfying

$$P_{W|\mathcal{X}_n}\left((\sqrt{n}/c)(\widehat{\theta}^*-\widehat{\theta})\leq\kappa_{n\alpha}^*\right)=\alpha.$$

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Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples Bootstrap Confidence Set

• We define  $\kappa_{n\alpha}^*$  satisfying

$$P_{W|\mathcal{X}_n}\left((\sqrt{n}/c)(\widehat{\theta}^* - \widehat{\theta}) \leq \kappa_{n\alpha}^*\right) = \alpha.$$

Similarly, we can approximate the α-th quantile of √n(θ − θ<sub>0</sub>) by κ<sup>\*</sup><sub>nα</sub>. Thus we construct the (1 − α) hybrid-type bootstrap confidence set as

$$BC_h(\alpha) = \left[\widehat{\theta} - \frac{\kappa_{n(1-\alpha/2)}^*}{\sqrt{n}}, \widehat{\theta} - \frac{\kappa_{n(\alpha/2)}^*}{\sqrt{n}}\right]$$

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

# Remark 3:

Both the *percentile* bootstrap confidence set BC<sub>p</sub>(α) and hybrid bootstrap confidence set BC<sub>h</sub>(α) can be computed easily through routine bootstrap sampling.

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

# Remark 3:

- Both the *percentile* bootstrap confidence set BC<sub>p</sub>(α) and hybrid bootstrap confidence set BC<sub>h</sub>(α) can be computed easily through routine bootstrap sampling.
- We can avoid estimating the asymptotic variance of  $\hat{\theta}$ , i.e.,  $\tilde{l}_0^{-1}$ , in both  $BC_p(\alpha)$  and  $BC_h(\alpha)$ .

Introduction
Bootstrapping Semiparametric MLE
More General Conclusions
Examples
Bootstrap Confidence Set

The distributional consistency Theorem together with the quantile convergence Theorem implies the consistency of percentile-type and hybrid-type bootstrap confidence sets.

Bootstrap Confidence Set Corollary (Corollary I): Under the conditions in Theorem 1, we have

$$P_{XW}(\theta_0 \in BC_p(\alpha)) \longrightarrow 1-\alpha,$$
  
$$P_{XW}(\theta_0 \in BC_h(\alpha)) \longrightarrow 1-\alpha,$$

as  $n \to \infty$ .

### Remark 4:

Provided the consistent estimator for the asymptotic covariance is available, we can show that the t-type bootstrap confidence set is also consistent by considering the Slutsky's Theorem.

Exchangeably Weighted Bootstrap Bootstrap Distributional Consistency Bootstrap Confidence Set

Before presenting more general results, let us summarize our contributions in the likelihood framework so far:

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▶ We first show that the bootstrap distribution of  $(\sqrt{n}/c)(\hat{\theta}^* - \hat{\theta})$ , conditional on the observed data, asymptotically imitates the unconditional distribution of  $\sqrt{n}(\hat{\theta}_n - \theta_0)$  in Theorem 1.

Before presenting more general results, let us summarize our contributions in the likelihood framework so far:

- ▶ We first show that the bootstrap distribution of  $(\sqrt{n}/c)(\hat{\theta}^* \hat{\theta})$ , conditional on the observed data, asymptotically imitates the unconditional distribution of  $\sqrt{n}(\hat{\theta}_n \theta_0)$  in Theorem 1.
- We next establish in Corollary 1 that the coverage probabilities of the percentile and hybrid bootstrap confidence sets for θ converge to the nominal level as a consequence of Theorem 1.

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- ▶ We first show that the bootstrap distribution of  $(\sqrt{n}/c)(\hat{\theta}^* \hat{\theta})$ , conditional on the observed data, asymptotically imitates the unconditional distribution of  $\sqrt{n}(\hat{\theta}_n \theta_0)$  in Theorem 1.
- We next establish in Corollary 1 that the coverage probabilities of the percentile and hybrid bootstrap confidence sets for θ converge to the nominal level as a consequence of Theorem 1.
- Note that the above conclusions hold no matter η has √n convergence rate or slower than √n convergence rate.

