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Odds Ratio as Measure of Strength of Association in Diagnostic Screening Test

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Abstract: *I here propose an odds ratio based on false rates as a measure of the strength of association between state of nature or condition in a population and test results in diagnostic screening tests. The method provides an estimate for the proposed odds ratio that depends only on the estimated sensitivity and specificity of the test in the event that the prevalence rate is not known. The proposed method unlike the traditional odds ratio provides estimates of not only the proposed false rates based odds ratio-type measure of association, but also alternative sample estimates of its associated standard deviation and test statistic for significance that intrinsically and structurally partials out, that is, does not include in its formulation the number of subjects in the sample known or believed to actually have the condition in nature but test negative or actually do not have the condition in nature but test positive to the condition in the screening test. The proposed method given that the prevalence rate of the condition in the population is known, provides sample estimates of the false positive rate, false negative rate and their odds as well as the proportion of the population expected to test positive to the condition in the screening test which are additional useful information to guide policy formulation and implementation over and above the traditional odds ratio method. Modified estimates of the standard deviation and test statistic for the proposed measure that adjust for the fact that some sample observations in a screening test are not known and cannot therefore validly be used in traditional odds ratio estimation method are provided. The proposed method which is shown to provide more information and to be at least as efficient as the traditional odds ratio method is illustrated with some sample data.*

Key words*: chi-square test of independence, false negative rate, false positive rate, odds ratio, specificity, sensitivity.*

I. Introduction

When sample data is collected for use in either prospective or retrospective study design, one will preferably use the odds ratio or relative risk rather than the phi-coefficient which unlike the former two measures is not invariant under the three study methods, to assess the degree of association between a predisposing or antecedent factor and condition of interest in a population (Fleiss 1973; Agresti, 2007; Kestenbaum 2009). However, the use of the traditional odds ratio and relative risk in their direct usual formulations as measures of level of association between state of nature or condition and test results is sometimes not possible in diagnostic screening tests. This is because these measures as formulated do not immediately reflect or incorporate existing or known prevalence rate and the proportion of subjects expected to test positive to the condition of interest in the population (Fleiss, 1973; Kestenbaum, 2009). The prevalence rate is either known or estimated from some related data obtained earlier from previous studies while the expected proportion of the population responding positive to the test for the condition is estimated indirectly as a function of the prevalence rate. Hence any measure of association including the odds ratio used for this purpose needs to be adjusted to incorporate these rates or adjusted for their effects. Ideally such tests should correctly and absolutely identify all subjects with the condition and similarly correctly identify all subjects which are free of the condition. However, most clinical tests fall short of these ideals (Lalkhen and McCluskey, 2008). When evaluating a clinical test, the terms sensitivity and specificity are used (Lalkhen and McCluskey, 2008). Sensitivity (clinical sensitivity) is positivity test for a condition, while true positive rate is the ability of a test to correctly identify a condition at a particular decision threshold. Specificity (clinical specificity) is negativity test in health and true-negative rate is the ability of a test to correctly identify the absence of a condition at a particular decision threshold (Akobeng 2007). Sensitivity and specificity are proportions, so confidence intervals can be calculated for them using standard methods for proportions (Gardner and Altman, 1989). A test can have considerable ability to discriminate, yet not be of practical value for patient care. This could happen for several reasons. For instance, the cost or undesirability of false results can be so huge that there are no decision thresholds for the test where the trade-off between sensitivity and specificity is acceptable (Zweig et al, 1995). Sensitivity and specificity are independent of the population of interest being tested. However, the terms positive predictive value (PPV) and negative predictive value (NPV) are used when considering the value of a test to a clinician and are dependent on the prevalence of the disease in the population of interest(Lalkhen and McCluskey 2008). Public health workers may often need clearer and more definitive measures of association

