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A COMPARISON OF PLANS FOR HYPERTENSION SCREENING

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Abstract—Correcting to the work by Donner and Bull [1], it is reported that, in the setting they considered, screening plans based on the mean have higher power (probability of identifying a true hypertensive) than screening plans based on the minimum. However, for any reasonable size (probability of a false diagnosis of hypertension) the powers of the two plans are close.

INTRODUCTION

DONNER and BULL [1] compare two plans for screening hypertensive patients in which n blood pressure readings are taken at each of k clinic visits. The first plan is a multi-stage plan based on the mean of the n readings at each visit. The basis of this plan was described earlier by Rosner [2] and by Donner *et al.* [3]. The second plan is similar to the first, except that it is based on the minimum reading at each visit. In comparing the two plans, Donner and Bull show that in both the one visit and two visit cases, the minimum exhibits a superior probability of detecting a true hypertensive (the power of the plan) subject to a fixed probability of not detecting a true normotensive (the size of the plan).

The setting assumed by Donner and Bull [1] may be described as a random effects model of the form $X_{ij} = \theta + \epsilon_j + \eta_{ij}$ where $i = 1, \ldots, n$ readings per visit and $j = 1, \ldots, k$ visits. The ϵ_j are independent and $N(0, \sigma_B^2)$, the η_{ij} are independent and $N(0, \sigma_W^2)$ and the ϵ_j are independent of the η_{ij}. In other words, the patient's readings are assumed to have a Gaussian distribution with mean θ, between visit variance component σ_B^2 and within visit variance component σ_W^2.

For this model, when n blood pressure readings at a given visit are considered only within the context of that particular visit, then any two readings within that visit are statistically independent. However, when the total $n\ k$ readings over all visits are considered then any two readings within a visit are not statistically independent, indeed they have a correlation of $\sigma_B^2/(\sigma_B^2 + \sigma_W^2)$ [8]. In this case, the n readings within a visit do not constitute a sample of *independent* readings. The readings are *conditionally* independent within a visit but they are not *marginally* independent when considered over all visits.

In comparing the two plans, Donner and Bull [1] evaluate two competing statistical tests of the null hypothesis that a patient is normotensive ($\theta \leq \theta_0$ = lower threshold) against the alternative hypothesis that a patient is hypertensive ($\theta \geq \theta_1$ = upper threshold). Our recent research has indicated that plans based on the *mean* will in fact be superior to plans based on the minimum, within the setting described above. We attribute the discrepancy between this recent research and the Donner and Bull result to an assumption made by the latter authors in the evaluation of this plan based on the minimum.

THE CORRECT DISTRIBUTIONS

Donner and Bull, in deriving the probability that the minimum M_j exceeds a cut off value V_j at visit j (Appendix, Section (ii) of [1]) assume the n readings at visit j are independent. They give the distribution of M_j as

$$nf(M_j|\theta)[1 - F(M_j|\theta)]^{n-1}$$

where f and F are the density and cumulative distribution function of the Gaussian distribution. The above expression for the distribution of M_j is valid only if the n observations at visit j are independent.

The correct expression for the distribution of the minimum is proportional to the multiple integral (with respect to all order statistics other than the minimum) of the joint distribution of the n readings at visit j. This joint distribution reflects the dependence of these n readings and is actually multivariate normal, with mean of any reading equal to θ, variance of any reading equal to $\sigma_B^2 + \sigma_W^2$ and covariance between any two readings equal to σ_B^2. It should be noted that the distribution for the mean that is presented in Donner and Bull is derived from this multivariate normal distribution. The covariance between the readings within visits serves to increase the variance of the mean from $(\sigma_B^2 + \sigma_W^2)/n$ (if they were independent) to $\sigma_B^2 + \sigma_W^2/n$ (as in Donner and Bull [1]).