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Our bootstrap consistency conclusions in the likelihood setup can be extended to the more general scenario as follows.

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Our bootstrap consistency conclusions in the likelihood setup can be extended to the more general scenario as follows.

G1. (Penalized) M-estimation:

$$(\widehat{ heta}_{\lambda_n}, \widehat{\eta}_{\lambda_n}) = \arg \max_{\theta \in \Theta, \eta \in \mathcal{H}} \sum_{i=1}^n m_{\lambda_n}(\theta, \eta)(X_i).$$

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Example II.  $Y = W'\theta + f(T) + \epsilon$ .

If f is smooth, we can estimate  $(\theta, f)$  by penalizing its roughness J(f) [partial smoothing spline]:

$$(\widehat{ heta}_{\lambda_n}, \widehat{\eta}_{\lambda_n}) = \arg\min_{ heta \in \Theta, \eta \in \mathcal{H}} \left\{ \sum_{i=1}^n (Y_i - W'_i \theta - f(T_i))^2 + \lambda_n J(f) \right\}$$

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## G2. Estimation Equation:

$$\widehat{ heta}$$
 solves  $\sum_{i=1}^{n} z( heta, \widehat{\eta}( heta))(X_i) = 0,$ 

where  $\hat{\eta}(\theta)$  is an estimate for  $\eta$  given any fixed  $\theta$  (satisfying some convergence rate condition).

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G3. The nuisance parameter  $\eta$  can be finite dimensional (conditions can be relaxed in this special case).

Example III (GEE). This is a natural example of G2 & G3 in which  $\theta$  is the mean regression parameter of interest and  $\eta$  is the finite dimensional *nuisance* correlation parameter.

Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
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## ▶ In the first Cox regression model, $(\hat{\theta}, \hat{\eta}) = \arg \max_{\theta \in \Theta, \eta \in \mathcal{H}} \sum_{i=1}^{n} \log lik(\theta, \eta)(X_i).$

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Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
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- ▶ In the second partial smoothing spline model,  $(\widehat{\theta}_{\lambda_n}, \widehat{\eta}_{\lambda_n}) = \arg \max_{\theta \in \Theta, \eta \in \mathcal{H}} \sum_{i=1}^n m_{\lambda_n}(\theta, \eta)(X_i).$

Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
------------------------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------------

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- ▶ In the last GEE model,  $\hat{\theta}$  solves  $\sum_{i=1}^{n} z(\theta, \hat{\eta}(\theta))(X_i) = 0$ .

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Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data

### Model I. Cox Regression Model with Current Status Data

The hazard function of the survival time T of a subject with covariate Z is modelled as:

$$\lambda(t|z) \equiv \lim_{\Delta \to 0} rac{1}{\Delta} \Pr(t \leq T < t + \Delta | T \geq t, Z = z) = \lambda(t) \exp(\theta' z),$$

where  $\lambda$  is an unspecified baseline hazard function.

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Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data

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▶ In this model, we are usually interested in the regression parameter  $\theta$  while treating the cumulative hazard function  $\eta(y) = \int_0^y \lambda(t) dt$  as the nuisance parameter.

Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data

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- ▶ In this model, we are usually interested in the regression parameter  $\theta$  while treating the cumulative hazard function  $\eta(y) = \int_0^y \lambda(t) dt$  as the nuisance parameter.
- The nonparametric bootstrap is applied to this model, e.g., Efron and Tibshirani (1986), but without any theoretical justifications.

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Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
------------------------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------------

Consider the current status data in which the event time *T* is unobservable but we know whether the event has occurred at the examination time *C* or not. Thus, we observe *X* = (*C*, δ, *Z*), where δ = *I*{*T* ≤ *C*}.

Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
------------------------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------------

- Consider the current status data in which the event time T is unobservable but we know whether the event has occurred at the examination time C or not. Thus, we observe X = (C, δ, Z), where δ = I{T ≤ C}.
- ► Note that, in the case of current status data, the nonparametric MLE î is n<sup>1/3</sup> convergent.

