Adaptive confidence intervals for nonregular parameters

Eric B. Laber\textsuperscript{1} \& Susan A. Murphy\textsuperscript{2}

\textsuperscript{1}North Carolina State University, Raleigh
\textsuperscript{2}University of Michigan, Ann Arbor

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Introduction

- Modern statistical analysis is rife with non-regularity
  1. Test error of a learned classifier
  2. Parameters in a treatment policy
  3. Inference based on thresholded estimators
  4. ...

- Ignoring or assuming away this non-regularity can lead to poor small sample inference under many realistic generative models

- An asymptotic framework that faithfully represents small sample behavior is needed for the development and evaluation of inferential procedures
Two Examples

1. Confidence intervals for the test error in classification
2. Confidence intervals for parameters in optimal treatment policies
Example I: Classification

1. Observe iid training data $\mathcal{D} = \{(x_i, y_i)\}_{i=1}^n$
   - inputs $X \in \mathbb{R}^p$
   - outputs $Y \in \{-1, 1\}$
2. Construct classifier $\hat{c}_D(X) : \mathbb{R}^p \mapsto \{-1, 1\}$
3. Use classifier for prediction at new inputs
Example I: Classification

1. Observe iid training data \( \mathcal{D} = \{(x_i, y_i)\}_{i=1}^{n} \)
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2. Construct classifier \( \hat{c}_D(X) : \mathbb{R}^p \mapsto \{-1, 1\} \)

3. Use classifier for prediction at new inputs

Goal:

- **Interval estimator:** for test error \( \tau(\hat{c}_D) \triangleq P1_{Y \neq \hat{c}_D(X)} \)
The problem

- Focus on linear approximations to the Bayes decision boundary
  - We do not assume the approximation space is correct
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  - We do not assume the approximation space is correct
- Construct a classifier using surrogate loss \( L(X, Y, \beta) \)
  1. \( \hat{\beta} \triangleq \arg \min_{\beta \in \mathbb{R}^p} \mathbb{P}_n L(X, Y, \beta) \)
  2. \( \hat{c}_D(X) = \text{sign} \left( X^T \hat{\beta} \right) \)
The problem

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  1. $\hat{\beta} \triangleq \arg\min_{\beta \in \mathbb{R}^p} \mathbb{P}_n L(X, Y, \beta)$
  2. $\hat{c}_D(X) = \text{sign}(X^T \hat{\beta})$
- Review: surrogate loss function $L(X, Y, \beta)$
  - like to minimize error rate $\mathbb{P}_n 1_{Y \neq \text{sign}(X^T \beta)}$
  - non-smoothness $\Rightarrow$ computational difficulty
  - replace $1_{Y \neq \text{sign}(X^T \beta)} = 1_{Y X^T \beta < 0}$ with smooth surrogate
    - Support Vector Machines:
      \[ L(X, Y, \beta) = (1 - YX^T \beta)_+ + \gamma \|\beta\|^2 \]
    - Binomial Deviance:
      \[ L(X, Y, \beta) = \log(1 + e^{-YX^T \beta}) \]
    - Squared Error:
      \[ L(X, Y, \beta) = (1 - YX^T \beta)^2 \]
The problem cont’d

- Test error

\[ \tau(\hat{\beta}) \triangleq P_{1_{YX^T\hat{\beta}<0}} = \int 1_{yX^T\hat{\beta}<0} dP(x, y) \]
The problem cont’d

- Test error

\[ \tau(\hat{\beta}) \triangleq P 1_{YX^T\hat{\beta} < 0} = \int 1_{yx^T\hat{\beta} < 0} dP(x, y) \]

- Averages over new input-output pair \((X, Y)\) but not training data—evaluates the performance of the learned classifier
The problem cont’d

- Test error

\[ \tau(\hat{\beta}) \triangleq P\{Y_{X^T\hat{\beta}<0} = \int 1_{y_{x^T\hat{\beta}<0}} dP(x, y) \]  

- Averages over new input-output pair \((X, Y)\) but not training data—evaluates the performance of the learned classifier

- The test error \(\tau(\hat{\beta})\) is random quantity
  - Data-dependent parameter (Dawid 1994)
The problem cont’d

- Test error

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\tau(\hat{\beta}) \triangleq P 1_{YX^T \hat{\beta} < 0} = \int 1_{yX^T \hat{\beta} < 0} dP(x, y)
\]

- Averages over new input-output pair \((X, Y)\) but not training data—evaluates the performance of the learned classifier

- The test error \(\tau(\hat{\beta})\) is random quantity
  - Data-dependent parameter (Dawid 1994)

- Contrast with expected test error which averages over training data—evaluates performance of the algorithm used to construct the classifier
The problem cont’d

- Goal: given $\alpha \in (0, 1)$ construct $\hat{u}$ and $\hat{l}$ so that

$$P_D \left\{ \hat{l} \leq \tau(\hat{\beta}) \leq \hat{u} \right\} \geq 1 - \alpha$$
The problem cont’d

