

# The Population and Personalized Areas Under the Receiving Operating Characteristic Curve

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**ABSTRACT:** We consider two generalizations of the area under the receiving operating characteristic curve (“AUC”), a popular measure of discrimination, to accommodate clustered data. We describe situations in which the two cluster AUCs diverge and other situations in which they coincide. Differences are described using concrete models and visualizations, while quantitative results are used to relate the two generalizations. Procedures for joint estimation and inference are also presented, along with a simulation study. We apply the results to data collected on urban policing behavior.

**KEYWORDS:** AUC, Confounding, Clustered data, Simpson’s paradox

## 1 Introduction

The AUC is a widely used measure of how well a scalar predictor discriminates between two outcomes. As a population parameter, the AUC is the probability that the value of a randomly sampled predictor from one of the outcome classes is less than an independently sampled predictor from the other outcome class. There are several ways to generalize the AUC to accommodate clustered data. What we refer to as the “population AUC” appears to be the most commonly studied. The population AUC evaluates the predictor’s typical effect on an entire population, as further discussed below.

While the population AUC is an important part of understanding the usefulness of a predictor, the medical field has lately focused on personalizing treatment. For example, in 2018 the National Academy of Medicine concluded: “The individuality of the patient should be at the core of every treatment decision. One-size-fits-all approaches to treating medical conditions are inadequate; instead, treatments should be tailored to individuals based on heterogeneity of clinical characteristics and their personal preferences.”

We examine a “personalized AUC” in conjunction with the population AUC. These two evaluations may give different accounts of the usefulness of a marker. In the extreme case, the phenomenon known as Simpson’s paradox may occur: The personalized AUC may be nearly uninformative while the population AUC is nearly perfectly predictive, or vice versa. Modern accounts of Simpson’s paradox, working in the framework of causal inference,

delineate situations in which the personalized AUC is appropriate, and other situations in which the population AUC is appropriate.

Obuchowski (1997) proposes a nonparametric, asymptotic estimator for the variance of an estimator for the population AUC. We give an alternate derivation here. We also clarify the statistical model and target of inference. Rosner and Grove (1999) give a formula for the finite-sample variance under certain distributional assumptions. Lee and Dehling (2005) discuss the asymptotic behavior of generalized U-statistics with clustered data, a class which includes the estimator for the population AUC discussed in Obuchowski (1997) and below. Liu et al. (2005) suggest a bootstrap approach, provided the data follow a generalized linear model. Toledano (2003) summarizes techniques in use for analyzing clustered ROC curves. Pearl (2014) gives an overview of Simpson’s paradox, an effect illustrated by the examples in Section 3 below, from the standpoint of causal inference. Michael et al. (2019) analyzes population and personalized versions of the ROC curve which may, in principle, be used to obtain estimates of the population and personalized AUCs discussed here under certain distributional assumptions. The analysis here is nonparametric and further avoids the inefficiency introduced by first estimating the entire ROC curve, which may not be feasible for many smaller data sets.

The remainder of the article is as follows. In Section 2 we introduce the AUC and the two generalizations to clustered data considered here, the population and personalized AUCs. In Section 3 we discuss several examples of data-generating processes that highlight the differences between the two AUCs. In Section 4 we describe two results available under the assumption of independence between the cluster sizes and the values of the predictor of interest. In Section 5 we give the asymptotic joint distribution of estimators for the two AUCs. The performance of these estimators are then analyzed using synthetic data generated under two models in Section 6. In Section 7 with directions for future work. The Supplementary Material contains an application of the methods to data on urban policing.

## 2 Setting and Notation

Let  $\psi : \mathbb{R}^2 \rightarrow \mathbb{R}$  denote the function  $(x, y) \mapsto \{x < y\} + \frac{1}{2}\{x = y\}$ , using  $\{\cdot\}$  to denote the indicator function. Given independent draws  $X$  and  $Y$  from two distributions  $F_X$  and  $F_Y$ , the AUC is defined as

$$\theta = E(\psi(X, Y)) = P(X < Y) + \frac{1}{2}P(X = Y).$$

Given samples  $X_1, X_2, \dots, X_M$ , IID as  $F_X$  and  $Y_1, Y_2, \dots, Y_N$ , IID as  $F_Y$ , an unbiased estimator of the AUC of  $F_X$  and  $F_Y$  is

$$\frac{1}{MN} \sum_{i=1}^M \sum_{j=1}^N \psi(X_i, Y_j).$$

The function  $\psi$  is referred to as the “kernel.” The AUC is often used to evaluate how effectively the data distinguish the two distributions. The AUC is close to  $1/2$  when the distinction is poor, and equals  $1/2$  in the extreme case that  $F_X = F_Y$ . The AUC is close to

1 when the distinction is better. In the extreme, there is a number  $c \in \mathbb{R}$  such that always  $X < c$  and  $Y > c$ , and then  $\theta = 1$ . We informally refer to these two classes given by the two distributions as “control” and “case,” and the scalar predictor as “marker.” Switching the observations designated “control” and “case” reflects the AUC across  $1/2$ ,  $AUC \mapsto 1 - AUC$ , so  $|AUC - \frac{1}{2}|$  is often of greater interest than the AUC itself.

We extend the AUC to accommodate 1) vectors of case and control observations and 2) dependence between case and control observations. Examples of data of this type are:

1. The predictors are longitudinal measurements of tumor antigens (CEA, CA15-3, TPS), and the outcomes are progression or non-progression of breast cancer (Emir et al., 2000).
2. The predictors are longitudinal measurements of levels of vascular endothelial growth factor and a soluble fragment of Cytokeratin 19, and the outcomes are progression or non-progression of non-small cell lung cancer (Wu and Wang, 2011).
3. The predictors are longitudinal measurements of an HIV positive patient’s CD4 counts, and the outcome is “blip” status, a binary measurement representing a transient spike in viral load (Michael et al., 2019).

Let  $(X, Y, M, N)$  be a random vector with joint distribution  $P$  such that  $X$  and  $Y$  are sequences and  $M$  and  $N$  are counting numbers.

$$\begin{aligned} (X, Y, M, N) &\sim P \\ X &= (X_1, X_2, \dots) \in \mathbb{R}^{\mathbb{N}}, Y = (Y_1, Y_2, \dots) \in \mathbb{R}^{\mathbb{N}} \\ M, N &\in 1, 2, 3, \dots \end{aligned} \tag{1}$$

Informally, we regard  $X$  and  $Y$  as vectors of length  $M$  and  $N$ , ignoring the rest of the sequences. The formulation (1) lets us avoid working with vectors of variable length.

Extend the AUC kernel  $\psi(\cdot, \cdot)$  to vector arguments as

$$\psi(x, y) = \psi((x_1, \dots, x_m), (y_1, \dots, y_n)) = \sum_{i=1}^m \sum_{j=1}^n \left( \{x_i < y_j\} + \frac{1}{2} \{x_i = y_j\} \right). \tag{2}$$

We define the personalized AUC as

$$\theta_{11}(P) = E \left( \frac{\psi(X, Y)}{MN} \right). \tag{3}$$

With  $(X_1, Y_1, M_1, N_1)$  and  $(X_2, Y_2, M_2, N_2)$ , being two independent draws from  $P$ , we define the population AUC as

$$\begin{aligned} \theta_{12}(P) &= \frac{E\psi(X_1, Y_2)}{E(M_1)E(N_2)} \\ (X_1, Y_1, M_1, N_1), (X_2, Y_2, M_2, N_2) &\stackrel{\text{iid}}{\sim} P. \end{aligned} \tag{4}$$

The personalized AUC may be undefined if  $M$  or  $N$  can take the value 0 with positive probability, which is the reason for restricting them to counting numbers. The population

AUC may still be well-defined and when analyzed without regard to the personalized AUC the possibility of  $M = 0$  or  $N = 0$  may be allowed (Obuchowski, 1997). In applications where  $M = 0$  or  $N = 0$  is possible, our analysis is therefore conditional on  $M > 0, N > 0$ , a sub-population in which all clusters have at least 1 case and 1 control observation.

For estimation, suppose a sample is given,

$$(X_1, Y_1, M_1, N_1), \dots, (X_I, Y_I, M_I, N_I) \stackrel{\text{IID}}{\sim} P.$$

An unbiased estimator of  $\theta_{11}$  is

$$\hat{\theta}_{11} = \frac{1}{I} \sum_{i=1}^I \frac{\psi(X_i, Y_i)}{M_i N_i}.$$

A consistent estimator of  $\theta_{12}$  is

$$\hat{\theta}_{12} = \frac{\sum_i \sum_{i \neq j} \psi(X_i, Y_j)}{\sum_i M_i \sum_i N_i}. \quad (5)$$

Both the population and personalized AUC, like the usual AUC, are bounded between 0 and 1,  $\frac{1}{2}$  represents poor discrimination, and distance from  $\frac{1}{2}$  represents increasing discrimination. However, they describe distinct measures of discrimination. It is possible for one to be informative and therefore far from  $1/2$ , while the other is non-informative, or close to  $1/2$ . Whereas the personalized AUC is the average AUC of a typical cluster, the population AUC is, setting aside ties in the data, the probability that a typical control observation in the population is less than a typical case observation. The following proposition makes this description precise. The consistency of  $\hat{\theta}_{12}$  follows from Corollary 8.