ONE VISIT

For the case of one visit with two readings per visit ($k = 1, n = 2$), the joint distribution of the two readings (X_{11}, X_{21}) is bivariate normal with mean (θ, θ) and covariance matrix

$$\begin{pmatrix} \sigma_B^2 + \sigma_W^2 & \sigma_B^2 \\ \sigma_B^2 & \sigma_B^2 + \sigma_W^2 \end{pmatrix}.$$

The probability that $M_1 = \min(X_{11}, X_{21})$ exceeds some constant V_1 may be evaluated as follows:

$$P(M_1 > V_1) = P[\min(X_{11}, X_{21}) > V_1] = P(X_{11} > V_1 \text{ and } X_{21} > V_1).$$

This probability may be evaluated from tables of the cumulative bivariate normal distribution [6] or by using the IMSL program MDBNOR [7]. Using these computed probabilities, a comparison of the powers of the two plans based on the mean and minimum for $k = 1$ and $n = 2$ is given in Table 1. We have used the following values from Donner and Bull [1]:

$$\sigma_B^2 = 12.3, \sigma_W^2 = 8.7, \theta_0 = 90\text{ mm}, \ \theta_1 = 105\text{ mm}$$

TABLE 1. CUTOFF VALUES AND POWERS FOR ONE VISIT SCREENING PLANS BASED ON MEAN AND MINIMUM, BY SIZE

	Based on mean		Based on minimum	
Size	Cutoff	Power	Cutoff	Power
0.10	95.23	0.992	92.71	0.987
0.05	96.71	0.979	93.81	0.969
0.02	98.37	0.948	95.03	0.929
0.01	99.49	0.911	95.85	0.885
0.005	100.51	0.864	96.60	0.831
0.001	102.61	0.721	98.14	0.677

This table indicates that, for a given size, the power of the plan based on the mean will always exceed the power of the plan based on the minimum. In fact, we know this must occur, because the Neyman-Pearson fundamental lemma [4, 5] states that the power of the plan based on the mean will exceed the power of a plan based on *any* other statistic.

TABLE 2. CUTOFF VALUES AND POWER FOR TWO VISIT SCREENING PLANS BASED ON MEAN AND MINIMUM, BY SIZE

	Based on mean		Based on minimum	
Size	Cutoff	Power	Cutoff	Power
0.10	96.66	1.000	93.77	0.999
0.05	97.98	0.998	94.74	0.997
0.02	99.48	0.992	94.84	0.987
0.01	100.51	0.982	96.60	0.972
0.005	101.46	0.963	97.29	0.947
0.001	103.46	0.874	98.74	0.843

TWO VISITS

For the case of two visits with two readings per visit ($k = 2$, $n = 2$), we utilize the following results that are obtainable from the model:

(a) Readings taken from different visits *are* independent both marginally and conditionally.
(b) The power of either plan will be maximized by using the same cutoff values for each visit (i.e. $V_1 = V_2$).

The required probabilities were calculated using the same thresholds and variance components as in the one visit case. Our results are summarized in Table 2.

DISCUSSION

Rosner [2] and Donner *et al.* [3] have discussed the limitation of the model as presented in this paper. Biological change in θ, both within and between visits, is not taken into account in the model. While it may be theoretically possible to model effects which potentially depend on temporal and environmental factors, such models could form a basis for future research.

We have considered the evaluation of screening plans with a hypothesis testing framework. In this setting, the Neyman–Pearson theory implies that statistical tests based on the mean are more powerful than tests based on any other statistic, such as the minimum. The mean carries with it optimal properties for classifying patients as normotensive or hypertensive.

It is clear that the differences in power between the two plans are not large. It also seems reasonable to suggest that such differences will not be disturbing to clinicians. Presumably, cutoff values used in practice would be rounded according to the accuracy of the measuring instrument. Such rounding together with alternate estimates for variance components or alternate choices for thresholds would apparently place the choice of criterion with the clinician.

The results do suggest that two visit plans are to be preferred to one visit plans.

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