 ► Goal: given $\alpha \in (0, 1)$ construct $\hat{u}$ and $\hat{l}$ so that

$$\mathbb{P}_D \left\{ \hat{l} \leq \tau(\hat{\beta}) \leq \hat{u} \right\} \geq 1 - \alpha$$

Context

 ► Model space may not be correct
 ► Low dimensional setting ($p$ fixed)
 ► Cannot afford a test set
Non-regularity

- Simple estimate of $\tau(\hat{\beta})$ is $\hat{\tau}(\hat{\beta}) \triangleq P_n1_{YX^T\hat{\beta}<0}$
- Natural starting point for inference:
  \[
  \sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta})) \triangleq \sqrt{n}(P_n - P)1_{YX^T\hat{\beta}<0} = \sqrt{n}(P_n - P)1_{X^T\hat{\beta}^\neq 01_{YX^T\hat{\beta}<0}} + \sqrt{n}(P_n - P)1_{X^T\hat{\beta}^*=01_{YX^T\sqrt{n}(\hat{\beta}-\beta^*)<0}}
  \]
- $P1_{X^T\beta^*=0} > 0$ implies $\sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta}))$ has non-regular limit
  - points near the boundary cause jittering
  - $P1_{YX^T\hat{\beta}<0}$ need not concentrate about its mean
  - bootstrap and normal approximations are invalid
Illustration

Suppose

- \((X_1, X_2) \sim \text{Unif}[0, 5]^2\)
- \(\epsilon \sim N(0, 1/4)\)
- \(Y = \text{sign}(X_2 - (4/25)X_1^2 - 1 + \epsilon)\)

Properties of this example

- \(P1_{X^T\beta^* = 0} = 0\) (seemingly regular)
- Linear classifier is a good fit
- E.g. if \(n = 30\)
  - \(\mathbb{E}(\tau(\hat{\beta})) \approx .11\)
  - Bayes error \(\approx .09\)
Illustration cont’d

Under “regular” framework

- Centered bootstrap $\sqrt{n}(\hat{P}_n^{(b)} - P_n)1_{YX^T\hat{\beta}^{(b)} < 0}$

- Normal approximation $\hat{\tau}(\hat{\beta}) \pm z_{1-\gamma/2} \sqrt{\frac{\hat{\tau}(\hat{\beta})(1-\hat{\tau}(\hat{\beta}))}{n}}$

are both asymptotically valid
Illustration cont’d

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Coverage estimated using 1000 Monte Carlo data sets
- Below nominal coverage even for \( n = 250 \)
- Coverage especially poor for small samples
Illustration cont’d

Why do these methods fail?
Illustration cont’d

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- Non-smoothness $\Rightarrow$ non-regularity
- Performance inversely proportional to smoothness
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- Non-smoothness $\Rightarrow$ non-regularity
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Continuing our example
- Instead of test error $\tau(\hat{\beta})$ consider

$$\tau_{\text{smooth}}(\hat{\beta}) \triangleq P \left( 1 + \exp(aYX^T\hat{\beta}) \right)^{-1}$$

- $\tau_{\text{smooth}}(\hat{\beta})$ is smooth for fixed $a > 0$
- If $a \to \infty$ then $\tau_{\text{smooth}}(\hat{\beta}) \to \tau(\hat{\beta})$
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- Instead of test error $\tau(\hat{\beta})$ consider

$$
\tau_{\text{smooth}}(\hat{\beta}) \triangleq P \left( 1 + \exp(a Y X^T \hat{\beta}) \right)^{-1}
$$

- $\tau_{\text{smooth}}(\hat{\beta})$ is smooth for fixed $a > 0$
- If $a \rightarrow \infty$ then $\tau_{\text{smooth}}(\hat{\beta}) \rightarrow \tau(\hat{\beta})$
- **Conjecture:** Bootstrap coverage should deteriorate as $a$ grows
Illustration cont’d

Smoothed Loss Functions

Estimated Coverage Quadratic Example: Smoothed

Sample Size

Estimated Coverage
Illustration cont’d

Smoothed Loss Functions

Estimated Coverage Quadratic Example: Smoothed

- Smoothed Loss Functions
  - Margin
  - Smoothed Loss
  - \( a = 0.1 \)
  - \( a = 1.0 \)
  - \( a = 10 \)
  - \( a = \infty \)

- Estimated Coverage Quadratic Example: Smoothed
  - Sample Size
  - Estimated Coverage
  - \( a = 0.1 \)
  - \( a = 1.0 \)
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  - \( a = \infty \)
Two Examples

1. Confidence intervals for the test error in classification
2. Confidence intervals for parameters in optimal treatment policies
Example II: Treatment Policies

- Motivation: treatment of chronic illness
  - Some examples: HIV/AIDS, cancer, depression, schizophrenia, drug and alcohol addiction, ADHD, etc.
- Multistage decision making problem
- Longer-term treatment requires balancing present and future benefit as opposed to focusing only on present benefit.