**Proposition 1.** *1. Let  $(X_1, Y_1, M_1, N_1), \dots, (X_I, Y_I, M_I, N_I)$ , be a random sample of size  $I$  IID according to  $P$ . Let  $P_I$  be the joint distribution of independent random selections from among the elements of  $X_1, \dots, X_I$ , and  $Y_1, \dots, Y_I$ , and let  $(\xi_I, \eta_I) \sim P_I$ . Then  $\theta(P_I) = \Pr(\xi_I < \eta_I) + \frac{1}{2}\Pr(\xi_I = \eta_I) \rightarrow \theta_{12}(P)$  as  $I \rightarrow \infty$ .*

*2. Let  $(X_1, Y_1, M_1, N_1), \dots$ , be an infinite random sequence sampled IID according to  $P$ . Let  $P_\infty$  be the joint distribution of independent random selections from among the elements of  $X_1, \dots$ , and  $Y_1, \dots$ , and let  $(\xi_\infty, \eta_\infty) \sim P_\infty$ . Then  $\theta(P_\infty) = \Pr(\xi_\infty < \eta_\infty) + \frac{1}{2}\Pr(\xi_\infty = \eta_\infty) = \theta_{12}(P)$ .*

The definition of the population AUC (4) allows for dependence between  $(M, N)$  and  $(X, Y)$  in capturing a population-level AUC in the sense of Proposition 1. Practical reasons to avoid assuming  $(X, Y) \perp\!\!\!\perp (M, N)$  include informative censoring, imbalanced designs, and confounding by indication. As an alternative definition of the population AUC, consider

$$\theta'_{12} = E \left( \frac{\psi(X_1, Y_2)}{M_1 N_2} \right). \quad (6)$$

This parameter is formally a closer counterpart to the personalized AUC (3), but does not take into account different cluster sizes, with a small cluster contributing as much as a large

cluster. This estimator would not therefore represent discrimination at the population level, except in case  $(X, Y) \perp\!\!\!\perp (M, N)$ .

Similar to the population AUC estimator (5), Obuchowski (1997) presents the estimator

$$\frac{\sum_i \sum_j \psi(x_i, y_j)}{\sum_i m_i \sum_i n_i} = \hat{\theta}_{12} + \frac{\sum_i \psi(x_i, y_i)}{\sum_i m_i \sum_i n_i}. \quad (7)$$

This estimator may be obtained as  $\theta_{12}(P_I)$ , where  $P_I$  is the empirical distribution given a sample of size  $I$ . It differs from  $\hat{\theta}_{12}$  only in including the diagonal terms, an asymptotically negligible  $O(1/I)$  bias. The definition (4) was chosen in part as the probability limit of (7). Though Obuchowski (1997) does not enunciate a clear statistical model, the analysis of (7) rather than the simpler (6) perhaps suggests that Obuchowski (1997) too contemplates  $(X, Y) \not\perp\!\!\!\perp (M, N)$ .

The population AUC, which appears more prominently in past research, may lay a claim to being the more natural generalization of the usual AUC since it equals the usual AUC when  $M = N = 1$ . Below we argue that in general the population and personalized AUCs are both important, complementary tools in evaluating an estimator. In the other direction, we give inequalities that may be used in some situations to relate the two cluster AUCs.

## 3 Examples

### 3.1 Random effects model

We illustrate the population and personalized AUCs and their differences using a generic random effects model with a location shift parameter. We show that the location shift can be used to control the personalized AUC while separately the random effect can be used to control the population AUC.

Let the distribution of  $(X, Y, M, N)$  given  $M, N$  be

$$\begin{aligned} X \mid M, N &\sim Z(M, N) + \xi_i^x, i = 1, \dots, M \\ Y \mid M, N &\sim Z(M, N) + \xi_j^y + \Delta, j = 1, \dots, N \end{aligned} \quad (8)$$

Here,  $\Delta > 0$  is a non-random location shift between the control and case values,  $Z$  is a random, cluster-level effect, and  $\xi_i^x, \xi_j^y, i = 1, \dots, M, j = 1, \dots, N$ , are IID individual effects. The within-cluster dependence is induced by  $Z$ . The individual effects  $\xi_i^x, \xi_j^y$  are assumed to be independent of  $(M, N)$ , but  $Z$  is not assumed to be so. To keep things simple, we assume continuous densities are available, and so  $\psi(x, y) = \{x < y\}$ .

The personalized AUC is

$$\begin{aligned}
\theta_{11} &= E\left(\frac{\psi_{11}}{M_1 N_1}\right) = E\left(\frac{1}{M_1 N_1} \sum_{i=1}^{M_1} \sum_{j=1}^{N_1} \{X_{1i} < Y_{1j}\}\right) \\
&= E\left(\frac{1}{M_1 N_1} \sum_{i=1}^{M_1} \sum_{j=1}^{N_1} \{Z_1 + \xi_i^x < Z_1 + \xi_j^y + \Delta\}\right) \\
&= E\left(\frac{1}{M_1 N_1} \sum_{i=1}^{M_1} \sum_{j=1}^{N_1} P(\xi_i^x - \xi_j^y < \Delta \mid M_1, N_1)\right) \\
&= P(\xi_1 - \xi_2 < \Delta).
\end{aligned} \tag{9}$$

Lemma 9 was used to pull the conditional expectation inside the double sum.

The population AUC is

$$\begin{aligned}
\theta_{12} &= \frac{1}{E(M)E(N)} E\left(\sum_{i=1}^{M_1} \sum_{j=1}^{N_2} \{X_{1i} < Y_{2j}\}\right) \\
&= \frac{1}{E(M)E(N)} E\left(\sum_{i=1}^{M_1} \sum_{j=1}^{N_2} P(Z_1 + \xi_i^x < Z_2 + \xi_j^y + \Delta \mid M_1, N_1, M_2, N_2)\right) \\
&= \frac{1}{E(M)E(N)} E(M_1 N_2 P(Z_1 + \xi^x < Z_2 + \xi^y + \Delta \mid M_1, N_1, M_2, N_2)) \\
&= E\left(\frac{M_1 N_2}{E(M)E(N)} \{Z_1 - Z_2 + (\xi^x - \xi^y) < \Delta\}\right)
\end{aligned} \tag{10}$$

The last expression is a covariance-like term lying between 0 and 1.

### 3.1.1 Informative personalized AUC, uninformative population AUC

From (9),  $\theta_{11} \rightarrow 1$  as  $\Delta \rightarrow \infty$ .

Letting  $Z$  be independent of  $(M, N)$ ,  $\theta_{12} = P(Z_1 + \xi^x - (Z_2 + \xi^y) < \Delta)$ . As a difference of two IID random variables,  $Z_1 + \xi^x - (Z_2 + \xi^y)$  is symmetric about 0, and  $\theta_{12} = P(Z_1 + \xi^x - (Z_2 + \xi^y) < \Delta) = 1 - P(Z_1 + \xi^x - (Z_2 + \xi^y) \geq \Delta) = 1 - 1/2 P(|Z_1 + \xi^x - (Z_2 + \xi^y)| \geq \Delta)$ . As  $P(|Z_1 + \xi^x - (Z_2 + \xi^y)| \geq \Delta) \geq 1 - 2\Delta |f_{Z+\xi}|_\infty \geq 1 - 2\Delta |f_Z|_\infty$ , a sufficient condition for  $\theta_{12} \rightarrow 1/2$  is  $|f_Z|_\infty \rightarrow 0$ . For example, suppose  $Z$  belongs to a scale family,  $f_Z = f_{Z_0}(Z/\sqrt{\text{Var}(Z)})/\sqrt{\text{Var}(Z)}$  for a fixed density  $f_{Z_0}$ ,  $|f_{Z_0}|_\infty < \infty$ , and  $\text{Var}(Z) \rightarrow \infty$ .

Therefore, for  $\Delta = E(Y_{11}) - E(X_{11})$  large enough,  $\theta_{11}$  is arbitrarily close to 1, while for any fixed  $\Delta$ , for  $\text{Var}(Z)$  large enough,  $\theta_{12}$  approaches 1/2.

### 3.1.2 Informative population AUC, uninformative personalized AUC

From (9),  $\theta_{11} \rightarrow 1/2$  as  $\Delta \rightarrow 0$ ,  $\xi^x - \xi^y$  being symmetric about 0.

