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Nonparametric Regression Method for Broad Sense Agreement

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Abstract

Characterizing the correspondence between an ordinal measurement and a continuous measurement is often of interest in mental health studies. To this end, Peng, Li, Guo, and Manatunga (2011) introduced the concept of broad sense agreement (BSA) and developed nonparametric estimation and inference for a BSA measure. In this work, we propose a nonparametric regression framework for BSA, which provides a robust tool to further investigate population heterogeneity in BSA. We develop inferential procedures including regression function estimation and hypothesis testing. Extensive simulation studies demonstrate satisfactory performance of the proposed method. We also apply the new method to a recent Grady Trauma Study and reveal an interesting impact of depression severity on the alignment between a self-reported symptom instrument and clinician diagnosis in posttraumatic stress disorder (PTSD) patients.

Keywords

Broad sense agreement; Jackknife; Nonparametric regression; U-statistic

AMS Subject Classification

Primary: 62G08; Secondary: 62G20

1. Introduction

In recent years, there has been a tremendous interest in improving assessment and diagnosis of mental health disorders (Gillespie et al. 2009). For example, Posttraumatic stress disorder (PTSD) is a complex, heterogeneous disorder and is one of the most prevalent mental health disorder among combat veterans (Kessler, Sonnega, Bromet, Hughes, and Nelson 1995). The Clinician-Administered PTSD scale (CAPS) is currently the best available standard for diagnosing PTSD (yes vs. no), but requires considerable time and efforts of clinicians and trained clinical researchers who have working knowledge of PTSD (Foa, Riggs, Dancu, and Rothbaum 1993; Foa and Tolin 2000). The PTSD Symptom Scale Interview (PSS) is an alternative self-reported measure of PTSD severity, which demands much less assessment

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time than the CAPS and provides a continuous score to indicate the severity of PTSD (Foa et al. 1993). Investigating the alignment between CAPS diagnosis and PSS can lead to enhanced utility of these instruments. For instance, if there is a good alignment between PSS and CAPS diagnosis, PSS may be used as a less costly surrogate of CAPS with reasonable reliability or validity. Addressing such a problem can not be accomplished through the traditional agreement methods (Cohen 1960, 1968; Fleiss et al. 1971; Kraemer 1980; Lin 1989, among others) because they typically require measurements to be on the same scale.

The broad sense agreement (BSA) framework, introduced by Peng et al. (2011), is specifically designed to characterize the correspondence between a continuous measurement and an ordinal measurement. For example, the BSA measure proposed by Peng et al. (2011) can depict the capacity of interpreting PSS according to the CAPS diagnosis of PTSD. The BSA measure is scaled between -1 and 1 by its definition and is easy to interpret. The BSA measure equaling 1 corresponds to the perfect BSA scenario where there exists a definite way to discretize PSS to produce a concordant one-to-one correspondence with CAPS diagnosis. Peng et al. (2011) proposed a nonparametric estimator and jackknife based inference procedures for their BSA measure. Their methods are primarily focused on the one-sample case.

Mental health disorders, such as PTSD, are typically prone to a large population heterogeneity as manifested by highly variable disease phenotypes. Therefore, in many mental health studies, the estimator proposed in Peng et al. (2011) can provide a good overall summary of BSA but may suffer a loss of precision due to the potential variations of BSA among different subpopulations. The heterogeneity pattern of BSA, if exists, can also be of great scientific interest. For example, in the recent Grady Trauma Study (Gillespie et al. 2009), referred to as PTSD study hereafter, 8091 trauma exposed subjects were recruited in the waiting rooms of primary care of Grady hospital, an inner-city health care facility. Data collected from these subjects include several clinical assessments such as CAPS, PSS and other information such as depression disorder score measured by Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, and Erbaugh 1961). In an exploratory analysis, we estimated the BSA measure between PSS and CAPS diagnosis for four subgroups stratified by the BDI depression score and obtained the corresponding confidence intervals; see Figure 1. It is shown that the BSA measure may vary considerably across different BDI groups. The results suggest that there may be a good alignment between PSS and CAPS diagnosis in PTSD patients with no/little depression symptoms, but this is not true for those suffering from severe depression. Such a heterogeneous pattern of BSA can help the understanding of these instruments, but it cannot be uncovered from a simple one-sample study of BSA.

Motivated by the PTSD example, we propose to extend the current BSA framework by developing a robust regression tool for BSA. As shown in the PTSD example, the changing pattern of BSA with a covariate may not be linear. Therefore, we study a nonparametric regression method of BSA to allow for nonlinear covariate effects. There are some important subtlety in formulating a nonparametric regression model for BSA and developing its estimation. That is, unlike common association or agreement measures (e.g. correlation coefficient, kappa coefficient), the BSA measure in the one-sample case is not defined upon

the distribution of measurements from a single unit/subject. Instead it is constructed based on a comparison of data from multiple units/subjects. When the study population is allowed to be heterogenous, one needs to appropriately adapt the concept of BSA. For example, one tricky task is to identify comparable units/subjects when defining the BSA measure while accounting for population heterogeneity. This poses some conceptual complications to the modeling, estimation and inference of BSA in the regression setting.

In Section 2, we first review the existing BSA framework, followed by an introduction of covariate-adjusted BSA measure and our formulation of a nonparametric regression model. In Section 3, we propose a nonparametric estimator for the regression function in the proposed model, which employs the idea of kernel regression in the context of regressing BSA. We study the asymptotic properties of the proposed estimator, and develop inference procedures including variance estimation, confidence intervals, and hypothesis testing. In Section 4, we present simulation studies, which demonstrate good finite sample performance of the proposed method. An application of our methods to the PTSD study is presented in Section 5. We conclude this paper with a few remarks in Section 6.

2. The Proposed Regression Framework

2.1. Review of broad sense of agreement

The concept of broad sense agreement (BSA) extends the paradigm of classical agreement studies which only concern measurements on the same scale. Let X and Y be continuous and ordinal measurements of a common trait from the same subject. Let $\mathcal{D}_X$ and $\mathcal{D}_Y$ be the domain of X and Y , respectively. By the definition of Peng et al. (2011), X and Y are in perfect broad sense agreement (or disagreement) if and only if there exists an increasing (or decreasing) step function Ψ from $\mathcal{D}_X$ to $\mathcal{D}_Y$ such that $Y = \Psi(X)$ with probability 1. This definition implies that when there is a perfect agreement (disagreement), one can identify a set of cut-points for the continuous X such that the discretized X has an exact one-to-one concordant (or discordant) correspondence with the ordinal Y .

Peng et al. (2011) introduced a measure to characterize the broad sense agreement between a continuous measurement and an ordinal measurement. The key idea underlying Peng et al. (2011)'s BSA measure is to quantify the departure from perfect broad sense agreement by using the distance between the observed ranks in X and the ranks expected under perfect BSA given a group of randomly selected observations, one from each category of Y . That is, suppose the ordinal Y takes values $1 < \dots < L$. Let $\check{X}_{[l]}$ denote the randomly selected X given $Y = l$ ($l = 1, 2, \dots, L$). Denote the ranks of $\{\check{X}_{[1]}, \check{X}_{[2]}, \dots, \check{X}_{[L]}\}$ by $(R_{[1]}, R_{[2]}, \dots, R_{[L]})$. The BSA measure between X and Y (Peng et al. 2011) is defined as

$$\rho_{bsa}(X, Y) = 1 - \frac{E\{\sum_{l=1}^L (l - R_{[l]})^2\}}{E_{X \perp Y}\{\sum_{l=1}^L (l - R_{[l]})^2\}}, \quad (1)$$

where $E(\cdot)$ denotes the expectation and $E_{X \perp Y}(\cdot)$ denotes the expectation under the independence between X and Y . When X and Y are independent, $\rho_{bsa}(X, Y) = 0$. Peng et al.

(2011) showed that $E_{X \perp Y} \{ \sum_{l=1}^L (l - R_{[l]})^2 \}$ equals a constant $C_L \equiv (L^3 - L)/6$, and $-1 \leq \rho_{bsa}(X, Y) \leq 1$ with $\rho_{bsa}(X, Y) = 1$ (or -1) corresponding to the perfect broad sense agreement (disagreement) scenario. Peng et al. (2011) proposed a nonparametric estimator of $\rho_{bsa}(X, Y)$. They established the theoretical properties of their estimator, and develop the inference procedures for $\rho_{bsa}(X, Y)$ accordingly.

2.2. The Proposed Regression Framework for BSA measure

Let Z denote a vector of explanatory variables. The observed data consist of n random samples of (X, Y, Z) , denoted by $\{(X_i, Y_i, Z_i) : i = 1, 2, \dots, n\}$.