- Treatment Policies
  - Operationalize multistage decision making via a sequence of decision rules
    - One decision rule for each time (decision) point
    - A decision rule is a function inputs patient history and outputs a recommended treatment
  - Aim to optimize some cumulative clinical outcome
Construction and inference for policies have applications beyond medicine

1. Artificial Intelligence and Reinforcement Learning (autonomous helicopter, drones, etc., Ng 2003)
2. Marketing (Simester, Sun and Tsitsiklis, 2003)
3. Active labor market policies (Lechner and Miquel, 2010)
4. Recruitment and retention policies in Survey Research (Wagner, 2012?)
5. . . .
An Example Policy for ADHD

Prior medication?

Adequate response?

High adherence?

Low dose MEDS

Intensify MEDS

Add BMOD

Low dose BMOD

No

Yes

Yes

Yes

Continue MEDS

Continue BMOD

Intensify BMOD

Add BMOD

Add MEDS

No

No

No

No

High adherence?
ADHD Trial (Pelham, PI)

Treatment A
Low Intensity BMOD
Response?

Yes
- Continue
  - Low Intensity BMOD

No
- Treatment AA
  - Augment with MEDS

- Treatment AB
  - Intensify BMOD

Treatment B
Low Intensity MEDS
Response?

Yes
- Continue
  - Low Intensity MEDS

No
- Treatment BA
  - Augment with BMOD

- Treatment BB
  - Intensify MEDS
Data

- $(X_1, A_1, X_2, A_2, Y)$ for each individual
  - $X_j$: Observations available at stage $j$
  - $A_j$: Treatment at stage $j$, with known distribution (usually uniform)
  - $Y$: Primary outcome (larger is better)
  - $H_j$: History at stage $j$, $H_1 = X_1$, $H_2 = (X_1, A_1, X_2)$

- The policy, $\pi = \{\pi_1, \pi_2\}$, $\pi_j : H_j \rightarrow A_j$, should have high Value: $V^\pi = E^\pi (Y)$
Constructing a policy from data: Q-Learning

- Generalization of regression to multiple treatment stages
- Backwards induction like dynamic programming
- Approximate conditional expectation with regression
Constructing a policy from data: Q-Learning

- Generalization of regression to multiple treatment stages
- Backwards induction like dynamic programming
- Approximate conditional expectation with regression

- In computer science there are many variations; almost always presented as part of a stochastic approximation algorithm for solving an infinite number of stages (infinite horizon) Watkins (1989), Sutton & Barto (1998)

- In statistics there are a few variations, with a finite number of stages, appearing in Murphy (2003), Robins (2004), Henderson et al. (2009) + more
Simple Version of Q-Learning

Two stages; linear regressions; $A_j \in \{0, 1\}$, $H_{j1}$, $H_{j2}$ features of patient history, $H_j$:

- **Stage 2 regression**: Regress $Y$ on $H_{21}$, $H_{22}$ to obtain
  \[
  \hat{Q}_2(H_2, A_2) = \beta_{21}^T H_{21} + \beta_{22}^T H_{22} A_2
  \]
  \[
  \hat{\pi}_2(H_2) = \arg \max_{a_2} \hat{Q}_2(H_2, a_2) = \arg \max_{a_2} \beta_{22}^T H_{22} a_2
  \]
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  \]

- \( \tilde{Y} = \hat{\beta}_{21}^T H_{21} + \text{max}_{a_2} \hat{\beta}_{22}^T H_{22} a_2 \) (\( \tilde{Y} \) is a predictor of \( \text{max}_{a_2} Q_2(H_2, a_2) \))
Simple Version of Q-Learning

Two stages; linear regressions; \( A_j \in \{0, 1\} \), \( H_{j1}, H_{j2} \) features of patient history, \( H_j \):

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- **Stage 1 regression:** Regress \( \tilde{Y} \) on \( H_{11}, H_{12} \) to obtain
  \[
  \hat{Q}_1(H_1, A_1) = \hat{\beta}_{11}^T H_{11} + \hat{\beta}_{12}^T H_{12} A_1
  \]
  \[
  \hat{\pi}_1(H_{12}) = \arg \max_{a_1} \hat{Q}_1(H_1, a_1) = \arg \max_{a_1} \hat{\beta}_{12}^T H_{12} a_1
  \]
GOAL: confidence interval for a contrast of stage 1 parameters: $c^T \beta^*_1$

- Non-regular due to non-differentiable max operator used in Q-learning; recall
  - $\hat{Y} = \hat{\beta}_{21}^T H_{21} + \max_{a_2} \hat{\beta}_{22}^T H_{22} a_2$

