

## Power Calculations for Matched Case-Control Studies

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### SUMMARY

Power calculations are derived for matched case-control studies in terms of the probability  $p_0$  of exposure among the control patients, the correlation coefficient  $\phi$  for exposure between matched case and control patients, and the odds ratio  $\psi$  for exposure in case and control patients. For given Type I and Type II error probabilities  $\alpha$  and  $\beta$ , the odds ratio that can be detected with a given sample size is derived as well as the sample size needed to detect a specified value of the odds ratio. Graphs are presented for paired designs that show the relationship between sample size and power for  $\alpha = .05$ ,  $\beta = .2$ , and different values of  $p_0$ ,  $\phi$ , and  $\psi$ . The sample size needed for designs involving  $M$  matched control patients can be derived from these graphs by means of a simple equation.

These results quantify the loss of power associated with increasing correlation between the exposure status of matched case and control patients. Sample size requirements are also greatly increased for values of  $p_0$  near 0 or 1. The relationship between sample size,  $\psi$ ,  $\phi$ , and  $p_0$  is discussed and illustrated by examples.

### 1. Introduction

This paper presents a new series of isographs for power calculations and sample size estimation from matched  $2 \times M$  case-control studies. The question of sample size determination in matched  $2 \times 2$  tables has been considered by Schlesselman (1982) and more recently by Parker and Bregman (1986) and Connett, Smith, and McHugh (1987). All of these authors express their sample size calculations in terms of the true odds ratio that is to be detected with a given power and Type I error probability level. Schlesselman estimates the number of discordant case-control pairs and then assumes independence in the exposure probabilities for cases and controls to obtain total sample size estimates. Connett et al. (1987) use an unconditional approach that requires an estimate of the probability that a case-control pair will have an unexposed case patient and an exposed control patient. When such an estimate is unavailable, they also assume independence in the exposure probabilities of cases and controls. This assumption is unrealistic because in most matched studies, exposure in a case patient is correlated with exposure in his matched control. Also, estimating the probability of a discordant pair can be very difficult in the absence of pilot data. Parker and Bregman (1986) avoid the independence assumption by permitting the user to specify a heterogeneous exposure distribution in different subgroups of the control population. Although this approach is a great improvement over previous methods, it is sometimes difficult to make plausible estimates of this exposure distribution. Parker and Bregman also assume that the disease incidence in unexposed patients does not vary with different values of the matching variables. This assumption is often unrealistic. For example, in an age-matched study of smoking and lung cancer it would imply that lung cancer incidence among nonsmokers does not increase with age.

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*Key words:* Case-control studies; Matching; Sample size estimation; Power calculations.



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Miettinen (1968), Duffy (1984), and Connor (1987) have also considered the problem of power calculations for matched tables. In these papers the alternative hypothesis is expressed in terms of the difference between the probabilities of obtaining the two different types of discordant case-control pairs. For epidemiologic studies it is perhaps more useful to express power calculations in terms of odds ratios.

This paper gives the derivation of the odds ratio that can be detected with power  $1 - \beta$  given a two-sided Type I error probability  $\alpha$ ,  $N$  case patients,  $M$  matched control patients per case, the probability of exposure  $p_0$  among control patients, and the correlation coefficient  $\phi$  for exposure in matched pairs of case-control patients. The corresponding number of case patients needed to detect a given odds ratio  $\psi$  with power  $1 - \beta$  and Type I error probability  $\alpha$  is also derived. A major advantage of this approach is that power calculations are expressed directly in terms of the correlation coefficient for exposure between matched case and control subjects and the prevalence of exposure in the control group. This facilitates the drawing of isographs, which greatly simplify the task of sample size estimation in matched case-control studies, and which permit epidemiologists to gain an insight into the relationship between power, sample size, and these other variables.

## 2. Notation and Assumptions

Consider a population of case patients with some disease and control patients who do not have this illness. Some of these patients have had prior exposure to a risk factor of interest, and all subjects can be classified by different levels of a variable that confounds the association between the risk factor and the disease. We wish to estimate the odds ratio  $\psi$  of developing the disease in exposed and unexposed patients who have equal values of the confounding variable (see Breslow and Day, 1980). To do this we first select a random sample of  $N$  case patients. We then stratify the population by the confounding variable and assume that  $\psi$  is constant across all strata. For each selected case patient we randomly sample  $M$  matched control patients from the same stratum as the corresponding case patient. Let  $x_k = 1$  or 0 if the  $k$ th sampled case patient was or was not exposed, respectively, and let  $y_k = 1$  or 0 denote the corresponding exposure status of the first matched control for this patient. Let  $p_{ij}$  denote the probability that  $x_k = i$  and  $y_k = j$ . Let  $p_0 = p_{11} + p_{01}$  denote the probability that a sampled control patient is exposed. Let  $p_1 = p_{11} + p_{10}$  denote the probability that a sampled case patient is exposed and let  $q_0 = 1 - p_0$  and  $q_1 = 1 - p_1$ . Let  $\phi$  denote the phi coefficient between  $x_k$  and  $y_k$ . (It is easily shown that  $\phi$  is algebraically identical to the Pearson product-moment correlation coefficient  $\rho$  between  $x_k$  and  $y_k$ .) Let  $\alpha$  and  $\beta$  denote the Type I and Type II error probabilities, respectively. In the remainder of this paper the terms *case* and *control patient* refer to sampled subjects as opposed to members of the target population.

