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COMPARISON OF RELATIVE RISK, ATTRIBUTABLE RISK AND LOGISTIC RESPONSE PROCEDURES FOR $2\times2\times2$ AND c $2\times2\times2$ CONTINGENCY TABLES*

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Summary

A numerical evaluation was made on three different χ^2 statistics in order to compare mutagenic risk frequencies between two experimental groups in a $2\times2\times2$ contingency table and c $2\times2\times2$ contingency tables. The three methods involve 1) a relative risk approach, 2) an attributable risk approach and 3) a logistic response approach. A relatively large difference was observed among χ^2 statistics in the three approaches using actual data under the hypothesis that there is no difference between the two groups under scrutiny. With regard to approximate power, it appears that approaches 2) and 3) give fairly stable results. Approach 1) has greater power if there is a small difference in the control groups. It was confirmed that the approximate power of approach 1) is extremely large when the difference in the relative risk frequencies between the two groups under contrast is constant and each relative risk frequency is small.

1. Introduction

It is very interesting, as a clue in elucidating the origins of the difference in sensitivity to mutagens among strains, to compare the difference in mutation rates in mutagen treated offspring using two strains whose sensitivity to chemical substances and radiation are different. This study originated in an inquiry from the Zoology Department, Faculty of Science, Hiroshima University about a feasible statistical method to evaluate the frequency of lethal mutants in two strains. Comparison of these frequencies has much in common with the study of the relative biological effectiveness (RBE) of neutrons, one of the major concerns of RERF. A large difference in neutron component

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exists between the Hiroshima uranium bomb and the Nagasaki plutonium bomb. The difference in the radiation effect between the two bombs can be evaluated by comparing the relative risk frequencies or attributable risk frequencies observed in the two cities.

In this paper, interest is focused on different approaches to the comparison of risk frequencies in a two-strain experiment or any two-group classification replicated c times.

2. Contingency table and notation

Let a $2\times2\times2$ contingency table for a single two-strain experiment be denoted by

(2.1)

	A-strain		B-strain	
	Control	Exposed†	Control	Exposed†
Hatched	x_{11}	x_{12}	x_{21}	x_{22}
Not hatched	$n_{11}-x_{11}$	$n_{12}-x_{12}$	$n_{21}-x_{21}$	$n_{22}-x_{22}$
Number of eggs laid	n_{11}	n_{12}	n_{21}	n_{22}

† denotes that one of the parents is exposed.
A-strain is "Hikone strain" with the force of resistance and B-strain "sensitive strain" with genes of bw (brown), st (scarlet) and ss (spineless).

It is assumed that the numbers of eggs hatched $\{x_{ij};\ i, j=1, 2\}$ have independent binomial distributions with parameters P_{ij} $(0<P_{ij}<1)$ and n_{ij} respectively in the contingency table (2.1).

3. Relative risk comparison approach

From the contingency table (2.1) the estimate of the relative risk, $\hat{\psi}_i$, is defined as the ratio of hatching rates between the control and the exposed groups, i.e.,

$$\hat{\psi}_i=\frac{\hat{P}_{i2}}{\hat{P}_{i1}} \tag{3.1}$$

where $\hat{P}_{i1}=x_{i1}/n_{i1}$ and $\hat{P}_{i2}=x_{i2}/n_{i2}$.

In this procedure we are interested in a comparison of the relative risk frequency (CRR) between the two strains. One measure of CRR, say $\hat{\psi}$, is obtained from the ratio of the relative risks for the two strains,

$$\hat{\psi}=\frac{\hat{\psi}_2}{\hat{\psi}_1} \tag{3.2}$$

where $\hat{\phi}_1$ denotes the relative risk for strain A in which $i=1$ and $\hat{\phi}_2$ is the relative risk for strain B where $i=2$.

