INDIVIDUAL MATCHING WITH MULTIPLE CONTROLS IN THE CASE OF ALL-OR-NONE RESPONSES

OLLI S. MIETTINEN

Departments of Epidemiology and Biostatistics, Harvard School of Public Health, and Cardiology Division, Department of Medicine, Children's Hospital Medical Center, Boston, Massachusetts, U. S. A.

SUMMARY

The one-to-one individual matching principle of the matched pairs design is generalized to R-to-one individual matching in the case of all-or-none responses and fixed sample size procedures. A test is given; its asymptotic power function is derived; the selection of the matching ratio (R) is considered in relation to the unit costs in the two comparison groups; and finally, procedures for sample size determination are described.

1. INTRODUCTION

Matching is a common feature in the design of nonexperimental studies concerned with the evaluation of causal propositions (such as hypotheses on disease etiology). Its main purpose typically is the attainment of validity for the inferences, but it has implications for design efficiency as well.

As nonexperimental studies with matched comparison series are frequently quite expensive, it is important to understand the properties of matching designs so as to be able to make the best use of them. The matched pairs design in the case of all-or-none responses and fixed sample size has recently been studied rather extensively (Worcester [1964], Billewicz [1964, 1965], Miettinen [1966, 1968a, b], Bennett [1967], Chase [1968]). The present paper deals with the extension of this design to the case where the number of control subjects obtained for each propositus is not necessarily one but some general number R. We will use the term 'R-to-one individual matching design.' This generalization and an intelligent choice of R are important whenever several control subjects can be obtained at a unit cost substantially lower than that of the propositi.

2. BASIC CONCEPTS, TERMINOLOGY, AND NOTATION

In a study with R-to-one individual matching one obtains J sets of $1 + R$ subjects. Of each of these $(1 + R)$-tuples, one unit belongs to one and R units to the other of the two comparison groups. The first group, consisting of J subjects (propositi), is here termed Series 1, and the latter group, with RJ subjects (controls) is called Series 2.

The matching is based on some matching variate M (which need not be unidimensional). The jth $(1 + R)$-tuple shows some realization m_j for M, and this implies a realization $(p_{1j}, p_{2j}) = [p_1(m_j), p_2(m_j)]$ for the random pair (P_1, P_2) of underlying response probabilities, the numerals in the subscripts referring to Series 1 and Series 2, respectively.

Each subject is characterized by a code value of either 0 or 1 for a (dichotomous) response variate Y. Thus, in the jth matched group a realization $(y_{1j}, y_{2j1}, \cdots, y_{2jR})$ is obtained for the random response vector $(Y_{1j}, Y_{2j1}, \cdots, Y_{2jR})$.

3. THE MODEL, THE HYPOTHESES, AND THE TEST

The model under which the results are derived in the present work is completely analogous to that considered by Miettinen [1966; 1968a, b] in the special case of the matched pairs design. It consists of the assumptions that

(1) the distribution of M is independently identical for all the J sample positions, and that
(2) conditionally on the realizations $\{m_j\}$ for M the observation (response) variates corresponding to the $(1 + R)J$ units are independent within as well as among the J sample positions.

To state this model in another way, it is assumed that

(1) the J vectors $(Y_{1j}, Y_{2j1}, \cdots, Y_{2jR})$ are independently and identically distributed, and that
(2) $Y_{1j}, Y_{2j1}, \cdots, Y_{2jR}$ are mutually independent conditionally on $(P_1, P_2) = (p_{1j}, p_{2j}), j = 1, \cdots, J$.

As before (Miettinen [1968a, b]), the object of statistical inference is taken to be

$$\delta = \theta_1 - \theta_2 ,$$

where $\theta_i = E(Y_i) = E_M[E(Y_i \mid M)] = E_M[p_i(M)] = E(P_i), i = 1, 2$, and the expectation is taken with respect to the distribution of the matching variate in the source population of the propositi. The null hypothesis is taken as

$$H_0 : \delta = 0,$$

and the alternatives considered are $\delta < 0$, $\delta > 0$ and $\delta \neq 0$.

Information in terms of a two-by-two table of frequencies is sufficient for each matched group. For the jth group the table is a realization for

		Series 1	Series 2	Total
Y	1	X_{1j}	X_{2j}	X_j
	0	$1 - X_{1j}$	$R - X_{2j}$	$1 + R - X_j$
Total		1	R	$1 + R$

where $X_{1j} = Y_{1j}$ and $X_{2j} = \sum_k Y_{2jk}$.

In terms of the above hypotheses the interest lies in the contrast

$$\sum_j (RX_{1j} - X_{2j}).$$

On the null hypothesis its expectation is zero. Conditionally on $\{X_i\}$ its variance is

$$\begin{aligned} \operatorname{var}\,[\sum_i (RX_{1i} - X_{2i}) \mid \{X_i\}] &= \sum_i \operatorname{var}\,[(1 + R)X_{1i} - X_i \mid X_i] \\ &= \sum_i (1 + R)^2 \frac{X_i}{1 + R} \frac{1 + R - X_i}{1 + R} \\ &= \sum_i X_i(1 + R - X_i). \end{aligned}$$

Thus, the test statistic in the case of large J can be taken as

$$T = [\sum_i (RX_{1i} - X_{2i})]/[\sum_i X_i(1 + R - X_i)]^{\frac{1}{2}}, \tag{3.1}$$

and its value referred to tables of the standard normal distribution. (The Central Limit Theorem for unequally distributed variates applies here by the Lindeberg criterion.) If a continuity correction were to be applied to this statistic, it would mean reducing the absolute value of the numerator by $\frac{1}{2}(1 + R)$.

The square of the above test statistic can be thought of as representing one degree of freedom in the chi square statistic which Cochran [1950] gave for comparing proportions among several individually matched series, each represented by one unit at each of the observed levels of the matching variate. Moreover, it is a special case of the method which Mantel and Haenszel [1959] suggested for accumulating information from a number of hypergeometric experiments.

The results of Birch [1964] on the properties of the Mantel–Haenszel test imply that the statistic in (3.1) is optimal if $P_1(1 - P_2)/(1 - P_1)P_2$ is constant.

It may be noted that the Mantel–Haenszel test applies also in the case where R varies among the matched groups. Alternative analyses for that case were considered by Cox [1966].

The exact test corresponding to (3.1) is considered in sections 4.1 and 8.

4. THE TWO-TO-ONE INDIVIDUAL MATCHING DESIGN

4.1. *The test*

The two-to-one individual matching design merits special attention among the R-to-one matching designs with $R > 1$. It is to be regarded as the most frequently applicable alternative for the commonly used matched pairs design in the category of individual matching designs with a fixed matching ratio. Also, as the simplest nonsymmetrical R-to-one matching design it serves well the purpose of introducing the principles of the general asymmetrical case.