For any given values of  $\alpha$ ,  $\beta$ ,  $\psi$ ,  $\phi$ , and  $p_0$ , the value of  $N$  needed to detect  $\psi$  with power  $1 - \beta$  can be decreased by increasing  $M$ . Suppose  $N_1$  and  $N_M$  denote the number of case patients needed to attain the required power given 1 and  $M$  matched controls, respectively. Let  $F_M = N_M/N_1$  denote the reduction in  $N$  relative to a paired design that can be obtained by selecting  $M$  controls per case.

## 3. Derivation of Results

By definition  $\phi = \text{cov}(x_k, y_k)/(\sigma_x \sigma_y)$ . It can be easily shown that

$$\phi = \frac{p_{11}p_{00} - p_{10}p_{01}}{\sqrt{p_1 q_1 p_0 q_0}}, \quad (1)$$

which is consistent with equation (5.3) of Fleiss (1981). It follows from the definitions of  $p_i$  and  $q_i$  in terms of  $p_{ij}$  that  $p_{11}p_{00} - p_{10}p_{01} = p_{11} - p_1p_0 = p_1q_0 - p_{10} = q_1p_0 - p_{01} = p_{00} - q_1q_0$ . Substituting these expressions into equation (1) gives

$$p_{11} = p_1p_0 + \phi\sqrt{p_1q_1p_0q_0}; \quad (2)$$

$$p_{10} = p_1q_0 - \phi\sqrt{p_1q_1p_0q_0}; \quad (3)$$

$$p_{01} = q_1p_0 - \phi\sqrt{p_1q_1p_0q_0}; \quad (4)$$

$$p_{00} = q_1q_0 + \phi\sqrt{p_1q_1p_0q_0}. \quad (5)$$

Now  $p_1$  can be written as a function of  $\psi$ ,  $p_0$ , and  $\phi$  (see Appendix). Substituting equation (13) from the Appendix into equations (2)–(5) allows us to write  $p_{ij}$  as a function of  $\psi$ ,  $p_0$ , and  $\phi$ . Thus  $\psi$ ,  $p_0$ , and  $\phi$  uniquely determine  $p_{ij}$ . (Note, however, that not all values of  $\psi$ ,  $p_0$ , and  $\phi$  yield values of  $p_{ij}$  that lie between 0 and 1.)

Let  $p_{0+}$  and  $p_{0-}$  denote the probability that a control patient is exposed given that his matched case patient is or is not exposed, respectively. Then

$$p_{0+} = p_{11}/p_1 = p_0 + \phi\sqrt{q_1p_0q_0/p_1} \quad \text{and} \quad p_{0-} = p_{01}/q_1 = p_0 - \phi\sqrt{p_1p_0q_0/q_1}.$$

Let  $q_{0+} = 1 - p_{0+}$  and  $q_{0-} = 1 - p_{0-}$ . Then the probability of observing  $m$  exposed subjects among a case patient and his  $M$  matched controls is

$$t_m = p_1 \binom{M}{m-1} p_{0+}^{m-1} q_{0+}^{M-m+1} + q_1 \binom{M}{m} p_{0-}^m q_{0-}^{M-m}$$

for  $m = 1, \dots, M$ . Let  $n_{ij}$  denote the number of matched sets of subjects in which the case patient was ( $i = 1$ ) or was not ( $i = 0$ ) exposed and  $j$  of the  $M$  control subjects were exposed. Let

$$y = \sum_{m=1}^M n_{1,m-1}$$

be the number of discordant sets in which the case patient was exposed and let  $T_m = n_{1,m-1} + n_{0,m}$  be the number of sets in which  $m$  subjects were exposed. The expected value of  $T_m$  is  $E(T_m) = Nt_m$ . Let  $E_\psi$  and  $s_\psi$  denote the conditional mean and standard deviation of  $y$  given  $T_m = E(T_m)$ ,  $m = 1, \dots, M$ . Then it follows from equation (5.16) of Breslow and Day (1980) that  $E_\psi = Ne_\psi$  and  $s_\psi = \sqrt{N}v_\psi$ , where

$$e_\psi = \sum_{m=1}^M \frac{mt_m\psi}{m\psi + M - m + 1} \quad \text{and} \quad v_\psi = \sum_{m=1}^M \frac{mt_m\psi(M - m + 1)}{(m\psi + M - m + 1)^2}.$$

Let  $z_x$  be the value of the standard normal variate exceeded with probability  $x$  and let  $\Phi(z_x) = 1 - x$ . Equation (5.19) of Breslow and Day (1980) provides a  $\chi^2$  test of the null hypothesis that  $\psi = 1$ . This test can be rewritten as a  $z$  statistic involving  $y$  and its conditional mean and standard deviation. It follows by a standard argument that for given  $\alpha$ ,  $p_0$ ,  $\phi$ ,  $N$ , and  $M$  that this test will have power

$$1 - \beta = \Phi\left(\frac{E_1 - E_\psi - z_{\alpha/2}s_1}{s_\psi}\right) + 1 - \Phi\left(\frac{E_1 - E_\psi + z_{\alpha/2}s_1}{s_\psi}\right). \quad (6)$$