A statistical test of the hypothesis of equal relative risks, i.e., $\phi_1=\phi_2$, can be based on the logarithm of the estimated CRR, that is,

$$\hat{\lambda}=\log(\hat{\phi}_2)-\log(\hat{\phi}_1) \tag{3.3}$$

which has the asymptotic variance,

$$V(\hat{\lambda})=\frac{1}{\hat{\omega}}=\frac{(n_{11}-x_{11})}{n_{11}x_{11}}+\frac{(n_{12}-x_{12})}{n_{12}x_{12}}+\frac{(n_{21}-x_{21})}{n_{21}x_{21}}+\frac{(n_{22}-x_{22})}{n_{22}x_{22}}\,. \tag{3.4}$$

Thus, a χ^2 statistic for testing the null hypothesis H_0: $\lambda=0$, equality of relative risk frequencies of the two strains, is given by

$$\chi^2=\frac{\hat{\lambda}^2}{V(\hat{\lambda})}=\hat{\omega}\hat{\lambda}^2 \tag{3.5}$$

which has an asymptotic χ^2 distribution with 1 degree of freedom. The value obtained by this method is equivalent to the test statistic used by Ratnayake [4] in 1968. He states in his paper that "the significance of the difference in relative dominant lethal frequency between any two series within an experiment was estimated by using a χ^2 test kindly provided by Dr. Barnett Woolf", but the method was not clearly demonstrated. This point was confirmed through personal communication with him [5].

4. Partitioning of χ^2 statistics in c $2\times2\times2$ contingency tables

Consider now the χ^2 statistic when the experiment in contingency table (2.1) is repeated c times. We assume the c experiments to be independent.

From the contingency table (2.1) we assume that the numbers of eggs hatched in c experiments, $\{x_{ij}^l;\ i,j=1,2;\ l=1,2,\cdots,c\}$, have mutually independent binomial distributions with parameters P_{ij}^l $(0<P_{ij}^l<1)$ and n_{ij}^l, respectively. For each of the c experiments, from (3.3) the log CRR is given by

$$\hat{\lambda}_l=\log(\hat{\phi}_2^l)-\log(\hat{\phi}_1^l) \tag{4.1}$$

where $l=1,2,\cdots,c$. From (3.4) the asymptotic variance of $\hat{\lambda}_l$ is $V(\hat{\lambda}_l)=1/\hat{\omega}_l$. A χ^2 statistic based on the summation of the statistics from the independent c experiments is

$$\chi^2_{\text{total}}=\sum_{l=1}^{c}\hat{\omega}_l\hat{\lambda}_l^2 \tag{4.2}$$

and has approximately a χ^2 distribution with c degrees of freedom. The total χ^2 statistic (4.2) may be divided into two component χ^2 values (Fleiss [3]). That is

$$\chi^2_{\text{total}}=\chi^2_{\text{assoc}}+\chi^2_{\text{homog}} \tag{4.3}$$

where $\chi^2_{\text{assoc}}=\left(\sum_{l=1}^{c}\hat{\omega}_l\hat{\lambda}_l\right)^2\Big/\sum_{l=1}^{c}\hat{\omega}_l$ is a χ^2 value with 1 degree of freedom and $\chi^2_{\text{homog}}=\chi^2_{\text{total}}-\chi^2_{\text{assoc}}$ a χ^2 value with $c-1$ degrees of freedom. The $\sum_{l=1}^{c}\hat{\omega}_l\hat{\lambda}_l$ assesses not only the significance of the average degree of the difference in relative risk frequencies among the c experiments, but also provides an important measure of determining whether or not the risk difference among the c experiments are in the positive or negative direction. The χ^2_{homog} corresponds to a statistic which measures the degree of homogeneity of the difference in relative risk frequencies among the c experiments.

