Epidem. Inf. (1987), **99**, 485–499
Printed in Great Britain

An assessment of methods for routine local monitoring of vaccine efficacy, with particular reference to measles and pertussis

By J. A. CLARKSON and P. E. M. FINE

Ross Insitute, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT

(*Accepted 1 May 1987*)

SUMMARY

The efficacy of measles and pertussis vaccines was investigated using several different procedures based upon data routinely available at Local Health Authority level in England and Wales. It is demonstrated that such estimates can be derived by methods which can be carried out simply and routinely by local health department staff. Several theoretical and practical difficulties in the procedures are discussed. It is recommended that Health Authorities consider monitoring by a routine procedure based on crude case-control analysis of recorded vaccination status of notified cases compared with that of the population in the Child Health computer file, or of matched controls drawn from Child Health Registers. A simple protocol for such studies is provided.

INTRODUCTION

The ultimate measure of the value of a vaccination programme is its impact on disease incidence. But for operational purposes it may be more appropriate to monitor those parameters upon which such a fall in disease incidence depends – vaccine coverage (uptake statistics by age) and vaccine efficacy (the degree of protection imparted by the vaccination).

To facilitate appropriate corrective action, operational monitoring of vaccine efficacy should be carried out separately for different administrative areas. Public health officers will wish to know whether a local outbreak is attributable to vaccine failure or to some other factor, perhaps a chance aggregation of non-vaccinated individuals. It is always useful to have local information for health education purposes – for encouragement of providers to do better (if vaccine efficacy is poor) or for the public to participate (if efficacy is high). It should be possible to identify areas using poor vaccines (perhaps attributable to improper storage conditions), areas where vaccines are being improperly administered, or areas experiencing a change in infection pattern (for example a shift in serotype of *Bordetella pertussis* away from those included in the vaccine). Finally, there are additional advantages if all the data processing involved in monitoring vaccine efficacy can itself be carried out at local level. This should reduce the delay involved in centralized information systems, and it should encourage the clerical

Address for correspondence: Mrs J. A. Clarkson, Ross Institute, London School of Hygiene & Tropical Medicine, Keppel Street (Gower Street), London WC1E 7HT.

staff of local Health Authorities by demonstrating the direct use of records which they work hard to maintain.

The protective efficacy of a vaccine, or vaccine efficacy (VE), is conventionally defined as the percent reduction in disease incidence in vaccinated as compared to unvaccinated but otherwise similar individuals. Thus $VE = (R_{nv} - R_v)/R_{nv}$, where R_{nv} and R_v are the incidence rates of disease among non-vaccinated and vaccinated individuals respectively. There are two general methods for the estimation of VE: cohort studies, in which populations of unvaccinated and of vaccinated children are followed over time, to provide direct estimates of R_{nv} and R_v; and case-control studies, in which the relative risk R_v/R_{nv} is estimated by the ratio of the odds of a positive vaccination history in cases compared with an appropriate control group. The theoretical basis of these two general approaches has been discussed in several recent publications (Smith, Rodrigues & Fine, 1984; Orenstein *et al.* 1985). The literature contains many examples of studies employing variants of both these approaches (Fine & Clarkson, in press). On the other hand, little attention has been given to the mechanics of adapting these general methods for routine application at local level. Orenstein and his colleagues describe a screening method (essentially a case-control method) for monitoring vaccine uptake in a group of cases in a narrow age band and comparing it with that in the population (Orenstein *et al.* 1985). This idea is developed below.

In principle, both cohort and case-control methods require only the appropriate linking of local vaccinations and disease notifications data, as recommended for England and Wales in the 1983 Körner Report on Community Health Services Information (DHSS/NHS, 1983). In practice, these methods are limited by the nature of available records. In this paper we follow the Körner recommendation and evaluate different protocols for the local monitoring of vaccine efficacy by analysis of routinely collected data. Though the study was carried out with particular reference to measles and pertussis vaccines in England and Wales, and is thus most relevant to data systems in this country, many of the methodological points should be applicable to other immunizable diseases and to other areas of the world.