When  $\beta$  is reasonably small and  $\psi > 1$ , the first term on the right-hand side in (6) is negligible. In this case

$$-z_\beta = \frac{E_1 - E_\psi + z_{\alpha/2}s_1}{s_\psi} = \frac{N^{1/2}(e_1 - e_\psi) + z_{\alpha/2}v_1^{1/2}}{v_\psi^{1/2}}.$$

It follows that

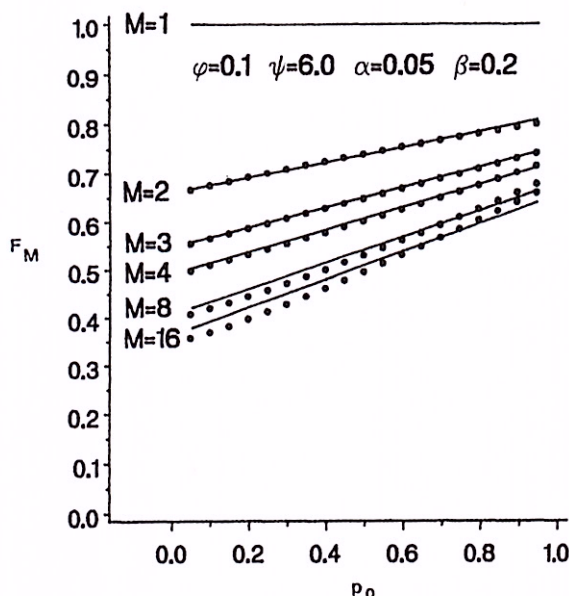
$$N = \frac{(z_{\beta} v_{\psi}^{1/2} + z_{\alpha/2} u_1^{1/2})^2}{(e_1 - e_{\psi})^2}. \quad (7)$$

Substituting the preceding expressions into equation (7) permits us to write  $N$  as a function of  $p_0$ ,  $\phi$ ,  $\psi$ ,  $\alpha$ , and  $\beta$ . Thus, equation (7) can be used to determine the number of case patients needed to detect  $\psi$  with power  $1 - \beta$  given  $\alpha$ ,  $p_0$ ,  $\phi$ , and  $M$ .

$F_M = N_M/N_1$  can also be calculated from equation (7) by taking the ratio of sample sizes needed using 1 and  $M$  controls per case, respectively. The dots in Figure 1 show values of  $F_M$  plotted as a function of  $p_0$  for  $\alpha = .05$ ,  $\beta = .2$ ,  $\psi = 6$ ,  $\phi = .1$ , and  $M = 2, 3, 4, 8$ , and 16. This figure is typical of similar figures for a wide range of values of  $\alpha$ ,  $\beta$ ,  $\psi$ ,  $\phi$ , and  $M$ . For given values of  $\alpha$ ,  $\beta$ ,  $\psi$ , and  $\phi$ , these figures indicate that  $F_M$  can be closely approximated by linear functions  $\hat{F}_M(p_0)$  that have a common intersection point on the line  $F_1 \equiv 1$  and for which  $\hat{F}_M(c) = (M + 1)/(2M)$  for some positive  $c$ . This latter condition can be met by setting  $\hat{F}_M(p_0) = (M + 1)/(2M) + b_M(p_0 - c)$ . The common intersection of these curves at some point  $p_0 = k + c$  implies that  $1 = (M + 1)/(2M) + b_M k$ , giving

$$\hat{F}_M(p_0) = \frac{M + 1}{2M} + \frac{(M - 1)}{2Mk} (p_0 - c), \quad (8)$$

where  $k$  and  $c$  are both functions of  $\alpha$ ,  $\beta$ ,  $\phi$ , and  $\psi$ . The accuracy and utility of this expression are discussed in the next section. The straight lines drawn on Figure 1 give  $\hat{F}_M(p_0)$  for  $M = 2, 3, 4, 8$ , and 16. The accuracy of  $\hat{F}_M$  as an estimate of  $F_M$  is remarkable.



**Figure 1.** This figure shows  $F_M$ , the reduction in  $N$  relative to a paired design that can be obtained by selecting  $M$  controls per case. The dots show the true values of  $F_M$  for  $M = 2, 3, 4, 8$ , and 16. The straight lines show the estimated value of  $F_M$  using equation (8) with  $c = .573$  and  $k = 1.620$ . In this example,  $\phi = .1$ ,  $\psi = 6.0$ ,  $\alpha = .05$ , and  $\beta = .2$ .

#### 4. Using the Isographs

Figures 2-7 present sample size isographs for paired case-control studies that were derived using equation (7). The value of  $\phi$  is constant in each graph and equals 0, .1, .2, .3, .4, and .5 in Figures 2 through 7, respectively. The values of  $\alpha$  and  $\beta$  equal .05 and .2, respectively, in all graphs and test the null hypothesis that  $\psi = 1$  against a two-sided alternative hypothesis. The abscissa of each graph is  $p_0$  while the ordinate is the value of  $\psi$  that can be detected with 80% power. Each figure shows isographs of constant case sample size  $N$  as a function of  $p_0$  and  $\psi$ . By interpolating between these lines the reader can either determine the value of  $\psi$  that can be detected with a given sample size or the sample size required to detect a given value of  $\psi$ .