Let  $\Delta$  be fixed. The covariance-like term (10) approaches 1 when there is a large negative covariance between  $M, N$ , and  $Z_1 - Z_2$ , i.e., a large negative covariance between  $M$  and  $Z$  or large positive covariance between  $N$  and  $Z$ , or both.



Figure 1: Two visualizations contrasting the individual and population AUCs. Each gives rug plots of fifteen clusters of data, each cluster sampled IID according to a bivariate normal model, with the unclustered data combined at the bottom. Case observations are represented with “—” and control observations with “|”. On the left, the personalized AUC is informative and the population AUC uninformative. The reverse situation is presented on the right.

Figure 1 presents a simulation using gaussian data to demonstrate the discussed differences between the population and personalized AUCs. The normal model is an example of the random effects model (8) and is discussed further in Section 6. Though a large location shift can push the personalized AUC close to 1, large inter-cluster variance relative to intra-cluster variance keeps the population AUC uninformative. Similarly, if the number of case observations relative to control is positively associated with the observation values, the population AUC may approach 1 irrespective of the personalized AUC.

### 3.2 Binary response model

Models for case and control data are often given by specifying the status conditional on the marker, rather than vice versa as in Example 3.1. Let  $\sigma$  denote a monotone link such as the probit or logistic function. Fixing the cluster size  $M + N$ , let continuous cluster effects  $Z$ , continuous within-cluster effects  $\xi$ , and within-cluster status indicators  $D$  specify the

distribution of a cluster as follows:

$$\begin{aligned}
\vec{\xi} &= (\xi_1, \dots, \xi_{M+N}) \text{ IID} \\
Z &\perp\!\!\!\perp (\xi_1, \dots, \xi_{M+N}) \\
B_i &= Z + \xi_i, i = 1, \dots, M + N \\
D_i \mid \vec{Z}, \vec{\xi} &\sim \text{bernoulli with parameter } \sigma(\beta_0 Z + \beta_1 \xi_i), i = 1, \dots, M + N \\
M &= \sum_{i=1}^{M+N} (1 - D_i), \quad N = \sum_{i=1}^{M+N} D_i.
\end{aligned}$$

The control and case observations in a cluster,  $X_i$  and  $Y_i$ , are then those  $B_i$  such that  $D_i = 0$  and  $D_i = 1$ , respectively. Here the cluster allocations  $M$  and  $N$  and the markers  $\vec{B}$  are dependent, both being functions of  $Z$  and  $\vec{\xi}$ , though they are conditionally independent given the statuses  $\vec{D}$ .

Suppose first that  $\beta_0 > 0$  and  $\beta_1 = 0$ , so  $P(D_i = 1 \mid Z, \vec{\xi}) = \sigma(\beta_0 Z)$ . The population AUC is

$$\begin{aligned}
\theta_{12} &= \frac{1}{E(M)E(N)} E \left( \sum_{i=1}^{M+N} \sum_{j=1}^{M+N} \{B_{1i} < B_{2j}\} \{D_{1i} = 0\} \{D_{2j} = 1\} \right) \\
&= \frac{1}{E(M)E(N)} E \left( \sum_{i=1}^{M+N} \sum_{j=1}^{M+N} P(B_{1i} < B_{2j} \mid D_{1i} = 0, D_{2j} = 1) \{D_{1i} = 0\} \{D_{2j} = 1\} \right) \\
&= P(B_{11} < B_{21} \mid D_{11} = 0, D_{21} = 1) \\
&= P(Z_{11} - Z_{21} < \xi_{21} - \xi_{11} \mid D_{11} = 0, D_{21} = 1).
\end{aligned}$$

Since  $Z_{11} \mid D_{11} = 0$  is stochastically less than  $Z_{21} \mid D_{21} = 1$ , with the difference increasing in  $\beta_0$ , and since the  $\xi$ s are independent of the  $Z$ s and  $D$ s, the last line is  $> \frac{1}{2}$ , with the difference increasing in  $\beta_0$ .

On the other hand,  $\vec{\xi} \perp\!\!\!\perp (\vec{D}, M, N)$ , so

$$\begin{aligned}
\theta_{11} &= E \left( \frac{1}{MN} \sum_{i=1}^{M+N} \sum_{j=1}^{M+N} \{B_{1i} < B_{1j}\} \{D_{i1} = 0 \text{ and } D_{ij} = 1\} \mid M > 0, N > 0 \right) \\
&= E \left( \frac{1}{MN} \sum_{i=1}^{M+N} \sum_{j=1}^{M+N} \{\xi_{1i} < \xi_{1j}\} \{D_{i1} = 0 \text{ and } D_{ij} = 1\} \mid M > 0, N > 0 \right) \\
&= P(\xi_{11} < \xi_{12}) = 1/2.
\end{aligned}$$

Two possible instances of the model:

- (a) The cluster effect  $Z$  represents a genuine signal of disease status  $D$ , such as viral load does for HIV status, and  $\xi$  represents non-systematic measurement error on instruments measuring  $Z$ . In this case, the population AUC better matches expectations of an AUC measurement than the personalized AUC. The biomarker  $B$  isn't completely uninformative, as  $\theta_{11}$  suggests.



- (b) The cluster effect  $Z$  is a subject's dose of a possibly ineffective drug, and larger doses are administered to sicker patients. The subject-specific measurements  $\xi$  represent non-systematic measurement error again. Here the association between the marker and disease status implied by the population AUC is spurious, and may or may not be of value to the analyst. It is possible that the personalized AUC, which does not convey any association, is preferable.

Reversing the roles of the cluster-level effect  $Z$  and within-cluster effects  $\xi$ , suppose  $\beta_0 = 0$  and  $\beta_1 > 0$ , so that  $\theta_{12} \approx 1/2$  and  $\theta_{11} > 1/2$ . Two instances of this model:

- (c) The markers  $B$  are measurements on a patient,  $D$  indicates the presence of a disease that depends little or not at all on a baseline measure  $Z$  but is indicated by the deviations  $\xi$  from the baseline. As a second example, the markers  $B$  are post-test measurements on a population that has been stratified by pre-test measurement  $Z$ . The subject effects  $\xi_i = B_i - Z$  represent the difference between post-test and pre-test measurements, and the status indicators  $D$  represent an effective or ineffective intervention. Here the personalized AUC probably carries the correct interpretation.
- (d) A population clustered along any given dimension  $Z$ , and, analogous to (b), uptake of a possibly ineffective drug is confounded by indication. That is, sicker individuals, those for which  $D_i$  is more likely to be 1, take higher doses  $\xi_i$  of the drug. Here again a causal analysis would suggest the population AUC as less misleading than the personalized AUC, though a non-causal analysis, e.g., an intention-to-treat analysis, may point to the personalized AUC.

## 4 Simplifications when $(X, Y) \perp\!\!\!\perp (M, N)$

Under some conditions, the cluster AUC parameters  $\theta_{12}$  and  $\theta_{11}$  may simplify to the  $M = N = 1$  case. An example is given in Section 3, where the exchangeable cluster structure enables the simplification.

**Proposition 2.** *Given  $(X, Y, M, N) \sim P$ , suppose that  $E(\psi(X_{1k}, Y_{1l}) \mid M, N)$  and  $E(\psi(X_{1k}, Y_{2l}) \mid M, N)$  do not depend on  $k, l$ . Then  $\theta_{11}(P) = E\psi(X_{11}, Y_{11})$  and  $\theta_{12}(P) = E\psi(X_{11}, Y_{21})$ .*

In order for  $\hat{\theta}_{12} \rightarrow 1$  while  $\hat{\theta}_{11} \not\rightarrow 1$  in the random effects model discussed in Section 3, it was necessary that  $(X, Y) \not\perp\!\!\!\perp (M, N)$ . Theorem 3 below bounds  $\theta_{12}$  by  $\theta_{11}$  under one case of  $(X, Y) \perp\!\!\!\perp (M, N)$ , namely, when  $M$  and  $N$  are each constant.