We first introduce the concept of covariate-adjusted broad sense agreement as the foundation of the proposed regression framework. Specifically, we define covariate-adjusted broad sense agreement (BSA) as

$$\rho_{bsa}(X, Y|Z) = 1 - \frac{E\{\sum_{l=1}^L (l - R_{[l]})^2 | Z\}}{E_{X \perp Y|Z}\{\sum_{l=1}^L (l - R_{[l]})^2 | Z\}}, \quad (2)$$

where $E(\cdot|Z)$ stands for the conditional expectation given Z and $E_{X \perp Y|Z}(\cdot|Z)$ stands for the conditional expectation given Z under the independence between X and Y given Z .

It is easy to interpret the covariate-adjusted BSA measure defined in (2). Intuitively, $\rho_{bsa}(X, Y|Z)$ may be viewed as the BSA measure for the subgroup with a common value of Z . Like its unadjusted counterpart $\rho_{bsa}(X, Y)$, $\rho_{bsa}(X, Y|Z)$ is a standardized measure satisfying $-1 \leq \rho_{bsa}(X, Y|Z) \leq 1$. A large magnitude of $\rho_{bsa}(X, Y|Z = z)$ would suggest a high feasibility of interpreting the continuous measurement X according to the ordinal scale Y for a subpopulation characterized by $Z = z$.

Based on the concept of covariate-adjusted BSA, a natural approach to formulating the regression framework for BSA is to specify $\rho_{bsa}(X, Y|Z)$ as a function of Z (i.e. regression function). That is, we assume

$$\rho_{bsa}(X, Y|Z=z) = m(z), \quad (3)$$

where $m(z)$ is a smooth regression function, the functional form of which is unspecified. Model (3) is a nonparametric model which allows for a robust and flexible investigation of the heterogeneity in BSA. Estimating the regression function $m(\cdot)$ can help reveal how the BSA between X and Y changes with Z . It can also provide a more precise measure to describe the alignment between X and Y with covariate Z taken into account.

Without loss of generality and for ease of presentation, hereafter we shall focus on the case where Z is a single continuous covariate. Accommodating discrete covariates in model (3) is equivalent to conducting stratified analysis with only continuous covariates. Extending our

proposals in Section 2.3 to incorporate multiple continuous covariates is quite straightforward and is remarked in Section 6.

3. Estimation and Inference

3.1. Estimation of the regression function

In the subsection, we propose a nonparametric estimator of $m(\cdot)$ based on an appropriate adaptation of kernel regression technique (Nadaraya 1965; Watson 1964) in the context of regressing BSA.

To apply the kernel regression technique to derive a nonparametric estimator of $m(\cdot)$, we first

note that $E_{X \perp Y|Z} \{ \sum_{l=1}^L (l - R_{[l]})^2 | Z \} = C_L$. This can be shown along the lines of Peng et al. (2011). Given this result, model (3) can be rewritten as

$$1 - \frac{E \{ \sum_{l=1}^L (l - R_{[l]})^2 | Z \}}{C_L} = m(z).$$

This means, to estimate $m(z)$, we only need to derive an estimator of

$E \{ \sum_{l=1}^L (l - R_{[l]})^2 | Z = z \}$. The involvement of the rank statistics $R_{[l]}$ ($l = 1, \dots, L$) in $E \{ \sum_{l=1}^L (l - R_{[l]})^2 | Z = z \}$ entails a comparison of multiple distributions, namely the distributions of X given $Y = l$ ($l = 1, \dots, L$) when $Z = z$. In the one-sample setting, Peng et al. (2011) adopted the stratified resampling idea and examined all possible groups of L observations of (X, Y) with distinct Y values. To generalize this strategy to the regression setting, we propose to further employ the idea of kernel regression, by which we borrow information from observations with covariate values close to $Z = z$ to construct an estimate for $m(z)$.

More specifically, let $\vec{S} = (1, 2, \dots, L)$. Without loss of generality, we first arrange the observed data as follows:

$$\left. \begin{array}{l} (Y_1=1, X_1, Z_1), \dots, (Y_{n_1}=1, X_{n_1}, Z_{n_1}), \\ (Y_{n_1+1}=2, X_{n_1+1}, Z_{n_1+1}), \dots, (Y_{n_1+n_2}=2, X_{n_1+n_2}, Z_{n_1+n_2}), \\ \vdots \quad \dots \quad \vdots \\ (Y_{\sum_{l=1}^{L-1} n_l+1}=L, X_{\sum_{l=1}^{L-1} n_l+1}, Z_{\sum_{l=1}^{L-1} n_l+1}), \dots, (Y_{\sum_{l=1}^L n_l}=L, X_{\sum_{l=1}^L n_l}, Z_{\sum_{l=1}^L n_l}) \end{array} \right\} \quad (4)$$

where n_l denotes the number of observations with $Y = l$ and $\sum_{l=1}^L n_l = n$. Define

$\tilde{X}_{s,t_s} = X_{\sum_{l=1}^{s-1} n_l + t_s}$, with $1 \leq t_s \leq n_s$ ($1 \leq s \leq L$). Let $\tilde{Z}_{s,t_s}$ denote the sample covariate associated with $\tilde{X}_{s,t_s}$. For $\vec{x} = (x_1, x_2, \dots, x_L)'$, we define $R(\vec{x}) = (\tau_{[1]}, \tau_{[2]}, \dots, \tau_{[L]})$ where

$r_{[l]} \equiv \sum_{j=1}^L I(x_{[l]} \geq x_{[j]})$ denotes the rank of x_l among $\{x_1, x_2, \dots, x_L\}$. We propose to estimate $E\{\sum_{l=1}^L (l - R_{[l]})^2 | Z = z\}$ by

$$G_{n,h_n}(z) = \frac{\sum_{j_1=1}^{n_1} \dots \sum_{j_L=1}^{n_L} \left\{ k_{h_n}(\tilde{Z}_{1,j_1} - z) \times \dots \times k_{h_n}(\tilde{Z}_{L,j_L} - z) \|\vec{S} - \vec{R}(\tilde{X}_{1,j_1}, \dots, \tilde{X}_{L,j_L})\|^2 \right\}}{\sum_{j_1=1}^{n_1} \dots \sum_{j_L=1}^{n_L} \left\{ k_{h_n}(\tilde{Z}_{1,j_1} - z) \times \dots \times k_{h_n}(\tilde{Z}_{L,j_L} - z) \right\}},$$

where $\|\cdot\|$ is Euclidean norm in $\mathcal{R}^L$, h is a smoothing parameter (bandwidth), and $k_h(z) = h_n^{-1} k(h_n^{-1} z)$. Here $k(\cdot)$ is a nonnegative symmetric continuous kernel function satisfying $\int \|k(z)\| dz < \infty$ and $\int k(z) dz = 1$. By the definition above, $G_{n,h_n}(z)$ may be viewed as a weighted average of random samples of $\|\vec{S} - \vec{R}(\tilde{X}_{1,j_1}, \dots, \tilde{X}_{L,j_L})\|^2$ with $Z \in [z - h_n, z + h_n]$. When bandwidth $h_n \rightarrow 0$ as n increases, we expect $G_{n,h_n}(z)$ approaches $E\{\sum_{l=1}^L (l - R_{[l]})^2 | Z = z\}$. An estimator of $m(z)$ is then given by

$$\hat{m}(z) = 1 - \frac{G_{n,h_n}(s)}{C_L}. \quad (5)$$

We can show that $\|\vec{S} - \vec{R}(\tilde{X}_{1,j_1}, \dots, \tilde{X}_{L,j_L})\|^2 \leq 2C_L$ (Peng et al. 2011), and therefore $-1 \leq \hat{m}(z) \leq 1$.

3.2. Asymptotic properties

We first introduce necessary notation and regularity conditions. Let $p_l = P(Y = l)$. Let $f_{(X,Z)|Y=l}(x, z)$ denote the conditional joint density of X and Z given $Y = l$. Likewise, we adopt notation taking the form $f_V(v)$ to denote the density function of random variable V . Let $\{(\check{X}_{[l]}, \check{Z}_{[l]})\}_{l=1}^n$ be independent pairs of random variables, where $(\check{X}_{[l]}, \check{Z}_{[l]})$ follows the joint density $f_{(X,Z)|Y=l}(x, z)$. Define $V_i = (X_i, Y_i, Z_i)^T$. Let $\sigma_n^2(z) = n \text{Var}[\xi_{n,1}(z, V_1)]$, where $\xi_{n,1}(z, V_1)$ is defined in (8) in Appendix A.

Define

$$m_*(z_1, z_2, \dots, z_L) = E \left[\sum_{l=1}^L (l - R_{[l]})^2 | \check{Z}_{[1]} = z_1, \check{Z}_{[2]} = z_2, \dots, \check{Z}_{[L]} = z_L \right].$$

By the definition of $\rho_{bsd}(X, Y | Z)$, under model (3), we have $m_*(z, z, \dots, z) = C_L \{1 - m(z)\}$.