between screening test results and state of nature or health condition, disease or biological entity being measured that use all available information from the screening test. In this paper we propose to develop an odds ratio-type measure of association based on false rates. Now in diagnostic screening tests the data or observations immediately available to the medical researcher for use are the total number of subjects screened which consist of the number of subjects known or believed to actually have and not to actually have the condition in the population and the number who actually have the condition and test positive as well as the number of subjects who do not actually have the condition and test negative in the screening test. The number of subjects who do not have the condition but test positive and the number of subjects who have the condition but test negative in the screening test are usually not known, so that the total number of subjects who either test positive or negative in the screening test are usually not completely known. Hence the traditional odds ratio and other similarly calculated measures of association cannot be validly and properly used without modifications as measures of the strength of association between state of nature or condition and test results in diagnostic screening tests. For the same reasons the usual estimates of the precision and chi-square test statistics for these measures (Fleiss, 1973; Akobeng, 2007) cannot be validly used directly. Although the proposed measure of association is dependent on the prevalence rate of the condition of interest if known, an alternative measure of association that is independent of the prevalence rate but depends only on the sensitivity and specificity of the test is also developed. Estimates of the precision of the proposed measure and an appropriate test statistic that depend only on the sensitivity and specificity of the test are also developed. Given that the prevalence rate of the condition in the population is known or a reliable estimate can be obtained from previous studies, an estimate of the proportion of the population expected to test positive in the screening test is also here provided.

Decision Matrix Table For Diagnostic Test Results

If a research scientist or clinician collects from a certain population a random sample of $n_{.1}$ subjects known or believed to actually have a certain condition in a population and similarly collects a random sample of $n_{.2}$ subjects from the same population known or believed not to actually have the condition in the population giving a total sample size of $n = n_{..} = n_{.1} + n_{.2}$ subjects to be screened. Research interest is in conducting a diagnostic screening test to determine whether or not each of the randomly selected subjects actually responds positive or negative to the test for the condition, disease, biological entity, make-up etc.

Let B be the event that a randomly selected subject from this population has the condition of interest and $\overline{B}$ be the event that the subject does not have the condition in nature. Let A be the event that the randomly selected subject tests positive to the screening test and $\overline{A}$ be the event that the subject tests negative to the test. The results from such a screening test may then be presented in a 2 x 2 table as in Table 1.

Table 1: Format for Presentation of Results of a Diagnostic Screening Test

Screening Test Result	**State of Nature(Condition)**		
	Present (B)	**Absent($\overline{B}$)**	**Total**
Positive (A)	n_{11}	n_{12}	$n_{1.}$
Negative($\overline{A}$)	n_{21}	n_{22}	$n_{2.}$
Total	$n_{.1}$	$n_{.2}$	$n_{..}(=n)$

In Table 1 out of $n_{1.}$ subjects testing positive to the test, n_{11} actually have the condition while n_{12} do not have the condition and out of $n_{2.}$ subjects testing negative, n_{21} actually have the condition, while n_{22} actually do not have the condition. Of the $n = n_{..}$ subjects studied $n_{.1}$ subjects actually have the condition while $n_{.2}$ subjects do not have the condition in nature. The sensitivity, Se of a test is defined as the proportion of those actually having the condition that test positive. The specificity, Sp of a test is the proportion out of those not actually having the condition, which test negative. (Akobeng 2007) The false positive rate, F_{+ve} of a test is the proportion out of those testing positive who are actually free from the disease and the false negative rate, F_{-ve}, is the proportion out of those testing negative who actually have the disease (Akobeng 2007). These rates may be expressed notationally as:

$$Se = P(A/B); Sp = P(\overline{A}/\overline{B}) \qquad (1)$$

The larger the $P(A/B)$, the more sensitive is the test and the larger the $P(\overline{A}/\overline{B})$, the more specific is the test(Altman and Bland 1994). Sample estimates of these rates using the notations of Table 1 are respectively given as

$$\hat{S}e = \frac{n_{11}}{n_{.1}}; \hat{S}p = \frac{n_{22}}{n_{.2}} \quad (2)$$

Of greater public health importance however is the false positive, F_{+ve} and false negative, F_{-ve} rates of a test. F_{+ve} is defined as the probability that a randomly selected subject who tests positive to the test does not actually have the condition, while F-ve is the probability that a randomly selected subject who tests negative to the test in fact has the condition in nature. Notationally we have that:

$$F_{+ve} = P(\bar{B} / A); F_{-ve} = P(B / \bar{A}) \quad (3)$$

Using the conditional and multiplication rules of probability (Altman and Bland 1994), we have that:

$$F_{+ve} = \frac{P(A / \bar{B})P(B)}{P(A)} = \frac{\left(1 - P(\bar{A} / \bar{B})\right)\left(1 - P(B)\right)}{P(A)} \quad (4)$$

$$where\ P(\bar{B}) = 1 - P(B)\ and\ P(\bar{A} / \bar{B}) = 1 - P(A / \bar{B})$$

$$And$$

$$F_{-ve} = \frac{P(\bar{A} / B)P(B)}{P(\bar{A})} = \frac{\left(1 - P(A / B)\right)P(B)}{1 - P(A)} \quad (5)$$

$$where$$

$$P(\bar{A}) = 1 - P(A)\ and\ P(\bar{A} / B) = 1 - P(A / B)$$

Now unless the available data are a result of a representative random sample obtained in a well-designed controlled clinical trial, it is often not possible to obtain P (A) and P (B) directly from these data. P (B) is usually obtained from a reliable census or health survey while P(A) which is a function of P(B) is obtained as follows using Baye's rule (Miller, 1986; Uche, 2004).