**Theorem 3.** *Let  $(X, Y, M, N) \sim P$  be given as in (1). Assume further that  $M = m$  and  $N = n$  are constant. Then*

$$\frac{1}{2} \left( \theta_{11} + \frac{\sum_{k,l} P(X_{1k} = Y_{1l})}{2mn} \right)^2 \leq \theta_{12} \leq 1 - \frac{1}{2} \left( 1 - \theta_{11} + \frac{\sum_{k,l} P(X_{1k} = Y_{1l})}{2mn} \right)^2$$

The theorem follows from the lemma,

**Lemma 4.** *Given a pair of scalar random variables  $(X, Y)$  with joint distribution  $P$ , let  $P_{\perp}$  be the product measure of the marginals, i.e., for all real  $a, b$ ,*

$$P_{\perp}(\{x < a\} \cap \{y < b\}) = P(\{x < a\})P(\{y < b\}).$$

*Then*

$$\frac{1}{2}(P(X < Y) + P(X = Y))^2 \leq P_{\perp}(X < Y) + \frac{1}{2}P(X = Y) \leq 1 - \frac{1}{2}(1 - P(X < Y))^2.$$

With the random vector  $(X, Y, M, N) \sim P$ , with constant  $M = N = 1$  so that  $P$  may be regarded as the joint distribution of  $(X, Y)$ , assumed continuous, the conclusion of the Lemma is

$$\frac{1}{2}(\theta_{11}(P))^2 \leq \theta_{12}(P) \leq 1 - \frac{1}{2}(1 - \theta_{11}(P))^2, \quad (11)$$

equivalently,

$$1 - \sqrt{2(1 - \theta_{12})} \leq \theta_{11} \leq \sqrt{2\theta_{12}}.$$

When the personalized AUC is completely uninformative,  $\theta_{11} = 1/2$ , the informativity of the population AUC is limited,  $1/8 \leq \theta_{12} \leq 7/8$ . However, when the population AUC is completely uninformative,  $\theta_{12} = 1/2$ , the above bounds on the personalized AUC, which are tight, are vacuous,  $0 \leq \theta_{11} \leq 1$ . Situations as described in Section 3, where the population AUC  $\rightarrow 1$  while the personalized AUC  $\rightarrow 1/2$ , appear to require some dependence between  $M, N$  and  $X, Y$ .

## 5 Asymptotic Distribution of $(\theta_{12}, \theta_{11})$

Theorem 5 gives the asymptotic joint distribution of the individual and population AUCs. It is stated in somewhat greater generality for any square-integrable kernel, not just the AUC kernel (2). The proof is the same for any random variables  $M, N$ , such that  $EM \neq 0, EN \neq 0, EM^{-2} < \infty, EN^{-2} < \infty$ , i.e.,  $M$  and  $N$  need not be the lengths of  $X$  and  $Y$ . Let  $W_i = (X_i, Y_i, M_i, N_i), i = 1, \dots, I$ , and let  $V$  denote the space of finite sequences.

**Theorem 5.** *Let  $\psi : V \times V \rightarrow \mathbb{R}$ ,  $(X, Y, M, N) \sim P$  with  $(X, Y) \in V \times V$ ,  $\psi \in L^2(P)$ ,  $M$  and  $N$  counting numbers  $> 0$  with finite means. Then:*

$$\sqrt{I}(\hat{\theta}_{12} - \theta_{12}, \hat{\theta}_{11} - \theta_{11}) \rightsquigarrow \mathcal{N}(0, \Sigma)$$

*with*

$$\begin{aligned} \Sigma_{11} &= \lim_{I \rightarrow \infty} I \text{Var}(\hat{\theta}_{12}) = E \left( \frac{E(\psi_{12} | W_1) + E(\psi_{21} | W_1)}{E(M)E(N)} - \theta_{12} \left( \frac{M_1}{E(M)} + \frac{N_1}{E(N)} \right) \right)^2 \\ \Sigma_{22} &= \lim_{I \rightarrow \infty} I \text{Var}(\hat{\theta}_{11}) = \text{Var}(\psi_{11}/(M_1 N_1)) \\ \Sigma_{12} &= \lim_{I \rightarrow \infty} I \text{Cov}(\hat{\theta}_{12}, \hat{\theta}_{11}) = \theta_{12} E \left( \frac{\psi_{11}}{M_1 N_1} \left( \frac{\psi_{12} + \psi_{21}}{E\psi_{12}} - \frac{M_1}{E(M)} - \frac{N_1}{E(N)} \right) \right) \end{aligned}$$

**Corollary 6.** *Under the assumptions of Theorem 5, let  $(X_1, Y_1, M_1, N_1), \dots, (X_I, Y_I, M_I, N_I)$ , be IID according to  $P$ . For  $1 \leq i \leq I$  define*

$$\begin{aligned}\psi_{i.} &= I^{-1} \sum_{j=1}^I \psi(X_i, Y_j), \\ \psi_{.i} &= I^{-1} \sum_{j=1}^I \psi(X_j, Y_i), \\ \phi_i &= \frac{\psi(X_i, Y_i)}{M_i N_i},\end{aligned}$$

*and analogously for  $M_{.}, N_{.}$ , and  $\psi_{..}$ . The asymptotic covariance matrix  $\Sigma$  of  $(\hat{\theta}_{12}, \hat{\theta}_{11})$  may be consistently estimated by  $\hat{\Sigma}$  given by:*

$$\begin{aligned}\hat{\Sigma}_{11} &= \frac{1}{I-1} \sum_{i=1}^I \left( \frac{\psi_{i.} + \psi_{.i}}{M_{.} N_{.}} - \hat{\theta}_{12} \left( \frac{M_i}{M_{.}} + \frac{N_i}{N_{.}} \right) \right)^2 \\ \hat{\Sigma}_{22} &= \frac{1}{I-1} \sum_{i=1}^I (\phi_i - \phi_{.})^2 \\ \hat{\Sigma}_{12} &= \frac{1}{I} \sum_{i=1}^I \left( \frac{\phi_i}{\phi_{.}} \left( \frac{\psi_{i.} + \psi_{.i}}{\psi_{..}} - \frac{M_i}{M_{.}} - \frac{N_i}{N_{.}} \right) \right)\end{aligned}$$

*Proof.* See Sen (1960) for convergence results for random variables  $\psi_{i.}$  and  $\psi_{.i}$ . □

The estimator  $\hat{\Sigma}_{11}$  of the asymptotic variance of  $\hat{\theta}_{12}$  is the same as given by Obuchowski (1997), derived by a different method. The finite-sample performance of this estimator is examined in Section 6.

## 6 Simulation

We examine estimation and inference on the population and personalized AUCs jointly. Many of the choices and parameters follow the simulation in Obuchowski (1997) examining what is here referred to as the population AUC. Key differences include: 1) In our model  $M > 0, N > 0$ , to ensure that the personalized AUC is well-defined; 2) Whereas Obuchowski (1997) take  $I = 100$ , we take the number of clusters to be  $I = 60$  in the coverage simulation, Section 6.2, and  $I = 10$  in the power simulation, Section 6.3.

### 6.1 Data models

To generate  $(M, N)$ , first a preliminary number  $\overline{M} + \overline{N}$  of combined case and control observations belonging in a sample is randomly selected from among  $k \in \{2, 3, 4, 5\}$ . Next, to obtain the allocation to case and control observations,  $\overline{M} + \overline{N}$  normal variables are sampled with unit variance and common pairwise correlation  $\rho_{MN} \in \{0, 0.1, 0.4, 0.8\}$ . A preliminary number  $\overline{M}$  of control observations is taken to be those greater than 0, and the remainder

the preliminary number  $\overline{N}$  of case observations. Finally, 1 is added to each to obtain the final number of control and case observations,  $M = \overline{M} + 1, N = \overline{N} + 1$ . The greater the correlation  $\rho_{MN}$ , the greater the imbalance between case and control observations within the clusters.

Two related models were considered for  $(X, Y) \mid (M, N)$ .

### 6.1.1 Bivariate normal model

A popular parametric model for the AUC is the bivariate normal model, where the case and control observations are both assumed to follow a normal distribution (Hanley, 1988). Following Obuchowski (1997) we extend this model to accommodate clustered data by modeling the observations as multivariate normal vectors with an exchangeable correlation structure.

$$(X, Y) \mid (M, N) \sim \mathcal{N}_{M+N} \left( \begin{pmatrix} 0 \cdot \mathbb{1}_M \\ \Delta \cdot \mathbb{1}_N \end{pmatrix}, \rho \mathbb{1}_{M+N} \mathbb{1}_{M+N}^T + (1 - \rho) Id_{M+N} \right) \quad (12)$$

That is, the case and control observations of a given cluster all have unit variance and share the same pairwise correlation  $\rho$ , all the case observations have mean  $\Delta > 0$ , and all the control observations mean 0. The bivariate normal model is in fact an example of the random effect model described in Section 3, though the random effect is not given explicitly in (12). As the impact of the random effect discussed there is only to change the intra-cluster correlation or mean in (12), it is redundant to the usual multivariate normal parameters. Moreover, further parameters such as for a non-zero control mean  $E(X_{11})$  or non-unit variances  $\text{Var}(X_{11})$  and  $\text{Var}(Y_{11})$  are redundant for our purpose of modeling AUCs.