We assume the following regularity conditions:

- C1** $p_l > 0$ for $l = 1, \dots, L$.
- C2** $\lim_{n \rightarrow \infty} h_n \rightarrow 0$ and $\lim_{n \rightarrow \infty} n h_n^L = \infty$.

- C3** $f_{Z[l]}(z)$, $l = 1, \dots, L$, are positive bounded continuous and have bounded continuous first and second order derivatives.
- C4** $m^*(z_1, z_2, \dots, z_L)$ is a bounded continuous function of $(z_1, z_2, \dots, z_L)$, which has bounded continuous first and second order partial derivatives.
- C5** $\lim_{n \rightarrow \infty} h_n^2 \sqrt{nh_n^L} = \lambda, 0 < \lambda < \infty$.
- C6** $\lim_{n \rightarrow \infty} \sigma_n(z) = \sigma(z) > 0$.

We establish the consistency and asymptotic normality of the proposed estimator $\hat{m}(z)$ in the following theorems:

Theorem 1—Under regularity conditions C1 – C4,

$$\hat{m}(z) \rightarrow_p m(z).$$

Theorem 2—Under the regularity conditions C1 – C6,

$$\sqrt{nh_n^L}[\hat{m}(z) - m(z)] + \lambda C_L^{-1} \left\{ \prod_{l=1}^L f_{Z[l]}(z) \right\}^{-1} B(z) \xrightarrow{d} N(0, \sigma^2(z)),$$

where $B(z)$ is defined in Appendix A (see Lemma 1).

To prove Theorems 1 and 2, the main idea is to approximate $\hat{m}(z)$ by a U-statistic, $\hat{m}^{[1]}(z)$ (defined in (7) in Appendix A). Using the U-statistic theory, and the standard arguments for kernel regression, we establish the consistency of $\hat{m}(z)$. For the asymptotic distribution of $\hat{m}(z)$, we derive the influence function of $\sqrt{nh_n^L}[\hat{m}(z) - m(z)]$ appropriately adjusting for the difference between $\hat{m}^{[1]}(z)$ and $\hat{m}(z)$. Detailed proofs for Theorems 1 and 2 are provided in Appendix A.

As suggested by one referee, one may improve the convergence rate of $\hat{m}(z)$ by imposing higher order smoothness assumptions on $m^*(\cdot)$ and $f_{Z[l]}(\cdot)$ and adopting a different bandwidth selection and higher order kernel. Such an asymptotic refinement is promising and merits further research

3.3. Bandwidth selection

How to select the smoothing parameter (bandwidth) h is an important practical problem. The typical strategy is to identify an objective function that measures the estimation performance with a given bandwidth and then select the bandwidth that produces the optimal objective function value. Compared to usual regression models, the design of the estimation performance objective function is less straightforward in the BSA regression setting. This is because the $\{R_{[1]}, \dots, R_{[L]}\}$ with $Z = z$ in (2) is not directly observable.

To assess the performance of a given bandwidth, we utilize the fact that $\rho_{bsa}(X, Y) = E\{\rho_{bsa}(X, Y | Z)\}$. By this fact, we first estimate the unadjusted BSA measure $\rho_{bsa}(X, Y)$ by $\hat{\rho}_{bsa}(X, Y)$ using Peng et al. (2011)'s method and then compare it with $\hat{m}_{**}(h) \equiv n^{-1} \sum_{i=1}^n \hat{m}(z_i)$. We choose h as

$$h_{opt} = \arg \min_h |\hat{\rho}(X, Y) - \hat{m}_{**}(h)|. \quad (6)$$

In practice, we suggest starting with an initial bandwidth h_0 , and then searching in a grid over the interval $[h_0/3, 3h_0]$ to find the optimal bandwidth h_{opt} defined in (6). Our recommended initial bandwidth is $h_0 = (\hat{\sigma}^2/n)^{1/L+4}$, where $\hat{\sigma}$ is the standard deviation estimate for $\hat{\rho}_{bsa}(X, Y)$ (Peng et al. 2011). Such a selection of h_0 is motivated by our results on the asymptotic mean-integrated-squared-error (AMISE) of $\hat{m}(\cdot)$. In Appendix B, we show that AMISE is minimized at a bandwidth, which has the same order as the h_0 described above.

3.4. Inference

Given the complicated analytic form of $\sigma^2(z)$, we propose to estimate the asymptotic variance of $\hat{m}(z)$ using the jackknife method. That is, let $\hat{m}^{-i}(z)$ denote the proposed estimator of $m(z)$ obtained from the data excluding (X_i, Y_i, Z_i) . The jackknife variance estimator of $\hat{m}(z)$ is given by

$$\hat{V}(\hat{m}(z)) = \frac{n-1}{n} \sum_{i=1}^n \left\{ \hat{m}^{-i}(z) - \frac{1}{n} \sum_{k=1}^n \hat{m}^{-k}(z) \right\}^2.$$

Normal approximation can be used to construct a confidence interval of $m(z)$. That is, we can construct a confidence interval of level $1 - \alpha$ as

$$\left[\hat{m}(z) - z_{1-\alpha/2} \sqrt{\hat{V}(\hat{m}(z))}, \hat{m}(z) + z_{1-\alpha/2} \sqrt{\hat{V}(\hat{m}(z))} \right],$$

where $z_{1-\alpha/2}$ denotes the $100(1 - \alpha/2)$ th percentile of $N(0, 1)$.

We also propose a hypothesis testing procedure to examine whether $m(z)$ is constant over z . This can help us understand whether the BSA of interest varies with its potential confounder. Specifically, let $z^{(1)}, z^{(2)}, \dots, z^{(d)}$ be distinct values of Z . We consider testing the following null hypothesis:

$$H_0: m(z^{(1)}) = m(z^{(2)}) = \dots = m(z^{(d)}).$$

To test H_0 , we construct a test statistic based on

$$D_{n,h_n} = \sqrt{nh_n^L} \begin{pmatrix} \hat{m}(z^{(2)}) - \hat{m}(z^{(1)}) \\ \hat{m}(z^{(3)}) - \hat{m}(z^{(1)}) \\ \vdots \\ \hat{m}(z^{(d)}) - \hat{m}(z^{(1)}) \end{pmatrix}.$$

Following the lines for proving Theorem 2, we can show that D_{n,h_n} converges to a multivariate Normal distribution, which has mean zero when H_0 holds. We may use bootstrap to approximate the limit distribution of D_{n,h_n} . Specially, letting $\hat{D}_b^*$ denote the estimate for D_{n,h_n} based on the b th bootstrap sample ($b = 1, \dots, B$), we may estimate the asymptotic variance of D_{n,h_n} by

$$\hat{\Sigma}_n = \frac{1}{B-1} \sum_{b=1}^B \left(\hat{D}_b^* - \frac{1}{B} \sum_{b=1}^B \hat{D}_b^* \right)^T \left(\hat{D}_b^* - \frac{1}{B} \sum_{b=1}^B \hat{D}_b^* \right).$$

Therefore, the proposed test statistic is $T_n = D_{n,h_n}^T \hat{\Sigma}_n^{-1} D_{n,h_n}$. We can show that under the null hypothesis H_0 , the limit distribution of T_n is χ_{d-1}^2 . Therefore, one can reject the null hypothesis when T_n is greater than the $100(1 - \alpha)$ th percentile of χ_{d-1}^2 .

4. Simulation Studies

We conducted simulation studies to assess the finite sample performance of the proposed methods. We considered two simulation setups. In both setups, we set $L = 3$ and generate Y from the multinomial distribution with probability $(1/3, 1/3, 1/3)$ and Z from a uniform distribution, $Unif(0, 1)$. In setup (I), we generated X given $Y = 1$ and $Z = z$ from $Unif(0, 1)$, X given $Y = 2$ and $Z = z$ from $Unif(1 - 0.5z, 1 + 0.5z)$, and X given $Y = 3$ and $Z = z$ from $Unif(1, 2)$. In setup (II), we generated X given $Y = 1$ and $Z = z$ from $Unif(0, 1)$, X given $Y = 2$ and $Z = z$ from $Unif(0.5, 1.5)$, and X given $Y = 3$ and $Z = z$ from $Unif(1, 2)$. By some algebraic manipulations, we can show that $m(z) = 1 - z/8$ under setup (I) and $m(z) = 0.875$ under setup (II).

We applied the proposed method to estimate $m(z)$ under both setup (I) and setup (II), adopting the Gaussian kernel (second order) function. The proposed bandwidth selection procedures based on (6) yielded bandwidths $h = 0.20$ and 0.15 for $n = 100$ and 200 , respectively. In Table 1, we present $\hat{m}(z)$ for $z = 0.1, 0.3, 0.5, 0.7$, and 0.9 , the corresponding empirical standard deviations, the average standard deviation estimates based on jackknife, and the empirical coverage probabilities of 95% confidence intervals based on 500 simulated datasets of size $n = 100$ and 200 . From Table 1, we see that $\hat{m}(z)$ is virtually unbiased. The estimated standard deviations based on the jackknife method agree well with the empirical standard deviations. The magnitude of the empirical standard deviations suggest pretty good estimation efficiency of $\hat{m}(z)$ with a sample size of 100. As expected, the standard deviations

decrease as the sample size increases. The 95% confidence intervals have coverage probabilities close to the nominal level.

