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Recommendations for the use of Taylor series confidence intervals for estimates of vaccine efficacy*

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A simple formula for calculating confidence intervals by means of a Taylor series variance approximation has been recommended for gauging the precision of estimates of vaccine efficacy. To evaluate the performance of Taylor series 95% confidence intervals for vaccine efficacy, we conducted a simulation study for commonly expected values of vaccine efficacy, risk of disease in the unvaccinated population, and sample sizes of the vaccinated and unvaccinated groups. In the first simulation, the sample size in the vaccinated group was 500 or 1000, whereas that in the unvaccinated group ranged from 10 to 1000. The confidence intervals were accurate when the sample size in the unvaccinated group was $\geqslant 50$ *and the risk of disease was 0.3–0.9. In contrast, the intervals were too narrow when all three of the following situations occurred: the number of unvaccinated was small (10 or 20), the true vaccine efficacy was relatively low (60% or 80%), and the risk of disease was 0.5–0.9. Furthermore, when the true vaccine efficacy was high (90% or 95%) and the disease risk in the unvaccinated was low (0.1 and 0.2), the confidence intervals were too broad, especially when the unvaccinated sample size was* < 50. *Additional simulations with a sample size in the vaccinated group of 200 gave broad intervals for 95% vaccine efficacy (for all values of disease risk) and for 90% vaccine efficacy when the disease risk was* $\leqslant 0.3$.

INTRODUCTION

Immunization represents one of the most cost-effective means of disease prevention. Successful immunization programmes can save lives and reduce the severe morbidity of vaccine-preventable diseases; however, for a programme to be successful, it must be monitored closely. Generally, such monitoring involves determination of vaccine coverage and estimation of disease reduction through careful surveillance. In addition, epidemiological assessment of clinical vaccine efficacy has become a useful adjunct to coverage and surveillance for evaluating the impact of immunization programmes. Field evaluation of vaccine efficacy can be particularly useful if surveillance data suggest little impact on disease, despite increasing coverage levels, and if the proportion of reported cases that are vaccine failures appears to be higher than expected.

One common technique used to measure vaccine efficacy (such as that against measles) is a cohort investigation during an outbreak. Whereas the methodology for such studies has been well developed, evaluation of the techniques used to determine the precision of the estimated vaccine efficacy, i.e., confidence intervals, has been incomplete. Information about the precision of an estimate of vaccine efficacy is important, since narrow limits permit greater confidence in the estimate. The Taylor series method has been recommended for determining 95% confidence intervals for vaccine efficacy (*1*) and it has the advantage that the calculations can be done in the field using a simple formula without the need for extensive computer programs.

BACKGROUND

In a cohort study, it is assumed that the risks of the disease in the vaccinated and unvaccinated samples arise from two independent binomial populations. Let NV vaccinated and NU unvaccinated individuals be included in the study and let ARV and ARU be the risks of disease in the samples of vaccinated and unvaccinated, respectively. The sample estimate of

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the risk ratio, or relative risk (RR), for the vaccinated is ARV/ARU. Relative risks that are decreasingly less than unity indicate that the vaccine has an increasingly protective effect.

The data are displayed in a (2×2) table using the following notation:

	Cases	*Non-cases*	*Total*	*Risk*
Vaccinated	a	b	$a+b=NV$	$ARV=a/(a+b)$
Unvaccinated	c	d	$c+d=NU$	$ARU=c/(c+d)$

where $RR=ARV/ARU=[a/(a+b)]/[c/(c+d)]$.

The upper and lower confidence limits on sample estimates are commonly reported in order to gauge precision; however, confidence intervals on estimates of relative risks present special problems since only approximate methods for their calculation are available (*2, 3*). Katz et al. evaluated several such methods for calculating confidence intervals for relative risk estimates (*3*) and recommended the use of a Taylor series approximation for determining the variance of the relative risk. The Taylor series variance approximation is obtained by first noting that

$$\text{var}[\log_e(RR)]=\text{var}[\log_e(ARV)-\log_e(ARU)].$$

Then, assuming that the risk of disease in the vaccinated and unvaccinated populations are statistically independent, i.e., that the covariance between the two risks is zero,

$$\text{var}[\log_e(ARV)-\log_e(ARU)]=\text{var}[\log_e(ARV)]+\text{var}[\log_e(ARU)].$$