Using Proposition 2,

$$\begin{aligned} \theta_{12}(P) &= \Phi \left( \frac{\Delta}{\sqrt{2}} \right) \\ \theta_{11}(P) &= \Phi \left( \frac{\Delta}{\sqrt{2(1 - \rho)}} \right) \end{aligned} \quad (13)$$

The formulas (13) show that  $\theta_{11} > \theta_{12}$  and further that  $\theta_{12}$  and  $\theta_{11}$  are simultaneously  $> 1/2$ ,  $= 1/2$ , or  $< 1/2$ . We give two benefits. The first is that  $(\theta_{12}, \theta_{11})$  can be restricted without loss of generality to  $[1/2, 1] \times [1/2, 1]$ , switching control and case labels if necessary. The pair  $(\theta_{12}, \theta_{11})$  may then serve as a parameterization of the bivariate normal model (12), solving for  $\Delta$  and  $\rho$  in (13). The second involves testing. Though AUCs are often compared by magnitude, e.g.,  $H_0 : AUC_1 - AUC_2 > 0$ , one is usually interested in the discrimination, i.e.,  $|AUC_1 - 1/2|$  versus  $|AUC_2 - 1/2|$ . The hypothesis  $H_0 : AUC_1 - AUC_2 > 0$  is ambiguous, indicating that  $AUC_1$  than is more discriminating than  $AUC_2$  when both are greater than  $1/2$ , but less discriminating if both are less than  $1/2$ . A further complication, which will not be solved by switching the class designations, is that one AUC may be greater than  $1/2$  and the other less. These complications are avoided in the bivariate normal model for the personalized and population AUCs. A test of  $\theta_{12} = \theta_{11}$  versus  $\theta_{12} < \theta_{11}$  is also a test of discrimination,  $|\theta_{12} - 1/2| = |\theta_{11} - 1/2|$  versus  $|\theta_{12} - 1/2| < |\theta_{11} - 1/2|$ .

### 6.1.2 Censored bivariate normal model

We also examine the bivariate normal model under censoring, a mixed discrete-continuous distribution. Let  $a > 0$ , let  $(\bar{X}, \bar{Y}) \mid (M, N)$  be sampled as in (12), and let

$$(X, Y) \mid (M, N) = (-a\{\bar{X} \leq -a\} + \bar{X}\{-a < \bar{X} < a\} + a\{\bar{X} \geq a\}, \\ -a\{\bar{Y} \leq -a\} + \bar{Y}\{-a < \bar{Y} < a\} + a\{\bar{Y} \geq a\}). \quad (14)$$

That is, observations  $(\bar{X}, \bar{Y})$  are generated as in the bivariate normal model (12), and the values are then clipped to  $\pm a$ . This type of data-generating process is used by Obuchowski (1997) to model radiologists' scores, which lie on a 0—100% scale and often accumulate at 0% and 100%.

Let

$$(X_{11}, Y_{11}) \sim \mathcal{N}_2 \left( \begin{pmatrix} 0 \\ \Delta \end{pmatrix}, \begin{pmatrix} 1 & \rho \\ \rho & 1 \end{pmatrix} \right).$$

Again using Proposition 2 to reduce to the  $M = N = 1$  case,

$$\begin{aligned} \theta_{12}(P) &= - \int_{-a}^a \Phi(x - \Delta) \phi(x) dx + \frac{1}{2} (\Phi(a) - \Phi(a - \Delta) - \Phi(-a - \Delta) \\ &\quad + \Phi(a)(\Phi(-a - \Delta) + \Phi(a - \Delta)) + 1) \\ \theta_{11}(P) &= \int_{-a}^a \int_x^a f_{X_{11}, Y_{11}}(x, y) dy dx + \Phi(-a) + 1 - \Phi(a - \Delta) - \frac{1}{2} P(X_{11} < -a, Y_{11} < -a) \\ &\quad - \frac{1}{2} P(X_{11} > a, Y_{11} > a) - P(X_{11} < -a, Y_{11} > a). \end{aligned}$$

Due to the censoring, the AUCs may be bounded below 1 in this model, regardless of the magnitude of the location shift between the underlying control and case observations. As  $\Delta \rightarrow \infty$ ,  $\theta_{12}$  and  $\theta_{11}$  both tend to  $\frac{1}{2}(1 + \Phi(a))$ .

## 6.2 Coverage

The parameters  $\Delta$  and  $\rho$  were set to correspond to a population AUC of  $\theta_{12} \in \{0.7, 0.8\}$  and personalized AUCs of  $\theta_{11} \in \{0.7, 0.8, 0.9\}$  with  $\theta_{11} \geq \theta_{12}$ . For each setting of  $\rho_{MN}, \theta_{12}, \theta_{11}$ , 1,000 replicates of size  $I = 60$  were sampled and used to form a confidence ellipse for  $(\theta_{12}, \theta_{11})$ . Specifically, with  $\hat{\theta}_{12}, \hat{\theta}_{11}$  computed as in Section 2 and  $\Sigma$  as in Theorem 5, under  $P$ ,

$$\left| \Sigma^{-1/2} \begin{pmatrix} \begin{pmatrix} \theta_{12} \\ \theta_{11} \end{pmatrix} - \begin{pmatrix} \hat{\theta}_{12} \\ \hat{\theta}_{11} \end{pmatrix} \end{pmatrix} \right|^2 \quad (15)$$

has a chi-squared distribution with 2 degrees of freedom. If  $q$  is an upper  $\alpha$  quantile of this distribution, then

$$\left\{ \begin{pmatrix} x \\ y \end{pmatrix} : \left| \Sigma^{-1/2} \begin{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix} - \begin{pmatrix} \hat{\theta}_{12} \\ \hat{\theta}_{11} \end{pmatrix} \end{pmatrix} \right|^2 < q \right\}$$

is a level  $1 - \alpha$  confidence region for  $(\theta_{12}, \theta_{11})$ , which then covers  $(\theta_{12}, \theta_{11})$  when (15) is  $< q$ . In the simulation, we substitute for  $\Sigma$  the asymptotic approximation  $\hat{\Sigma}$  given in Corollary

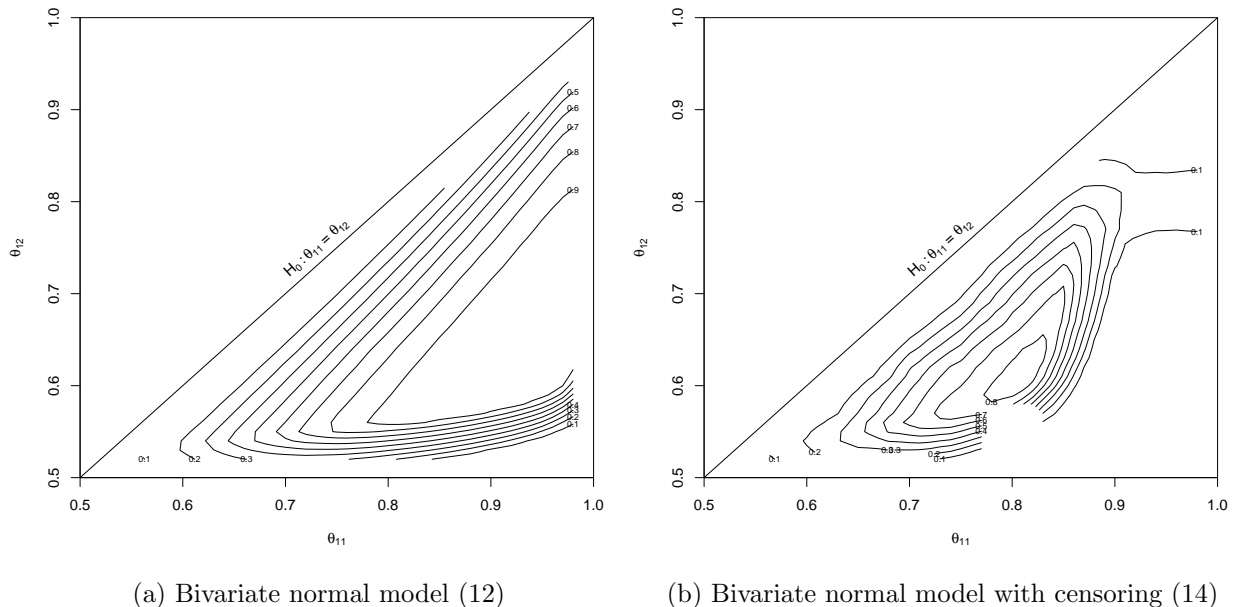


Figure 2: Empirical power function of the test of  $H_0 : \theta_{12} = \theta_{11}$  versus  $\theta_{12} < \theta_{11}$  using the asymptotic estimator given in Section 5. In the bivariate normal model with or without censoring, the null is equivalent to  $H_0 : |\theta_{12} - 1/2| = |\theta_{11} - 1/2|$ , equal informativity.

6. Results are presented in Table 1. The bias is on the order of a hundredth at this sample size, and the coverage is generally close to .95. There is some degradation in the coverage as  $(\theta_{12}, \theta_{11})$  approach  $(1, 1)$ .