5. Attributable risk comparison approach

The difference in hatching rates between the exposed and control groups is a measure of the risk of mutation attributable to exposure,

$$\hat{\phi}_i=\hat{P}_{i1}-\hat{P}_{i2}\,. \tag{5.1}$$

Therefore, the comparison of the difference in attributable risk frequencies between two strains (CAR) is defined from (5.1) as

$$\hat{\lambda}=\hat{\phi}_2-\hat{\phi}_1\,. \tag{5.2}$$

The estimated variance of λ is

$$\mathrm{V}(\hat{\lambda})=\frac{1}{\hat{\omega}}=\frac{\hat{P}_{11}(1-\hat{P}_{11})}{n_{11}}+\frac{\hat{P}_{12}(1-\hat{P}_{12})}{n_{12}}+\frac{\hat{P}_{21}(1-\hat{P}_{21})}{n_{21}}+\frac{\hat{P}_{22}(1-\hat{P}_{22})}{n_{22}}\,. \tag{5.3}$$

A χ^2 statistic for testing the null hypothesis H_0: $\lambda=0$, i.e., no difference in attributable risk frequencies between the two strains, is given by

$$\chi^2=\frac{\hat{\lambda}^2}{\mathrm{V}(\hat{\lambda})}=\hat{\omega}\hat{\lambda}^2 \tag{5.4}$$

and has approximately a χ^2 distribution with 1 degree of freedom. As in the previous section, a one degree of freedom χ^2 value for the null hypothesis of no difference of attributable risk frequencies between two strains in c independent experiments is obtained from (5.2) and (5.3) as

$$\chi^2_{\text{assoc}}=\frac{\left(\sum_{l=1}^{c}\hat{\omega}_l\hat{\lambda}_l\right)^2}{\sum_{l=1}^{c}\hat{\omega}_l}\,. \tag{5.5}$$

When χ^2 statistic (5.5) is significant, $\sum_{l=1}^{c}\hat{\omega}_l\hat{\lambda}_l<0$ means that the A-strain shows a greater decrease in hatching rate than the biologically sensitive B-strain.

6. Logistic response comparison approach

In this section the same problem will be evaluated by a simple mathematical model usually used in mass experimental data, i.e., logistic model (Berkson [1] and Cox [2]).

We shall assume that the numbers of hatched eggs in the contingency table (2.1), $\{x_{ij};\ i, j=1, 2\}$, have independent binomial distributions with parameters P_{ij} and n_{ij} as in the former section. The structure of the P_{ij} which is expressed by the logit transformation is

$$\log\left[P_{i1}/(1-P_{i1})\right]=\mu_i\,, \qquad \log\left[P_{i1}/(1-P_{i2})\right]=\mu_i-\beta_{i2} \tag{6.1}$$

where μ_i denotes the transformed hatching rate for the control group for each strain and β_{i2} the decrease in the transformed hatching rate in the treated group. The joint distribution of the numbers of observed independent hatched eggs, $\{x_{ij}\}$, is given by the product of the binomial distributions from (6.1), i.e.,

$$L=\prod_{i=1}^{2}\prod_{j=1}^{2}\left[\binom{n_{ij}}{x_{ij}}\exp\left(\mu_i-\beta_{ij}\right)^{x_{ij}}\{1+\exp\left(\mu_i-\beta_{ij}\right)\}^{-n_{ij}}\right] \tag{6.2}$$

where $\beta_{i1}=0$ for the control group. These estimated parameters can be easily obtained by

$$\hat{\mu}_i=\log\left[\hat{P}_{i1}/(1-\hat{P}_{i1})\right]\,, \qquad \hat{\beta}_{i2}=\hat{\mu}_i-\log\left[\hat{P}_{i2}/(1-\hat{P}_{i2})\right]$$

where $\hat{P}_{i1}=x_{i1}/n_{i1}$ and $\hat{P}_{i2}=x_{i2}/n_{i2}$.