The variances of $\log_e$ (ARV) and $\log_e$ (ARU) are then estimated using a Taylor series approximation as described by Kleinbaum et al. (*4*). With the Taylor series approximate variance and the previous notation, the two-sided 95% confidence limits are given by:

$$\exp[\log_e RR \pm 1.96\sqrt{(1-ARV)/a+(1-ARU)/c)}\,].$$

Vaccine efficacy (VE) can be shown to be a simple transformation of the relative risk and is defined as:

$$VE=[(ARU-ARV)/ARU]\times 100=(1-RR)\times 100.$$

A confidence interval for the relative risk of vaccination can be transformed into one for vaccine efficacy in a few simple steps. First, the two-sided confidence interval for the relative risk of vaccination given by:

$$RR_L<RR<RR_U$$

is multiplied by -1 to give:

$$-RR_L>-RR>-RR_U$$

and 1 is added to each element:

$$1-RR_L>1-RR>1-RR_U.$$

Finally, each element is multiplied by 100 (if the vaccine efficacy is to be expressed as a percentage) to give:

$$(1-RR_L)\times 100>(1-RR)\times 100>(1-RR_U)\times 100.$$

This gives the confidence interval for the vaccine efficacy expressed as a percentage. Notice that the *lower* limit of the confidence interval for the relative risk is used to compute the *upper* limit of the interval for the vaccine efficacy, and vice versa, i.e.,

$$VE_L=(1-RR_U)\times 100 \text{ and}$$

$$VE_U=(1-RR_L)\times 100.$$

Typical point estimates of measles vaccine efficacy have been $\geq 80\%$, which corresponds to relative risks of ≤ 0.2. While prior evaluation of the Taylor series intervals suggests that they give a valid upper 95% confidence limit if the relative risk is ≥ 0.25, i.e., the vaccine efficacy is $\leq 75\%$ (*3*), there has been no evaluation for relative risks less than 0.25. Furthermore, there has been no systematic evaluation of two-sided confidence intervals. Finally, no studies have taken into account the distributions of vaccinated and unvaccinated subjects that apply to cohort studies of vaccine efficacy. We therefore carried out simulation studies using a variety of conditions likely to occur in vaccine efficacy investigations to determine under what circumstances Taylor series intervals should be used to calculate 95% confidence limits for estimates of vaccine efficacy.

METHODS

Four factors—vaccine efficacy, disease risk in the unvaccinated population, and the sample sizes of the vaccinated and the unvaccinated populations—determine the width of the 95% Taylor series confidence interval. Simulations were therefore carried out using a wide range of common values for all four factors, as outlined below. The following four values of the population or true vaccine efficacy (VE) were used: 95%, 90%, 80%, and 60%. For each of these values, disease risks (attack rates) in the unvaccinated population were selected that ranged from 0.1 to 0.9 (10–90%) in increments of 0.1 (10%). Three situations were evaluated: the first, in which both vaccinated and unvaccinated subjects were common in the population under study; the second, in which vaccinees were common but unvaccinated persons were infrequent; and the third, in which all sample sizes of unvaccinated persons were considered, but only 200 subjects were included in the vaccinated sample. The first situation applies to areas where vaccine coverage is relatively low (around 50%), the

Table 1. Estimated confidence coefficients obtained by using the Taylor series method for studies with a large number of unvaccinated subjects