### 6.3 Power

We examine the power of testing the null hypothesis  $H_0 : \theta_{12} = \theta_{11}$  using the proposed variance estimators under the bivariate normal model (12). Restricting to  $\rho > 0$  in (12), the set of alternatives to  $H_0 : 1/2 < \theta_{12} = \theta_{11}$  is  $H_A : 1/2 < \theta_{12} < \theta_{11}$ , i.e., where the personalized AUC is more discriminating than the population AUC.

The data is generated under (12) using  $(\theta_{12}, \theta_{11})$  selected from points randomly and uniformly selected in  $[\frac{1}{2}, 1] \times [\frac{1}{2}, 1], \{\theta_{11} \geq \theta_{12}\}$ . Estimates  $\hat{\theta}_{12}, \hat{\theta}_{11}$ , and  $\hat{\Sigma}$  were then obtained as described above. The test is carried out by testing the significance of the z-statistic

$$(\hat{\theta}_{12} - \hat{\theta}_{11}) / \sqrt{c^t \hat{\Sigma} c}$$

where the contrast vector  $c$  is  $(1, -1)^t$ .

The observed power functions are plotted in Fig. 2. The number of clusters was chosen to be  $I = 10$ , few relative to the setting in Obuchowski (1997), since the qualitative behavior of the power surface appears clearer with fewer clusters.

parameters			coverage	bias				
$\theta_{12}$	$\theta_{11}$	$\rho_{MN}$		$\theta_{12}$	$\theta_{11}$	$\Sigma_{11}$	$\Sigma_{12}$	$\Sigma_{22}$
0.70	0.70	0.00	0.94	0.00	-0.00	0.00	-0.00	-0.00
0.70	0.70	0.10	0.93	0.00	0.00	-0.01	-0.00	0.00
0.70	0.70	0.40	0.94	0.00	0.00	0.01	0.01	0.01
0.70	0.70	0.80	0.94	0.00	0.00	0.00	-0.00	-0.00
0.70	0.80	0.00	0.94	0.00	0.00	0.00	0.00	0.00
0.70	0.80	0.10	0.93	0.00	0.00	0.00	0.00	0.00
0.70	0.80	0.40	0.93	0.00	0.00	-0.01	-0.00	0.00
0.70	0.80	0.80	0.93	-0.00	-0.00	0.01	0.00	0.00
0.80	0.80	0.00	0.92	0.00	-0.00	-0.00	0.00	0.00
0.80	0.80	0.10	0.94	0.00	-0.00	0.00	0.00	0.00
0.80	0.80	0.40	0.93	0.00	0.00	0.00	0.00	0.00
0.80	0.80	0.80	0.93	0.00	-0.00	0.00	-0.00	-0.00
0.80	0.90	0.00	0.92	0.00	0.00	0.00	-0.00	-0.00
0.80	0.90	0.10	0.92	0.00	-0.00	0.00	0.00	0.00
0.80	0.90	0.40	0.91	0.00	-0.00	0.00	0.00	-0.00
0.80	0.90	0.80	0.90	0.01	0.00	-0.00	-0.00	0.00

(a) Binormal model (12)

parameters			coverage	bias				
$\theta_{12}$	$\theta_{11}$	$\rho_{MN}$		$\theta_{12}$	$\theta_{11}$	$\Sigma_{11}$	$\Sigma_{12}$	$\Sigma_{22}$
0.70	0.70	0.00	0.94	0.00	0.00	0.00	0.00	0.00
0.70	0.70	0.10	0.94	0.00	0.00	-0.00	0.00	0.01
0.70	0.70	0.40	0.93	0.00	0.00	-0.00	-0.01	-0.00
0.70	0.70	0.80	0.94	0.00	0.00	-0.00	-0.00	-0.00
0.70	0.80	0.00	0.94	0.00	0.00	0.00	-0.00	-0.00
0.70	0.80	0.10	0.91	0.00	0.00	-0.01	-0.00	-0.01
0.70	0.80	0.40	0.94	0.00	-0.00	0.00	0.00	0.00
0.70	0.80	0.80	0.93	0.00	0.00	0.00	-0.00	-0.00
0.80	0.80	0.00	0.94	0.00	-0.00	0.00	0.00	0.00
0.80	0.80	0.10	0.93	0.00	-0.00	0.00	0.00	0.00
0.80	0.80	0.40	0.95	-0.00	-0.00	0.00	-0.00	0.00
0.80	0.80	0.80	0.92	0.00	-0.00	-0.01	-0.00	-0.00
0.80	0.90	0.00	0.93	0.00	-0.01	-0.00	-0.00	0.00
0.80	0.90	0.10	0.92	0.00	-0.01	-0.00	-0.00	-0.00
0.80	0.90	0.40	0.92	0.00	-0.01	-0.00	-0.00	0.00
0.80	0.90	0.80	0.93	0.00	-0.01	0.00	0.00	0.01

(b) Binormal model with censoring (14)

Table 1: The results of a simulation examining the coverage of a nominal 95% confidence ellipse obtained using the asymptotic estimator given in Section 5. For  $\theta_{11}$  and  $\theta_{12}$ , the bias is computed as the mean difference between the estimates and the known true values. For the elements of the covariance matrix  $\Sigma_{ij}$ , the bias is the mean difference between the estimates given by Theorem 5 and the empirical covariance.

## 7 Discussion

We have compared and contrasted two generalizations of the AUC to accommodate clustered, paired data. Straightforward extensions include allowing for multiple dependent AUCs, clusters that are only exchangeable or otherwise fall short of being IID, and covariate-adjusted AUCs. A more delicate extension would allow for estimation of the personalized AUC when some clusters have no control or no case observations. As the personalized AUC is not currently defined for such clusters either the definition would need to be re-worked or a model would need to be introduced for the missing values corresponding to those clusters. No major changes would be required of the analysis under a strong enough assumption such as ignorability, i.e., the assumption that the behavior of the personalized AUC (or the pair) is the same on  $M > 1, N > 1$  as on the entire population.

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*Proof of Proposition 1.* 1. By the LLN  $I^2/MN \rightarrow 1/(E(M)E(N))$  almost surely and by Lemma 8  $\sum_{i,j} \psi_{ij}/I^2 \rightarrow E\psi_{12}$  almost surely. Conditioning on the sample,

$$\begin{aligned} E\psi(\xi_I, \eta_I) &= E(E(\psi(\xi_I, \eta_I) \mid (X_1, Y_1, M_1, N_1), \dots, (X_I, Y_I, M_I, N_I))) \\ &= E\left(\frac{\sum_{1 \leq i, j \leq I} \sum_{1 \leq k \leq M_i, 1 \leq l \leq N_j} \psi(X_{ik}, Y_{jl})}{\sum_{i=1}^I M_i \sum_{i=1}^I N_i}\right) \\ &= E\left(\frac{\sum_{1 \leq i, j \leq I} \psi_{ij}}{\sum_{i=1}^I M_i \sum_{i=1}^I N_i}\right) \rightarrow \frac{E\psi_{12}}{E(M)E(N)} = \theta_{12}. \end{aligned}$$

The limit is justified since  $\sum_{i,j} \psi_{i,j}/(\sum_i M_i \sum_i N_i) \leq 1$ .

2. The second part follows on showing that  $(\xi_I, \eta_I) \rightarrow (\xi_\infty, \eta_\infty)$  setwise. For  $a, b \in \mathbb{R}$ , by a similar argument as above,

$$\begin{aligned} P(\xi_I < a, \eta_I < b) &= E\left(\frac{\sum_{1 \leq i, j \leq I} \sum_{1 \leq k \leq M_i, 1 \leq l \leq N_j} \{X_{ik} < a, Y_{jl} < b\}}{\sum_{i=1}^I M_i \sum_{i=1}^I N_i}\right) \\ &\rightarrow \frac{E\left(\sum_{k=1}^{M_1} \{X_{1k} < a\}\right)}{E(M)} \frac{E\left(\sum_{l=1}^{N_1} \{Y_{1l} < b\}\right)}{E(N)}. \end{aligned}$$

The probability of sampling an element from a cluster of size  $M = m$  given an initial segment of  $I$  samples  $(X_1, Y_1, M_1, N_1), \dots, (X_I, Y_I, M_I, N_I)$ , is  $\frac{m \sum_{i=1}^I \{M_i = m\}}{\sum_{i=1}^I M_i}$ . Along almost any sequence of samples as  $I \rightarrow \infty$  this relative frequency tends to  $\frac{mP(M=m)}{E(M)}$ .