The odds for the hatching and non-hatching rates in the control group is expressed by

$$\hat{\Omega}_{i1}=\frac{\hat{P}_{i1}}{1-\hat{P}_{i1}}=\exp\left(\hat{\mu}_i\right)\,; \qquad i=1, 2 \tag{6.3}$$

where $\hat{P}_{i1}=x_{i1}/n_{i1}$; whereas, the odds for the hatching and non-hatching rates in the treated group is given by

$$\hat{\Omega}_{i2}=\frac{\hat{P}_{i2}}{1-\hat{P}_{i2}}=\exp\left(\hat{\mu}_i-\hat{\beta}_{i2}\right) \tag{6.4}$$

where $\hat{P}_{i2}=x_{i2}/n_{i2}$. Thus, the ratio defined by (6.3) and (6.4) becomes corresponding to (3.1),

$$\hat{\Omega}_i=\frac{\hat{\Omega}_{i2}}{\hat{\Omega}_{i1}}=\exp(-\hat{\beta}_{i2}) \tag{6.5}$$

and is a function which depends on only the treatment response. The risk estimate corresponding to CRR (3.2) and CAR (5.2) is expressed by

$$\hat{\Omega}=\frac{\hat{\Omega}_2}{\hat{\Omega}_1}=\exp\{-(\hat{\beta}_{22}-\hat{\beta}_{12})\} \tag{6.6}$$

where $\hat{\Omega}_1$ denotes the odds ratio of the A-strain and $\hat{\Omega}_2$ that of the B-strain. A test statistic for the null hypothesis of no difference in treatment responses between the two strains is

$$\chi^2=\frac{(\hat{\beta}_{22}-\hat{\beta}_{12})^2}{\mathrm{V}(\hat{\beta}_{22}-\hat{\beta}_{12})}=\hat{\omega}(\hat{\beta}_{22}-\hat{\beta}_{12})^2 \tag{6.7}$$

which has approximately a χ^2 distribution with 1 degree of freedom, where $\mathrm{V}(\hat{\beta}_{22}-\hat{\beta}_{12})$ denotes the asymptotic variance of the difference in treatment effects in the two-strain experiment. The χ^2 statistic with 1 degree of freedom corresponding to the χ^2 values (4.3) and (5.5) in the c independent experiments is given by

$$\chi^2_{\text{assoc}}=\frac{\left[\sum_{l=1}^{c}\hat{\omega}_l(\hat{\beta}_{22}-\hat{\beta}_{12})_l\right]^2}{\sum_{l=1}^{c}\hat{\omega}_l} \tag{6.8}$$

where $\hat{\omega}_l=1/\mathrm{V}(\hat{\beta}_{22}-\hat{\beta}_{12})_l$ for $l=1, 2, \cdots, c$.

7. Numerical evaluation

Table 1 was obtained from the paper of Uchibori [6]. The numerical evaluation involves a comparison between two strains of Drosophila whose sensitivity to radiation is different. The Hikone strain (A-strain) was used as a strain with resistance and B-strain with genes bw (brown), st (scarlet) and ss (spineless) as a radiation sensitive strain. Both the A- and the B-strains were irradiated with 500 rad in the pupal stage, and the hatched males and nonirradiated females were mass mated for 24 hours. The number of eggs laid and the number of hatched eggs are shown in Table 1. Table 2 gives the results of three approaches, i.e., 1) a relative risk comparison approach (3.5) and (4.3), 2) an attributable risk comparison approach (5.4) and (5.5) and 3) a logistic response comparison approach (6.7) and (6.8). No significant difference

Table 1. Frequency distribution of hatched eggs after exposure of pupae to X-ray in two strains

Experiment No.	Strain	Control			Exposed (500 rad: Male only)		
		Eggs laid	Hatched	%	Eggs laid	Hatched	%
1	A	3964	2877	72.6	3213	1137	35.4
	B	1426	810	56.8	652	245	37.6
2	A	1812	1662	91.7	6738	3078	45.7
	B	3614	2364	65.4	5775	1932	33.5
3	A	2998	2726	90.9	3256	1047	32.2
	B	665	491	73.8	579	96	16.6
4	A	4905	2831	57.7	5728	1843	32.2
	B	3674	2080	56.6	5089	1606	31.6
Total	A	13679	10096	73.8	18935	7105	37.5
	B	9379	5745	61.3	12095	3879	32.1

A-strain: "Hikone strain" with resistance and
B-strain: a "sensitive strain" with genes bw (brown); st (scarlet); ss (spineless).

was observed in the CRR statistic (4.3). However, a large significant difference was observed for both statistics (5.5) and (6.8).