No. unvaccinated	No. vaccinated	Risk in the unvaccinated group								
		0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
Vaccine efficacy 95%										
500	500	0.974	0.976	0.968	0.952	0.947	0.958	0.945	0.953	0.954
500	1000	0.971	0.962	0.954	0.951	0.952	0.955	0.946	0.948	0.946
1000	500	0.971	0.976	0.966	0.959	0.957	0.952	0.948	0.951	0.954
1000	1000	0.975	0.959	0.947	0.951	0.951	0.953	0.950	0.953	0.949
Vaccine efficacy 90%										
500	500	0.973	0.955	0.954	0.950	0.943	0.952	0.950	0.950	0.954
500	1000	0.954	0.954	0.953	0.956	0.954	0.949	0.947	0.946	0.948
1000	500	0.975	0.959	0.951	0.953	0.950	0.953	0.945	0.948	0.943
1000	1000	0.958	0.949	0.951	0.960	0.956	0.950	0.951	0.945	0.947
Vaccine efficacy 80%										
500	500	0.952	0.949	0.957	0.950	0.945	0.952	0.951	0.946	0.950
500	1000	0.951	0.956	0.950	0.956	0.953	0.952	0.949	0.948	0.953
1000	500	0.959	0.948	0.950	0.956	0.954	0.949	0.953	0.948	0.948
1000	1000	0.951	0.955	0.955	0.950	0.957	0.954	0.947	0.949	0.954
Vaccine efficacy 60%										
500	500	0.952	0.953	0.945	0.950	0.948	0.949	0.951	0.946	0.944
500	1000	0.953	0.946	0.956	0.949	0.954	0.951	0.946	0.956	0.952
1000	500	0.953	0.943	0.947	0.948	0.952	0.953	0.951	0.945	0.948
1000	1000	0.953	0.952	0.952	0.947	0.955	0.948	0.953	0.948	0.958

second to areas with high vaccine coverage ($\geq 90\%$), while the third evaluates the effect of having a relatively small sample size in the group that has the lowest disease risk. For each combination of vaccine efficacy and risk in the unvaccinated, we examined sample sizes for the unvaccinated (NU) of 10, 20, 50, 100, 500, and 1000, while for the vaccinated group sample sizes (NV) of 200, 500, and 1000 were taken.

For each combination of vaccine efficacy, risk in the unvaccinated, and sample size in each group we generated 5000 random (2×2) tables. The independent pairs of random binomial observations were generated on a computer[a] using the Statistical Analysis System (SAS). Since the number of vaccinated (NV) and unvaccinated (NU) subjects were fixed, we generated a random binomial observation for the a and c cells of each table (the number of cases in the vaccinated and unvaccinated groups) and obtained the b and d cells (the noncases in each group) by subtraction. As a result, each table could have had an observed value of the vaccine efficacy and ARU that were different from the population parameters, i.e., the true values. We next calculated the approximate upper and lower 95% confidence limits from the observed table and checked whether it contained the population vaccine efficacy. Finally, for the 5000 tables we determined the proportion of times that the confidence interval contained the population vaccine efficacy, i.e., the observed confidence coefficient whose expectation value was 0.95 (or 95%). If the proportion was much less than 95%, the confidence intervals were, on the average, too narrow, while if it was much greater than 95% the confidence intervals were too wide (or conservative).

If an observed table had no vaccinated cases ($a=0$), the upper limit of the confidence interval was taken to be 100% and the lower limit−9999, since the variance was undefined. In contrast, if the table had no unvaccinated cases ($c=0$), we used $c=0.5$ in the calculations. This followed the procedure described by Katz et al. (*3*).

[a] IBM 3081.

RESULTS

For sample sizes that involved large numbers of both vaccinated and unvaccinated subjects, the observed confidence coefficients of the approximate confidence intervals are presented in Table 1. Over-

all, the approximate two-sided 95% confidence intervals have observed confidence coefficients that are quite close to 95%. If the population vaccine efficacy is 80% or 60%, the confidence coefficient is always within 0.7% of the expected value of 95%. However, as the vaccine efficacy approaches 100%, and the risk in the unvaccinated decreases, the observed confidence coefficients tend to exceed the expected confidence coefficient. Under these conditions, the confidence intervals are, on the average, too broad. On the other hand, even when the vaccine efficiency is 90% or 95%, if the risk in the unvaccinated group is ≥ 0.3, the observed confidence coefficient is still always within 2% of 95%.