In the case of two-to-one individual matching, the test statistic (3.1) takes the form

$$T = \left[\sum_1^J (2X_{1i} - X_{2i}) \right] \Big/ \left[\sum_1^J X_i(3 - X_i) \right]^{\frac{1}{2}}. \tag{4.1}$$

A useful alternative expression for this statistic may be obtained by considering the multinomial distribution of the response vector (X_{1j}, X_{2j}). There are six possible realizations, and their random frequencies are here denoted as follows:

		X_2: 2	1	0	Total
X_1	1	Z_{12}	Z_{11}	Z_{10}	
	0	Z_{02}	Z_{01}	Z_{00}	
Total					J

In terms of this layout and notation, the statistic in (4.1) may be recast in the form

$$T = [2Z_{10} - Z_{01} + Z_{11} - 2Z_{02}]/[2(Z_{10} + Z_{01} + Z_{11} + Z_{02})]^{\frac{1}{2}}. \qquad (4.2)$$

The square of this latter statistic, with possible continuity correction of 3/2, is completely analogous to the McNemar [1947] statistic for the matched pairs design.

The above multinomial formulation also permits ready construction of an exact test. Regarding $\{X_j\}$ as fixed in (3.1) and (4.1) implies that the sums $Z_{10} + Z_{01} = S_1$ (say) and $Z_{11} + Z_{02} = S_2$ (say) are taken to be fixed in (4.2), and that Z_{10} and Z_{11} have independent binomial distributions whose parameters under the null hypothesis are $(S_1, \frac{1}{3})$ and $(S_2, \frac{2}{3})$, respectively. The corresponding joint probability function, $\Pr(Z_{10} = z_{10}, Z_{11} = z_{11} \mid S_1 = s_1, S_2 = s_2)$, is

$$\binom{s_1}{z_{10}}\left(\frac{1}{3}\right)^{z_{10}}\left(\frac{2}{3}\right)^{s_1 - z_{10}}\binom{s_2}{z_{11}}\left(\frac{2}{3}\right)^{z_{11}}\left(\frac{1}{3}\right)^{s_2 - z_{11}}.$$

This permits the computation of the p-value for hypothesis testing. E.g., with $\delta > 0$ as H_1, $p = \Pr(Z_{10} + Z_{11} \geq z_{10} + z_{11} = v)$, i.e.,

$$p = \sum_{k_1 + k_2 \geq v}\sum \binom{s_1}{k_1}\left(\frac{1}{3}\right)^{s_1}\left(\frac{2}{3}\right)^{s_1 - k_1}\binom{s_2}{k_2}\left(\frac{2}{3}\right)^{k_2}\left(\frac{1}{3}\right)^{s_2 - k_2}. \qquad (4.3)$$

4.2. *The asymptotic unconditional power function*

From the above exact test it is apparent that any assessment of power at the conclusion of a study with two-to-one individual matching would best be made conditionally on S_1 and S_2. That conditional power function involves nuisance parameters (see Birch [1964]) whose evaluation in practice would tend to be quite problematic. However, in the present context we are concerned with design problems (cf. sections 4.3, 5.2, and 7) and they call for the unconditional power function. It is seen below that this function can be approximated in terms of rather simple expressions.

One approach to the asymptotic unconditional power function, $\Pi(\delta)$, is that of taking

$$\Pi(\delta) = E_S \Pi(\delta \mid S),$$

where $S = S_1 + S_2$, i.e.,

$$S = Z_{10} + Z_{01} + Z_{11} + Z_{02}.$$

It is shown in Proofs 1 and 2 of Appendix A that, for the statistic in (4.2),

$$E(T \mid S) = (2S)^{\frac{1}{2}}\delta/(\psi + \tfrac{1}{2}\psi_2)$$

and

$$\text{var}\,(T \mid S) = [(\psi + \tfrac{1}{2}\psi_2)(2\psi - \tfrac{1}{2}\psi_2) - 2\delta^2]/(\psi + \tfrac{1}{2}\psi_2)^2,$$

where

$$\psi = E(P_1 + P_2 - 2P_1P_2) = \theta_1 + \theta_2 - 2\theta_1\theta_2 - 2\,\text{cov}\,(P_1, P_2) \tag{4.4}$$

and

$$\psi_2 = E(P_2 + P_2 - 2P_2P_2) = 2\theta_2(1 - \theta_2) - 2\,\text{var}\,(P_2). \tag{4.5}$$

Therefore, for a one-sided test,

$$\Pi(\delta \mid S) = \Phi\left[\frac{-u_\alpha(\psi + \frac{1}{2}\psi_2) + (2S)^{\frac{1}{2}}\,|\delta|}{[(\psi + \frac{1}{2}\psi_2)(2\psi - \frac{1}{2}\psi_2) - 2\delta^2]^{\frac{1}{2}}}\right], \tag{4.6}$$

where Φ denotes the distribution function of a standard normal variate, and u_α is the $100(1 - \alpha)$ percentile of the standard normal distribution.

A first approximation to $\Pi(\delta)$ may now be obtained by evaluating $\Pi(\delta \mid S)$ at $S = E(S) = JE[P_1(1 - P_2)^2 + (1 - P_1)2P_2(1 - P_2) + P_12P_2(1 - P_2) + (1 - P_1)P_2^2] = J(\psi + \frac{1}{2}\psi_2)$. Thus, for a one-sided test,

$$\Pi(\delta) \doteq \Phi\left[\frac{-u_\alpha(\psi + \frac{1}{2}\psi_2) + [2J(\psi + \frac{1}{2}\psi_2)]^{\frac{1}{2}}\,|\delta|}{[(\psi + \frac{1}{2}\psi_2)(2\psi - \frac{1}{2}\psi_2) - 2\delta^2]^{\frac{1}{2}}}\right]. \tag{4.7}$$

From the definitions of ψ and ψ_2 in (4.4) and (4.5), it is apparent that in the vicinity of the null state one may take $\psi \doteq \psi_2$. Thus, in the assessment of local power, (4.7) may be further approximated as

$$\Pi(\delta) \doteq \Phi\left[\frac{-u_\alpha\psi + 2(J\psi/3)^{\frac{1}{2}}\,|\delta|}{(\psi^2 - 8\delta^2/9)^{\frac{1}{2}}}\right]. \tag{4.8}$$

An alternative approach may be based on finding the parameters of the asymptotic normal distribution of T. Using the above conditional results we obtain

$$E(T) = E_S(T \mid S) = 2^{\frac{1}{2}}E(S^{\frac{1}{2}})\delta/(\psi + \tfrac{1}{2}\psi_2),$$

and

$$\begin{aligned}\text{var}\,(T) &= E_S[\text{var}\,(T \mid S)] + \text{var}\,[E(T \mid S)]\\ &= [(\psi + \tfrac{1}{2}\psi_2)(2\psi - \tfrac{1}{2}\psi_2) - 2\delta^2]/[\psi + \tfrac{1}{2}\psi_2)^2 + [2^{\frac{1}{2}}\delta/(\psi + \tfrac{1}{2}\psi_2)]^2\,\text{var}\,(S^{\frac{1}{2}})\\ &= \{(\psi + \tfrac{1}{2}\psi_2)(2\psi - \tfrac{1}{2}\psi_2) - 2\delta^2[1 - \text{var}\,(S^{\frac{1}{2}})]\}/[\psi + \tfrac{1}{2}\psi_2)^2.\end{aligned}$$