Each of the three χ^2 values obtained here depends on the corresponding hypothesis. However, their respective hypotheses support only the statement or claim about the state of nature. From the radiobiological standpoint three different hypotheses were considered to compare the difference in mutation rates in mutagen treated offspring between the two strains, but it is difficult to select the most appropriate (reasonable) or suitable hypothesis among the three hypotheses introduced here because the data in a two-strain experiment give only incomplete information about a population and can easily be misleading. Based on this statistical consideration, it is of interest to evaluate numerically three χ^2 statistics by using various artificial risk frequencies. Table 3 gives four different artificial risk rates. Table 4 shows by sample size the three χ^2 statistics corresponding to the data when we assume that the four different risks in Table 3 were observed. Relatively large values of the χ^2 statistic for the three different approaches were noted for four artificial data. Furthermore, we can see the relation between sample size and each χ^2 value of one degree of freedom at $\alpha\%$ significant level ($\chi^2=3.84$ with 5% level) corresponding to each hypothesis in the artificial examples. These χ^2 values corresponding to sample size n are easily obtained, being solely dependent on sample size. In the risk data (1) of Table 3 the same risks were assigned to the control levels. We can easily see that all the hypotheses in three approaches are equivalent if $P_{11}=P_{21}$ is true. Then the χ^2 values in approach 1)

Table 2. Comparison of relative risks, attributable risks and logistic responses between two strains

Experiment No.	Relative risks				Attributable risks				Logistic responses			
	$\hat{\lambda}=\log(\hat{\psi}_2/\hat{\psi}_1)$	$V(\hat{\lambda})\times10^{-3}$	$\hat{\omega}$	χ^2	$(\hat{\psi}_2-\hat{\psi}_1)$	$V(\hat{\psi}_2-\hat{\psi}_1)\times10^{-4}$	$\hat{\omega}$	χ^2	$(\hat{\beta}_{22}-\hat{\beta}_{12})$	$V(\hat{\beta}_{22}-\hat{\beta}_{12})\times10^{-2}$	$\hat{\omega}$	χ^2
1	.3051	3.7448	267.04	24.86***	−.1797	6.5321	1530.91	49.41***	−.7940	1.2025	83.16	52.43***
2	2.655×10^{-2}	.7170	1394.64	.98NS	−.1408	1.7988	5559.20	110.25***	−1.2534	.9867	101.35	159.22***
3	−.4542	9.9037	100.97	20.83***	-1.517×10^{-2}	6.2391	1602.79	.37NS	−.3983	2.5722	38.88	6.17*
4	-7.497×10^{-5}	1.1521	867.97	.00NS	-4.855×10^{-3}	1.9715	5072.27	.12NS	-1.661×10^{-2}	.3653	273.73	.08NS
	$\chi^2_{total}(df=4)=46.67$***				$\chi^2_{total}(df=4)=160.15$***				$\chi^2_{total}(df=4)=217.90$***			
	$\chi^2_{assoc}(df=1)=\left(\sum_{l=1}^{4}\hat{\omega}_l\hat{\lambda}_l\right)^2\Big/\sum_{l=1}^{4}\hat{\omega}_l$				$\chi^2_{assoc}(df=1)=\left(\sum_{l=1}^{4}\hat{\omega}_l(\hat{\psi}_2-\hat{\psi}_1)_l\right)^2\Big/\sum_{l=1}^{4}\hat{\omega}_l$				$\chi^2_{assoc}(df=1)=\left(\sum_{l=1}^{4}\hat{\omega}_l(\hat{\beta}_{22}-\hat{\beta}_{12})_l\right)^2\Big/\sum_{l=1}^{4}\hat{\omega}_l$			
	$=72.57^2/2630.62=2.00$NS				$=(-1106.78)^2/13765.17=88.99$***				$=(-213.09)^2/497.12=91.34$***			

Significance level of tests is expressed by NS ($P>.10$), * ($P<.05$), ** ($P<.01$) and *** ($P<.001$).