The value of  $\psi$  in Figures 2-7 ranges from 1 through 6. However, these graphs can also be used for studies of factors that are thought to reduce disease risk. For example, if factor  $X$  reduces disease risk with odds ratio  $\psi < 1$ , then the absence of  $X$  increases the disease risk with odds ratio  $1/\psi > 1$ . Thus, sample size calculations using these figures can be based on the risk associated with not having factor  $X$ .

For the values of  $\phi$  and  $\psi$  described in Figures 2-7, it can be shown empirically that  $F_M$  can be closely approximated by equation (8). The values of  $k$  and  $c$  needed in equation (8) are given in Table 1. Equation (8) and Table 1 can be used in combination with Figures 2-7 to determine the sample size needed to detect a given value of  $\psi$  using more than one

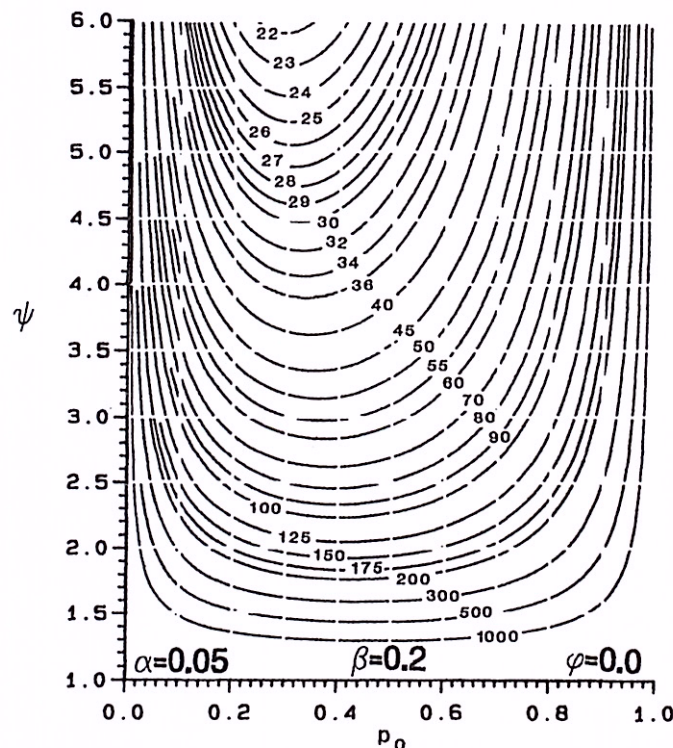


Figure 2. The numbers on the lines on this graph indicate constant sample sizes for paired case-control studies. Each line shows the value of the odds ratio  $\psi$  that can be detected with 80% power as a function of exposure prevalence  $p_0$  for control subjects. These curves are derived assuming a two-sided Type I error probability of  $\alpha = .05$  and a correlation coefficient for exposure between matched subjects of  $\phi = 0$ .

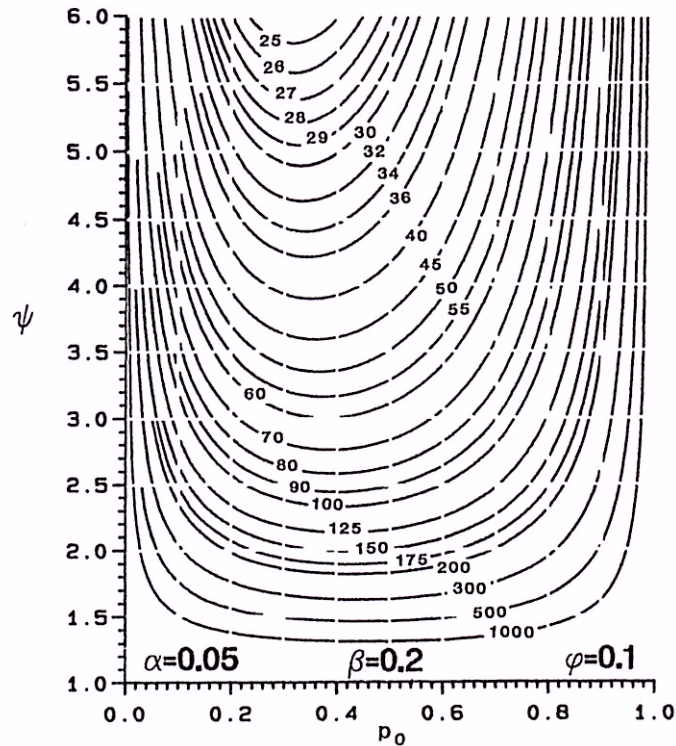


Figure 3. Isographs of constant sample size for paired case-control studies. This figure differs from Figure 2 only in that the correlation coefficient  $\phi$  equals .1.