It follows that the asymptotically exact unconditional power function for the case of a one-sided test is

$$\Pi(\delta) = \Phi\left[\frac{-u_\alpha(\psi + \frac{1}{2}\psi_2) + 2^{\frac{1}{2}}E(S^{\frac{1}{2}})\,|\delta|}{\{(\psi + \frac{1}{2}\psi_2)(2\psi - \frac{1}{2}\psi_2) - 2\,\delta^2[1 - \text{var}\,(S^{\frac{1}{2}})]\}^{\frac{1}{2}}}\right]. \quad (4.9)$$

A first-order approximation to this function is obtained by replacing $E(S^{\frac{1}{2}})$ and var $(S^{\frac{1}{2}})$ by their first-order approximations from Taylor series expansions about $E(S)$:

$$E(S^{\frac{1}{2}}) \doteq [J(\psi + \tfrac{1}{2}\psi_2)]^{\frac{1}{2}} \qquad \text{and} \qquad \text{var}\,(S^{\frac{1}{2}}) = \tfrac{1}{4}(1 - \psi - \tfrac{1}{2}\psi_2).$$

Thus,

$$\Pi(\delta) \doteq \Phi\left[\frac{-u_\alpha(\psi + \frac{1}{2}\psi_2) + [2J(\psi + \frac{1}{2}\psi_2)]^{\frac{1}{2}}\,|\delta|}{\{(\psi + \frac{1}{2}\psi_2)(2\psi - \frac{1}{2}\psi_2) - \delta^2(3 + \psi + \frac{1}{2}\psi_2)/2\}^{\frac{1}{2}}}\right]. \quad (4.10)$$

The further approximation corresponding to $\psi \doteq \psi_2$ is

$$\Pi(\delta) \doteq \Phi\left[\frac{-u_\alpha\psi + 2(J\psi/3)^{\frac{1}{2}}\,|\delta|}{[\psi^2 - \delta^2(2 + \psi)/3]^{\frac{1}{2}}}\right]. \quad (4.11)$$

The numerical evaluations in Appendix C indicate that the approximations from this latter approach, (4.10) and (4.11), are more accurate than (4.7) and (4.8), respectively.

Second-order approximations are given in Appendix B and evaluated in Appendix C. They afford only slight refinements of the above first-order approximations.

Regarding the case of a two-sided alternative hypothesis, each of the additive power contributions from the two tails may be evaluated by using $\Pi(\delta)$, with $u_{\frac{1}{2}\alpha}$ in place of u_α, and with $-|\delta|$ in place of $|\delta|$ for the lower tail contribution.

4.3. *Sample size determination*

The sample size which, with α level of significance, yields the power $1 - \beta$ against δ is, from (4.7),

$$J \doteq \{u_\alpha(\psi + \tfrac{1}{2}\psi_2) + u_\beta[(\psi + \tfrac{1}{2}\psi_2)(2\psi - \tfrac{1}{2}\psi_2) - 2\delta^2]^{\frac{1}{2}}\}^2/2(\psi + \tfrac{1}{2}\psi_2)\delta^2.$$

The corresponding approximation from (4.8) is

$$J \doteq 3[u_\alpha\psi + u_\beta(\psi^2 - 8\psi\delta^2/9)^{\frac{1}{2}}]/4\psi\delta^2.$$

The alternative first-order approximation to the power function, (4.10), yields

$$J \doteq \{u_\alpha(\psi + \tfrac{1}{2}\psi_2) + u_\beta[(\psi + \tfrac{1}{2}\psi_2)(2\psi - \tfrac{1}{2}\psi_2) - \delta^2(3 + \psi + \tfrac{1}{2}\psi_2)/2]^{\frac{1}{2}}\}^2/2(\psi + \tfrac{1}{2}\psi_2)\delta^2.$$

The approximation to this expression from (4.11) is

$$J \doteq 3\{u_\alpha\psi + u_\beta[\psi^2 - \delta^2(2 + \psi)/3]^{\frac{1}{2}}\}^2/4\psi\delta^2.$$

The second-order approximations to the asymptotic power function (see

Appendix B) are not readily applicable to sample size determination.

As to the case of a two-sided alternative hypothesis, α and β are usually small enough so that all the power is derived essentially from one of its two components, and in such situations the above sample-size formulas apply upon substituting $u_{\frac{1}{2}\alpha}$ for u_α.

5. THE GENERAL CASE

5.1. *The asymptotic unconditional power function*

In section 4.2 as well as in earlier work on the matched pairs design (Miettinen [1968a, b]) results for unconditional power were derived through results on the conditional distribution of T. In the general case of $R:1$ individual matching designs this approach does not seem to be readily applicable (cf. Miettinen [1968b]). Therefore, in the present context a result for the unconditional power will be derived without the intermediary of the conditional distribution of T. Due to the nature of the approach, the immediate result applies well only when $|\delta|$ is small relative to ψ.

For a derivation of the result for local unconditional power, it is convenient to write the test statistic (3.1) as

$$T = U_J/V_J,$$

where

$$U_J = J^{-\frac{1}{2}} \sum_1^J (RX_{1i} - X_{2i}) \quad \text{and} \quad V_J = \left[J^{-1} \sum_1^J X_i(1 + R - X_i)\right]^{\frac{1}{2}}.$$

The expectation of U_J is

$$E(U_J) = J^{-\frac{1}{2}} \sum_1^J (R\theta_1 - R\theta_2) = RJ^{\frac{1}{2}}\delta,$$

and by Proof 3 of Appendix A, var $(U_J) = R^2(\psi - \delta^2) - \frac{1}{2}R(R-1)\psi_2$. It follows that if $J \to \infty$ and $\delta \to 0$ in such a manner that $J^{\frac{1}{2}}\delta$ remains fixed, then the distribution function $F_J(u)$ of U_J tends to

$$F(u) = \Phi\left[\frac{u - RJ^{\frac{1}{2}}\delta}{[R^2(\psi - \delta^2) - \frac{1}{2}R(R-1)\psi_2]^{\frac{1}{2}}}\right].$$

On the other hand, the sequence V_J converges stochastically to the constant $[(R+1)E(X) - E(X^2)]^{\frac{1}{2}}$, and by Proof 4 of Appendix A this limit equals $R^{\frac{1}{2}}[\psi + \frac{1}{2}(R-1)\psi_2]^{\frac{1}{2}}$.