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Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
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- ► Note that, in the case of current status data, the nonparametric MLE î is n<sup>1/3</sup> convergent.
- Our theory implies that Bootstrapping the regression parameter θ in the Cox regression model with current status data based on the exchangeable weights, e.g., nonparametric bootstrap & bayesian bootstrap, is consistent.

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Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data

### Model II. Partly Linear Model

We assume that

$$Y = \theta' W + f(Z) + \epsilon,$$

where  $\epsilon$  is independent of (W, Z) and f is an unknown smooth function belonging to second order Sobolev space. The distribution of  $\epsilon$  is assumed to satisfy some orthogonality condition.

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Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data

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• Estimate  $(\theta, f)$  using the penalized least square criterion:

$$\sum_{i=1}^{n} (y_i - \theta' w_i - f(z_i))^2 + \lambda_n \int_0^1 [f^{(2)}(s)]^2 ds.$$
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Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data

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• Our theory implies that Bootstrapping the *partial smoothing spline estimator*  $\hat{\theta}_{\lambda_n}$  is consistent.

Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data

Model III. Generalized Estimating Equation for Longitudinal Data

In longitudinal data sets, we observe  $m_i$  repeated measurements for the *i*-th subject, i.e.

Outcome 
$$Y_i = \begin{pmatrix} Y_{i1} \\ \vdots \\ Y_{im_i} \end{pmatrix}$$
 and  $m_i \times p$  Covariate  $X_i = \begin{pmatrix} X'_{i1} \\ \vdots \\ X'_{im_i}, \end{pmatrix}$ 

for i = 1, ..., n. Each subject/cluster is assumed to be independent. However, the repeated measurements within each subject/cluster are assumed to be correlated.

Model assumptions for the longitudinal data:

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Introduction	Cox Regression Model with Current Status Data
Bootstrapping Semiparametric MLE	Partly Linear Model
More General Conclusions	Generalized Estimating Equation for the Longitudinal Data
Examples	Generalized Estimating Equation for the congitudinal Data

Model assumptions for the longitudinal data:
 M1. E(Y<sub>i</sub>|X<sub>i</sub>) = μ<sub>i</sub>(β<sub>0</sub>);

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 M2. Var(Y<sub>i</sub>|X<sub>i</sub>) = Σ<sub>i</sub>(β<sub>0</sub>).

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- Due to the difficulty in specifying Σ<sub>i</sub>(β<sub>0</sub>), Liang and Zeger (1986) introduced an additional correlation parameter α to form the so called "working covariance matrix" V<sub>i</sub>(α, β) in order to approximate Σ<sub>i</sub>(β), and thus estimate β by solving

$$\sum_{i=1}^{n} D_i'(\beta) V_i^{-1}(\widehat{\alpha}(\beta), \beta) S_i(\beta) = 0,$$
(5)

where  $D_i(\beta) = \partial \mu_i(\beta) / \partial \beta$ ,  $S_i(\beta) = Y_i - \mu_i(\beta)$ .
Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
------------------------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------------

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where  $D_i(\beta) = \partial \mu_i(\beta) / \partial \beta$ ,  $S_i(\beta) = Y_i - \mu_i(\beta)$ .

•  $\widehat{\alpha}(\beta)$  may be obtained by GEE2 (Zhao and Prentice, 1990).

Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
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Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
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Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
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- In this scenario, it is natural to view the correlation parameter α as the nuisance parameter. Note that, in this particular example, α can be estimated at the parametric rate.
- Our general theory implies that
   In the framework of GEE, *cluster* bootstrap estimate of the
   mean regression parameter β [Sherman and le Cessie (1997)]
   based on the exchangeable weights is consistent.

Introduction Bootstrapping Semiparametric MLE More General Conclusions Examples	Cox Regression Model with Current Status Data Partly Linear Model Generalized Estimating Equation for the Longitudinal Data
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## Thank you for your attention....

Assistant Professor Guang Cheng Department of Statistics, Purdue University chengg@purdue.edu

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3