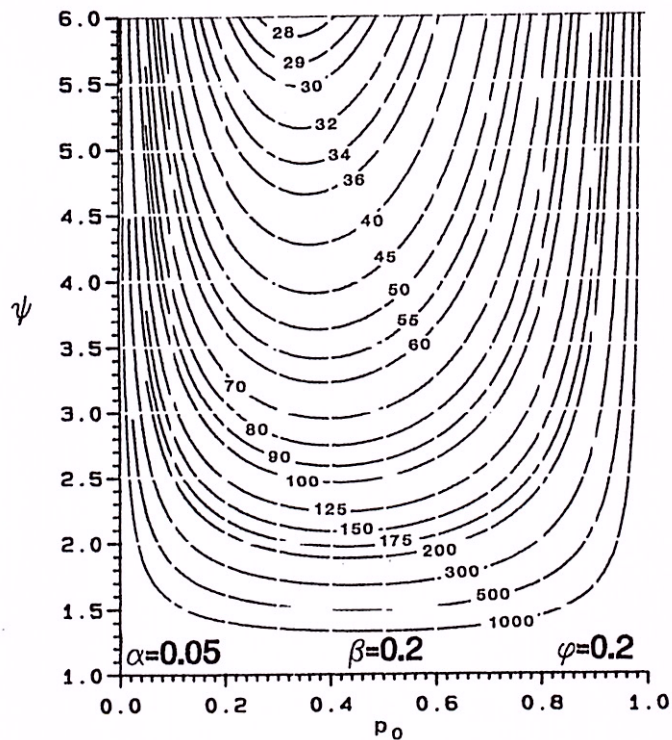


Figure 4. Isographs of constant sample size for paired case-control studies. This figure differs from Figure 2 only in that the correlation coefficient  $\phi$  equals .2.

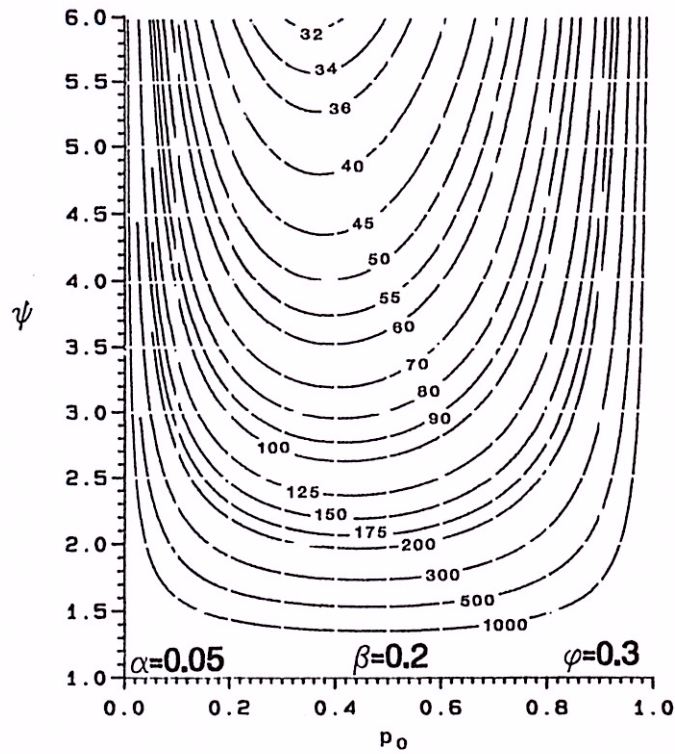


Figure 5. Isographs of constant sample size for paired case-control studies. This figure differs from Figure 2 only in that the correlation coefficient  $\phi$  equals .3.

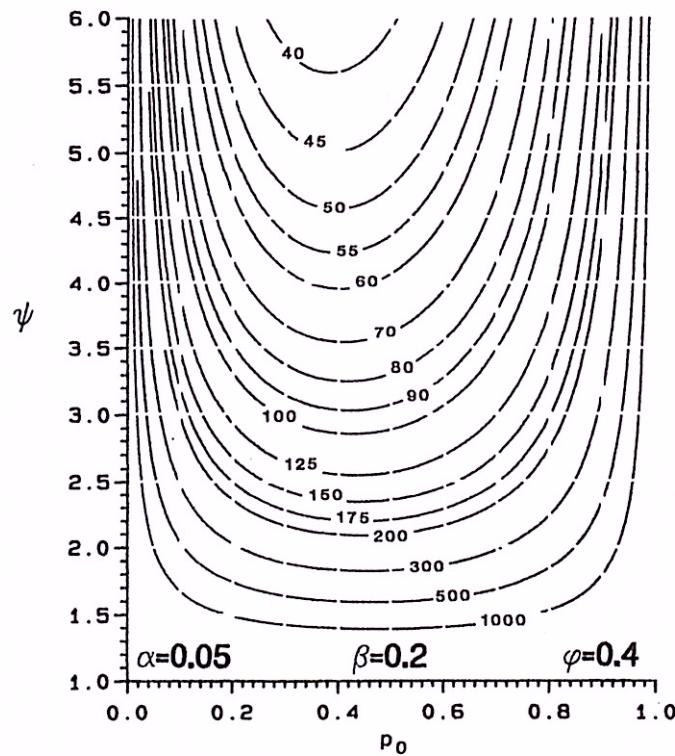


Figure 6. Isographs of constant sample size for paired case-control studies. This figure differs from Figure 2 only in that the correlation coefficient  $\phi$  equals .4.