Table 2 shows the observed confidence coefficients for samples with large numbers of vaccinated but small numbers of unvaccinated subjects, a situation which is common in developed countries, where immunization levels are high. Regardless of the true vaccine efficacy, if the risk in the unvaccinated is

Table 2. Estimated confidence coefficients obtained by using the Taylor series method for studies with a small number of unvaccinated subjects

No. unvaccinated	No. vaccinated	Risk in the unvaccinated group								
		0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
Vaccine efficacy 95%										
10	500	0.993	0.976	0.974	0.972	0.962	0.956	0.958	0.951	0.951
10	1000	0.975	0.966	0.957	0.952	0.952	0.947	0.948	0.951	0.956
20	500	1.000	0.992	0.968	0.960	0.958	0.953	0.961	0.956	0.950
20	1000	0.982	0.971	0.960	0.956	0.954	0.959	0.953	0.952	0.955
50	500	0.989	0.971	0.961	0.956	0.954	0.953	0.953	0.961	0.945
50	1000	0.984	0.957	0.951	0.953	0.951	0.952	0.950	0.951	0.949
100	500	0.982	0.972	0.963	0.958	0.956	0.948	0.951	0.949	0.954
100	1000	0.971	0.952	0.948	0.952	0.950	0.946	0.953	0.946	0.950
Vaccine efficacy 90%										
10	500	0.978	0.966	0.951	0.953	0.948	0.955	0.944	0.949	0.955
10	1000	0.953	0.952	0.949	0.945	0.943	0.934	0.929	0.919	0.937
20	500	0.987	0.972	0.961	0.957	0.954	0.951	0.959	0.957	0.951
20	1000	0.964	0.962	0.960	0.955	0.954	0.948	0.950	0.948	0.953
50	500	0.986	0.951	0.957	0.951	0.949	0.958	0.955	0.957	0.955
50	1000	0.971	0.958	0.952	0.950	0.954	0.954	0.944	0.954	0.953
100	500	0.976	0.952	0.952	0.953	0.952	0.953	0.955	0.955	0.949
100	1000	0.959	0.950	0.952	0.950	0.959	0.954	0.946	0.946	0.949
Vaccine efficacy 80%										
10	500	0.959	0.954	0.949	0.941	0.938	0.933	0.930	0.924	0.923
10	1000	0.944	0.944	0.942	0.938	0.932	0.928	0.913	0.894	0.875
20	500	0.961	0.960	0.960	0.953	0.949	0.944	0.945	0.948	0.951
20	1000	0.959	0.960	0.957	0.942	0.946	0.945	0.940	0.935	0.936
50	500	0.973	0.955	0.951	0.954	0.950	0.950	0.958	0.952	0.950
50	1000	0.968	0.954	0.952	0.953	0.949	0.951	0.939	0.950	0.955
100	500	0.955	0.957	0.951	0.948	0.955	0.953	0.946	0.950	0.953
100	1000	0.952	0.953	0.954	0.951	0.956	0.954	0.957	0.948	0.954
Vaccine efficacy 60%										
10	500	0.949	0.947	0.948	0.938	0.938	0.935	0.906	0.891	0.856
10	1000	0.945	0.954	0.948	0.942	0.933	0.935	0.890	0.899	0.753
20	500	0.952	0.963	0.952	0.946	0.946	0.936	0.938	0.932	0.928
20	1000	0.959	0.956	0.955	0.946	0.941	0.942	0.932	0.922	0.897
50	500	0.966	0.955	0.956	0.948	0.956	0.950	0.944	0.955	0.952
50	1000	0.963	0.952	0.949	0.949	0.949	0.949	0.946	0.945	0.948
100	500	0.959	0.951	0.952	0.950	0.958	0.950	0.953	0.948	0.949
100	1000	0.948	0.947	0.952	0.950	0.951	0.950	0.946	0.948	0.945

$\geqslant 0.3$ and NU $\geqslant 50$, the observed confidence coefficient is reasonably close, i.e., within 2%, to 95%. However, the observed confidence coefficients become considerably greater than 95% as the true vaccine efficacy increases and the disease risk in the unvaccinated decreases, and both NU and NV become small. Under these circumstances, the confidence intervals are too broad. In contrast, the observed confidence coefficient drops considerably below 95%, which implies that the confidence intervals are too narrow, as the true vaccine efficacy decreases, and the disease risk in the unvaccinated increases, and NU becomes small. The problem is more marked the larger the value of NV.