Thus,

$$P(A) = P(A / B).P(B) + P(A / \bar{B})P(\bar{B})$$

$$= P(A / B).P(B) + P(A / \bar{B})\left(1 - P(B)\right) \quad (6)$$

Or in terms of sensitivity and specificity

$$P(A) = P(A / B).P(B) + \left(1 - P(\bar{A} / \bar{B})\right)\left(1 - P(B)\right)$$

$$= 1 - P(\bar{A} / \bar{B}) - \left(1 - P(A / B) - P(A / B) - P(\bar{A} / \bar{B})\right).P(B) \quad (7)$$

Now putting equation (6) in equation (4) we have that

$$F_{+ve} = P(\bar{B} / A) = \frac{\left(1 - P(\bar{A} / \bar{B})\right)\left(1 - P(B)\right)}{P(A / B)P(B) + P(A / \bar{B})\left(1 - P(B)\right)} \quad (8)$$

Or when expressed in terms of the often more familiar sensitivity and specificity becomes

$$F_{+ve} = \frac{\left(1 - P(\bar{A} / \bar{B})\right)\left(1 - P(B)\right)}{P(A / B)P(B) + P(\bar{A} / \bar{B})\left(1 - P(B)\right)}$$

$$= \frac{\left(1 - P(\bar{A} / \bar{B})\right)\left(1 - P(B)\right)}{1 - P(\bar{A} / \bar{B}) - \left(1 - P(A / B)\right) - P(\bar{A} / \bar{B})\left(1 - P(B)\right)} \quad (9)$$

Similarly using Equation 6 in Equation 5, we have that

$$F_{-ve} = P(B / \bar{A}) = \frac{\big(1 - P(A / B)\big) P(B)}{1 - P(A / B)P(B) + P(A / \bar{B})\big(1 - P(B)\big)} \qquad (10)$$

Similarly which when expressed in terms of sensitivity and specificity becomes

$$F_{-ve} = \frac{\big(1 - P(A / B)\big) P(B)}{1 - P(A / B)P(B) + \big(1 - P(\bar{A} / \bar{B})\big)\big(1 - P(B)\big)}$$

$$= \frac{\big(1 - P(A / B)\big) P(B)}{P(\bar{A} / \bar{B}) + \big(1 - P(A / B) - P(\bar{A} / \bar{B})\big) P(B)} \qquad (11)$$

II. The Proposed Method

Now to develop the proposed measure of association between test results and existing condition we note that the odds that a randomly selected subject who tests positive to the test actually has the condition is

$$\Omega_A = \frac{P(B / A)}{P(\bar{B} / A)} = \frac{True\ Positive\ Rate\,(TPR)}{False\ Positive\ Rate(FPR)}$$

Expressed in terms of false positive rate we have that

$$\Omega_{\bar{A}} = \frac{1 - P(\bar{B} / A)}{P(B / A)} = \frac{1 - F_{+ve}}{F_{+ve}} \qquad 12$$

When interpreted, we have that among all subjects testing positive to the test, Ω_A measures the number of subjects who actually have the condition for every subject who actually does not have the condition in nature. Similarly, the odds that a randomly selected subject who tests negative to the test actually has the condition is

$$\Omega_{\bar{A}} = \frac{P(B / \bar{A})}{P(\bar{B} / \bar{A})} = \frac{False\ Negative\ Rate(FNR)}{True\ Negative\ Rate\ (TNR)}$$

Expressed in terms of false negative rate we have that

$$\Omega_{\bar{A}} = \frac{P(B / \bar{A})}{1 - P(B / \bar{A})} = \frac{F_{-ve}}{1 - F_{-ve}} \qquad 13$$