We also examined the performance of the proposed test statistic for testing the constancy of the regression function $m(z)$ over z . For both setups, we let $z^{(1)} = 0.20$, $z^{(2)} = 0.40$, $z^{(3)} = 0.60$, and $z^{(4)} = 0.80$, which respectively are the 20th, 40th, 60th, and 80th quantile of Z . In Table 2, we report the empirical rejection rates of H_0 . Note that $m(z)$ is a constant function in setup (II). Therefore the empirical rejection rates under setup (II) correspond to the empirical sizes of the proposed test.

Results presented in Table 2 demonstrate satisfactory performance of the proposed constancy test for $m(z)$. In setup (II), the empirical sizes are pretty close to the nominal level, 0.05. Under setup (I), the empirical rejection rates are 41%, and 77% for $n = 100$ and 200, respectively. This result demonstrate good power of the proposed constancy test.

5. An Application to the Grady Trauma Study

The Grady Trauma Study is a cross-sectional study, originally designed to determine the relative contribution of genetic and trauma-related risk factors for posttraumatic stress disorder (PTSD) of a highly traumatized civilian urban population of low socioeconomic status, predominantly African-American men and women. Participants in this study were asked to complete a 17-item PTSD symptom scale self-report (PSS-SR) questionnaires, a self-report measure of PTSD symptoms, while waiting in the waiting rooms of primary care or obstetrical-gynecological clinics of Grady Memorial Hospital in Atlanta, Georgia, USA. Clinician Administered 17-item PTSD Scale (CAPS) (Foa and Tolin 2000; Foa et al. 1993)) were administered by trained clinicians for a subgroup of the study subjects who consented for more rigorous assessment of PTSD diagnosis. Clinical depression severity of the study participants was also measured by a 21-item self-report inventory measuring BDI (Beck et al. 1961).

A categorical diagnosis of PTSD based on CAPS (i.e. PTSD vs. No PTSD) is the best available psychiatric diagnosis of PTSD. However, administering CAPS is timeconsuming and requires specially trained personnel. Therefore, it is practically appealing to investigate how the simpler and less costly self-measured PSS scores can serve as a potential surrogate of CAPS, while taking into account subject characteristics measured in this study. One characteristic of particular interest is the depression severity measured by total BDI scores. This is because PTSD often comorbid with major depressive disorder (MDD) (Breslau, Davis, Andreski, and Peterson 1991; Kessler et al. 1995, 2005). As a result, PTSD patients can present highly variable phenotypes in the domain of depression. For example, the BDI scores in our dataset range from 0 to 48, reflecting a wide range of depression severity from no or little depression symptoms to severe depression symptoms. Adjusting for the population heterogeneity captured by BDI scores when assessing the alignment between CAPS and PSS would lead to a refined view regarding the utility of PSS as a potential surrogate of CAPS.

Motivated by these considerations, we performed analyses to assess the BSA between the ordinal PTSD diagnosis based on CAPS and the continuous PSS score and how it varies by the total BDI score. Our analyses included 956 subjects of the Grady Trauma Study who had complete information on the CAPS diagnosis (PTSD vs. no PTSD), PSS total scores (0–51), and total BDI scores (0–63). Without adjusting for BDI scores, the estimated BSA between CAPS diagnosis and PSS score is 0.617 with standard error, 0.034, and the 95% confidence interval, (0.550, 0.684).

To explore how the BSA between CAPS diagnosis and BDI may change with BDI score, we first calculated BSA estimates separately for four subject groups defined by the BDI score (i.e. $0 \leq \text{BDI} < 10$, $10 \leq \text{BDI} < 20$, $20 \leq \text{BDI} < 30$, $\text{BDI} \geq 30$). In Figure 1, we depict the BSA estimates and the corresponding 95% confidence intervals for these four BDI groups. It is shown that the estimated BSA between CAPS based diagnosis and PSS score is pretty high for the group with low BDI score (i.e. $0 \leq \text{BDI} < 10$), around 0.63, while the BSA estimates are much lower for the high BDI groups. For example, for the group with BDI score between 20 and 30, the estimated BSA is only around 0.25.

We applied the proposed nonparametric regression method to investigate how the BSA between CAPS diagnosis and PSS changes with BDI score. In Figure 2, we plot the estimates for $m(z)$ with $z = 0, 1, \dots, 40$, along with the corresponding 95% confidence intervals. The bandwidth selected by the proposed procedure is $h = 6$ in this example. Figure 2 demonstrates an overall decreasing trend of the BSA as the BDI score increases, which is consistent with the exploratory analysis in Figure 1. In Table 3, we also present the estimates for $m(z)$ with $z = 1, 5, 10, 15, 25, 40$ and the corresponding standard errors and 95% confidence intervals. Both Figure 2 and Table 3 suggest considerable misalignment (or discrepancies) between CAPS diagnosis and PSS scores in subjects with severe depression symptoms. Some confirmatory descriptive data are also provided in Figure 3, which presents the boxplots of PSS scores separately for subjects diagnosed with PTSD and without PTSD (based on CAPS), stratified by BDI scores. It is shown that subjects with severe depression symptoms (e.g. $\text{BDI} \geq 30$) have quite similar self-reported PSS between the group with PTSD diagnosis and the group without PTSD diagnosis. This suggests that PSS is much less indicative of CAPS diagnosis for subjects with severe depression symptoms than those with low depression symptoms. This interesting finding cannot be revealed by unadjusted BSA analysis.

We also applied our proposals in Section 3.4 to evaluate whether the BSA of interest is constant over BDI score. We set $z^{(1)}$, $z^{(2)}$, $z^{(3)}$ and $z^{(4)}$ as the 20th, 40th, 60th, and 80th percentiles of the observed BDI scores, which are 4, 8, 14, and 22 respectively. We obtained the test statistic $T_n = 7.99$, which yields the p -value = 0.046. This result suggests that the BSA between CAPS diagnosis and PSS may change with BDI score. A practical implication is that PSS may serve as a reasonable surrogate for CAPS in PTSD patients with low depression symptoms. However, PSS and CAPS diagnosis can be poorly aligned in subjects with severe depression. These findings provide a much more refined view regarding the relationship between CAPS and PSS, as compared to those from a simple one-sample study of BSA.

6. Concluding Remarks

In this article we proposed a nonparametric regression method for broad sense agreement (BSA). We adapted the kernel regression technique in the context of BSA and provided thorough justifications for our proposals. The new method provides a robust tool for exploring population heterogeneity in the correspondence between an ordinal measurement and a continuous measurement, which may shed useful scientific insight.

For ease of presentation, we present the new BSA regression framework in the case with one single continuous covariate. Our proposals can be readily generalized to situations with multiple continuous covariates, for example, by adopting a multivariate product kernel function. When dealing with multiple covariates, the new method, given its modeling flexibility, may demand a large sample size to attain reasonably accurate estimation. A promising practical use of the proposed method is to explore an appropriate functional form of a continuous covariate's effect on the BSA of interest. The resulting findings may help guide the development of a more restrictive regression model for BSA that offers better interpretability and estimation efficiency.

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Appendix A: Asymptotic Proofs

Notation

Define $\check{V}_{[l]} = (\check{X}_{[l]}, \check{Y}_{[l]} = I, \check{Z}_{[l]})^T$. Let $\check{\mathbf{X}} = (\check{X}_{[1]}, \check{X}_{[2]}, \dots, \check{X}_{[L]})^T$, $\check{\mathbf{Z}} = (\check{Z}_{[1]}, \check{Z}_{[2]}, \dots, \check{Z}_{[L]})^T$, and $\check{\mathbf{z}} = (\check{z}_{[1]}, \dots, \check{z}_{[L]})^T$. Then $f_{\mathbf{z}}(\check{\mathbf{z}}) = \prod_{l=1}^L \{f_{\check{z}_{[l]}}(\check{z}_{[l]})\}$. Note that $R_{[l]} = \sum_{j=1}^L I(\check{X}_{[l]} \geq \check{X}_{[j]})$. Let Θ_L denote the sample space of $\vec{R} = (R_{[1]}, \dots, R_{[L]})$ which consists of $L!$ permutations of $\{1, 2, \dots, L\}$ and $\Omega_{n,L} = \{(j_1, j_2, \dots, j_L) : 1 \leq j_l \leq n, j_1, \dots, j_L \text{ are all distinct}\}$. Let $\gamma_L = 1/(L!C_L)$.