The effect of decreasing the number of vaccinated subjects in the study to 200 is shown for various sample sizes in Table 3; not surprisingly, the confidence intervals become broader. Since the vaccinated group has the lowest disease risk, the number of expected cases is very low for the higher vaccine efficacies. In the most extreme case, when the true vaccine efficacy is 95% and the disease risk is 0.1 in the unvaccinated group, only one case is expected in the vaccinated sample of 200, since their disease risk is only 0.005. This situation becomes less decisive and the performance of the Taylor series confidence intervals improves as either the disease risk increases or the true vaccine efficacy decreases.

DISCUSSION

The goal of the study was to evaluate the performance of the Taylor series confidence intervals for determining vaccine efficacy (and the corresponding

Table 3. Estimated confidence coefficients obtained by using the Taylor series method for studies with 200 vaccinated subjects

	Risk in the unvaccinated group								
No. unvaccinated	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
Vaccine efficacy 95%									
10	1.000	1.000	0.999	0.995	0.990	0.981	0.974	0.974	0.960
20	1.000	0.990	0.983	0.975	0.981	0.976	0.972	0.962	0.960
50	0.981	0.979	0.976	0.976	0.972	0.972	0.967	0.956	0.956
100	0.976	0.972	0.975	0.971	0.973	0.974	0.968	0.965	0.960
500	0.973	0.969	0.980	0.973	0.975	0.971	0.975	0.961	0.960
1000	0.974	0.968	0.979	0.967	0.978	0.972	0.972	0.961	0.958
Vaccine efficacy 90%									
10	0.999	0.993	0.977	0.973	0.969	0.958	0.960	0.949	0.957
20	1.000	0.992	0.979	0.965	0.956	0.962	0.955	0.957	0.961
50	0.983	0.976	0.970	0.960	0.961	0.954	0.952	0.954	0.947
100	0.978	0.972	0.973	0.963	0.956	0.961	0.951	0.952	0.950
500	0.977	0.971	0.974	0.959	0.956	0.953	0.952	0.950	0.957
1000	0.976	0.972	0.970	0.959	0.955	0.955	0.952	0.944	0.954
Vaccine efficacy 80%									
10	0.977	0.962	0.960	0.957	0.963	0.951	0.953	0.949	0.950
20	0.989	0.973	0.962	0.960	0.953	0.953	0.951	0.945	0.950
50	0.989	0.962	0.955	0.957	0.955	0.959	0.953	0.950	0.948
100	0.973	0.960	0.958	0.957	0.946	0.953	0.952	0.950	0.953
500	0.974	0.959	0.955	0.949	0.954	0.951	0.949	0.951	0.946
1000	0.974	0.961	0.957	0.955	0.948	0.949	0.951	0.952	0.952
Vaccine efficacy 60%									
10	0.956	0.957	0.958	0.951	0.947	0.936	0.930	0.930	0.937
20	0.969	0.963	0.956	0.953	0.947	0.946	0.951	0.947	0.951
50	0.970	0.959	0.953	0.956	0.952	0.956	0.952	0.949	0.951
100	0.966	0.954	0.951	0.955	0.957	0.956	0.954	0.953	0.954
500	0.957	0.948	0.947	0.951	0.950	0.949	0.949	0.951	0.948
1000	0.958	0.959	0.945	0.950	0.951	0.950	0.956	0.954	0.942

relative risks) under a wide variety of circumstances in order to define the conditions under which the technique will perform reliably.

Investigators should consider the methodology to be used for calculating confidence intervals during the planning stages of a study. Once sample size estimates are obtained using the desired Type I and Type II errors, along with some estimate of the true vaccine efficacy, all of the information needed to make a decision is available. Unfortunately, in the absence of data an investigator is obligated during the planning stages to "guess" the true vaccine efficacy in order to assess how many subjects are needed and decide what methodology will be used to assess the precision of the estimates. Fortunately, however, under most circumstances the guess need only be approximate, since the confidence intervals give misleading results only under combinations of extreme values of the study factors, e.g., very small unvaccinated group combined with a low vaccine efficacy and a risk that exceeds 0.5. Most investigators will probably know intuitively whether their study could potentially fall into one of these "danger zones."