From the above results it follows—e.g., by Theorem 20.6, Cramér [1946]—that as $J \to \infty$ and $\delta \to 0$ in such a manner that $N^{\frac{1}{2}}\delta$ remains fixed, Pr $(U_J/V_J < u_\alpha) = \Pr(T < u_\alpha)$ tends to

$$\Phi\left[\frac{u_\alpha[\psi + \frac{1}{2}(R-1)\psi_2]^{\frac{1}{2}} - (RJ)^{\frac{1}{2}}\delta}{[R(\psi - \delta^2) - \frac{1}{2}(R-1)\psi_2]^{\frac{1}{2}}}\right].$$

The corresponding approximation to the asymptotic unconditional power function for a one-sided test is

$$\Pi(\delta) \doteq \Phi\left[\frac{-u_\alpha[\psi + \frac{1}{2}(R - 1)\psi_2]^{\frac{1}{2}} + (RJ)^{\frac{1}{2}}\,|\delta|}{[R(\psi - \delta^2) - \frac{1}{2}(R - 1)\psi_2]^{\frac{1}{2}}}\right]. \tag{5.1}$$

As this result was derived in a manner which is adequate for small $|\delta|$ only, it is interesting and pertinent to compare it to earlier results without such limitation for the cases of 1:1 and 2:1 individual matching design. For this purpose it is expedient to rewrite (5.1) as $\Pi(\delta) \doteq$

$$\Phi\left[\frac{-u_\alpha[\psi + \frac{1}{2}(R - 1)\psi_2] + \{RJ[\psi + \frac{1}{2}(R - 1)\psi_2]\}^{\frac{1}{2}}\,|\delta|}{\{[\psi + \frac{1}{2}(R - 1)\psi_2][R\psi - \frac{1}{2}(R - 1)\psi_2] - R[\psi + \frac{1}{2}(R - 1)\psi_2]\,\delta^2\}^{\frac{1}{2}}}\right]. \tag{5.2}$$

If in this result the latter term in the denominator, $-R[\psi + \frac{1}{2}(R - 1)\psi_2]\delta^2$, is replaced by $-R\delta^2$, it gives exactly the earlier first-order approximation (4.7) as well as its equivalent for the matched pairs design (cf. Miettinen [1968a, b]). This modification is, as was to be expected, immaterial with small $|\delta|$, but for relatively large values of $|\delta|$ it may be important.

Making the above modification in (5.2) yields

$$\Pi(\delta) \doteq \Phi\left[\frac{-u_\alpha[\psi + \frac{1}{2}(R - 1)\psi_2] + \{RJ[\psi + \frac{1}{2}(R - 1)\psi_2]\}^{\frac{1}{2}}\,|\delta|}{\{[\psi + \frac{1}{2}(R - 1)\psi_2][R\psi - \frac{1}{2}(R - 1)\psi_2] - R\delta^2\}^{\frac{1}{2}}}\right]. \tag{5.3}$$

It was seen above that this formula applies well in the cases of $R = 1$ and $R = 2$' without the limitation that $|\delta|$ be small. One may surmise that this is the case also for larger R, particularly for practical purposes, as the frequency with which a particular $R : 1$ individual matching design is optimal decreases sharply with increasing R so that designs with, say, $R > 4$ are of very little interest.

In the vicinity of the null state one may again set $\psi \doteq \psi_2$, and the result in (5.3) becomes

$$\Pi(\delta) \doteq \Phi\left[\frac{-u_\alpha(1 + R)\psi + [2R(1 + R)J\psi]^{\frac{1}{2}}\,|\delta|}{[(1 + R)^2\psi^2 - 4R\delta^2]^{\frac{1}{2}}}\right]. \tag{5.4}$$

But setting $\psi \doteq \psi_2$ presupposes also that $|\delta|$ is small relative to ψ, so that it is reasonable for some purposes to make the further simplification of deleting the latter term in the denominator. This yields

$$\Pi(\delta) \doteq \Phi\{-u_\alpha + [2RJ/(1 + R)\psi]^{\frac{1}{2}}\,|\delta|\}. \tag{5.5}$$

5.2. *Selection of the design constants*

Suppose again that the desired degree of information is specified in terms of the level α of the test, whether the test is to be one-sided or two-sided, and the power level $1 - \beta$ to be attained against some alternative δ. The design problem then is to choose the constants R and J in such a manner that this information is obtained at a minimum cost.

Only the simple (and useful) cost model is considered where

C_0 = 'set-up' cost,
c_1 = unit cost in Series 1, and
c_2 = unit cost in Series 2,

so that the total cost of the study is

$$C = C_0 + (c_1 + Rc_2)J. \tag{5.6}$$

The first problem is to choose R in such a way that C is minimized for the particular combination of α, β, and the parameters. From (5.3),

$$J \doteq \{u_\alpha[\psi + \tfrac{1}{2}(R - 1)\psi_2]^{\frac{1}{2}} + u_\beta[R\psi - \tfrac{1}{2}(R - 1)\psi_2 - R\delta^2/(\psi + \tfrac{1}{2}(R - 1)\psi_2)]^{\frac{1}{2}}\}^2/R\delta^2. \tag{5.7}$$

Substituting this expression for J in (5.6) permits a trial-and-error solution for the integer value of R which minimizes C for the case of a one-sided alternative.

The above approach to the selection of R has the drawback that the solution depends on the nuisance parameters, and typically good estimates of them are not available in the planning stage of the study. These problems are avoided by using the somewhat less accurate power function in (5.5). The corresponding expression for the total cost (5.6) is

$$C \doteq C_0 + (c_1 + Rc_2)(1 + R)\psi(u_\alpha + u_\beta)^2/2R\delta^2, \tag{5.8}$$

and this cost function is minimized by taking

$$R = (c_1/c_2)^{\frac{1}{2}}. \tag{5.9}$$

R is, of course, an integer, and in practice one could, thus, choose that matching ratio which best corresponds to the square root of the inverse of the unit cost ratio. In case of ambivalence, the integer value of R which minimizes C in (5.8) may be obtained by trial-and-error minimization of $(R + c_1/c_2)(1 + R)/R$.

With R selected, the corresponding J for the case of a one-sided test is specified by (5.7). This formula has the obvious drawback that it involves two nuisance parameters, ψ and ψ_2. However, in the vicinity of the null state, with $|\delta|$ small relative to ψ, it is appropriate to use the power expressions in (5.4) and (5.5). They yield

$$\begin{aligned} J &\doteq \{u_\alpha[(1 + R)\psi]^{\frac{1}{2}} + u_\beta[(1 + R)\psi - 4R\delta^2/(1 + R)\psi]^{\frac{1}{2}}\}^2/2R\delta^2 \\ &\doteq (1 + R)\psi(u_\alpha + u_\beta)^2/2R\delta^2. \end{aligned} \tag{5.10}$$

6. EVALUATION OF THE NUISANCE PARAMETERS

It is seen from the power functions in (5.1) and (5.3) that with $R = 1$ there is only one nuisance parameter, ψ. Moreover, it was concluded on the basis of the definitions in (4.4) and (4.5) that in the vicinity of the null state one may take $\psi_2 = \psi$ and thereby have a single nuisance parameter even when $R > 1$.