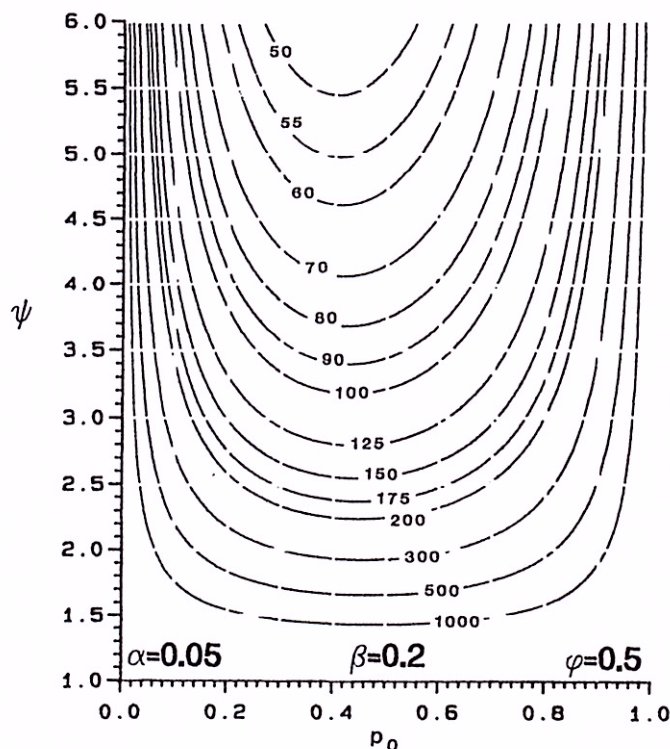


Figure 7. Isographs of constant sample size for paired case-control studies. This figure differs from Figure 2 only in that the correlation coefficient  $\phi$  equals .5.

matched control per case. For example, suppose  $p_0 = .6$ ,  $\phi = .2$ , and that we wish to detect  $\psi = 3$  with power .8. Then Figure 4 shows that we should select 80 case patients using a paired design. If we select 3 control patients per case, then Table 1 gives  $k = 3.669$  and  $c = 1.028$  when  $\phi = .2$  and  $\psi = 3$ . Substituting these values into equation (8) with  $M = 3$  and  $p_0 = .6$  gives  $\hat{F}_3(.6) = .6278$ . Thus, with  $N = 80\hat{F}_3(.6) = 50$  cases and 3 controls per case we can detect  $\psi = 3$  with 80% power. In this example the true value of  $F_3$  equals .6264, which also yields  $N = 50$ . Thus, in this example, the estimate of  $N$  obtained by using Table 1 is correct to the nearest integer. Table 2 shows the maximum percentage error in  $\hat{F}_M$  for values of  $M$  between 2 and 16 and the values of  $p_0$ ,  $\phi$ , and  $\psi$  given in the figures. For 2, 3, or 4 controls per case, the error in  $\hat{F}_M$  is always less than 3%. Larger values of  $M$  are associated with higher errors when  $p_0$  is small. In this case  $\hat{F}_M$  overestimates  $F_M$  and hence overestimates the required number of case patients.

Schlesselman (1982, p. 168) recommends multiplying the paired-case sample size by  $(M + 1)/(2M)$  to obtain the equivalent case sample size with  $M$  matched controls per group. Equation (8) shows that this approach provides an acceptable approximation if  $p_0$  is near  $c$  or when  $k$  is large. From Table 1 we see that  $k$  increases as  $\psi$  approaches 1. Thus, Schlesselman's multiple control correction is asymptotically correct for large  $N$  since  $N$  approaches infinity as  $\psi$  approaches 1. Equation (8) shows, however, that Schlesselman's adjustment is inaccurate for many reasonable values of  $p_0$  and  $\psi$ . For small values of  $p_0$  this adjustment will greatly overestimate the number of case patients needed to achieve the required power.

Software is available from the author on request which derives the value of  $\psi$  that can be detected with power  $1 - \beta$  given  $\alpha$ ,  $\phi$ ,  $p_0$ ,  $N$ , and  $M$ , as well as the case sample size  $N$ .

**Table 1**  
Coefficients  $k$  and  $c$  for power calculations with multiple controls per case. These coefficients are used in equation (8), with  $\alpha = .05$  and  $\beta = .2$ .

$\psi$		Correlation coefficient $\phi$					
		0	.1	.2	.3	.4	.5
1.5	$k$	6.148	8.098	10.827	14.754	20.610	29.760
	$c$	.486	1.238	2.404	4.235	7.173	12.062
2.0	$k$	3.568	4.651	6.158	8.304	11.446	16.223
	$c$	.479	.890	1.517	2.485	4.003	6.455
3.0	$k$	2.218	2.829	3.669	4.834	6.477	8.848
	$c$	.472	.697	1.028	1.515	2.240	3.339
6.0	$k$	1.332	1.620	2.002	2.498	3.143	3.997
	$c$	.471	.573	.704	.870	1.080	1.350

**Table 2**  
Maximum percentage error in efficiency ratio  $\hat{F}_M(p_0)$

		$1 < \psi \leq 3$	$3 < \psi \leq 6$
$0 \leq \phi \leq .2$	$2 \leq M \leq 4$	1.2	1.2
	$M = 8$	4.4	5.7
	$M = 16$	7.5	11.
$.2 < \phi \leq .5$	$2 \leq M \leq 4$	1.9	2.7
	$M = 8$	6.7	11.
	$M = 16$	11.	18.

needed to detect a true value of  $\psi$  with power  $1 - \beta$  given  $\alpha$ ,  $\beta$ ,  $p_0$ , and  $M$ . These programs calculate the exact power associated with  $M$  controls per case without using the approximation of  $F_M$  given in equation (8).