Thus among all subjects testing negative to the test $\Omega_{\bar{A}}$ measures the number of subjects who actually have the condition for every subject who actually does not have the condition. Hence a good measure of the strength of association between screening test results and state of nature or existing condition is the ratio of these odds, or the so called odds ratio, namely

$$\omega = \frac{\Omega_A}{\Omega_{\bar{A}}} = \frac{\big(1 - F_{+ve}\big)\big(1 - F_{-ve}\big)}{F_{+ve} F_{-ve}} = \frac{P(A / B).P(\bar{B} / \bar{A})}{\big(1 - P(A / B)\big)\big(1 - P(\bar{A} / \bar{B})\big)} \qquad 14$$

Notice that the last expression on the right hand side of Equation 14 is independent of the prevalence rate P(B) of the condition in the population, but it is a function of only the sensitivity and specificity of the test. Hence even when the prevalence rate of a condition in the population is not known, one is still able to use the value of $'\omega'$ as a measure of the strength of association between the condition of interest and screening test results using the values of sensitivity and specificity of the test. Now since F_{+ve} and F_{-ve} are both probabilities and hence non-negative

$$\omega \geq 0 \qquad 15$$

Note that as any other odds ratio, ω is invariant under the three types of study designs namely; the cross sectional; prospective and retrospective studies(Allan 1996).When the screening test results and the existing condition are not in any way associated, in which case the diagnostic test is unable to correctly screen a subject having the condition as actually having the condition and a subject free of the condition as actually not having the condition. In these cases, knowing a subject's test result is of no use in predicting the subject's existing condition. Hence the smaller the value of ω, the lower and weaker the association between test results and state of nature; the greater the value of ω, the higher and stronger the association.

III. Modified Odds Ratio From Sample Estimates

In diagnostic screening tests the only sample data or observations in Table 1 usually known and used by the researcher in an analysis are the total sample size n= n.. consisting of $n_{.1}$ and $n_{.2}$ subjects, the number of subjects from the sampled population known or believed to have and not to have the condition, n_{11} the number of subjects known to have the condition who test positive and n_{22} the number of subjects known not to have the condition who test negative. The sample value n_{12}, the number of subjects in the sample known not to have the condition who test positive and n_{21}, the number of subjects known to have the condition who test negative and their derivatives $n_{1.}$ and $n_{2.}$, the total numbers of subjects testing positive and negative respectively are usually not known and hence cannot properly and validly be directly used in estimating measures of association in diagnostic screening tests. Hence the traditional odds ratio, relative risk and other such usual measures of association which rely on these sample values for their estimation cannot without modifications be properly calculated and used as measures of association in screening tests. We therefore here estimate the proposed modified odds ratio type measure of association in terms of only the available sample data n, $n_{.1}$, $n_{.2}$, n_{11} and n_{22}. Use is also made of the prevalence rate P(B) of the condition in the population if known, otherwise the proposed measure of association is calculated in terms of the estimated sensitivity and specificity of the test. Thus as already shown in Equations 3 and 4 sensitivity and specificity of the test are estimated respectively as

$$\hat{Se} = \frac{n_{11}}{n_{.1}} \; and \; \hat{Sp} = \frac{n_{22}}{n_{.2}}.$$

The proportion of the population expected to test positive to the condition is estimated from Equations 9 and 10 as;

$$\hat{P}(A) = P(A) = \frac{n_{11}}{n_{.1}}P(B) + \left(1 - \frac{n_{22}}{n_{.2}}\right)\left(1 - P(B)\right) = 1 - \hat{Sp} - \left(1 - \hat{Se} - \hat{Sp}\right).P(B) \qquad 16$$

Sample estimates of F_{+ve} and F_{-ve} are obtained using sample estimates of sensitivity and specificity of equations (3) and (4) together with the values of (A) of Equation 19 and P(B) obtained from perhaps some census data on health survey data. Thus, using equations (3), (4) and (19) in equations (12) and (13) we have that the estimates of F_{+ve} and F_{-ve} expressed in terms of the often more familiar sensitivity and specificity of the test are respectively.

$$\hat{F}_{+ve} = \frac{\left(1 - \frac{n_{22}}{n_{.2}}\right)\left(1 - P(B)\right)}{\frac{n_{11}}{n_{.1}}P(B) + \left(1 - \frac{n_{22}}{n_{.2}}\right)\left(1 - P(B)\right)} = \frac{\left(1 - \hat{Sp}\right)\left(1 - P(B)\right)}{1 - \hat{Sp} - \left(1 - \hat{Se} - \hat{Sp}\right).P(B)} \qquad 17$$