For applications involving large numbers of both vaccinated and unvaccinated subjects, reliable confidence intervals are produced whenever the disease risk in the unvaccinated group is ≥ 0.3 (≥ 0.2 for true vaccine efficacies of 90% and ≥ 0.1 with true efficacies of 80% or 60%). These intervals are therefore widely applicable in such studies. However, the combination of low risk in the unvaccinated group and a high vaccine efficacy results in confidence intervals that are too broad. If a study is to be conducted under these conditions, another method of computing the confidence intervals should be used, such as that described by Bailey (*5*) (which can also be carried out using a pocket calculator) or by Thomas & Gart (*6*) (or the refinement in the computing algorithm reported by Mehta et al. (*7*)). None of these methods has been evaluated under conditions appropriate for vaccine efficacy confidence intervals, but of the two, the calculations are easier to perform using Bailey's method (although they are more difficult than the Taylor series approach) and the intervals obtained are very accurate (*5*). It should be noted, however, that the 95% Taylor series confidence interval has at least a 95% chance of containing the true vaccine efficacy.

For applications that involve large numbers of vaccinated and smaller numbers of unvaccinated subjects, very reliable confidence intervals are obtained when the number of unvaccinated subjects is ≥ 50 and the disease risk in the unvaccinated group is ≥ 0.3, regardless of the efficacy of the vaccine. Of course, many other conditions give reliable confidence intervals (see Table 2); however, as the risk and the sample size in the unvaccinated group decrease and the vaccine efficacy increases, the confidence coefficient becomes considerably greater than 95%, indicating that the confidence intervals are too broad. Under these conditions, the true variation in the point estimate of the vaccine efficacy will be overestimated.

Only rarely were the confidence intervals obtained too narrow. This occurred when the number of unvaccinated persons in a sample was ≤ 20, the number vaccinated was ≥ 500, the attack rate in the unvaccinated was 50–90%, and the true vaccine efficacy was $\leq 80\%$. Under these conditions, other methods for calculating 95% confidence intervals should be considered (*5–7*).

As shown in Table 3, reducing the sample size in the vaccinated group tends to increase the breadth of the confidence intervals. Ideally, the estimated confidence coefficient should not be a function of sample size, but that this is not the case for an approximate procedure under extreme conditions is not surprising. Confidence intervals calculated using the Taylor series method should be used very carefully for studies that involve a true vaccine efficacy of $\geq 95\%$ or a true efficacy of approximately 90% and a disease risk of ≤ 0.3, since the true variation will then be overestimated. In contrast, for studies that involve a true vaccine efficacy of 80%, the intervals will be too broad when the disease risk is ≤ 0.1. Otherwise, the confidence intervals calculated using the Taylor series method are quite accurate.

Table 4 summarizes the recommendations for the use of Taylor series 95% confidence intervals. Shown are the general conditions under which the intervals obtained are usable or specific circumstances under which alternative methods should be considered. The performance of the confidence intervals under conditions not covered in Table 4 were too variable to make blanket recommendations and, if a study is planned under such conditions, Tables 1, 2, or 3 should be consulted to assess whether or not the Taylor series intervals should be used.

The results we have reported show that, under virtually all conditions examined, the 95% Taylor series confidence limits determined are never too narrow if the unvaccinated group has ≥ 50 subjects. Investigators should therefore note that the intervals obtained will not underestimate the variation in their estimates and that the calculated interval has at least a 95% chance of including the true vaccine efficacy. However, under extreme conditions, e.g., small sample size for the unvaccinated combined with low risk and a high true vaccine efficacy or a high risk and a low true vaccine efficacy, the intervals may be either too broad or too narrow, respectively.

Table 4. Recommendations for the use of 95% Taylor series confidence levels

Sample category[a]	Risk in the unvaccinated	True vaccine efficacy (%)	Results and recommendations
1. NU ⩾ 50, NV ⩾ 500	0.2–0.9	60–90	Taylor series approximation provides accurate intervals
NU ⩾ 20, NV ⩾ 500	0.3–0.9	95	
All NU, NV = 200	0.2–0.9	60–80	
All NU, NV = 200	0.4–0.9	90	
2. All NU, NV ⩾ 500	0.1 and 0.2	95	Intervals are too broad; will affect ability to show good precision
All NU, NV ⩾ 500	0.1	90	
All NU, NV = 200	0.1–0.7	95	
All NU, NV = 200	0.1–0.3	90	
3. NU = 10, NV ⩾ 500	0.5–0.9	80	Intervals are too narrow; consider alternative methods
NU ⩽ 20, NV ⩾ 500	0.5–0.9	60	

[a] NU = number unvaccinated; NV = number vaccinated.