MATERIALS AND METHODS

Estimation of vaccine efficacy requires vaccination status information of a group of cases of the disease against which the vaccine should protect, and also on the population from which the cases are drawn. The latter may be estimated from total population statistics or from a control group selected by one means or another. We have explored several methods for estimating vaccine efficacy in five Health Authorities: three in London (Hampstead, Paddington/North Kensington and Tower Hamlets) and two in rural areas (Shropshire and Sedgemoor District, in Somerset). Each of these Health Authorities had different procedures of capturing and holding the relevant data, although the underlying structure of all these procedures was similar (as it is throughout England and Wales). All the data used in this study were extracted from routinely available records by JAC.

Information on cases

Physicians in England and Wales are obliged to notify their Medical Officer for Environmental Health (MOEH) of any case of approximately 30 infectious diseases which they diagnose (Clarkson & Fine, 1985, 1987). The preprinted notification slips request information on the diagnosis, date of onset, name, age, sex and address of the case, and they are usually date-stamped on arrival at the Health Authority. The information may be copied into a Notification Register, but in none of the areas visited was any of this information computerized. The slips are usually kept for at least 5 years, and most current notification registers began with the reorganization of the National Health Service (NHS) in 1974. For this study, data on diagnosis, age, sex and date of notification of measles and pertussis cases notified during defined periods were transcribed on to cards. In Hampstead and Paddington/North Kensington the names and addresses had also to be copied to identify each individual in the Child Register (see below). To preserve confidentiality, this personal information was removed before the cards were taken away for analysis. In the other three Health Authorities the notification slips themselves were used to trace individuals and no identifying information was transcribed.

Information on vaccination

All Health Authorities have some form of birth or child health register, recording live births and movements of children (up to age 16) in and out of the Authority. Vaccination information is added to these registers from forms sent in by child health clinics or general practitioners. At the time of our study (1984–5), one Authority was still totally dependent on a card file (but was about to change to its own computer system), one used an interactive computer system designed locally, and three used the National Health Service Standard Child Health System (NCHCS) (DHSS/NHS, 1983).

Sources of controls

We assessed three different methods of selecting controls.

1. *Vaccine uptake statistic controls.* The vaccine uptake statistic routinely used in England and Wales is defined for each annual birth cohort x and Health Authority a (let us call this statistic P_{xa}) as the total number of courses of vaccine given in a to all children who were born in year x, and completed before the end of year $x+2$, divided by the total number of live births in a during year x. These statistics are available for each District Health Authority (for each Area Health Authority prior to the 1980 birth control cohort), and each birth cohort (except 1972 and 1973, because of the reorganization of the NHS in 1974) (DHSS, unpublished documents). They are not sex-specific. They were used to predict the vaccination status of a theoretical, age-matched control group from the District population. Therefore, for each notified case born in year x, we estimated P_{xa} vaccinated controls and $1-P_{xa}$ unvaccinated controls. This is analagous to the method used by Orenstein *et al.* (1985), but controls for varying vaccine uptake by age. If the vaccine uptake is constant over time, the two methods are identical.

2. *Child register controls.* For each case identified in a Child Health Register, two

individuals were selected of the same age (usually within a few days and always within one year), sex and area (i.e. register). These were, in general, selected as the first two children, who satisfied the criteria and appeared after the case in a birth order listing of the Register.

3. *Notification Register controls.* In order to control for any factors associated with a case having been notified, children notified for non-immunizable diseases (NIDs) were identified in each area and later matched to measles and pertussis cases by age. Because of the scarcity of NIDs, up to four index cases of each disease were matched to each NID. The vaccination status of each of these individuals was then obtained as for the index cases.

Data linkage

A link was considered to have been established between a notified individual and an entry in the Child Register if the full name and age agreed. If the surname was common or there was no age on the notification slip, the address had also to match. A child was considered vaccinated if there was a record of vaccination having been given before the reported date of onset of the notified illness. The onset date for the cases was used in assessing the vaccination status of the matched controls (if more than one index case was matched to a NID, the vaccination status of the NID was ascertained at the mean age of onset of the index cases). No attempt was made to verify either the vaccination record or the diagnosis.

Methods of analysis

Three methods were used to calculate the vaccine efficacies. Each was essentially a case-control procedure.