And

$$\hat{F}_{-ve} = \frac{\left(1 - \frac{n_{11}}{n_{.1}}\right)P(B)}{1 - \left(\frac{n_{11}}{n_{.1}}P(B) + \left(1 - \frac{n_{22}}{n_{.2}}\right)\left(1 - P(B)\right)\right)} = \frac{\left(1 - \hat{Se}\right)P(B)}{\hat{Sp} + \left(1 - \hat{Se} - \hat{Sp}\right).P(B)} \qquad 18$$

The estimated odds of positive response is from equation (17)

$$\hat{\Omega}_A = \frac{1-\hat{F}_{+ve}}{\hat{F}_{+ve}} \qquad 19$$

Similarly the estimated odds of negative response is from equation (18)

$$\hat{\Omega}_{\bar{A}} = \frac{1-\hat{F}_{-ve}}{\hat{F}_{-ve}} \qquad 20$$

Hence from Equation 14 the sample estimate of the false rates based odds ratio-type measure of association between condition and results in a diagnostic screening test is

$$\hat{\omega} = o = \frac{\hat{\Omega}_A}{\hat{\Omega}_{\bar{A}}} = \frac{\left(1-\hat{F}_{+ve}\right)\left(1-\hat{F}_{-ve}\right)}{\hat{F}_{+ve}.\hat{F}_{-ve}} = \frac{\hat{Se}.\hat{Sp}}{\left(1-\hat{Se}\right)\left(1-\hat{Sp}\right)} \qquad 21$$

Using equations (19), (20) and (21), the sample estimates of , and are readily obtained. Note as pointed out above that even if the prevalence rate P(B) of the condition is not known to enable estimation of false rates, the proposed odds ratio type measure of association can still be estimated from Equation 21 using the estimated sensitivity and specificity of the test which are independent of the population of interest.

Estimate Of Standard Error And Test Statistics For ω

If the traditional odds ratio or relative risk is used as a measure of the strength of association between sample data obtained using any of the three common study methods, then the estimate of the standard error of the sample odds ratio $\omega = 0$ or such similar measures of association, which is used only in gauging the precision of the estimated sample measure but not in hypothesis testing for its significance or in certain confidence intervals is

$$se\,(o) = o\sqrt{\frac{1}{n_{11}} + \frac{1}{n_{12}} + \frac{1}{n_{21}} + \frac{1}{n_{22}}} \qquad 22$$

For the traditional odds ratio measure of association, the test statistic for testing the significance of the association, that is, for testing the significance of $\hat{\omega} = 0$ (that is, $H_0 : \omega = 1$) is done using the usual chi-square test statistic based on the sample data of Table 1, namely

$$\chi^2 = \frac{n\left(n_{11}.n_{22} - n_{12}n_{21}\right)^2}{n_{1.}n_{2.}n_{.1}n_{.2}} \qquad 23$$

which under H_0 has approximately the chi-square distribution with 1 degree of freedom. However as already noted above, in diagnostic screening tests, the sample values n_{12} *and* n_{21} usually are not known, so are the sample values $n_{1.}$ *and* $n_{2.}$ derived from them. Hence the sample estimates of the standard error of $\hat{\omega} = 0$ given in Equation 22 and its associated test statistic given in Equation 23 cannot properly and validly be estimated using those sample values. Now a modified estimate of the standard error of $\hat{\omega} = 0$ which is appropriate for use with the estimated odds ratio type measure of association $\hat{\omega} = 0$ for assessing the strength of association in diagnostic screening tests is obtained by eliminating n_{12} *and* n_{21} from Equation 22, which after a few simple algebraic manipulations yields in terms of $n_{.1}, n_{.2}, \hat{Se}$ *and* $\hat{Sp}$, the value

$$se\,(\hat{\omega}) = se\,(o) = o\sqrt{\frac{1}{n_{.1}\hat{Se}\left(1-\hat{Se}\right)} + \frac{1}{n_{.2}\hat{Sp}\left(1-\hat{Sp}\right)}} \qquad 24$$