**5. Comparison with Schlesselman's Method**

Suppose  $\phi = .2$  and  $p_0 = .6$ . Figure 4 shows that  $\psi = 3$  can be detected with 80% power when  $N = 80$ . Substituting these values of  $\phi$ ,  $p_0$ , and  $\psi$  into equations (2)-(5) gives the following  $2 \times 2$  table of exposure probabilities for a matched pair of case-control patients:

		Case		Total
		+	-	
Control	+	$p_{11} = .509$	$p_{01} = .091$	$p_0 = .6$
	-	$p_{10} = .272$	$p_{00} = .128$	$q_0 = .4$
Total		$p_1 = .781$	$q_1 = .219$	1

[It is worth noting as a check on the validity of equations (2)-(5) that  $\psi = p_{10}/p_{01} = 3.0$  and that  $\phi = .20$  using equation (1).] The probability of a discordant pair is thus  $p_{10} + p_{01} = .363$  and hence the expected number of discordant pairs given a sample size of  $N = 80$  case patients equals  $80 \times .363 = 29.0$ . In comparison, equation (6.20) of Schlesselman

(1982) gives that the number of discordant pairs needed to detect  $\psi = 3.0$  with 80% power is

$$m = \left[ \frac{z_{.025}}{2} + z_{.2} \sqrt{\frac{\psi}{(1+\psi)^2}} \right]^2 / \left[ \frac{\psi}{(1+\psi)} - \frac{1}{2} \right]^2 = 28.9,$$

which is in close agreement with the expected number of discordant pairs given above. Thus, the method presented in this paper can be thought of as a generalization of Schlesselman's method to the case in which  $\phi \neq 0$ . Equation (6.23) of Schlesselman estimates  $N$  to be  $m/(p_0q_1 + p_1q_0) = 65$ . This estimate, which is derived under the assumption that  $\phi = 0$ , overestimates the expected number of discordant pairs and hence underestimates the sample size needed for the required power.

## 6. Estimating $p_0$ and $\phi$

$p_0$  is the probability that a sample control patient will be exposed. The control sample is not, however, a random sample from the control population but, rather, is matched to a random sample of case patients from the case population. Thus, an unbiased estimate of the exposure prevalence in the control population is not necessarily an unbiased estimate of  $p_0$ . Let  $p_0(\mathbf{c})$  denote the probability that a control subject with confounding variable  $\mathbf{c}$  is exposed,  $D_{\text{case}}(\mathbf{c})$  and  $D_{\text{ctl}}(\mathbf{c})$  denote the probability density functions of  $\mathbf{c}$  among the case and control populations, respectively, and let  $p_0^*$  denote the exposure prevalence in the control population. Then

$$p_0 = \int p_0(\mathbf{c})D_{\text{case}}(\mathbf{c}) d\mathbf{c} \quad (9)$$

while

$$p_0^* = \int p_0(\mathbf{c})D_{\text{ctl}}(\mathbf{c}) d\mathbf{c}.$$

When  $\mathbf{c}$  is positively associated with both disease incidence and exposure prevalence,  $p_0^*$  will underestimate  $p_0$ . Note, however, that if  $p_0(\mathbf{c})$  is constant, then  $p_0 = p_0^*$  and  $p_0^*$  will approximate  $p_0$  whenever the exposure prevalence in the control population does not vary greatly with  $\mathbf{c}$ . In many case-control studies, there is little association between the confounding variable and the exposure variable in the control population. For such studies it is reasonable to estimate  $p_0$  by the exposure prevalence in the general population. When a more accurate estimate of  $p_0$  is required, it may be estimated through equation (9). To do this it is necessary to obtain estimates of the confounder-specific exposure prevalence rates in the control population as well as estimates of the distribution of case patients with respect to  $\mathbf{c}$ . [Note that the method of Parker and Bregman (1986) also requires estimates of the confounder-specific exposure prevalence rates and that they estimate the distribution of case patients with respect to  $\mathbf{c}$  by assuming a constant disease incidence among unexposed subjects.]

The correlation coefficient  $\phi$  can be estimated from previous studies that publish matched  $2 \times 2$  contingency tables using equation (5.2) of Fleiss (1981). Of course, such data could also be used to estimate the proportion of discordant pairs, which in turn could be used to obtain sample size estimates using Schlesselman's (1982) method. However, the proportion of discordant pairs is likely to vary considerably between different studies since it depends not only on  $\phi$  but also on the exposure prevalence  $p_0$  and the odds ratio  $\psi$ . In contrast, estimates of  $\phi$  should be more stable between similar studies. When no estimate of  $\phi$  is available, investigators may prefer to perform their power calculations under the assumption

that  $\phi$  equals, say, .2 rather than make the questionable independence assumption required by most other methods.