- In this setting the centered percentile bootstrap confidence interval for $c^T \beta^*_1$ can be anticonservative, (95% confidence interval covers 90%-93% in two stages, each with two treatments; 84%-93% for two stages, each with three treatments)
Limiting Distribution of centered $c^T \sqrt{n} \hat{\beta}_1$

- Local Alternative:
  - $\beta_{22,n}^* = \beta_{22}^* + u/\sqrt{n}$
  - The limiting distribution of $c^T \sqrt{n}(\hat{\beta}_1 - \beta_{1,n}^*)$ is the distribution of
    $$c^T \Sigma_1^{-1} (\mathbb{W} + f(\mathbb{V}, u))$$

where

$$f(v, u) = E \left[ B_1 \left( [H_{22}^T v + H_{22}^T u]^+ - [H_{22}^T u]^+ \right) 1_{H_{22}^T \beta_{22}^* = 0} \right]$$

and $B_1 = (H_{11}^T, H_{12}^T A_1)^T$ (e.g. the design matrix) and $\mathbb{W}$, $\mathbb{V}$ are jointly normal vectors

- The fact that the limiting distribution depends on the direction, $u$, means that $\hat{\beta}_1$ is a *nonregular* estimator (unless $P [H_{22}^T \beta_{22}^* = 0] = 0$)
Ideas
Idea

This work builds on ideas from

- Generalization error bounds
  - Construct smooth data-based upper and lower bounds on a centered estimator:
    - $\sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta}))$ (centered estimator of test error)
    - $\sqrt{n}(c^T\hat{\beta}_1 - c^T\beta_1)$ (centered stage 1 regression coefficient)
  - If generative model induces regularity, then bounds collapse to centered parameter

- Pretests (e.g. hypothesis tests) for use in inference concerning weakly identified parameters in econometrics (Andrews 2001, Andrews and Soares 2007; Cheng 2008). We use the pretest idea to test if the parameter is near a “bad” parameter value.
Ideas

- Confidence interval is the primary focus

- Construct smooth data-based upper and lower bounds on a centered estimator:
  - $\sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta}))$ (centered estimator of test error)
  - $\sqrt{n}(c^T\hat{\beta}_1 - c^T\beta_1)$ (centered stage 1 regression coefficient)

- Confidence intervals are formed by bootstrapping these bounds

- Evaluate using an asymptotic framework that permits non-regularity
The Adaptive Confidence Intervals

1. Confidence intervals for the test error in classification
2. Confidence intervals for parameters in optimal treatment policies
Adaptive CI for the test error

Idea: construct smooth upper and lower bounds on \( \sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta})) \)

- Recall \( \sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta})) \) is equal to

\[
\sqrt{n}(\mathbb{P}_n - P)1_{YX^T\hat{\beta} < 0}
\]

- Take supremum/infimum only when \( X \) is in a region near the decision boundary \( X^T\beta^* = 0 \)

\[
\text{UB}_n \triangleq \sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta}))
\]

\[
- \sqrt{n}(\mathbb{P}_n - P)1_{n(X^T\beta)^2 \frac{1}{X^T\hat{\Sigma}X} \leq \lambda_n}1_{YX^T\hat{\beta} < 0}
\]

\[
+ \sup_{u \in \mathbb{R}^p} \sqrt{n}(\mathbb{P}_n - P)1_{\frac{n(X^T\beta)^2}{X^T\hat{\Sigma}X} \leq \lambda_n}1_{YX^Tu < 0}
\]

where \( \hat{\Sigma} = n\text{Cov}(\hat{\beta}) \)
Adaptive CI for the test error

Idea: construct smooth upper and lower bounds on $\sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta}))$

- Recall $\sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta}))$ is equal to
  $$\sqrt{n}(P_n - P)1_{YX^T\hat{\beta}<0}$$

- Take supremum/infimum only when $X$ is in a region near the decision boundary $X^T\beta^* = 0$

$$UB_n \triangleq \sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta})) - \sqrt{n}(P_n - P)1_{n(X^T\hat{\beta})^2 \leq \lambda_n} n(X^T\hat{\beta}) < 0 \cdot 1_{YX^T\hat{\beta}<0} + \sup_{u \in \mathbb{R}^p} \sqrt{n}(P_n - P)1_{n(X^T\hat{\beta})^2 \leq \lambda_n} n(X^T\hat{\beta}) \leq \lambda_n \cdot 1_{YX^Tu<0}$$

where $\hat{\Sigma} = nCov(\hat{\beta})$

(Replace supremum with infimum to obtain lower bound.)
Assumptions

Some technical assumptions:

(A1) $L(X, Y, \beta)$ is convex with respect to $\beta$ for each $(x, y) \in \mathbb{R}^p \times \{-1, 1\}$

(A2) $Q(\beta) \triangleq PL(X, Y, \beta)$ exists and is finite for all $\beta \in \mathbb{R}^p$

(A3) $\beta^* \triangleq \arg \min_{\beta \in \mathbb{R}^p} Q(\beta)$ exists and is unique

(A4) Let $g(X, Y, \beta)$ be a sub-gradient of $L(X, Y, \beta)$. Then $P\|g(X, Y, \beta)\|^2 < \infty$ for all $\beta$ in a neighborhood of $\beta^*$.