Let $H_f(\cdot)$ denotes the hessian of function f , and

$$\nu_2 = \begin{pmatrix} \int u_1^2 k(u_1) du_1 & 0 & \dots & 0 \\ 0 & \int u_1^2 k(u_2) du_2 & \dots & 0 \\ \vdots & \vdots & \dots & \vdots \\ 0 & 0 & \dots & \int u_L^2 k(u_L) du_L \end{pmatrix}.$$

For $(m_1, \dots, m_L) \in \Omega_{n,L}$, define

$$\begin{aligned} \psi_{h_n}(z, V_{m_1}, \dots, V_{m_L}) &= I\{(Y_{m_1}, \dots, Y_{m_L}) \in \Theta_L\} \times \\ &\quad \left[\{k_{h_n}(Z_{m_1} - z) \times \dots \times k_{h_n}(Z_{m_L} - z)\} \times \sum_{l'=1}^L \{Y_{m_{l'}} - \sum_{r=1}^L I(X_{m_{l'}} \geq X_{m_r})\}^2 \right], \\ \phi_{h_n}(z, V_{m_1}, \dots, V_{m_L}) &= [I\{(Y_{m_1}, \dots, Y_{m_L}) \in \Theta_L\} \{k_{h_n}(Z_{m_1} - z) \times \dots \times k_{h_n}(Z_{m_L} - z)\}], \end{aligned}$$

and

$$g(z, V_1, \dots, V_L) = 1 - \psi_{h_n}(z, V_1, \dots, V_L) \gamma_L \left[\prod_{l=1}^L \{f_{\tilde{z}_{[l]}}(z)\} \right]^{-1} \left(\prod_{l=1}^L p_l \right)^{-1}.$$

Define $W_{h_n}(z) = \sum_{(m_1, \dots, m_L) \in \Omega_{n,L}} [\phi_{h_n}(z, V_{m_1}, \dots, V_{m_L})]$,

$$M_{n,L}(z) = \frac{\binom{n}{L}}{W_{h_n}(z) C_L}, T_{n,h_n} = W_{h_n}(z) / \binom{n}{L},$$

$$\hat{m}^{[1]}(z) = \binom{n}{L}^{-1} \sum_{(m_1, \dots, m_L) \in \Omega_{n,L}} [g(z, V_{m_1}, \dots, V_{m_L})], \quad (7)$$

and

$$\hat{m}^{[2]}(z) = \left\{ \binom{n}{L}^{-1} \sum_{(m_1, \dots, m_L) \in \Omega_{n,L}} \psi_{h_n}(z, V_{m_1}, \dots, V_{m_L}) \right\} \times \left[M_{n,L}(z) - \frac{\gamma_L}{\left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\} \left(\prod_{l=1}^L p_l \right)} \right].$$

In addition, let $g_1(z, v_1) = E[g(z, v_1, V_2, \dots, V_L)]$, $\zeta_{h_n,1}(z) = \text{Var}[g_1(z, V_1)]$, $\tilde{g}_1(z, V_1) = g_1(z, V_1) - E[g(z, V_1, V_2, \dots, V_L)]$ and $\phi_{1,h_n}(z, v_1) = E[\phi_{h_n}(z, v_1, V_2, \dots, V_L)]$, and $\tilde{\phi}_{1,h_n}(z, V_1) = \phi_{1,h_n}(z, V_1) - E[\phi_{h_n}(z, V_1, \dots, V_L)]$.

Technical Lemmas and Proofs

Lemma 1

Under conditions C2 – C4,

$$E[\psi_{h_n}(z, V_1, \dots, V_L)] = a_L(z) + h_n^2 L! \left(\prod_{l=1}^L p_l \right) B(z) + O(h_n^3),$$

where $a_L(z) = L! \left(\prod_{l=1}^L p_l \right) \left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\} C_L \{1 - m(z)\}$ and

$B(z) = B_1(z) + \frac{1}{2} \left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\} B_2(z) + \frac{1}{2} m_*(\mathbf{z}) B_3(z)$ with $B_1(z) = [\nabla m_*(\mathbf{z})]^T \mathbf{v}_2 \nabla f_{\tilde{\mathbf{z}}}(\mathbf{z})$, $B_2(z) = \text{trace}\{H_{m^*}(\mathbf{z}) \mathbf{v}_2\}$, and $B_3(z) = \text{trace}\{H_{f_{\tilde{\mathbf{z}}}}(\mathbf{z}) \mathbf{v}_2\}$.

Proof of Lemma 1—First, we have

$$\begin{aligned}
& E[\psi_{h_n}(z, V_1, \dots, V_L)] \\
&= E\left[I\{(Y_1, \dots, Y_L) \in \Theta_L\} \times \{k_{h_n}(Z_1 - z) \times \dots \times k_{h_n}(Z_L - z)\} \times \right. \\
&\quad \left. \left\{ \sum_{l'=1}^L \{Y_{l'} - \sum_{r=1}^L I(X_{l'} \geq X_r)\}^2 \right\} \right] \\
&= P\{(Y_1, \dots, Y_L) \in \Theta_L\} \times E\left[\{k_{h_n}(Z_1 - z) \times \dots \times k_{h_n}(Z_L - z)\} \times \right. \\
&\quad \left. \left\{ \sum_{l'=1}^L \{Y_{l'} - \sum_{r=1}^L I(X_{l'} \geq X_r)\}^2 \right\} \mid (Y_1, \dots, Y_L) \in \Theta_L\right] \\
&= L! \left(\prod_{l=1}^L p_l \right) E\left[\{k_{h_n}(Z_1 - z) \times \dots \times k_{h_n}(Z_L - z)\} \times \right. \\
&\quad \left. \left\{ \sum_{l'=1}^L \{Y_{l'} - \sum_{r=1}^L I(X_{l'} \geq X_r)\}^2 \right\} \mid Y_1=1, \dots, Y_L=L\right].
\end{aligned}$$

By the definition of $(\check{Z}_{[1]}, \check{Z}_{[2]}, \dots, \check{Z}_{[L]})^T$, the conditional distribution of $(Z_1, \dots, Z_L)^T$ given $(Y_1 = 1, \dots, Y_L = L)$ is the same as the distribution of $(\check{Z}_{[1]}, \dots, \check{Z}_{[L]})^T$. Therefore,

$$\begin{aligned}
& E[\psi_{h_n}(z, V_1, \dots, V_L)] \\
&= L! \left(\prod_{l=1}^L p_l \right) \times E\left[\{k_{h_n}(\check{Z}_{[1]} - z) \times \dots \times k_{h_n}(\check{Z}_{[L]} - z)\} \times \sum_{l=1}^L \{l - \sum_{r=1}^L I(\check{X}_{[l]} \geq \check{X}_{[r]})\}^2\right] \\
&= L! \left(\prod_{l=1}^L p_l \right) \times E\left[\{k_{h_n}(\check{Z}_{[1]} - z) \times \dots \times k_{h_n}(\check{Z}_{[L]} - z)\} \times \sum_{l=1}^L (l - R_{[l]})^2\right] \\
&= L! \left(\prod_{l=1}^L p_l \right) \times E\left[\{k_{h_n}(\check{Z}_{[1]} - z) \times \dots \times k_{h_n}(\check{Z}_{[L]} - z)\} \times E\left\{\sum_{l=1}^L (l - R_{[l]})^2 \mid \check{Z}_{[1]}, \dots, \check{Z}_{[L]}\right\}\right] \\
&= L! \left(\prod_{l=1}^L p_l \right) \times E\left[\{(1/h_n)k((\check{Z}_{[1]} - z)/h_n) \times \dots \times (1/h_n)k((\check{Z}_{[L]} - z)/h_n)\} \times m_*(\check{Z}_{[1]}, \dots, \check{Z}_{[L]})\right].
\end{aligned}$$