## 7. Conclusions

The graphs presented in this paper demonstrate and quantify the complex relationship between sample size, power, the magnitude of the control exposure prevalence  $p_0$ , and the exposure correlation coefficient  $\phi$ . Figures 2-7 illustrate the substantial loss in power that occurs with increasing correlation between the exposure status of matched case-control pairs. For example, when  $\phi = 0$ , the minimum value of  $\psi$  that can be detected with 80% power and  $N = 50$  is 3.14. This minimum value increases steadily with increasing  $\phi$ , reaching 5.45 when  $\phi = .5$ . The value of  $p_0$  has little effect on power when  $\psi$  is low and  $p_0$  is not too extreme (say  $\psi < 2$  and  $.2 \leq p_0 \leq .8$ ). However, the precise value of  $p_0$  has a critical effect on the power when  $p_0$  is near 0 or 1, or when the sample size is small. This result is due to the influence of  $p_0$  and  $\psi$  on the expected number of discordant case-control pairs. The method presented here will provide accurate power calculations whenever reasonable estimates of  $p_0$  and  $\phi$  are available. Even when no appropriate estimates of  $\phi$  can be found, investigators can still avoid the independence assumption for exposure among matched subjects by selecting a reasonable value of  $\phi$ . This will produce sample size estimates that are more conservative and plausible than those based on the independence assumption.

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## RÉSUMÉ

La puissance des études cas-témoins appariées est déterminée en fonction de  $p_0$ , probabilité d'exposition chez les témoins,  $\phi$ , coefficient de corrélation entre les expositions chez les malades et témoins appariés, et  $\psi$ , "odds-ratio" mesurant la relation exposition-maladie. Pour des risques de première et seconde espèce donnés,  $\alpha$  et  $\beta$ , l'odds-ratio qui peut être détecté est calculé en fonction de la taille de l'échantillon et inversement. On présente des abaques qui, pour les études 1-1, montrent la relation entre la taille de l'échantillon et la puissance pour  $\alpha = .05$ ,  $\beta = .2$  et différentes valeurs de  $p_0$ ,  $\phi$ , et  $\psi$ . Le passage aux études 1-M se fait au moyen d'une équation simple.

Ces résultats quantifient la perte de puissance associée à une augmentation du coefficient de corrélation  $\phi$ . Des valeurs de  $p_0$  voisines de 0 au 1 nécessitent des effectifs importants. Des exemples illustrent ces résultats.

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#### APPENDIX

We wish to express  $p_1$  in terms of  $\psi$ ,  $p_0$ , and  $\phi$ . It follows from the definition of the terms  $p_{ij}$  that  $\psi = p_{10}/p_{01}$ ,  $p_1 - p_0 = p_{10} - p_{01} = (\psi - 1)p_{01}$ ,  $p_{11} = p_0 - p_{01}$ , and  $p_{00} = q_1 - p_{01}$ . Hence,  $p_{01} = (p_1 - p_0)/(\psi - 1)$ ,  $p_{10} = \psi(p_1 - p_0)/(\psi - 1)$ ,  $p_{11} = (\psi p_0 - p_1)/(\psi - 1)$ , and  $p_{00} = (\psi q_1 - q_0)/(\psi - 1)$ . When  $\psi \neq 1$  we can substitute these expressions into equation (1) to obtain

$$\phi = \frac{\psi^2 p_0 q_1 + p_1 q_0 - \psi(p_0 q_1 + p_1 q_0)}{(\psi - 1)^2 \sqrt{p_1 q_1 p_0 q_0}}. \quad (10)$$

Equation (10) can be rewritten in the form

$$\phi = \frac{A + Bp_1}{\sqrt{p_1 - p_1^2}}, \quad (11)$$

where  $A$  and  $B$  are functions of  $\psi$  and  $p_0$ . Squaring equation (11) yields

$$(B^2 + \phi^2)p_1^2 + (2AB - \phi^2)p_1 + A^2 = 0, \quad (12)$$

which is a quadratic equation in  $p_1$ . Equation (12) has two roots:

$$p_1 = \frac{2\psi p_0(\psi p_0 + q_0) + (\psi - 1)^2 p_0 q_0 \phi^2 - (\psi - 1)p_0 q_0 \phi \sqrt{\phi^2(\psi - 1)^2 + 4\psi}}{2[(\psi p_0 + q_0)^2 + (\psi - 1)^2 p_0 q_0 \phi^2]}, \quad (13)$$

which is also the solution to equation (11), and another root that solves  $-\phi = (A + Bp_1)/\sqrt{p_1 - p_1^2}$ . Thus, to prove that equation (13) is the solution to equation (11) it is sufficient to substitute (13) into the right-hand side of (11) and then show that this expression has the same sign as  $\phi$ . This is a straightforward exercise. It is interesting to note that when  $\psi = 1$ ,  $p_1 = p_0$ . Hence, equation (13) is correct for all positive values of  $\psi$ . Note also that when  $\phi = 0$ , (13) reduces to (6.2) in Schlesselman (1982).

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