(A5) $Q(\beta)$ is twice continuously differentiable at $\beta^*$ and $H \triangleq \nabla^2 Q(\beta^*)$ is positive definite.

(A6) The sequence $\lambda_n$ tends to infinity and satisfies $\lambda_n = o(n)$. 
Properties

Theorem (Convergence)

1. \( \sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta})) \sim W + V(z_{\infty}) \)
2. \( \sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta})) \leq UB_n \) for all \( n \)
3. \( UB_n \sim \sup_{u \in \mathbb{R}^p} W + V(u) \)
4. \( UB^{(b)}_n \sim \sup_{u \in \mathbb{R}^p} W + V(u) \) in probability.

where \( (V, W, z_{\infty}) \) is zero mean Gaussian; \( V \) is a Gaussian process, \( W \) is a normal random variable and \( z_{\infty} \) is \( p \)-dim normal.
Theorem (Convergence)

1. $\sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta})) \sim W + \mathcal{V}(z_\infty)$
2. $\sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta})) \leq UB_n$ for all $n$
3. $UB_n \sim \sup_{u \in \mathbb{R}^p} W + \mathcal{V}(u)$
4. $UB_n^{(b)} \sim \sup_{u \in \mathbb{R}^p} W + \mathcal{V}(u)$ in probability.

where $(\mathcal{V}, W, z_\infty)$ is zero mean Gaussian; $\mathcal{V}$ is a Gaussian process, $W$ is a normal random variable and $z_\infty$ is $p$-dim normal.

Theorem (Adaptation)

If either the Bayes decision boundary is linear or $P(X^T \beta^* = 0) = 0$ then $UB_n$ and $\sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta}))$ have the same limiting distribution.
Properties

The supremum in the upper bound $\mathbb{UB}_n$ can be viewed as a supremum over local alternatives:

Theorem (Convergence under local alternatives)

**Under $P_n$**

1. $\sqrt{n}(\hat{\tau}(\hat{\beta}) - \tau(\hat{\beta})) \rightsquigarrow \mathbb{W} + \mathbb{V}(z_{\infty} + u)$
2. $\mathbb{UB}_n \rightsquigarrow \sup_{u \in \mathbb{R}^p} \mathbb{W} + \mathbb{V}(u)$.

where $P_n$ is a sequence of local alternatives contiguous to $P$ for which $\beta^*_n \triangleq \arg \min_{\beta \in \mathbb{R}^p} P_n L(X, Y, \beta)$ satisfies $\beta^*_n = \beta^* + u/\sqrt{n}$. 
The Adaptive Confidence Intervals

1. Confidence intervals for the test error in classification
2. Confidence intervals for parameters in optimal treatment policies
Adaptive CI for the treatment effect

Idea: construct smooth upper and lower bounds on $c^T \sqrt{n}(\hat{\beta}_1 - \beta_1^*)$.

$$UB_n \triangleq c^T \sqrt{n}(\hat{\beta}_1 - \beta_1^*)$$

$$-c^T \hat{\Sigma}^{-1} \mathbb{P}_n B_1 \left( [H_{22}^T \sqrt{n} u + H_{22}^T u]_+ - [H_{22}^T u]_+ \right) \frac{1}{1} \frac{n(H_{22}^T \hat{\beta}_{22})^2}{H_{22}^T \hat{\Sigma} H_{22}} \leq \lambda_n \quad \bigg| \quad u = \sqrt{n} \beta_1^*$$

$$+ \sup_u c^T \hat{\Sigma}^{-1} \mathbb{P}_n B_1 \left( [H_{22}^T \sqrt{n} u + H_{22}^T u]_+ - [H_{22}^T u]_+ \right) \frac{1}{1} \frac{n(H_{22}^T \hat{\beta}_{22})^2}{H_{22}^T \hat{\Sigma} H_{22}} \leq \lambda_n$$

where the supremum is taken only when $H_{22}$ is in a region near the decision boundary $H_{22}^T \beta_{22}^* = 0$

- $B_1 = (H_{11}^T, H_{12}^T A_1)^T$
- $\sqrt{n} = \sqrt{n}(\hat{\beta}_{22} - \beta_{22}^*)$
- $\hat{\Sigma} = nCov(\hat{\beta}_{22})$
Adaptive CI for the treatment effect

Idea: construct smooth upper and lower bounds on $c^T \sqrt{n}(\hat{\beta}_1 - \beta_1^*)$.