The evaluation of ψ has been discussed in the context of the matched pairs design (Miettinen [1968a, b]), where it has the interpretation of being the probability that a pair will show discordant responses. It is usually reasonable to assume that cov $(P_1, P_2) \geq 0$. The corresponding range of ψ is

$$|\delta| \leq \psi \leq \theta_1 + \theta_2 - 2\theta_1\theta_2,$$

and in a priori evaluation it would generally be advisable to choose a value which is relatively close to the above upper bound. Furthermore, the maximum likelihood estimate of ψ based on matched pairs data has been shown (Miettinen [1968a]) to be

$$\hat{\psi} = [Z_{10} + Z_{01} + \delta(Z_{10} - Z_{01})]/2J + \{[Z_{10} + Z_{01} + \delta(Z_{10} - Z_{01})]^2/4J^2 - \delta[Z_{10} - Z_{01} - \delta(Z_{11} + Z_{00})]/J\}^{\frac{1}{2}}, \tag{6.1}$$

where Z_{fg} is the frequency of pairs with $Y_{1j} = f$ and $Y_{2j} = g$.

If data from an R:1 individual matching design with $R > 1$ are at hand, the estimate of ψ may be taken as

$$\hat{\psi} = \sum_{1}^{R} \hat{\psi}_k/R, \tag{6.2}$$

where $\hat{\psi}_k$ is computed according to (6.1), taking Z_{fg} as the frequency of matched groups with $Y_{1j} = f$ and $Y_{2jk} = g$.

The definition of ψ_2 in (4.5) may be put to the form $\psi_2 = E[P_2(1 - P_2)]$. Thus, it is the probability that a pair of control subjects within the same matched group show discordant responses. Its estimate, therefore, may be taken as the proportion of such pairs, i.e.,

$$\hat{\psi}_2 = \sum_{j=1}^{J} \sum_{k=1}^{R} \sum_{k'=1}^{R} (Y_{2jk} - Y_{2jk'})^2/R(R - 1)J. \tag{6.3}$$

7. THE CHOICE BETWEEN R-TO-ONE INDIVIDUAL MATCHING DESIGNS AND THE USE OF TWO INDEPENDENT SERIES

If matching is not needed for validity (comparability of the two series), it is pertinent to know under what conditions individual matching with the optimal fixed matching ratio would be indicated from the efficiency point of view. In the case of retrospective (case history) studies matching tends to decrease efficiency (cf. Miettinen [1968c]) and therefore the present discussion relates only to prospective (cohort) designs and experiments.

The answer depends on the cost model. As an example, consider the common nonexperimental situation where a set of propositi is obtained at a unit cost c_1 which does not depend on whether or not the control series is matched. Suppose also that the cost model in (5.6) is adequate for the matching designs. Then, by (5.9) and (5.10) the cost of the optimal R:1 individual matching design with a one-sided alternative hypothesis is approximately

$$C \doteq C_0 + (c_1^{\frac{1}{2}} + c_2^{\frac{1}{2}})^2\psi(u_\alpha + u_\beta)^2/2\delta^2.$$

The corresponding result for the case of two independent series may be taken as

$$C' \doteq C_0 + [c_1^{\frac{1}{2}} + (c_2')^{\frac{1}{2}}]^2\psi'(u_\alpha + u_\beta)^2/2\delta^2,$$

where

$$\psi' = \theta_1 + \theta_2 - 2\theta_1\theta_2$$

and c_2' is the unit cost of controls when no matching is attempted.

In terms of the above cost model and notation, matching is justified by an efficiency gain if $C < C'$, i.e., if

$$(\psi/\psi') < [1 + (c_2'/c_1)^{\frac{1}{2}}]/[1 + (c_2/c_1)^{\frac{1}{2}}].$$

It is to be understood here that in the unmatched case the allocation ratio R' can be essentially any positive rational number and its optimal value can, thus, well be approximated by $(c_1/c_2')^{\frac{1}{2}}$. On the other hand, however, substitution of $(c_1/c_2)^{\frac{1}{2}}$ for the optimal value of R in the derivation of the above results may not be very accurate because R is an integer.

8. EXAMPLE OF APPLICATION

Trichopoulos *et al.* [1969] tested the hypothesis that induced abortions increase the risk of ectopic implantation in subsequent pregnancies. Utilizing the case history (retrospective) approach, 18 propositi with ectopic pregnancy following at least one earlier pregnancy were identified in a large series collected for a breast cancer study. For each propositus, four control subjects were drawn from the rest of the available series, matching for order of pregnancy, age, and husband's education. E.g., for a woman whose third pregnancy was ectopic and occurred in the age interval of 30–34 years, and whose husband had between one and seven years of education, the control subjects had to have their third pregnancy in that same age interval in addition to the requirement that the husband have 1–7 years of education. The history of induced abortions terminating any of the preceding pregnancies was recorded for the propositi and the controls. The essential data are given in Table 1.

For testing whether the frequency of positive histories of induced abortion is significantly higher among the propositi, let us first apply the statistic in (3.1). In the numerator, the quantity $\sum_i RX_{1i} = R\sum_i X_{1i}$ is four times the number of '+' signs in the propositus column of Table 1, while $\sum_i X_{2i}$ is the total number of controls with a positive history. Thus, $\sum_i (RX_{1i} - X_{2i}) = 4(12) - 16 = 32$. As to the sum in the denominator of T, the contribution from each of the five matched groups with all histories negative is zero, as for these $X_i = 0$; there are four matched groups with one subject giving a positive history, and their total contribution to the sum is $4(1)(1 + 4 - 1) = 16$; etc. The value of the denominator is thus readily seen to be $(64)^{\frac{1}{2}} = 8$. The resulting value for T is $32/8 = 4.0$, and this corresponds to the one-sided p-value of 0.00003. Applying a continuity correction, the absolute value of the numerator is reduced by $\frac{1}{2}(1 + R) = 2.5$, and the result becomes $T = 3.7$ with $p = 0.00011$.

An exact test analogous to that in section 4.1 is also easy to apply here. Among the four matched groups with $X_i = 1$ there were three with $X_{1i} = 1$. The binomial probability for this under the null hypothesis is $\binom{4}{3}\left(\frac{1}{5}\right)^3\left(\frac{4}{5}\right)$.

TABLE 1

PREVIOUS HISTORY OF INDUCED ABORTION IN PROPOSITI WITH ECTOPIC PREGNANCY AND MATCHED CONTROLS. TRICHOPOULOS *et al.*

Index number	History of induced abortion				
	Propositus	Control number			
		1	2	3	4
1	−	−	−	−	−
2	+	−	+	−	−
3	+	−	−	−	−
4	−	−	−	−	−
5	−	+	−	−	−
6	+	−	−	−	−
7	+	−	−	−	−
8	−	−	−	−	−
9	+	+	−	−	+
10	+	−	+	−	−
11	+	−	+	+	−
12	−	−	−	−	−
13	+	+	+	+	+
14	+	−	−	+	−
15	+	−	−	+	−
16	+	+	−	−	−
17	−	−	−	−	−
18	+	+	−	−	+

Similarly for other values of X_i. Thus, the null probability of the observed outcome conditionally on the X_i's is

$$\left[\binom{4}{3}\left(\frac{1}{5}\right)^3\left(\frac{4}{5}\right)\right]\left[\binom{5}{5}\left(\frac{2}{5}\right)^5\left(\frac{3}{5}\right)^0\right]\left[\binom{3}{3}\left(\frac{3}{5}\right)^3\left(\frac{2}{5}\right)^0\right] = 4\left(\frac{1}{5}\right)^3\left(\frac{4}{5}\right)\left(\frac{2}{5}\right)^5\left(\frac{3}{5}\right)^3.$$

There are two other equally extreme outcomes (each with a total of 11 'successes' in the three binomials) and one more extreme outcome (with a total of 12 'successes'). Their probabilities, together with the one shown above, add up to the one-sided p-value of 0.00009. As this falls between the two values derived from the asymptotic test, the size of the series seems to be sufficient for the application of large-sample procedures with reasonably accurate results.