Table 3. Artificial risks between two strains

Strain	Exposure status	Absolute risk	Same control levels	Different control levels		
			Risk (1)	Risk (2)	Risk (3)	Risk (4)
A	Control	P_{11}	.9	.9	.9	.9
	Exposed	P_{12}	.7	.7	.7	.7
B	Control	P_{21}	.9	.7	.5	.4
	Exposed	P_{22}	.5	.5	.2	.1

Table 4. Three different χ^2 values by sample size and risk data

n	Relative risks $\hat{\lambda}=\log(\hat{\phi}_2/\hat{\phi}_1)$				Attributable risks $\hat{\lambda}=(\hat{\phi}_2-\hat{\phi}_1)$				Logistic responses $\hat{\beta}=(\hat{\beta}_{22}-\hat{\beta}_{12})$			
	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
	.3365	.08516	.6650	1.1350	.2	.0	.1	.1	.8473	−.5026	.03637	.4418
	χ^2 values with 1 d.f.											
10	.6858	.0368	.7982	1.1669	.6250	.0	.1408	.1587	.2317	.1025	.0005	.0627

n is equal to n_{ij} $(i, j=1, 2)$, i.e., $n=n_{11}=n_{12}=n_{21}=n_{22}$.
Each χ^2 value corresponding to sample size kn is easily obtained by $\chi^2(kn)=k\chi^2(n=10)$ where $k=2, 3, \cdots$. For example, $\chi^2(2\times 10)=2\times .6858=1.3716$.
(1), (2), (3) and (4) assume that the estimates $(\hat{P}_{ij})$ of risks (1), (2), (3) and (4) as shown in Table 3 were obtained.

are numerically close to those in approach 2), but not to those in approach 3). Approach 3) appears to provide a conservative result in an appropriate sample size. When the control level in B-strain was kept equal to or less than 50% as risks (3) and (4) in Table 3, approach 1) gains at all times large χ^2 values as compared with those in approaches 2) and 3).

From only such a numerical comparison of these χ^2 statistics, it is hard to decide which approach is more appropriate. Therefore, we evaluated the approximate powers of these χ^2 statistics on the basis of the parameters (P_{ij}) of population risks (1), (2), (3) and (4), respectively, as shown in Table 3. Table 5 gives the approximate powers of these three χ^2 statistics which were calculated by designating the distance from zero as $\log(.9/.8)$ when $d=.1$, $\log(.9/.6)$ when $d=.3$ and $\log(.9/.4)$ when $d=.5$ in approach 1), and as $\exp(d=.1)$, $\exp(d=.3)$ and $\exp(d=.5)$ in approach 3). The approximate power of approach 1) for population risk (1) is very close from the lower level to that of approach 2). The power value of approach 3) is smaller than those of approaches 1) and 2) when $d=.3$ and $d=.5$, but larger than them when $d=.1$. Under population risks (3) and (4), the most powerful method among the three approaches was approach 2) except when $d=.1$. The following was approach 3), but approach 1) was the smallest. With regard to comparison of approximate powers, only approach 1) has been evaluated on

Table 5. Approximate power of the two sided test at the 5% level for three test methods under the alternatives with .1, .3 and .5 positive distances from zero