Similarly an equivalent expression for the chi-square test statistic (Equation 23) for no association between state of nature and screening test results ($H_0 : \omega = 1$) in terms of sensitivity and specificity especially in diagnostic screening tests where n_{12}, n_{21}, $n_{1.}$ and $n_{2.}$ the total number of subjects testing positive and negative respectively are usually not known and not readily available for use in estimation is

$$\chi^2 = \frac{n_{..}\left(1-\hat{S}e-\hat{S}p\right)^2}{\hat{S}e.\hat{S}p\left(1+\frac{n_{.2}-n_{22}}{n_{11}}\right)\left(1+\frac{n_{.1}-n_{11}}{n_{22}}\right)}$$

$$= \frac{n\left(1-\hat{S}e.\hat{S}p\right)^2}{\hat{S}e.\hat{S}p\left(1+\left(\frac{n_{.2}}{n_{.1}}\right)\left(\frac{1-\hat{S}p}{\hat{S}e}\right)\right)\left(1+\left(\frac{n_{.1}}{n_{.2}}\right)\left(\frac{1-\hat{S}e}{\hat{S}p}\right)\right)} \qquad 25$$

which like equation (23) has the chi-square distribution, with 1 degree of freedom. The null hypothesis is rejected at the α level of significance if

$$\chi^2 \geq \chi^2_{1-\alpha;1} \qquad 26$$

otherwise H_O is accepted

As noted above it is not possible to estimate false rates, and the corresponding odds using sample data from diagnostic screening tests without prior knowledge or at least informed and reliable estimates of the prevalence rate P(B) and the proportion, P(A) of the population expected to test positive to the condition of interest. However, the present odds ratio type measure of association and the corresponding test statistic can never the less still be estimated, even when the prevalence rate is not known, now using the estimated sensitivity and specificity of the test. Notice that even when in diagnostic screening tests the prevalence rate of a condition in the population is not known, equation 21 can still be used to estimate the proposed false rates based measure of odds ratio type measure of association now using only the estimated sensitivity and specificity of the test which are independent of the prevalence rate of the condition in the population of interest. Hence the present method is more generalized than the traditional odds ratio approach, in that it enables the simultaneous estimation of sensitivity, specificity, false rates, the proportion of the population expected to test positive and the required measure of association, if the prevalence rate of the condition is known and also enables the estimation of the proposed odds ratio type measure of association using only sensitivity and specificity of the test when the prevalence rate of the condition in the population is not known. In all cases estimates including the standard error of the odds ratio type measure and the test statistics are made using sensitivity and specificity of the test which are always estimable in diagnostic screening tests. Furthermore as already noted above in diagnostic screening tests the number of subjects who test negative among the sample of subjects in the population known or believed to have the condition in nature and the number of subjects who test positive among the sample of subjects in the population who are known or believed not to have the condition in nature are usually not readily known or available and therefore cannot properly be directly used in the estimation of a measure of association between State of nature or condition and screening test results. Thus although the estimated odds ratio, its standard deviation and test statistic using the traditional methods would yield essentially the same values as the ones obtained using the odds ratio-type method, nevertheless, the traditional methods do not recommend themselves because of the problems with its estimation already highlighted above. Note finally for completeness of presentation that the sample estimate of the traditional odds ratio is given by Equation (27). The estimates of its standard deviation and associated test statistic for its significance are also given in Equations (22) and (23) respectively. These expressions by their presentation and formulation contain x_{12} and x_{21} and hence apparently and strictly speaking are not valid and may not be properly used in estimating values using data obtained from diagnostic screening test since in such studies x_{21} and x_{21} usually are not known. One however needs some knowledge of Algebra and familiarity with the concept and uses of sensitivity and specificity for one to find that dividing both the numerator and the denominator of Equation (27) with $n_{.1}\, n_{.2}$ yields the same expression as the second term on the right hand side of Equation (24) in terms of estimated sensitivity and specificity of the screening test which are always estimable from available sample data from screening tests, a result that may however not be immediately obvious and clear to the average user. This is the reason why the odds ratio type measure of association and the traditional odds ratio may often yield the same estimated values of the measure and the corresponding test statistic. However the traditional odds ratio is fundamentally faulty and invalid in its specification and estimation as

$$o = \frac{n_{11}.n_{22}}{n_{12}.n_{21}},$$

when used with sample data obtained from diagnostic screening tests. This is because its denominator, n_{12}, n_{21} strictly speaking does not exist because as pointed out above, n_{12} and n_{21} are usually not known. Thus strictly speaking, the results obtained from their use would be misleading and hence considered inadmissible.