One might next wish to estimate the sensitivity of this study. E.g., it might be asked what power it could have been expected to have against the alternative where the frequency of positive histories of induced abortions among women with ectopic pregnancy is 20 percentage points higher than among 'comparable' women without ectopic pregnancy ($\delta = 0.2$), using a one-sided test at the 5% level of significance. The first problem here is to estimate the nuisance parameters. Using (6.1) and the data for the propositi and the first set of controls in Table 1, the first estimate of ψ becomes

$$\hat{\psi}_1 = [8 + 1 + 0.2(8 - 1)]/2(18) + \{[8 + 1 + 0.2(8 - 1)]^2/4(18)^2 - 0.2[8 - 1 - 0.2(9)]/18\}^{\frac{1}{2}} = 0.44914.$$

The estimates obtainable by using the second, third, and fourth sets of controls are 0.33333, 0.33333, and 0.40000, respectively. Thus, upon averaging as in (6.2), the 'best' estimate of ψ becomes

$$\hat{\psi} = 0.37895.$$

As to the estimation of ψ_2 according to (6.3), the contributions to the numerator from those matched groups where one control has positive history is 6, while those with two '+' signs contribute 8. Quite immediately, therefore,

$$\hat{\psi}_2 = 60/216 = 0.27778.$$

Applying the above $\hat{\psi}$ and $\hat{\psi}_2$, together with $u_\alpha = 1.645$ and $R = 4$, to (5.3) yields the power estimate

$$\hat{\Pi}(0.2) \doteq \Phi(0.242) = 0.60.$$

(The formula for local power, (5.1), gives here $\hat{\Pi}(0.2) \doteq \Phi(0.237) = 0.59$, and the close agreement with the above result indicates rather wide applicability for this formula despite the theoretical limitation to the vicinity of the null state.)

It is of interest to consider here the sensitivity gain from the utilization of multiple controls, instead of just one, for each of the 18 available propositi. With $R = 1$ and other specifications as in the above, the formula in (5.3) yields $\hat{\Pi}(0.2) \doteq \Phi(-0.314) = 0.38$, substantially less than the above 0.60 for $R = 4$. On the other hand, $R = 10$ corresponds to $\hat{\Pi}(0.2) \doteq \Phi(0.386) = 0.65$, so that with increasing R the returns are rapidly diminishing.

ACKNOWLEDGMENTS

The author is indebted to Miss Linda Rosenstein for carrying out the computer work for Appendix C, and to the Editor and a referee for helpful suggestions.

This work was supported by Grants 5 T1 GM 7 and HE 10436-02 from the National Institutes of Health. It formed a part of the author's Ph.D. thesis submitted to the University of Minnesota in March, 1968.

APPARIEMENT INDIVIDUEL A DES TEMOINS MULTIPLES DANS LE CAS DES REPONSES EN TOUT-OU-RIEN

RESUME

Le principe d'appariement individuel, 'un à un,' des plans à couples de sujets appariés est généralisé à l'appariement de 'R sujets à un' dans le cas de réponses en tout-ou-rien et de procédures à taille de l'échantillon fixée. Un test est établi; sa fonction de puissance asymptotique également; le choix du rapport R d'appariement est étudié en relation avec les coûts unitaires dans les deux groupes à comparer et finalement les procédures pour déterminer la taille de l'échantillon sont décrites.

REFERENCES

Beard, R. E. [1947]. Some notes on approximate product-integration. *J. Inst. Actuar. 73*, 356–416.

Bennett, B. M. [1967]. Tests of hypotheses concerning matched samples. *J. R. Statist. Soc. B* 29, 468–74.

Billewicz, W. Z. [1964]. Matched samples in medical investigations. *Brit. J. Prev. Soc. Med. 18*, 167–73.

Billewicz, W. Z. [1965]. The efficiency of matched samples: an empirical investigation. *Biometrics 21*, 623–44.

Birch, N. W. [1964]. The detection of partial association, I: the 2 × 2 case. *J. R. Statist. Soc. B 26*, 313–24.

Chase, G. R. [1968]. On the efficiency of matched pairs in Bernoulli trials. *Biometrika 55*, 365–9.

Cochran, W. G. [1950]. The comparison of percentages in matched samples. *Biometrika 37*, 256–66.

Cox, D. R. [1966]. A simple example of comparison involving quantal data. *Biometrika 53*, 215–20.

Cramér, H. [1946]. *Mathematical Methods of Statistics*. Princeton University Press, Princeton, N. J.

Kendall, M. G. and Stuart, A. [1963]. *The Advanced Theory of Statistics. Vol. 1*. 2nd Edn. Hafner Publishing Company, New York.

Mantel, N. and Haenszel, W. [1959]. Statistical aspects of the analysis of data from retrospective studies of disease. *J. Nat. Cancer Inst. 22*, 719–48.

McNemar, Q. [1947]. Note on the sampling error of the difference between corrected proportions or percentages. *Psychometrika 12*, 153–7.

Miettinen, O. S. [1966]. Matched pairs vs. two independent series in the case of all-or-none responses. M. Sc. Thesis, Univ. of Minn. (Unpublished.)

Miettinen, O. S. [1968a]. The matched pairs design in the case of all-or-none responses. *Biometrics 24*, 339–52.

Miettinen, O. S. [1968b]. Some basic theory for matching designs in nonexperimental research on causation. Ph. D. Thesis, Univ. of Minn. University Microfilms, Inc., Ann Arbor, Mich.

Miettinen, O. S. [1968c]. Under- and overmatching in epidemiologic studies. *Atti 5° Cong. Internaz. Igiene Med. Prev. 1*, 49–61.

Patnaik, P. B. [1948]. Power function for the test for the difference between two proportions in a 2 × 2 table. *Biometrika 35*, 157–75.

Trichopoulos, D., Miettinen, O. S., and Polychronopoulou, A. [1969]. Induced abortions and ectopic pregnancy. (Unpublished.)

Worcester, J. [1964]. Matched samples in epidemiologic studies. *Biometrics 20*, 841–8.