\[
UB_n \triangleq c^T \sqrt{n}(\hat{\beta}_1 - \beta_1^*)
\]

\[-c^T \hat{\Sigma}^{-1} \text{P}_n B_1 \left( [H_{22}^T \sqrt{n} + H_{22}^T u]_+ - [H_{22}^T u]_+ \right) 1_{\frac{n(H_{22}^T \hat{\beta}_{22})^2}{H_{22}^T \hat{\Sigma} H_{22}} \leq \lambda_n} u = \sqrt{n} \beta_1^* \]

\[+ \sup_{u} c^T \hat{\Sigma}^{-1} \text{P}_n B_1 \left( [H_{22}^T \sqrt{n} + H_{22}^T u]_+ - [H_{22}^T u]_+ \right) 1_{\frac{n(H_{22}^T \hat{\beta}_{22})^2}{H_{22}^T \hat{\Sigma} H_{22}} \leq \lambda_n} \]

where the supremum is taken only when $H_{22}$ is in a region near the decision boundary $H_{22}^T \beta_{22}^* = 0$

\[B_1 = (H_{11}^T, H_{12}^T A_1)^T \]

\[\nabla_n = \sqrt{n}(\hat{\beta}_{22} - \beta_{22}^*) \]

\[\hat{\Sigma} = n \text{Cov}(\hat{\beta}_{22}) \]

(Replace supremum with infimum to obtain lower bound.)
Assumptions

(A1) The histories $H_j$ with $B_j = (H_{j1}^T, H_{j2}^T A_j)^T$, $j = 1, 2$ and primary outcome $Y$, satisfy the moment inequalities $P \| H_2 \|^2 \| B_1 \|^2 < \infty$ and $PY^2 \| B_j \|^2 < \infty$.

(A2) Define:

1. $\Sigma_j \triangleq PB_j^T B_j$ for $j = 1, 2$;
2. $g_2(B_2, Y_2; \beta_2^*) \triangleq B_2^T (Y_2 - B_2 \beta_2^*)$;
3. $g_1(B_1, Y_1, H_2; \beta_1^*, \beta_2^*) \triangleq B_1^T (H_{21}^T \beta_{21}^* + |H_{22}^T \beta_{22}^*| - B_1 \beta_1^*)$;

assume the matrices $\Sigma_j$ and $\Omega \triangleq \text{Var-cov} (g_1, g_2)$ are strictly positive definite.

(A3) The sequence $\lambda_n$ tends to infinity and satisfies $\lambda_n = o(n)$. 
Properties

Theorem (Convergence)

1. \( c^T \sqrt{n}(\hat{\beta}_1 - \beta_1^*) \sim c^T \Sigma_1^{-1} (W + f(V, 0)) \)
2. \( c^T \sqrt{n}(\hat{\beta}_1 - \beta_1^*) \leq UB_n \) for all \( n \)
3. \( UB_n \sim \sup_{u \in \mathbb{R}^p} c^T \Sigma_1^{-1} (W + f(V, u)) \)
4. \( UB_n^{(b)} \sim \sup_{u \in \mathbb{R}^p} c^T \Sigma_1^{-1} (W + f(V, u)) \) in probability.

where

\[
f(v, u) = E \left[ B_1 \left( [H_{22}^T v + H_{22}^T u]_+ - [H_{22}^T u]_+ \right) 1_{H_{22}^T \beta_{22}^* = 0} \right]
\]

and \( B_1 = (H_{11}^T, H_{12}^T A_1)^T \) (e.g. row of the design matrix) and \( W, V \) are jointly normal vectors.
Properties

Theorem (Adaptation)

If $P(H_{22}^\top \beta_{22}^* = 0) = 0$ then $\mathbb{UB}_n$ and $c^\top \sqrt{n}(\hat{\beta}_1 - \beta_1^*)$ have the same limiting distribution.
Properties

Theorem (Adaptation)

If \( P(H_{22}^T \beta_{22}^* = 0) = 0 \) then \( UB_n \) and \( c^T \sqrt{n}(\hat{\beta}_1 - \beta_1^*) \) have the same limiting distribution.

The supremum in the upper bound \( UB_n \) can be viewed as a supremum over local alternatives:

Theorem (Convergence under local alternatives)

Under \( P_n \) for which \( \beta_{22,n}^* = \beta_{22}^* + u/\sqrt{n} \),

1. \( c^T \sqrt{n}(\hat{\beta}_1 - \beta_1^{*n}) \sim c^T \Sigma_1^{-1} (W + f(V, u)) \)
2. \( UB_n \sim \sup_{u \in \mathbb{R}^p} c^T \Sigma_1^{-1} (W + f(V, u)) \).
Simulation Experiments

1. Confidence intervals for the test error in classification
2. Confidence intervals for parameters in optimal treatment policies
Experiments

Compare performance of

- Adaptive confidence interval (ACI)
- CV-Normal approximation [Yang 2006]
- BCCVP-BR approximation [Jiang 2008]
- ACI uses \( \lambda_n \triangleq \max(\sqrt{n}, \chi^2_{.995}) \)
Experiments