n	D.F.	Distance from zero (d)	Relative risks $\log(\psi_2/\psi_1)^+$				Attributable risks $(\psi_2-\psi_1)=d$				Logistic responses $\exp(\beta_{22}-\beta_{12})=\exp(d)$			
			(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
10	36	.1	.056	.055	.050	.049	.063	.061	.062	.064	.089	.100	.097	.089
		.3	.158	.139	.078	.063	.207	.180	.190	.209	.111	.128	.123	.110
		.5	.487	.419	.180	.111	.479	.413	.438	.485	.144	.170	.163	.143
20	76	.1	.066	.063	.053	.050	.083	.077	.079	.083	.139	.164	.157	.139
		.3	.286	.248	.116	.081	.377	.329	.348	.382	.187	.225	.215	.186
		.5	.794	.720	.330	.189	.786	.713	.742	.792	.257	.311	.296	.257
30	116	.1	.076	.071	.056	.051	.102	.093	.096	.103	.190	.229	.218	.189
		.3	.399	.348	.154	.099	.530	.461	.488	.537	.262	.315	.301	.261
		.5	.931	.882	.462	.265	.926	.877	.898	.930	.361	.434	.413	.360
50	196	.1	.097	.089	.062	.055	.142	.126	.132	.143	.290	.348	.332	.288
		.3	.605	.530	.231	.137	.748	.676	.704	.745	.398	.481	.458	.396
		.5	.994	.983	.677	.402	.993	.982	.987	.993	.552	.647	.623	.549
100	∞	.1	.151	.134	.077	.062	.244	.212	.224	.247	.511	.607	.579	.509
		.3	.885	.822	.404	.234	.965	.932	.947	.967	.676	.773	.748	.674
		.5	1.000	1.000	.933	.682	1.000	1.000	1.000	1.000	.841	.915	.895	.839
200	∞	.1	.258	.224	.108	.077	.421	.368	.388	.426	.799	.884	.864	.797
		.3	.994	.984	.680	.405	.999	.998	.999	.999	.931	.972	.964	.930
		.5	1.000	1.000	.998	.934	1.000	1.000	1.000	1.000	.988	.997	.995	.987
500	∞	.1	.537	.466	.204	.124	.796	.724	.752	.802	.994	.999	.998	.993
		.3	1.000	1.000	.972	.776	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
		.5	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
1000	∞	.1	.825	.753	.354	.204	.978	.954	.965	.980	1.000	1.000	1.000	1.000
		.3	1.000	1.000	1.000	.973	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
		.5	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000

n is equal to $n_{11}=n_{12}=n_{21}=n_{22}$.

(1), (2), (3) and (4) denote the parameters (P_{ij}) of population risks (1), (2), (3) and (4) respectively which are the same as shown in Table 3.

$^+$ means $\log(.9/.8)$ when $d=.1$, $\log(.9/.6)$ when $d=.3$ and $\log(.9/.4)$ when $d=.5$.

the basis of proper lower risks as given in Table 6. The results in Table 6 reveal that approach 1) has great power if there is a small difference in the levels of the control groups between the two strains, but it appears that the power is small when there is a great difference in risks between the control groups. It was confirmed that the approximate power of approach 1) is extremely large even if the level of the control group is highly different when the difference in risks is constant and the relative risk frequencies in the two strains are small. Based on the synthetic comparison of the approximate powers among three different approaches, fairly stable results can be obtained in approaches 2) and 3), especially in approach 2). However, approach 1) has greater power if there is a small difference in the control groups.

Lastly, it is emphasized that the experimental data in Table 1 used here are a numerical example which show a large fluctuation in the control levels of the A-strain. Radiobiologically speaking, approach 1)

Table 6. Approximate power of the two sided test at the 5% level under the alternatives with .1, .3 and .5 positive equal distance from zero when ψ_1 and ψ_2 are given in relative risk comparison approach