APPENDIX A

Proofs

Proof 1

Letting $\lambda_{fg} = \Pr(X_1 = f, X_2 = g)$ we have

$$\begin{aligned} E(T \mid S = s) &= (2s)^{-\frac{1}{2}} s(2\lambda_{10} - \lambda_{01} + \lambda_{11} - 2\lambda_{02})/(\lambda_{10} + \lambda_{01} + \lambda_{11} + \lambda_{02}) \\ &= (2s)^{-\frac{1}{2}} sE[2P_1(1 - P_2)^2 - (1 - P_1)2P_2(1 - P_2) \\ &\quad + P_1 2P_2(1 - P_2) - 2(1 - P_1)P_2^2]/E[P_1(1 - P_2)^2 \\ &\quad + (1 - P_1)2P_2(1 - P_2) + P_1 2P_2(1 - P_2) + (1 - P_1)P_2^2] \\ &= (2s)^{-\frac{1}{2}} sE[2(P_1 - P_2)]/E[(P_1 + P_2 - 2P_1P_2) + (P_2 - P_2^2)] \\ &= (2s)^{\frac{1}{2}} \delta/(\psi + \tfrac{1}{2}\psi_2). \end{aligned}$$

Proof 2

With λ's defined as in Proof 1, writing $\lambda_{10} + \lambda_{01} + \lambda_{11} + \lambda_{02} = \mu$, and realizing that conditionally on $S = s$ the Z's are frequencies in a multinomial distribution $(s, \lambda_{10}/\mu, \lambda_{01}/\mu, \lambda_{11}/\mu, \lambda_{02}/\mu)$, we may write

$$\begin{aligned}
\text{var}\,(T \mid S = s) \\
&= (2s)^{-1}s\mu^{-2}[4\lambda_{10}(\mu - \lambda_{10}) + \lambda_{01}(\mu - \lambda_{01}) + \lambda_{11}(\mu - \lambda_{11}) + 4\lambda_{02}(\mu - \lambda_{02}) \\
&\qquad + 4\lambda_{10}\lambda_{01} - 4\lambda_{10}\lambda_{11} + 8\lambda_{10}\lambda_{02} + 2\lambda_{01}\lambda_{11} - 4\lambda_{01}\lambda_{02} + 4\lambda_{11}\lambda_{02}] \\
&= (2\mu^2)^{-1}\{\mu[\mu + 3(\lambda_{10} + \lambda_{02})] - (2\lambda_{10} - \lambda_{01} + \lambda_{11} - 2\lambda_{02})^2\} \\
&= (2\mu^2)^{-1}\{\mu^2 + 3\mu E[P_1(1 - P_2)^2 + (1 - P_1)P_2^2] - [2E(P_1(1 - P_2)^2) \\
&\qquad - E((1 - P_1)2P_2(1 - P_2)) + E(P_1 2P_2(1 - P_2)) - 2E((1 - P_1)P_2^2)]^2\} \\
&= (2\mu^2)^{-1}\{\mu^2 + 3\mu E[(P_1 + P_2 - 2P_1P_2) - (P_2 - P_2^2)] - [2E(P_1 - P_2)]^2\} \\
&= (2\mu^2)^{-1}\{\mu^2 + 3\mu(\psi - \tfrac{1}{2}\psi_2)] - 4\,\delta^2\} \\
&= [(\psi + \tfrac{1}{2}\psi_2)(2\psi - \tfrac{1}{2}\psi_2) - 2\delta^2]/(\psi + \tfrac{1}{2}\psi_2)^2.
\end{aligned}$$

Proof 3

By the independence assumptions of the model,

$$\begin{aligned}
\text{var}\,(U_J) &= J^{-1}\sum_1^J [R^2\,\text{var}\,(X_{1j}) + \text{var}\,(X_{2j}) - 2R\,\text{cov}\,(X_{1j}\,, X_{2j})] \\
&= J^{-1}\sum_1^J \{R^2[E(\text{var}\,(X_1 \mid P_1)) + \text{var}\,(E(X_1 \mid P_1))] \\
&\qquad + E[\text{var}\,(X_2 \mid P_2)] + \text{var}\,[E(X_2 \mid P_2)] \\
&\qquad - 2R[E(\text{cov}\,(X_1\,, X_2 \mid P_1\,, P_2)) + \text{cov}\,(E(X_1 \mid P_1), E(X_2 \mid P_2))]\} \\
&= R^2\{E[P_1(1 - P_1)] + \text{var}\,(P_1)\} \\
&\qquad + RE[P_2(1 - P_2)] + R^2\,\text{var}\,(P_2) - 2R^2[0 + \text{cov}\,(P_1\,, P_2)] \\
&= R^2[\theta_1 + \theta_2 - 2\theta_1\theta_2 - 2\,\text{cov}\,(P_1\,, P_2) - \theta_1^2 - \theta_2^2 + 2\theta_1\theta_2] \\
&\qquad - R(R - 1)[\theta_2 - \theta_2^2 - \text{var}\,(P_2)] \\
&= R^2(\psi - \delta^2) - \tfrac{1}{2}R(R - 1)\psi_2\,.
\end{aligned}$$

Proof 4

$$\begin{aligned}
&[(R + 1)E(X) - E(X^2)]^{\frac{1}{2}} \\
&\quad = \{(R + 1)E(X_1 + X_2) - [E(X_1 + X_2)]^2 - \text{var}\,(X_1 + X_2)\}^{\frac{1}{2}} \\
&\quad = \{(R + 1)(\theta_1 + R\theta_2) - (\theta_1 + R\theta_2)^{\,2} \\
&\qquad\qquad - E[\text{var}\,(X_1 + X_2 \mid P_1\,, P_2)] - \text{var}\,[E(X_1 + X_2 \mid P_1\,, P_2)]\}_{\frac{1}{2}}
\end{aligned}$$

$$= \{(R + 1)(\theta_1 + R\theta_2) - (\theta_1 + R\theta_2)^2 - E[P_1(1 - P_1) + RP_2(1 - P_2)] - \text{var}(P_1 + RP_2)\}^{\frac{1}{2}}$$
$$= [(R + 1)(\theta_1 + R\theta_2) - (\theta_1 + R\theta_2)^2 - \theta_1 + \theta_1^2 + \text{var}(P_1) - \tfrac{1}{2}R\psi_2 - \text{var}(P_1) - R^2\,\text{var}(P_2) - 2R\,\text{cov}(P_1, P_2)]^{\frac{1}{2}}$$
$$= \{R[\theta_1 + \theta_2 - 2\theta_1\theta_2 - 2\,\text{cov}(P_1, P_2)] + R^2[\theta_2 - \theta_2^2 - \text{var}(P_2)] - \tfrac{1}{2}R\psi_2\}^{\frac{1}{2}}$$
$$= (R\psi + \tfrac{1}{2}R^2\psi_2 - \tfrac{1}{2}R\psi_2)^{\frac{1}{2}}$$
$$= R^{\frac{1}{2}}[\psi + \tfrac{1}{2}(R - 1)\psi_2]^{\frac{1}{2}}.$$

APPENDIX B

Second order approximations to the asymptotic unconditional power function of the 2:1 individual matching design