Therefore

$$\begin{aligned}
P(\xi_\infty < a) &= \sum_{m=1}^{\infty} P(\xi_\infty < a \mid \xi_\infty \text{ is sampled from a cluster of size } m) \cdot \\
&\quad P(\xi_\infty \text{ is sampled from a cluster of size } m) \\
&= \sum_{m=1}^{\infty} \frac{1}{m} \sum_{k=1}^m P(X_{1k} < a \mid M = m) \frac{mP(M = m)}{E(M)} \\
&= \frac{1}{EM} \sum_{m=1}^{\infty} \sum_{k=1}^m P(X_{1k} < a \mid M = m) P(M = m) \\
&= \frac{1}{E(M)} E \left( \sum_{k=1}^M \{X_{1k} < a\} \right).
\end{aligned}$$

Analogously,

$$P(\eta_\infty < a) = \frac{1}{E(N)} E \left( \sum_{l=1}^N \{X_{1l} < a\} \right).$$

The product is the limit of  $P(\xi_I < a, \eta_I < b)$  given above. □

The following lemma gives a convergence result for a two-sample  $U$ -statistic with kernel of degree  $(1, 1)$  where the data is paired. The corresponding definitions and result for independent samples is given in, e.g., Lee (2019). Let  $V$  denote the space of finite sequences.

**Lemma 7.** *Given a sample  $(X_0, Y_0), (X_1, Y_1), \dots, (X_I, Y_I)$  on  $V \times V$  IID according to  $P$  and a function  $\psi : V \times V \rightarrow \mathbb{R}$  in  $L^2(P)$ , define*

$$U_I = I^{-2} \sum_{\substack{1 \leq i, j \leq I \\ i \neq j}} \psi(X_i, Y_j), \quad V_I = I^{-2} \sum_{1 \leq i, j \leq I} \psi(X_i, Y_j),$$

and

$$\hat{U}_I = I^{-1} \sum_{i=1}^I (E(\psi(X_i, Y_0) \mid X_i, Y_i) + E(\psi(X_0, Y_i) \mid X_i, Y_i)) - 2E\psi(X_1, Y_2).$$

Then

$$E(U_I - EU_I - \hat{U}_I)^2 = O(I^{-2}) \text{ and } E(V_I - EV_I - \hat{U}_I)^2 = O(I^{-2}).$$

*Proof of Lemma 7.* Define

$$\bar{\psi}_{ij} = \psi(X_i, Y_j) - E(\psi(X_i, Y_0) \mid X_i, Y_i) - E(\psi(X_0, Y_j) \mid X_j, Y_j) + E\psi(X_0, Y_0).$$

Then, for  $i \neq j$ ,  $E(\bar{\psi}_{ij} \mid (X_i, Y_i)) = E(\bar{\psi}_{ij} \mid (X_j, Y_j)) = 0$ , implying

$$\begin{aligned}
E(U_I - EU_I - \hat{U}_I)^2 &= E \left( (I)_2^{-1} \sum_{i \neq j} \bar{\psi}_{ij} \right)^2 \\
&= (I)_2^{-2} \sum_{i \neq j} E\bar{\psi}_{ij}^2 + O(I^{-2}) \\
&= O(I^{-2}).
\end{aligned}$$

For the second equation,

$$\begin{aligned}
E(U_I - EU_I - V_I + EV_I)^2 &= I^{-2} E \left( (I)_2^{-1} \sum_{i \neq j} \psi_{ij} - E\psi_{11} + E\psi_{12} \right)^2 \\
&\leq I^{-2} E \left( (I)_2^{-1} \sum_{i \neq j} E(\psi_{ij} - E\psi_{11} + E\psi_{12})^2 \right) \\
&= O(I^{-2}).
\end{aligned}$$

□

**Corollary 8.** *With the same setup as Lemma 7,  $U_I - EU_I \rightarrow 0$  a.s. and  $\sqrt{I}(U_I - EU_I)/\sqrt{\text{Var}(U_I)} \rightarrow \mathcal{N}(0, 1)$  in distribution.*

*Proof of Corollary 8.* By Lemma 7,  $U_I - EU_I \rightarrow \hat{U}_I$  a.s. and  $\sqrt{I}(U_I - EU_I - \hat{U}_I) \rightarrow 0$  in quadratic mean, and  $\hat{U}_I$  is an IID sum subject to the usual LLN and CLT. □

*Proof of Proposition 2.*

$$\begin{aligned}
\theta_{11}(P) &= E \left( \frac{\sum_{k=1}^M \sum_{l=1}^N \psi(X_{1k}, Y_{1l})}{MN} \right) \\
&= E \left( \frac{1}{MN} E \left( \sum_{k=1}^M \sum_{l=1}^N \psi(X_{1k}, Y_{1l}) \mid M, N \right) \right) \\
&= E \left( \frac{1}{MN} MNE(\psi(X_{11}, Y_{11} \mid M, N)) \right) = E\psi(X_{11}, Y_{11}).
\end{aligned}$$

Similar to the above,

$$\begin{aligned}
\theta_{12}(P) &= \frac{E \left( \sum_{k=1}^{M_1} \sum_{l=1}^{N_2} \psi(X_{1k}, Y_{2l}) \right)}{E(M)E(N)} \\
&= \frac{E(M)E(N)E\psi(X_{11}, Y_{21})}{E(M)E(N)} = E\psi(X_{11}, Y_{21}).
\end{aligned}$$

□

**Lemma 9.** *Given integrable random variables  $M, V, X_1, X_2, \dots$ , such that  $M \in \{1, 2, \dots\}$  and  $\sum_{i=1}^{\infty} E(|X_i|; M \geq i) < \infty$ ,*

$$E \left( \sum_{i=1}^M X_i \mid M, V \right) = \sum_{i=1}^M E(X_i \mid M, V)$$

*Proof of Lemma 9.*

$$\begin{aligned}
E \left( \sum_{i=1}^M X_i \middle| M, V \right) &= E \left( \sum_{m=1}^{\infty} \{M = m\} \sum_{i=1}^m X_i \middle| M, V \right) \\
&= \sum_{m=1}^{\infty} E \left( \{M = m\} \sum_{i=1}^m X_i \middle| M, V \right) \\
&= \sum_{m=1}^{\infty} \sum_{i=1}^m \{M = m\} E(X_i | M, V) \\
&= \sum_{i=1}^M E(X_i | M, V),
\end{aligned}$$

the interchange in the second equality allowed since  $E \left| \sum_{i=1}^M X_i \right| \leq \sum_{i=1}^{\infty} E(|X_i|; M \geq i) < \infty$ .  $\square$

*Proof of Lemma 4.* Define for  $n \in \mathbb{N}$  approximations to  $\theta_{11}$  and  $\theta_{12}$  by

$$\begin{aligned}
A_{ij}^{(n)} &= \left\{ (x, y) : \frac{i}{2^n} \leq x < \frac{i+1}{2^n}, \frac{j}{2^n} \leq y < \frac{j+1}{2^n} \right\}, \quad -2^{2n} \leq i, j < 2^{2n} - 1 \\
\theta_{11}^{(n)} &= \sum_{i=-2^{2n}}^{2^{2n}-1} \sum_{j=i+1}^{2^{2n}-1} P(A_{ij}^{(n)}) + \frac{1}{2} \sum_{i=-2^{2n}}^{2^{2n}-1} P(A_{ii}^{(n)}) \\
\theta_{12}^{(n)} &= \sum_{i=-2^{2n}}^{2^{2n}-1} \sum_{j=i+1}^{2^{2n}-1} P_{\perp}(A_{ij}^{(n)}) + \frac{1}{2} \sum_{i=-2^{2n}}^{2^{2n}-1} P_{\perp}(A_{ii}^{(n)}).
\end{aligned}$$

Since  $\bigcup_n \bigcup_i \bigcup_{j>i} A_{ij}^{(n)} = \{x < y\}$  and  $\bigcap_n \bigcup_i A_{ii}^{(n)} = \{x = y\}$ , by continuity of measure  $\theta_{11}^{(n)} \rightarrow \theta_{11}$  and  $\theta_{12}^{(n)} \rightarrow \theta_{12}$ . Therefore, it is enough to establish the inequality (11) for  $\theta_{11}^{(n)}$  and  $\theta_{12}^{(n)}$ .

Fixing  $n$ ,

$$\begin{aligned}
\sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P_{\perp}(A_{ij}^{(n)}) &= \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P_{\perp}(A_{ij}^{(n)}) \\
&= \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P_{\perp}\left(\frac{i}{2^n} \leq x < \frac{i+1}{2^n}\right) P_{\perp}\left(\frac{j}{2^n} \leq y < \frac{j+1}{2^n}\right) \\
&\geq \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} (P(A_{ii}^{(n)}) + \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}))(P(A_{jj}^{(n)}) + \sum_{l=-2^{2n}}^{j-1} P(A_{lj}^{(n)})) \\
&= \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} \left( \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \sum_{l=-2^{2n}}^{j-1} P(A_{lj}^{(n)}) + P(A_{ii}^{(n)}) \sum_{l=-2^{2n}}^{j-1} P(A_{lj}^{(n)}) \right. \\
&\quad \left. + P(A_{jj}^{(n)}) \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) + P(A_{ii}^{(n)}) P(A_{jj}^{(n)}) \right).
\end{aligned}$$

We lower bound the first three terms in parentheses.