For $j = 1, 2, \dots, L$, let $(\check{Z}_{[j]} - z)/h_n = u_j$ and $\mathbf{u} = (u_1, \dots, u_L)^T$. Applying the Taylor expansion in the neighborhood of $\mathbf{z} = (\check{Z}_1 = z, \dots, \check{Z}_L = z)^T$, we obtain

$$\begin{aligned}
& E[\psi_{h_n}(z, V_1, \dots, V_L)] \\
&= L! \left(\prod_{l=1}^L p_l \right) \times \int \{k(u_1) \times \dots \times k(u_L)\} \times m_*(\mathbf{z} + h_n \mathbf{u}) f_{\mathbf{z}}(\mathbf{z} + h_n \mathbf{u}) du_1 \dots du_L \\
&= L! \left(\prod_{l=1}^L p_l \right) \times \int \{k(u_1) \times \dots \times k(u_L)\} \\
&\quad \times \left\{ m_*(\mathbf{z}) + h_n \mathbf{u}^T \nabla m_*(\check{\mathbf{z}})|_{\check{\mathbf{z}}=\mathbf{z}} + \frac{h_n^2}{2} \mathbf{u}^T H_{m_*}(\check{\mathbf{z}})|_{\check{\mathbf{z}}=\mathbf{z}} \mathbf{u} + O(h_n^3) \right\} \\
&\quad \times \left\{ f_{\check{\mathbf{z}}}(\mathbf{z}) + h_n \mathbf{u}^T \nabla f_{\check{\mathbf{z}}}(\check{\mathbf{z}})|_{\check{\mathbf{z}}=\mathbf{z}} + \frac{h_n^2}{2} \mathbf{u}^T H_{f_{\check{\mathbf{z}}}}(\check{\mathbf{z}})|_{\check{\mathbf{z}}=\mathbf{z}} \mathbf{u} + O(h_n^3) \right\} du_1 \dots du_L \\
&= L! \left(\prod_{l=1}^L p_l \right) \{m_*(\mathbf{z}) f_{\check{\mathbf{z}}}(\mathbf{z})\} \\
&+ L! \left(\prod_{l=1}^L p_l \right) h_n^2 \int [\nabla m_*(\mathbf{z})]^T \mathbf{u} \mathbf{u}^T [\nabla f_{\check{\mathbf{z}}}(\mathbf{z})] \{k(u_1) \times \dots \times k(u_L)\} du_1 \dots du_L \\
&+ L! \left(\prod_{l=1}^L p_l \right) \frac{h_n^2}{2} f_{\check{\mathbf{z}}}(\mathbf{z}) \int \mathbf{u}^T H_{m_*}(\mathbf{z}) \mathbf{u} \{k(u_1) \times \dots \times k(u_L)\} du_1 \dots du_L \\
&+ L! \left(\prod_{l=1}^L p_l \right) \frac{h_n^2}{2} m_*(\mathbf{z}) \int \mathbf{u}^T H_{f_{\check{\mathbf{z}}}}(\mathbf{z}) \mathbf{u} \{k(u_1) \times \dots \times k(u_L)\} du_1 \dots du_L + O(h_n^3)
\end{aligned}$$

Since $\int k(u) du_l = 1$ and $\int u_l k(u) du_l = 0$, for $l = 1, 2, \dots, L$, we have

$$\int \dots \int u_1 u_2 \{k(u_1) \times \dots \times k(u_L)\} du_1 du_2 \dots du_L = \int u_1 k(u_1) du_1 \times \int u_2 k(u_2) du_2 = 0$$

and

$$\int u_1^2 \{k(u_1) \times \dots \times k(u_L)\} du_1 du_2 \dots du_L = \int u_1^2 k(u_1) du_1.$$

These results lead to further simplification of $E[\psi_{h_n}(z, V_1, \dots, V_L)]$ after standard algebraic manipulations:

$$\begin{aligned}
& E[\psi_{h_n}(z, V_1, \dots, V_L)] \\
&= L! \left(\prod_{l=1}^L p_l \right) \left[C_L \{1 - m(z)\} \left\{ \prod_{l=1}^L f_{\check{\mathbf{z}}_{[l]}}(z) \right\} \right] \\
&+ h_n^2 L! \left(\prod_{l=1}^L p_l \right) \left[B_1(z) + \frac{1}{2} B_2(z) \left\{ \prod_{l=1}^L f_{\check{\mathbf{z}}_{[l]}}(z) \right\} + \frac{1}{2} m_*(\mathbf{z}) B_3(z) \right] + O(h_n^3).
\end{aligned}$$

Therefore, $E[\psi_{h_n}(z, V_1, \dots, V_L)] = a_L(z) + h_n^2 L! \left(\prod_{l=1}^L p_l \right) B(z) + O(h_n^3)$.

Lemma 2

Under conditions C2 and C4,

$$E[\phi_{h_n}(z, V_1, \dots, V_L)] = L! \left(\prod_{l=1}^L p_l \right) \left\{ \prod_{l=1}^L f_{z_{[l]}}(z) \right\} + O(h_n^2).$$

Proof of Lemma 2—The proof is similar to that of Lemma 1, and is thus omitted.

Lemma 3

Under conditions $C1 - C3$,

$$Var[\hat{m}^{[1]}(z)] \leq \frac{L^2}{nh_n^L} \left[\frac{36(L-1)^2}{L!(L+1)^2} \left\{ \prod_{l=1}^L f_{z_{[l]}}(z) \right\}^{-1} \left(\prod_{l=1}^L p_l \right)^{-1} \kappa_L^2 \right] + o\left(\frac{1}{nh_n^L}\right),$$

where $\kappa_L^2 = \int k^2(u_1) \times \dots \times k^2(u_L) du_1 \times \dots \times du_L$.

Proof of Lemma 3—By condition $C1$ and $C3$, $h_n^L \hat{m}^{[1]}(z)$ is a U-statistic with bounded kernel function. Given condition $C2$, it follows from Theorem 3.4 (Hoeffding's Theorem) of Shao (2003) that

$$Var[\hat{m}^{[1]}(z)] = \frac{L^2}{n} \zeta_{h_n,1} + O\left(\frac{1}{n^2 h_n^{2L}}\right) = \frac{L^2}{n} \zeta_{h_n,1} + o\left(\frac{1}{nh_n^L}\right).$$

Evaluating $\zeta_{h_n,1}$ gives that

$$\begin{aligned}
 & \leq \text{Var} [g(z, V_1, \dots, V_L)] \quad [\zeta_{h_n,1} = \text{Var}[g_1(z, V_1)] \text{ [Corollary 3.2 (i) of Shao (2003)}] \\
 & = \left[\gamma_L f_{\mathbf{z}}^{-1}(\mathbf{z}) \left(\prod_{l=1}^L p_l \right)^{-1} \right]^2 \text{Var} [\psi_{h_n}(z, V_1, \dots, V_L)] \\
 & \leq \left[\gamma_L f_{\mathbf{z}}^{-1}(\mathbf{z}) \left(\prod_{l=1}^L p_l \right)^{-1} \right]^2 E [\psi_{h_n}(z, V_1, \dots, V_L)]^2 \\
 & = L! \left(\prod_{l=1}^L p_l \right) \left[\gamma_L f_{\mathbf{z}}^{-1}(\mathbf{z}) \left(\prod_{l=1}^L p_l \right)^{-1} \right]^2 \\
 & \quad \times E \left[\{k_{h_n}(\check{Z}_{[1]} - z) \times \dots \times k_{h_n}(\check{Z}_{[L]} - z)\}^2 \times \left\{ \sum_{l=1}^L \{l - R_{[l]}\}^2 \right\}^2 \right] \\
 & \leq \left[\frac{1}{L! C_L^2} f_{\mathbf{z}}^{-2}(\mathbf{z}) \left(\prod_{l=1}^L p_l \right)^{-1} \right] \{L^2(L-1)^4\} E [\{k_{h_n}(\check{Z}_{[1]} - z) \times \dots \times k_{h_n}(\check{Z}_{[L]} - z)\}^2] \\
 & = \left[\frac{1}{L! C_L^2} f_{\mathbf{z}}^{-2}(\mathbf{z}) \left(\prod_{l=1}^L p_l \right)^{-1} \{L^2(L-1)^4\} \right] \times \frac{1}{h_n^L} \{f_{\mathbf{z}}(\mathbf{z}) \kappa_L^2 + O(h_n^2)\} \\
 & = \frac{1}{h_n^L} \left[\frac{1}{L! C_L^2} f_{\mathbf{z}}^{-1}(\mathbf{z}) \left(\prod_{l=1}^L p_l \right)^{-1} \kappa_L^2 \{L^2(L-1)^4\} \right] + O\left(\frac{h_n^2}{h_n^L}\right) \\
 & = \frac{1}{h_n^L} \left[\frac{36(L-1)^2}{L!(L+1)^2} f_{\mathbf{z}}^{-1}(\mathbf{z}) \left(\prod_{l=1}^L p_l \right)^{-1} \kappa_L^2 \right] + O\left(\frac{h_n^2}{h_n^L}\right),
 \end{aligned}$$

where $\kappa_L^2 = \int k^2(u_1) \times \dots \times k^2(u_L) du_1 \times \dots \times du_L$. Therefore, we have

$$\begin{aligned}
 \text{Var} [\hat{m}^{[1]}(z)] & \leq \frac{L^2}{n} \left\{ \frac{1}{h_n^L} \left[\frac{36(L-1)^2}{L!(L+1)^2} \left\{ \prod_{l=1}^L f_{\check{Z}_{[l]}}(z) \right\}^{-1} \left(\prod_{l=1}^L p_l \right)^{-1} \kappa_L^2 \right] + O\left(\frac{h_n}{h_n^L}\right) \right\} + o\left(\frac{1}{nh_n^L}\right) \\
 & = \frac{L^2}{nh_n^L} \left[\frac{36(L-1)^2}{L!(L+1)^2} \left\{ \prod_{l=1}^L f_{\check{Z}_{[l]}}(z) \right\}^{-1} \left(\prod_{l=1}^L p_l \right)^{-1} \kappa_L^2 \right] + o\left(\frac{1}{nh_n^L}\right).
 \end{aligned}$$