RÉSUMÉ

RECOMMANDATIONS RELATIVES À L'EMPLOI DES INTERVALLES DE CONFIANCE OBTENUS À PARTIR DES SÉRIES DE TAYLOR POUR L'ESTIMATION DE L'EFFICACITÉ DES VACCINS

Les études d'efficacité des vaccins effectuées sur des cohortes constituent un moyen important pour surveiller l'impact des programmes de vaccination. Pour déterminer la précision des estimations de l'efficacité des vaccins, il a été recommandé d'appliquer une formule simple pour le calcul des intervalles de confiance, à partir d'une approximation de la variance obtenue au moyen des séries de Taylor. Pour évaluer la qualité des intervalles de confiance ainsi calculés, nous avons effectué une simulation des valeurs de l'efficacité des vaccins auxquelles on peut normalement s'attendre, du risque de contracter la maladie dans la population non vaccinée, ainsi que de la taille des échantillons des groupes vaccinés et non vaccinés à étudier. Dans le premier cas, l'échantillon du groupe vacciné représentait 500 ou 1000 personnes, tandis que celui du groupe non vacciné allait de 10 à 1000 personnes. Les intervalles de confiance calculés étaient en général assez exacts pour toutes les valeurs réelles de l'efficacité du vaccin examinées, lorsque la taille de l'échantillon du groupe non vacciné était ⩾50 et le risque de maladie situé entre 0,3 et 0,9. En revanche ces intervalles étaient trop étroits lorsque les trois situations suivantes s'ajoutaient: le nombre de personnes non vaccinées était faible (10 ou 20), l'efficacité réelle du vaccin était relativement faible (60% ou 80%) et le risque de contracter la maladie se situait entre 0,5 et 0,9. D'autre part, avec une efficacité réelle du vaccin élevée (90% ou 95%) et un risque de contracter la maladie faible chez les non vaccinés (0,1 ou 0,2), ces intervalles de confiance étaient trop grands, en particulier lorsque l'échantillon de population non vaccinée était inférieur à 50. D'autres simulations dans lesquelles on a utilisé un échantillon de population vaccinée plus petit (<200) ont donné des intervalles trop grands pour un vaccin efficace à 95% (quelles que soient les valeurs du risque de contracter la maladie) et à 90% lorsque le risque était ⩽0,3. Dans le présent article figurent des recommandations concernant les circonstances dans lesquelles les intervalles de confiance obtenus à partir des séries de Taylor sont fiables, et des propositions d'autres méthodologies pour les situations dans lesquelles ces intervalles ne conviennent pas.

REFERENCES

1. ORENSTEIN, W. A. ET AL. Field evaluation of vaccine efficacy. *Bulletin of the World Health Organization*, **63**: 1055–1068 (1985).
2. GART, J. J. Statistical analyses of the relative risk. *Environmental health perspectives*, **32**: 157–167 (1979).
3. KATZ, D. ET AL. Obtaining confidence intervals for the risk ratio in cohort studies. *Biometrics*, **34**: 469–474 (1978).
4. KLEINBAUM, D. G. ET AL. *Epidemiologic research, principles and quantitative methods*. Lifetime Learning Publications, Belmont, CA, 1982.
5. BAILEY, B. J. R. Confidence limits to the risk ratio. *Biometrics*, **43**: 201–206 (1987).
6. THOMAS, D. G. & GART, J. J. A table of exact confidence limits for differences and ratios of two proportions and their odds ratio. *Journal of the American Statistical Association*, **72**: 73–76 (1977).
7. MEHTA, C. R. ET AL. Computing an exact confidence interval for the common odds ratio in several 2×2 contingency tables. *Journal of the American Statistical Association*, **80**: 969–973 (1985).