As in the matched pairs design (see Miettinen, 1968a, b), various second-order approximations to the asymptotic unconditional power function can be derived. Utilizing the relation $\Pi(\delta) = E_S\Pi(\delta \mid S)$ and expanding $\Pi(\delta \mid S)$ in a Taylor series about $E(S) = J(\psi + \frac{1}{2}\psi_2)$ gives the second-order approximation

$$\Pi(\delta) \doteq \Pi[\delta \mid S = J(\psi + \tfrac{1}{2}\psi_2)] + \tfrac{1}{2}\,\text{var}(S)\,\frac{d^2}{dS^2}\,\Pi(\delta \mid S)\,\Bigg|_{S=J(\psi+\frac{1}{2}\psi_2)}.$$

The corresponding explicit expression for the case of a one-sided alternative is obtained by using the power result in (4.6) and carrying out the algebra. The result, a refinement of (4.7), is

$$\Pi(\delta) \doteq \Phi(\gamma) - \varphi(\gamma)(1 - \psi - \tfrac{1}{2}\psi_2)\{[(\psi + \tfrac{1}{2}\psi_2)(2\psi - \tfrac{1}{2}\psi_2) - 2\delta^2] \cdot [2\delta^2/J(\psi + \tfrac{1}{2}\psi_2)]^{\frac{1}{2}} + 2\delta^2\gamma\}/8[(\psi + \tfrac{1}{2}\psi_2)(2\psi - \tfrac{1}{2}\psi_2) - 2\delta^2], \qquad \text{(B.1)}$$

where φ denotes the density function of the standard normal distribution and γ is the argument of Φ in (4.7).

Another second-order approximation is obtained by applying second-order approximations to $E(S^{\frac{1}{2}})$ and var $(S^{\frac{1}{2}})$ in (4.9). S has a binomial distribution with parameters J and $\psi^* = \psi + \frac{1}{2}\psi_2$. Thus, writing $S^{\frac{1}{2}} = f(S)$, the second-order approximation to $E(S^{\frac{1}{2}})$ from a Taylor series expansion about $E(S) = J\psi^*$ is

$$E(S^{\frac{1}{2}}) \doteq f(J\psi^*) + \tfrac{1}{2}\,\text{var}(S)f''(J\psi^*)$$
$$\doteq (J\psi^*)^{\frac{1}{2}} + \tfrac{1}{2}J\psi^*(1 - \psi^*)[-1/4(J\psi^*)^{\frac{3}{2}}]$$
$$\doteq [(8J + 1)\psi^* - 1]/8(J\psi^*)^{\frac{1}{2}}.$$

Similarly,

$$\text{var}(S^{\frac{1}{2}}) \doteq [f'(J\psi^*)]^2\,\text{var}(S) - [f''(J\psi)\,\text{var}(S)]^2/4 + f'(J\psi^*)f''(J\psi^*)E(S - J\psi^*)^3 + [f''(J\psi^*)]^2E(S - J\psi^*)^4/4.$$

Substituting $E(S - J\psi^*)^3 = J\psi^*(1 - \psi^*)(1 - 2\psi^*)$ and $E(S - J\psi^*)^4 = 3J^2\psi^{*2}(1 - \psi^*)^2 + J\psi^*(1 - \psi^*)[1 - 6\psi^*(1 - \psi^*)]$ (cf. Kendall and Stuart [1963] pp. 58–9) and carrying out the algebra yields var $(S^{\frac{1}{2}}) \doteq (1 - \psi^*)\,\{(8J + 7)\psi^* - 3 + [1 - 6\psi^*(1 - \psi^*)]/2J\psi^*\}/32J\psi^*$. Applying these results to (4.9) one obtains, for a one-sided test,

$$\Pi(\delta) \doteq \Phi\left[\frac{-u_\alpha\psi^* + \{[(8J+1)\psi^* - 1]/4(2J\psi^*)^{\frac{1}{2}}\}\ |\delta|}{\{\psi^*(2\psi - \frac{1}{2}\psi_2) - 2\delta^2 + 2\delta^2(1-\psi^*) \cdot [(8J+7)\psi^* - 3 + (1 - 6\psi^* + 6\psi^{*2})/2J\psi^*]/32J\psi^*\}^{\frac{1}{2}}}\right] \quad \text{(B.2)}$$

Finally, following Patnaik [1948] one may use Beard's [1947] approximate product-integration with the further approximation of setting $E(S - J\psi^*)^3 = E(S - J\psi^*)^5 = 0$. Patnaik's result, as adapted to the present problem, is

$$\Pi(\delta) \doteq \tfrac{1}{6}\Pi(\delta \mid s_1) + \tfrac{2}{3}\Pi(\delta \mid s_2) + \tfrac{1}{6}\Pi(\delta \mid s_3), \quad \text{(B.3)}$$

where, with a one-sided alternative, $\Pi(\delta \mid \cdot)$ is the conditional power function in (4.6), $s_1 = J\psi^* - [3J\psi^*(1 - \psi^*)]^{\frac{1}{2}}$, $s_2 = J\psi^*$, and $s_3 = J\psi^* + [3J\psi^*(1 - \psi^*)]^{\frac{1}{2}}$.

The various approximations to the asymptotic unconditional power function are compared numerically in Appendix C.

APPENDIX C

COMPARISON OF APPROXIMATIONS TO THE ASYMPTOTIC UNCONDITIONAL POWER FUNCTION OF THE 2:1 INDIVIDUAL MATCHING DESIGN

Parameters		Design constants*		Power approximations				
δ	$\psi = \psi_2$	α	J	(4.7)	(4.10)	(B.1)	(B.2)	(B.3)
.10	.20	.05	85.47	.800	.794	.789	.792	.792
.10	.20	.05	115.52	.900	.894	.891	.893	.893
.10	.20	.05	143.73	.950	.946	.943	.945	.945
.10	.40	.05	181.96	.800	.799	.798	.799	.799
.10	.40	.05	250.61	.900	.899	.898	.899	.899
.10	.40	.05	315.58	.950	.949	.949	.949	.949
.05	.20	.05	363.91	.800	.799	.798	.798	.798
.05	.20	.05	501.23	.900	.899	.898	.899	.899
.05	.20	.05	631.16	.950	.949	.949	.949	.949
.05	.40	.05	738.41	.800	.800	.800	.800	.800
.05	.40	.05	1021.40	.900	.900	.900	.900	.900
.05	.40	.05	1289.63	.950	.950	.950	.950	.950
.10	.20	.10	61.44	.800	.794	.789	.791	.791
.10	.20	.10	87.25	.900	.894	.890	.893	.893
.10	.20	.10	111.97	.950	.946	.943	.945	.945
.10	.40	.10	132.23	.800	.799	.798	.799	.799
.10	.40	.10	191.57	.900	.899	.898	.899	.899
.10	.40	.10	248.84	.950	.949	.949	.949	.949
.05	.20	.10	264.46	.800	.799	.798	.798	.798
.05	.20	.10	383.14	.900	.899	.898	.898	.898
.05	.20	.10	497.69	.950	.949	.949	.949	.949
.05	.40	.10	537.96	.800	.800	.799	.800	.800
.05	.40	.10	782.86	.900	.900	.900	.900	.900
.05	.40	.10	1019.63	.950	.950	.950	.950	.950

* The values of J were chosen to yield preselected power values when the simplest approximate power function, (4.7), is used.

Received April 1968, *Revised December* 1968