Lemma 4

Under conditions C1 – C5,

$$\sqrt{nh_n^L} [\hat{m}(z) - m(z)] = \sum_{i=1}^n \xi_{n,i}(z, V_i) - h_n^2 \sqrt{nh_n^L} C_L^{-1} \left\{ \prod_{l=1}^L f_{\check{Z}_{[l]}}(z) \right\}^{-1} B(z) + o_p(1),$$

where

$$\xi_{n,i}(z, V_i) = L\tilde{g}_1(z, V_i) \sqrt{h_n^L/n} + \frac{La_L(z)}{C_L \left[\left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\}^L \left(\prod_{l=1}^L p_l \right) \right]^2} \tilde{\phi}_{1,h_n}(z, V_i) \sqrt{h_n^L/n}.$$

(8)

Proof of Lemma 4—To prove the Lemma 4, we use the projection method to derive the influence function of $\sqrt{nh_n^L} [\hat{m}^{[1]}(z) - m(z)]$ and that of $\sqrt{nh_n^L} \cdot \hat{m}^{[2]}(z)$.

Let $\tilde{m}^{[1]}(z)$ denote the projection of U-statistic $\hat{m}^{[1]}(z)$ on the random vectors $V_1, \dots, V_n$ and is defined by (cf. definition 3.3 of Shao (2003))

$$\tilde{m}^{[1]}(z) = E \left[\hat{m}^{[1]}(z) \right] + \sum_{i=1}^n \left[E \{ \hat{m}^{[1]}(z | V_i) \} - E \{ \hat{m}^{[1]}(z) \} \right].$$

Note that $E [\hat{m}^{[1]}(z)] = 1 - \gamma_L \left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\}^{-1} \left(\prod_{l=1}^L p_l \right)^{-1} E [\psi_{h_n}(z, V_1, \dots, V_L)]$.

Using the result from the Lemma 1, we obtain

$$E [\hat{m}^{[1]}(z)] = E [g(z, V_1, \dots, V_L)] = m(z) - h_n^2 C_L^{-1} \left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\}^{-1} B(z) + O(h_n^2). \quad (9)$$

Therefore, $E [\tilde{m}^{[1]}(z)] = E [\hat{m}^{[1]}(z)] = m(z) - h_n^2 C_L^{-1} \left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\}^{-1} B(z) + O(h_n^3)$. By some simple algebraic manipulation (cf. equation 3.20 of Shao (2003)), we get

$\tilde{m}^{[1]}(z) = E [\hat{m}^{[1]}(z)] + \frac{L}{n} \sum_{i=1}^n \tilde{g}_1(z, V_i)$, and hence $Var \{ \tilde{m}^{[1]}(z) \} = \frac{L^2}{n} \zeta_{h_n,1}(z)$. On the other hand, the arguments in the proof of Lemma 3 imply that $Var [\hat{m}^{[1]}(z)] = \frac{L^2}{n} \zeta_{h_n,1}(z) + o(\frac{1}{nh_n^L})$. It then follows that

$$E \{ \hat{m}^{[1]}(z) - \tilde{m}^{[1]}(z) \}^2 = Var \{ \hat{m}^{[1]}(z) \} - Var \{ \tilde{m}^{[1]}(z) \} = o\left(\frac{1}{nh_n^L}\right).$$

This, combined with (9), gives

$$\hat{m}^{[1]}(z) - m(z) = n^{-1} \sum_{i=1}^n L \tilde{g}_1(z, V_i) - h_n^2 C_L^{-1} \left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\}^{-1} B(z) + O(h_n^3) + o_p\left(\frac{1}{\sqrt{nh_n^L}}\right) \quad (10)$$

Applying similar arguments to $T_{n,h_n}(z)$ and using Lemma 2, we obtain

$$T_{n,h_n}(z) - L! \left(\prod_{l=1}^L p_l \right) \left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\} = \frac{L}{n} \sum_{i=1}^n \tilde{\phi}_{1,h_n}(z, V_i) + O(h_n^2) + o_p\left(\frac{1}{\sqrt{nh_n^L}}\right). \quad (11)$$

Note that

$$\begin{aligned} M_{n,L}(z) - \frac{\gamma_L}{\left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\} (\prod_{l=1}^L p_l)} &= \frac{\binom{n}{L}}{W_{h_n}(z) C_L} - \frac{\gamma_L}{\left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\} (\prod_{l=1}^L p_l)} \\ &= \frac{-C_L^{-1}}{\left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\} L! \left\{ \prod_{l=1}^L p_l \right\}} \frac{1}{\left\{ W_{h_n}(z) / \binom{n}{L} \right\}} \times \left[T_{h,h_n}(z) - L! \left(\prod_{l=1}^L p_l \right) \left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\} \right] \end{aligned} \quad (12)$$

Mimicking the lines in the proof of Lemma 3, we can show that

$$\text{Var}[W_{h_n}(z) / \binom{n}{L}] = O(1/nh_n^L). \text{ This, coupled with Lemma 2, implies that}$$

$$\frac{W_{h_n}(z)}{\binom{n}{L}} = L! \left(\prod_{l=1}^L p_l \right) \left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\} + O(h_n^2) + O_p\left(\frac{1}{\sqrt{nh_n^L}}\right) \quad (13)$$

By (10), (12), (13), and condition C2, we have

$$M_{n,L}(z) - \frac{\gamma_L}{\left\{ \prod_{l=1}^L f_{\dot{Z}_{[l]}}(z) \right\} (\prod_{l=1}^L p_l)} = - \frac{1}{C_L \left[L! (\prod_{l=1}^L p_l) \left\{ \prod_{l=1}^L f_{\dot{Z}_{[l]}}(z) \right\} \right]^2} \times \frac{1}{n} \sum_{i=1}^n L \tilde{\phi}_{1,h_n}(z, V_i) + O(h_n^2) + O_p\left(\frac{1}{\sqrt{nh_n^L}}\right). \quad (14)$$

In addition, given condition C2, Lemma 1 and Lemma 2 imply

$$\binom{n}{L}^{-1} \sum_{(m_1, \dots, m_L) \in \Omega_{n,L}} \psi_{h_n}(V_{m_1}, \dots, V_{m_L}) - a_L(z) = O_p\left(\frac{1}{\sqrt{nh_n^L}}\right). \quad (15)$$

By (14) and (15), we get

$$\hat{m}^{[2]}(z) = - \frac{1}{n} \sum_{i=1}^n \frac{L a_L \tilde{\phi}_{1,h_n}(z, V_i)}{C_L \left[L! (\prod_{l=1}^L p_l) \left\{ \prod_{l=1}^L f_{\dot{Z}_{[l]}}(z) \right\} \right]^2} + O(h_n^3) + O_p\left(\frac{1}{\sqrt{nh_n^L}}\right) \quad (16)$$

Given C2 and C5, it follows from (10) and (16) that

$$\begin{aligned} \sqrt{nh_n^L} \{\hat{m}(z) - m(z)\} &= \sqrt{nh_n^L} \cdot [\hat{m}^{[1]}(z) - m(z)] - \sqrt{nh_n^L} \cdot \hat{m}^{[2]}(z) \\ &= \sum_{i=1}^n \xi_{n,i} - h_n^2 \sqrt{nh_n^L} C_L^{-1} \left\{ \prod_{l=1}^L f_{\dot{Z}_{[l]}}(z) \right\}^{-1} B(z) + o_p(1). \end{aligned}$$

This completes the proof of Lemma 4.