IV. Illustrative Example

A randomly selected screened sample of n.1 = 140 subjects from Abakaliki in Ebonyi State, Nigeria, known or believed to have breast cancer and n.2 = 245 subjects known or believed not to have breast cancer from the same community obtaining the results shown in Table 2. Interest is in determining whether the test results truly reflect actual prevalence of breast cancer in the community.

Table 2: Results of Screening Test for Breast Cancer by Clinicians in a certain Public Hospital at Abakaliki, Nigeria

Clinical diagnoses (Test results)	**Histologic diagnoses (State of Nature)**		
	Present(B)	Absent($\overline{B}$)	Total
positive(A)	116	35	151
Negative($\overline{A}$)	24	210	234
Total	140	245	385

V. Results

The sample data of table 2 were analyzed using the proposed method. Although the prevalence rate of breast cancer in Nigeria was reported to be 127 per 100,000 or about 1 per 1000, we here also provide estimates for the case in which the prevalence rate P (B) of breast cancer is 1 per 100 population, for comparative purposes. From Equations (3) and (4) we have that the sample estimates of the sensitivity and specificity of the test are respectively

$$\hat{S}e = \frac{116}{140} = 0.829; \hat{S}p = \frac{210}{245} = 0.857$$

values that indicate that the test is sufficiently sensitive and specific.

From Equation (19) the estimated proportion of the population expected to test positive to the test, with P (B) = 0.001, is

$$\hat{P}(A) = 1 - 0.857 - (1 - 0.829 - 0.857)(0.001) = 0.1437 \; or \; 0.144$$

From Equations 20 and 21 we have that the estimated false positive and false negative rates of the test with P (B) = 0.001 are respectively

$$\hat{F}_{+ve} = \frac{(1 - 0.857)(0.999)}{0.144} = 0.992$$

And

$$\hat{F}_{-ve} = \frac{(1 - 0.829)(0.001)}{1 - 0.144} = 0.0002$$

Thus if the prevalence rate of breast cancer of 1 in 1000 population in Nigeria is admissible then we would expect that for every 1000 subjects screened and found to test positive to breast cancer 992 would actually be free of the disease and for every 10,000 subjects screened and found not to have breast cancer only 2 would be expected to have the disease. The odds of positive and negative responses are similarly estimated from Equations (22) and (23) respectively. The proposed odds ratio type measure of association with P (B) = 0.001, is estimated from Equation (24)

as

$$\hat{\omega} = o = \frac{0.0058}{0.0002} = 29.00$$

Note from Equation (24) that $\hat{\omega} = o$ is also estimated from the second term on the right hand side of

$$\hat{\omega} = o = \frac{(0.829)(0.869)}{(1 - 0.829)(1 - 0.857)} = 29.06,$$

Only the proportion of the population expected to test positive, the false rates and their corresponding odds are affected by the prevalence rate of the condition in the population. Estimates of these rates and other measures for the case in which the prevalence rate is 1 per 100 population are similarly obtained. The results are shown in Table 3.

Table 3: Application of False Rates-Based Odds Ratio as Measure of Association in Breast Cancer Screening Data

Types of Measure	Prevalence rate unknown	Prevalence Rate P(B)	
		1 per 1,000	1 per 100
Sensitivity	0.829	0.829	0.829
Specificity	0.857	0.857	0.857
Proportion expected to test positive		0.144	0.150
False positive rate		0.992	0.945
False negative rate		0.0002	0.0020
Odds of positive response		0.0058	0.0586
Odds of negative response		0.0002	0.0020
Odds ratio 'O'	29.00	29.00	29.02
Standard deviation	8.381	8.352	8.358
Chi-square value	174.855	174.855	174.855
P-value	0.0000	0.0000	0.0000