n	Distance from zero (d)	Relative risks $\log(\psi_2/\psi_1)^{+}$				Relative risks $\log(\psi_2/\psi_1)^{++}$				Relative risks $\log(\psi_2/\psi_1)^{+++}$				Relative risks $\log(\psi_2/\psi_1)^{++++}$			
		(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
10	.1	.058	.057	.051	.049	.068	.065	.053	.050	.079	.074	.057	.052	.101	.092	.063	.055
	.3	.198	.173	.090	.068	.374	.325	.143	.090	.592	.516	.220	.130	.914	.860	.432	.246
	.5	.648	.575	.246	.143	.989	.975	.646	.374	—	—	—	—	—	—	—	—
20	.1	.072	.068	.054	.051	.093	.086	.061	.054	.117	.105	.067	.057	.165	.146	.081	.064
	.3	.363	.316	.140	.093	.661	.589	.255	.149	.884	.821	.400	.230	.997	.992	.736	.449
	.5	.923	.871	.448	.257	1.000	1.000	.921	.661	—	—	—	—	—	—	—	—
30	.1	.084	.078	.058	.053	.118	.106	.068	.057	.155	.137	.078	.063	.231	.200	.099	.073
	.3	.511	.440	.192	.118	.884	.762	.358	.206	.973	.946	.563	.323	1.000	.999	.894	.621
	.5	.986	.968	.620	.358	1.000	1.000	.986	.833	—	—	—	—	—	—	—	—
50	.1	.112	.101	.066	.057	.170	.150	.082	.065	.234	.203	.100	.074	.351	.296	.137	.091
	.3	.727	.653	.293	.169	.968	.937	.547	.314	.999	.996	.780	.491	1.000	1.000	.986	.835
	.5	.999	.998	.834	.549	1.000	1.000	.999	.968	—	—	—	—	—	—	—	—
100	.1	.182	.160	.086	.067	.298	.259	.121	.084	.409	.357	.159	.102	.611	.537	.235	.140
	.3	.957	.919	.515	.297	.999	.998	.837	.553	1.000	1.000	.975	.784	1.000	1.000	1.000	.987
	.5	1.000	1.000	.987	.839	1.000	1.000	1.000	1.000	—	—	—	—	—	—	—	—
200	.1	.316	.274	.126	.086	.519	.449	.197	.121	.687	.615	.272	.159	.837	.825	.406	.236
	.3	.999	.997	.804	.517	1.000	1.000	.987	.838	1.000	1.000	1.000	.975	1.000	1.000	1.000	1.000
	.5	1.000	1.000	1.000	.987	1.000	1.000	1.000	1.000	—	—	—	—	—	—	—	—
500	.1	.642	.570	.249	.145	.889	.827	.408	.236	.974	.947	.566	.326	.999	.996	.777	.490
	.3	1.000	1.000	.994	.887	1.000	1.000	1.000	.996	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	.5	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	—	—	—	—	—	—	—	—
1000	.1	.909	.853	.432	.250	.994	.985	.685	.409	1.000	.984	.850	.568	1.000	1.000	.973	.779
	.3	1.000	1.000	1.000	.994	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	.5	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	—	—	—	—	—	—	—	—

n and (1), (2), (3), (4) are the same description as those of Table 5.

+: $\log(.8/.7)$ when $d=.1$, $\log(.8/.5)$ when $d=.3$ and $\log(.8/.3)$ when $d=.5$.

++: $\log(.6/.5)$ when $d=.1$, $\log(.6/.3)$ when $d=.3$ and $\log(.6/.1)$ when $d=.5$.

+++: $\log(.5/.4)$ when $d=.1$, and $\log(.5/.2)$ when $d=.3$.

++++: $\log(.4/.3)$ when $d=.1$, and $\log(.4/.1)$ when $d=.3$.

gives an acceptable result, but approaches 2) and 3) present difficulties in interpretation of the experiments in that the quantity which significantly contributes much to the χ^2 statistic produced negative terms, $\sum_{l=1}^{4} \hat{\omega}_l \hat{\lambda}_l = -1106.78$ and $\sum_{l=1}^{4} \hat{\omega}_l (\hat{\beta}_{22} - \hat{\beta}_{12})_l = -213.09$, respectively. It is thought that the negative terms have been influenced by many factors other than radiation effects. In particular, approach 1) would have a weak power when there are large variations in the risks of the control groups between two strains. These experimental data suggest the need to establish experimental conditions not influenced by other factors insofar as possible for standing mutation induced by radiation among strains with vital sensitivity.

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