Compare performance of

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- CV-Normal approximation [Yang 2006]
- BCCVP-BR approximation [Jiang 2008]
- ACI uses $\lambda_n \triangleq \max(\sqrt{n}, \chi^2_{.995})$

Details

- 1000 Monte Carlo replications
- 10 data sets
Results

Target coverage .950, loss function $L(X, Y, \beta) = \log(1 + e^{-XY^T\beta})$, $n = 30$

<table>
<thead>
<tr>
<th>Data Set/Method</th>
<th>ACI</th>
<th>CV-Normal</th>
<th>BCCVP-BR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ThreePt</td>
<td>.976</td>
<td>.893</td>
<td>.914</td>
</tr>
<tr>
<td>Magic</td>
<td>.955</td>
<td>.999</td>
<td>.983</td>
</tr>
<tr>
<td>Mam.</td>
<td>.951</td>
<td>.993</td>
<td>.974</td>
</tr>
<tr>
<td>Ion.</td>
<td>.947</td>
<td>.995</td>
<td>.985</td>
</tr>
<tr>
<td>Donut</td>
<td>.968</td>
<td>.966</td>
<td>.908</td>
</tr>
<tr>
<td>Bal.</td>
<td>.979</td>
<td>.996</td>
<td>.972</td>
</tr>
<tr>
<td>Liver</td>
<td>.946</td>
<td>.997</td>
<td>.972</td>
</tr>
<tr>
<td>Spam</td>
<td>.985</td>
<td>.999</td>
<td>.981</td>
</tr>
<tr>
<td>Quad</td>
<td>.978</td>
<td>.997</td>
<td>.945</td>
</tr>
<tr>
<td>Heart</td>
<td>.960</td>
<td>.995</td>
<td>.976</td>
</tr>
</tbody>
</table>

Table: Estimated coverage of competing confidence procedures. Coverage is highlighted if not different from .950 at the .01 level.
### Results

Target coverage .950, loss function $L(X, Y, \beta) = \log(1 + e^{-YX^T\beta})$, $n = 30$

<table>
<thead>
<tr>
<th>Data Set/Method</th>
<th>ACI</th>
<th>CV-Normal</th>
<th>BCCVP-BR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ThreePt</td>
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<td>.551</td>
<td>.742</td>
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<tr>
<td>Magic</td>
<td>.466</td>
<td>.526</td>
<td>.504</td>
</tr>
<tr>
<td>Mam.</td>
<td>.373</td>
<td>.448</td>
<td>.387</td>
</tr>
<tr>
<td>Ion.</td>
<td>.305</td>
<td>.459</td>
<td>.401</td>
</tr>
<tr>
<td>Donut</td>
<td>.434</td>
<td>.485</td>
<td>.494</td>
</tr>
<tr>
<td>Bal.</td>
<td>.262</td>
<td>.349</td>
<td>.257</td>
</tr>
<tr>
<td>Liver</td>
<td>.533</td>
<td>.526</td>
<td>.518</td>
</tr>
<tr>
<td>Spam</td>
<td>.454</td>
<td>.494</td>
<td>.423</td>
</tr>
<tr>
<td>Quad</td>
<td>.310</td>
<td>.372</td>
<td>.267</td>
</tr>
<tr>
<td>Heart</td>
<td>.367</td>
<td>.476</td>
<td>.404</td>
</tr>
</tbody>
</table>

**Table:** Estimated width of competing confidence procedures. Width is highlighted if coverage is at least .950 and the interval is smallest.
Conclusions

- ACI achieves nominal coverage
- Non-trivial width
- Computationally efficient
- Robust to choice of $\lambda_n$
Simulation Experiments

1. Confidence intervals for the test error in classification
2. Confidence intervals for parameters in optimal treatment policies
Empirical study

- Compare performance of
  - Soft-thresholding (ST) (Chakraborty et al., 2009)
  - Centered percentile bootstrap (CPB)
  - Plug-in pretesting estimator (PPE) (uses idea of Chatterjee and Lahiri, 2011)
  - ACI uses $\lambda_n = \log \log n$
Empirical study

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  - Centered percentile bootstrap (CPB)
  - Plug-in pretesting estimator (PPE) (uses idea of Chatterjee and Lahiri, 2011)
  - ACI uses $\lambda_n = \log \log n$

- Generative models
  1. Non-regular (NR): $P(\mathbf{H}_{22}^T \beta_{22}^* = 0) > 0$
  2. Nearly non-regular (NNR): $P(\mathbf{H}_{22}^T \beta_{22}^* \approx 0) > 0$
  3. Regular (R): $P(\mathbf{H}_{22}^T \beta_{22}^* \approx 0) = 0$

- 1000 Monte Carlo replications
# Results

Target coverage .950 for coefficient of stage 1 treatment, \( n = 150 \)