VI. Discussion

The results obtained using the proposed method show that the estimated odds ratio-type measure of association is consistent with the rather high sample estimates of sensitivity and specificity of the test which are independent of the prevalence rate of a condition of interest in the population, but are however probably inconsistent with the low value of the prevalence rate of breast cancer of about 1 in 1000 reported for Nigeria. As expected, because of the independence of sensitivity and specificity and the prevalence rate of a condition in a population, the sample estimate of the odds ratio-type measure of association based on false rates and the one obtained using only sample estimates of sensitivity and specificity are essentially the same. For the same reason, as may be noticed from Table 2, the estimates of the proposed false rates based odds ratio-type measure are essentially invariant with prevalence rates. The proportion of subjects in the population expected to test positive to the condition (breast cancer) is seen to increase as prevalence rate decreases. This is because this rate is structurally always an inverse function of prevalence rates. Similarly as can be seen from Table 2, the estimated measures of association based on the usual odds ratio when the prevalence rate is not known as well as when it is known are virtually equal because of the dependence of these rates on only sensitivity and specificity. However, as already pointed out above, the traditional odds ratio method cannot, strictly speaking, be used in estimating any measure of association between screening test results and state of nature in a population because some of the required sample data normally used in the estimation of this measure are not usually available to the researcher. For the same reasons, although the sample estimates of the standard deviation of the estimated measures of association and the corresponding chi square values are essentially the same for both the traditional odds ratio method and the false rates based odds ratio-type measure method are virtually the same, the traditional estimates are structurally faulty and may not be validly calculated. The proposed method, unlike the traditional method enables the researcher as shown in Table 2 obtain sample estimates of false rates, their odds of positive response and negative response as well as the proportion of subjects in the population expected to test positive to the condition (breast cancer) if the prevalence rate of the condition in the population is known. These are useful and additional information that cannot possibly be obtained using the traditional odds ratio method.

VII. Summary And Conclusion

We have in this paper proposed and developed odds ratio-type measure of association in screening tests based on false positive rate, false negative rate, sensitivity and specificity of a test procedure. Unlike the traditional odds ratio, the proposed method takes into account in its formulation any existing prevalence rate of a condition of interest and incorporates an indirect estimate of the proportion of subjects in the population expected to test positive. Also unlike the traditional or conventional odds ratio method, the proposed method provides estimates of false rates for a condition and uses them to provide an estimate of the proposed odds ratio-type measure of association if the prevalence rate of the condition in the population expected to test positive. Also unlike the traditional or conventional odds ratio method, the proposed method provides estimates of false rates for a condition and uses them to provide an estimate of the proposed odds ratio-type measure of association if the prevalence rate of the condition in the population is known. Even when the prevalence rate is

not known, the proposed method is still able to provide estimate of the odds ratio-measure of association in terms of estimated sensitivity and specificity of the screening test. The proposed method unlike the traditional odds ratio approach provides sample estimates of the proposed odds ratio type measure, its standard deviation and test statistic for its significance that explicitly and structurally exclude in their formulation the usually unknown numbers of subjects in the sample obtained in a diagnostic screening test that are known or believed to actually have a condition but test negative or known or believed not to have a condition but test positive in the screening test. The fact that estimates of true and false rates, their odds and the proportion of the population expected to test positive to the condition in the screening test can be made when the prevalence rate of the condition in the population is known as well as estimates of the sensitivity and specificity of the test is an added advantage of the proposed method that provide additional useful information over and above the ones that are possible with the traditional odds ratio method.

References

[1]. Akobeng AK (2007).Understanding diagnostic tests 2: likelihood ratios, pre- and post-test probabilities and their use in clinical practice. Acta Paediatr 96(4):487-91.
[2]. Agresti, A (2007). Introduction to Categorical Data Analysis. John Wiley and Sons. Inc., Publications. New York.
[3]. Altman DG (1996). Statistics with Confidence. BMJ Publishing Group. 28-33.
[4]. Altman DG., Bland JM (1994). Diagnostic Tests I: Sensitivity and specificity. BMJ, 308(6943):1552. London.
[5]. Fleiss JL (1973). Statistical Method for Rates and Proportions. John Wiley, New York.
[6]. Gardner MJ, Altman DG (1989). Calculating confidence intervals for proportions and their differences. In: Gardner MJ,
[7]. Kestenbaum B (2009). Epidemiology and Biostatistics: an introduction to clinical research. Springer Science LLC.
[8]. Lalkhen AG, McCluskey A (2008). Clinical tests: sensitivity and specificity.Continuing Education in Anaesthesia.Critical
[9]. Care & Pain J. 8(6): 221-223
[10]. Miller J. Statistics for Advanced Level (1996). (2nd Edition) Cambridge University Press
[11]. Uche PI (2004). Probability: Theory and Practice. Longman Nig PLC
[12]. Zweig MH, Ashwood ER, Galen RS, Plous RH, Robinowitz M (1995). Assessment of the Clinical Accuracy of LaboratoryTests Using Receiver Operating Characteristics (ROC) Plots; Approved Guideline. NCCLS Standards and Guidelines.15(19): 1-27