Lemma 5

Under conditions C1 – C4,

$$\begin{aligned} E\{\xi_{n,1}(z, V_1)\}^2 &\leq 2L^2 \left[\frac{36(L-1)^2}{L!(L+1)^2} \left[\prod_{l=1}^L f_{\dot{Z}_{[l]}}(z) \right]^{-1} \left(\prod_{l=1}^L p_l \right)^{-1} \kappa_L^2 \right] + \\ &2 \left\{ \frac{L a_L(z)}{C_L \left[\left\{ \prod_{l=1}^L f_{\dot{Z}_{[l]}}(z) \right\} L! (\prod_{l=1}^L p_l) \right]^2} \right\}^2 L! \left(\prod_{l=1}^L p_l \right) \left[\prod_{l=1}^L f_{\dot{Z}_{[l]}}(z) \right]^{-1} \kappa_L^2 + O(h_n). \end{aligned}$$

Proof of Lemma 5—It is easy to see that $E\{\xi_{n,1}(z, V_1)\}^2$

$$\begin{aligned}
 &= E \left[L \tilde{g}_1(z, V_1) \sqrt{h_n^L} + \frac{L a_L(z)}{C_L \left[\left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\}^{L!} \left(\prod_{l=1}^L p_l \right) \right]^2} \tilde{\phi}_{1,h_n}(z, V_1) \sqrt{h_n^L} \right]^2 \\
 &\leq 2L^2 h_n^L E \{ \tilde{g}_1(z, V_1) \}^2 + 2h_n^L \left\{ \frac{L a_L(z)}{C_L \left[\left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\}^{L!} \left(\prod_{l=1}^L p_l \right) \right]^2} \right\}^2 E \{ \tilde{\phi}_{1,h_n}(z, V_1) \}^2
 \end{aligned}$$

Furthermore, following lines similar to those in the proof of Lemma 3, we get

$$\begin{aligned}
 E \{ \tilde{g}_1(z, V_1) \}^2 &= \text{Var}[g_1(z, V_1)] \leq \text{Var}[g(z, V_1, V_2, \dots, V_L)] \leq E[g(z, V_1, V_2, \dots, V_L)]^2 \\
 &\leq \frac{1}{h_n^L} \left[\frac{36(L-1)^2}{L!(L+1)^2} f_{\mathbf{Z}}^{-1}(\mathbf{z}) \left(\prod_{l=1}^L p_l \right)^{-1} \kappa_L^2 \right] + O(h_n^2)
 \end{aligned}$$

and

$$\begin{aligned}
 E \{ \tilde{\phi}_{1,h_n}(z, V_1) \}^2 &= \text{Var}[\phi_{1,h_n}(z, V_1)] \leq \text{Var}[\phi_{h_n}(z, V_1, \dots, V_L)] \leq E[\phi_{h_n}(z, V_1, \dots, V_L)]^2 \\
 &\leq \frac{1}{h_n^L} \left[L! \left(\prod_{l=1}^L p_l \right) f_{\mathbf{Z}}^{-1}(\mathbf{z}) \kappa_L^2 + O(h_n) \right],
 \end{aligned}$$

where κ_L is defined in Lemma 3. These results complete the proof of Lemma 5 and further imply that $E\{\xi_{n,h_n}(z, V_1)\}^2 < \infty$.

Proof of Theorems 1

First, we get from (13) that $M_{n,L}(z) - \frac{\gamma_L}{\left\{ \prod_{l=1}^L f_{\tilde{Z}_{[l]}}(z) \right\} \left(\prod_{l=1}^L p_l \right)} \rightarrow_p 0$. It then follows from (15) and an application of the Slutsky theorem that

$$\hat{m}^{[2]}(z) \rightarrow_p 0. \quad (17)$$

Next, by Lemma 3 and condition C2, we have $\text{Var}[\hat{m}^{[1]}(z)] \rightarrow 0$, which implies that $\hat{m}^{[1]}(z) - E[\hat{m}^{[1]}(z)] \rightarrow_p 0$. By (9), $E[\hat{m}^{[1]}(z)] = m(z) + O(h_n^2)$. Applying the Slutsky Theorem, we then obtain $\hat{m}^{[1]}(z) \rightarrow_p m(z)$. Combining this result with (17) leads to $\hat{m}(z) \rightarrow_p m(z)$.

Proof of Theorem 2

Since Lemma 5 implies that $E[\{\xi_{n,1}(z, V_1)\}^2] < \infty$, we can apply a variant of Lindeberg's Central Limit Theorem (i.e. Corollary 1.3 of Shao (2003)) to assess $\sum_{i=1}^n \xi_{n,i}(z, V_i)$. This, under condition C6, gives

$$\frac{\sum_{i=1}^n \xi_{n,i}(z, V_i)}{\sigma_n(z)} \xrightarrow{d} N(0, 1),$$

and consequently,

$$\sum_{i=1}^n \xi_{n,i}(z, V_i) \xrightarrow{d} N(0, \sigma^2(z)). \quad (18)$$

By the results of Lemma 4 and condition C5, we have

$$\sqrt{nh_n^L}[\hat{m}(z) - m(z)] = \sum_{i=1}^n \xi_{n,i}(z, V_i) - \lambda C_L^{-1} \left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\}^{-1} B(z) + o_p(1).$$

This, coupled with (18), immediately implies that

$$\sqrt{nh_n^L}[\hat{m}(z) - m(z)] + \lambda C_L^{-1} \left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\}^{-1} B(z) \xrightarrow{d} N(0, \sigma^2(z)).$$

Appendix B: Order of Asymptotically Optimal Bandwidth

An expression of asymptotic mean-squared-error (AMSE) of $\hat{m}(z)$, sum of leading term of bias squared and variance of $\hat{m}(z)$, follows from the Theorem 2 as given by

$$AMSE[\hat{m}(z)] \approx h^4 \left[C_L^{-1} \left\{ \prod_{l=1}^L f_{\tilde{z}_{[l]}}(z) \right\}^{-1} B(z) \right]^2 + \frac{\sigma^2(z)}{nh^L}.$$

AMSE is a pointwise measure of precision and a global measure of precision is the asymptotic mean-integrated-squared-error (AMISE) as defined by $AMISE = \int AMSE[\hat{m}(z)] dz$. Asymptotically optimal bandwidth of the kernel regression function is often obtained by minimizing the AMISE (Ruppert, Sheather, and Wand 1995). Note that $\frac{d}{dh} AMISE = 0$ implies that

$$h_{opt} = (L/A)^{1/L+4} [\int \sigma^2(z) dz]^{1/L+4} (1/n)^{1/L+4}, \quad (19)$$

where

$$A = 4C_L^{-2} \int \left[\left\{ \prod_{l=1}^L f_{\hat{z}_{[l]}}(z) \right\}^{-1} B(z) \right]^2 dz.$$

Thus, the optimal bandwidth h_{opt} is of order $O(\{\int \sigma^2(z) dz/n\}^{1/L+4})$. Motivated by this result, we propose to select the initial value for our bandwidth search as $h_0 = (\hat{\sigma}^2/n)^{1/L+4}$, where $\hat{\sigma}$ is the estimated standard deviation for unadjusted BSA estimate (Peng et al. 2011).

Figure 1.
Estimated BSA between PSS and CAPS diagnosis by BDI score and the corresponding 95% confidence intervals.

Figure 2.
Estimated regression function of BSA with respect to BDI score (solid line) and the corresponding pointwise 95% confidence intervals (dotted lines).

Figure 3.
Boxplots of PSS corresponding to CAPS diagnosis, stratified by BDI score.

Table 1

Simulation results on $\hat{m}(z)$: empirical biases (EmpBias), empirical standard deviation (EmpSD), estimated standard deviation (EstSD) and empirical coverage probabilities of 95% confidence interval (Cov95).

Setup	n	z	$m(z)$	EmpBias	EmpSD	EstSD	Cov95
(I)	100	0.1	0.988	0.011	0.015	0.015	0.93
		0.3	0.963	0.003	0.017	0.017	0.92
		0.5	0.938	0.001	0.021	0.022	0.94
		0.7	0.913	-0.003	0.026	0.027	0.92
		0.9	0.888	-0.013	0.034	0.037	0.89
	200	0.1	0.988	0.014	0.011	0.011	0.95
		0.3	0.963	0.003	0.012	0.013	0.97
		0.5	0.938	-0.002	0.015	0.017	0.96
		0.7	0.913	-0.006	0.017	0.021	0.97
		0.9	0.888	-0.012	0.021	0.028	0.93
(II)	100	0.1	0.875	0.000	0.038	0.040	0.94
		0.3	0.875	0.000	0.031	0.033	0.94
		0.5	0.875	0.000	0.030	0.031	0.95
		0.7	0.875	-0.001	0.031	0.032	0.94
		0.9	0.875	-0.001	0.037	0.040	0.94
	200	0.1	0.875	0.001	0.024	0.026	0.97
		0.3	0.875	0.000	0.020	0.022	0.95
		0.5	0.875	-0.003	0.021	0.021	0.95
		0.7	0.875	-0.001	0.021	0.022	0.96
		0.9	0.875	0.003	0.023	0.027	0.95

Table 2

Simulation results on empirical rejection rates of the constancy test.

Setup	Sample Size (n)	Rejection Rate
(I)	100	0.41
	200	0.77
(II)	100	0.04
	200	0.05

Table 3

PTSD example: point estimates for $m(z)$ ($z = 1, 5, 10, 15, 2$ with standard errors (SE) and 95% confidence intervals (CI)

z BDI	$m(z)$	SE	95% CI
1	0.62	0.073	(0.48, 0.76)
5	0.58	0.059	(0.46, 0.70)
10	0.54	0.052	(0.44, 0.64)
15	0.51	0.048	(0.42, 0.60)
25	0.40	0.060	(0.28, 0.52)
40	0.35	0.118	(0.12, 0.58)