<table>
<thead>
<tr>
<th>2 stages</th>
<th>2 txts</th>
<th>Ex1</th>
<th>Ex2</th>
<th>Ex3</th>
<th>Ex4</th>
<th>Ex5</th>
<th>Ex6</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB</td>
<td>NR</td>
<td>0.934</td>
<td>0.935</td>
<td>0.930</td>
<td>0.939</td>
<td>0.925</td>
<td>0.928</td>
</tr>
<tr>
<td>ST</td>
<td>NNR</td>
<td>0.948</td>
<td>0.945</td>
<td>0.938</td>
<td>0.919</td>
<td>0.759</td>
<td>0.762</td>
</tr>
<tr>
<td>PPE</td>
<td>NR</td>
<td>0.931</td>
<td>0.940</td>
<td>0.938</td>
<td>0.931</td>
<td>0.904</td>
<td>0.903</td>
</tr>
<tr>
<td>ACI</td>
<td>NNR</td>
<td>0.992</td>
<td>0.992</td>
<td>0.968</td>
<td>0.950</td>
<td>0.964</td>
<td>0.965</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3 txts</th>
<th>Ex1</th>
<th>Ex2</th>
<th>Ex3</th>
<th>Ex4</th>
<th>Ex5</th>
<th>Ex6</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB</td>
<td>NR</td>
<td>0.933</td>
<td>0.938</td>
<td>0.915</td>
<td>0.940</td>
<td>0.885</td>
</tr>
<tr>
<td>PPE</td>
<td>NNR</td>
<td>0.931</td>
<td>0.932</td>
<td>0.927</td>
<td>0.918</td>
<td>0.858</td>
</tr>
<tr>
<td>ACI</td>
<td>NNR</td>
<td>0.999</td>
<td>0.999</td>
<td>0.968</td>
<td>0.964</td>
<td>0.970</td>
</tr>
</tbody>
</table>

**Table**: Coverage is NOT highlighted if significantly below .95 at the .05 level.
Conclusion

- ACI achieved nominal or improved coverage on all examples
- ACI is conservative when there is no stage 2 treatment effect.
- Relative performance of ACI improves on examples with increasing numbers of stages and/or treatments
- Robust to choice of $\lambda_n$
Discussion

- Many modern statistical problems involve nonregular estimators. Most frequently these occur in $p$ large ($p < n$) or $p \gg n$ problems. Examples:
  - Inference based on estimators that involve the estimation of a matrix with eigenvalues that may be near zero,
  - Prediction intervals after using lasso or other variable selection methods,
  - Evaluation of the misclassification rate of a learned classifier
  - Constrained estimation

- Principled approaches to forming confidence intervals and hypothesis tests are currently lacking.
Questions: laber@stat.ncsu.edu, samurphy@umich.edu
A copy of this talk can be found at:
www.stat.lsa.umich.edu/~samurphy

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ADHD Dynamic Treatment Regime

Prior medication?
- Yes: Low dose MEDS
- No: Low dose BMOD

Adequate response?
- Yes: Continue MEDS
- No: Intensify MEDS

High adherence?
- Yes: Add BMOD
- No: Continue BMOD

Adequate response?
- Yes: Continue BMOD
- No: Intensify BMOD

High adherence?
- Yes: Add MEDS
- No: Add MEDS

No: Add MEDS
### Inference for ADHD Treatment Effects

<table>
<thead>
<tr>
<th>Stage</th>
<th>History</th>
<th>Lower (5%)</th>
<th>Upper (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Had prior med.</td>
<td>-0.51</td>
<td>0.14</td>
</tr>
<tr>
<td>1</td>
<td>No prior med.</td>
<td>-0.05</td>
<td>0.39</td>
</tr>
<tr>
<td>2</td>
<td>High adherence and BMOD</td>
<td>-0.08</td>
<td>0.69</td>
</tr>
<tr>
<td>2</td>
<td>Low adherence and BMOD</td>
<td>-1.10</td>
<td>-0.28</td>
</tr>
<tr>
<td>2</td>
<td>High adherence and MEDS</td>
<td>-0.18</td>
<td>0.62</td>
</tr>
<tr>
<td>2</td>
<td>Low adherence and MEDS</td>
<td>-1.25</td>
<td>-0.29</td>
</tr>
</tbody>
</table>

- Positive stage 1 effect favors BMOD ($A_1 = 1$ if BMOD; $A_1 = -1$ if MED)
- Positive stage 2 effect favors Intensify ($A_2 = 1$ if Intensify; $A_2 = -1$ if Augment)
ADHD Dynamic Treatment Regime

1. Prior medication? Yes → Low dose MEDS ∼ OR ∼ BMOD
   No → Low dose BMOD

2. Adequate response? Yes → Continue SAME
   No → Intensify SAME

3. High adherence? Yes → Add OTHER ∼ OR ∼ Intensify SAME
   No → Add MEDS

4. Adequate response? Yes → Add MEDS ∼ OR ∼ Intensify BMOD
   No → Continue BMOD