First term:

$$\begin{aligned}
& \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \sum_{l=-2^{2n}}^{j-1} P(A_{lj}^{(n)}) \\
&= \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \sum_{j=i+1}^{2^{2n}-1} \sum_{l=-2^{2n}}^{j-1} P(A_{lj}^{(n)}) \\
&\geq \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \sum_{j=i+1}^{2^{2n}-1} \sum_{l=i}^{j-1} P(A_{lj}^{(n)}) \\
&= \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \sum_{l=i}^{2^{2n}-2} \sum_{j=l+1}^{2^{2n}-1} P(A_{lj}^{(n)}) \\
&= \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \sum_{j=i+1}^{2^{2n}-1} P(A_{ij}^{(n)}) + \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \sum_{l=i+1}^{2^{2n}-2} \sum_{j=l+1}^{2^{2n}-1} P(A_{lj}^{(n)}) \\
&\geq \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P(A_{ij}^{(n)})^2 + \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{k=i+1}^{2^{2n}-2} \sum_{j=k+1}^{2^{2n}-1} P(A_{ij}^{(n)}) P(A_{ik}^{(n)}) + \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \sum_{l=i+1}^{2^{2n}-2} \sum_{j=l+1}^{2^{2n}-1} P(A_{lj}^{(n)}) \\
&= \sum \sum \sum \sum P(A_{ij}^{(n)}) P(A_{kl}^{(n)}) + \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P(A_{ij}^{(n)})^2 \\
&\quad \substack{i \neq k \text{ or } j \neq l \\ j > i \text{ and } l > k} \\
&= \frac{1}{2} \left( \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P(A_{ij}^{(n)}) \right)^2 + \frac{1}{2} \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P(A_{ij}^{(n)})^2.
\end{aligned}$$

Middle two terms:

$$\begin{aligned}
& \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} \left( P(A_{ii}^{(n)}) \sum_{l=-2^{2n}}^{j-1} P(A_{lj}^{(n)}) + P(A_{jj}^{(n)}) \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \right) \\
&= \sum_{i=-2^{2n}}^{2^{2n}-2} P(A_{ii}^{(n)}) \sum_{l=i}^{2^{2n}-2} \sum_{j=l+1}^{2^{2n}-1} P(A_{lj}^{(n)}) + \sum_{j=-2^{2n}+1}^{2^{2n}-1} P(A_{jj}^{(n)}) \sum_{i=-2^{2n}}^{j-1} \sum_{k=i+1}^{2^{2n}-1} P(A_{ik}^{(n)}) \\
&= \sum_{i=-2^{2n}}^{2^{2n}-2} P(A_{ii}^{(n)}) \sum_{l=i}^{2^{2n}-2} \sum_{j=l+1}^{2^{2n}-1} P(A_{lj}^{(n)}) + \sum_{i=-2^{2n}+1}^{2^{2n}-1} P(A_{ii}^{(n)}) \sum_{l=-2^{2n}}^{i-1} \sum_{j=l+1}^{2^{2n}-1} P(A_{lj}^{(n)}) \\
&= \left( \sum_{i=-2^{2n}}^{2^{2n}-1} P(A_{ii}^{(n)}) \right) \left( \sum_{l=-2^{2n}}^{2^{2n}-2} \sum_{j=l+1}^{2^{2n}-1} P(A_{lj}^{(n)}) \right).
\end{aligned}$$

The second-to-last equality is just renaming indices.

With these lower bounds,

$$\begin{aligned}
\theta_{12}^{(n)} &= \sum_{i=-2^{2n}}^{2^{2n}-1} \sum_{j=i+1}^{2^{2n}-1} P_{\perp}(A_{ij}^{(n)}) + \frac{1}{2} \sum_{i=-2^{2n}}^{2^{2n}-1} P_{\perp}(A_{ii}^{(n)}) \\
&\geq \frac{1}{2} \left( \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P(A_{ij}^{(n)}) \right)^2 + \left( \sum_{i=-2^{2n}}^{2^{2n}-1} P(A_{ii}^{(n)}) \right) \left( \sum_{l=-2^{2n}}^{2^{2n}-2} \sum_{j=l+1}^{2^{2n}-1} P(A_{lj}^{(n)}) \right) + \\
&\quad \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P(A_{ii}^{(n)}) P(A_{jj}^{(n)}) + \frac{1}{2} \sum_{i=-2^{2n}}^{2^{2n}-1} P(A_{ii}^{(n)})^2 \\
&= \frac{1}{2} \left( \sum_{i=-2^{2n}}^{2^{2n}-2} \sum_{j=i+1}^{2^{2n}-1} P(A_{ij}^{(n)}) + \sum_{i=-2^{2n}}^{2^{2n}-1} P(A_{ii}^{(n)}) \right)^2 \\
&= \frac{1}{2} \left( \theta_{11}^{(n)} + \frac{1}{2} \sum_{i=-2^{2n}}^{2^{2n}-1} P(A_{ii}^{(n)}) \right)^2 \\
&= \frac{1}{2} \left( \theta_{11}^{(n)} + \frac{1}{2} P(X=Y) \right)^2 + o(1).
\end{aligned}$$

The upper bound then follows by the same symmetry argument as given in Section 4.  $\square$

*Proof of Theorem 3.* With

$$\theta_{11} = \frac{1}{mn} E(\psi_{11}) = \frac{1}{mn} \sum_{i,j} (P(X_{1i} < Y_{1j}) + \frac{1}{2} P(X_{1i} = Y_{1j}))$$

Lemma 4 gives

$$\begin{aligned}
\theta_{12} &= \frac{1}{mn} E(\psi_{12}) = \frac{1}{mn} \sum_{i,j} (P(X_{1i} < Y_{2j}) + \frac{1}{2} P(X_{1i} = Y_{2j})) \\
&\geq \frac{1}{mn} \sum_{i,j} \frac{1}{2} (P(X_{1i} < Y_{1j}) + P(X_{1i} = Y_{1j}))^2 \\
&\geq \frac{1}{2} \left( \frac{1}{mn} \sum_{i,j} (P(X_{1i} < Y_{1j}) + P(X_{1i} = Y_{1j})) \right)^2 \\
&= \frac{1}{2} \left( \theta_{11} + \frac{1}{2mn} \sum_{i,j} P(X_{1i} = Y_{1j}) \right)^2.
\end{aligned}$$

The second inequality is Jensen's inequality, which is tight when the pairwise AUCs are all equal. The other bound follows similarly.  $\square$

*Proof of Theorem 5.* By Lemma 7,

$$\sqrt{I} \left( \frac{(I)_2^{-1} \sum_{i \neq j} \psi_{ij} - E\psi_{12}}{\text{sd}(\sqrt{I}(I)_2^{-1} \sum_{i \neq j} \psi_{ij})}, \frac{I^{-2} \sum_{i,j} M_i N_j - E(M)E(N)}{\text{sd}(I^{-3/2} \sum_{i,j} M_i N_j)}, \frac{I^{-1} \sum_i \psi_{ii}/(M_i N_i) - E(\psi_{11}/M_1 N_1)}{\text{sd}(\psi_{11}/M_1 N_1)} \right)$$

converges to

$$I^{-1/2} \sum_{i=1}^I \left( \frac{E(\psi_{i0} | W_i) + E(\psi_{0i} | W_i) - 2E\psi_{12}}{\text{sd}(E(\psi_{10} | W_1) + E(\psi_{01} | W_1))}, \frac{M_i E(N) + N_i E(M) - 2E(M)E(N)}{\text{sd}(M_1 E(N) + N_1 E(M))}, \frac{\psi_{ii}/(M_i N_i) - E(\psi_{11}/M_1 N_1)}{\text{sd}(\psi_{11}/M_1 N_1)} \right)$$

in mean-square. The latter is an IID sum with finite covariance matrix and is asymptotically normal by the usual CLT. Applying the delta method with the function  $(x, y, z) \mapsto (x/y, z)$ , with derivative

$$\begin{pmatrix} 1/y & -x/y^2 & 0 \\ 0 & 0 & 1 \end{pmatrix} \Big|_{(x,y)=(\theta_{12}, E(M)E(N))}$$

for  $y \neq 0$ , i.e.,  $E(M) \neq 0, E(N) \neq 0$ , gives the asymptotic normality of  $(\theta_{11}, \theta_{12})$ . The asymptotic covariance matrix is given by delta method.

□