The simplest was to neglect any matching of cases and controls and thus to estimate the relative risk by the conventional odds ratio (Orenstein *et al.* 1985; Schlesselman, 1982; Smith, Rodrigues & Fine, 1984):

$$VE = 1 - \frac{(\text{vaccinated cases}) \times (\text{unvaccinated controls})}{(\text{unvaccinated cases}) \times (\text{vaccinated controls})}.$$

This method was applied using each of the three control groups and for each Health Authority. We called this the crude method. To prevent a bias against the vaccine, only those cases (and controls) old enough to have been offered vaccine (1 year for pertussis and 18 months for measles) were included in the crude analyses. (Any bias would only be in its favour if the vaccine were harmful (Schlesselman, 1982).) All those aged less than 2 years were excluded from the crude analysis using the DHSS vaccine uptake figures because of the definition of uptake used in England and Wales.

The second and third methods recognized that the Child Register and the Notification Register control groups were each individually matched with the cases (matched for age, sex and residence, or for age, residence and attending a notifying health service, respectively). We thus applied the procedure proposed by

Table 1. *Numbers of notified cases of measles (M), pertussis (P) and non-immunizable diseases (NID) identified in Child Registers, and the percentages which these figures represent of all notifications, for each Health Authority*

Health Authority	Disease group	Period of ascertainment*	Number of cases notified	Number (%) of notified cases identified in child health registers	
Hampstead	M	1/83–12/83	135	54	(40%)
	P	1/82–2/84	86	49	(57%)
	NID	1/82–2/84	60	42	(70%)
Paddington/ N. Kensington	M	1/79–12/84	120	41	(34%)
	P	1/79–12/84	44	22	(50%)
	NID	1/79–12/84	151	63	(42%)
Tower Hamlets	M	1/84–12/84	206	153	(74%)
	P	1/83–12/84	88	52	(59%)
	NID	9/83–12/84	126	51	(41%)
Shropshire	M	1/84–12/84	218	184	(84%)
	P	1/83–12/84	148	122	(82%)
	NID	1/84–12/84	83	72	(87%)
Somerset	M	1/84–12/84	—	147	(*c.* 90%)
	P	1/81–12/84	—	105	(*c.* 90%)
	NID	1/78–12/84	—	51	(*c.* 90%)

* During which these cases were notified.

Mantel & Haenszel (1959) as adapted by Fleiss (1984) for situations with variable numbers of matched controls per case. The relative risk is estimated by:

$$\frac{\sum_r (\text{no. not vaccinated in sets with } r \text{ controls, the case vaccinated})/(r+1)}{\sum_r (\text{no. vaccinated in sets with } r \text{ controls, the case not vaccinated})/(r+1)}.$$

This procedure can be carried out with a hand calculator, but requires considerable manipulation of the data. We called this the 'Mantzel–Haenszel–Fleiss' method.

Finally we have estimated the relative risks using the mainframe computer package PECAN, following the method outlined in Breslow & Day (1980). This is perhaps the most sophisticated method available today, and performs regression analysis of conditional likelihood functions, and preserves the matching. We called this method 'PECAN'.

RESULTS

Numbers of measles and pertussis cases, of non-immunizable disease controls ascertained in the notification records and the numbers and percentages which could be identified in the Child Health Registers, are shown in Table 1. (The total number of notifications by disease groups were not noted in Somerset, but overall

Table 2. *Estimated efficacy (%) of measles vaccine, for the five Districts, by control group and method of analysis*

(Children aged less than 18 months are omitted from the crude analyses, and those under 2 years of age are omitted from the DHSS vaccine uptake figures calculation.)

Source of controls	DHSS vaccine uptake figures	Child Register			Notification Register		
Method of analysis	Crude	Crude	M-H-F	PECAN	Crude	M-H-F	PECAN
Hampstead	87 (47,97)*	74 (6,93)	68 (0,90)	68 (1,90)	84 (34,96)	88 (42,98)	83 (18,96)
Paddington/ N. Kensington	89 (16,99)	49 (−86,86)	64 (−45,91)	62 (−49,90)	93 (66,99)	−†	−†
Tower Hamlets	89 (75,95)	86 (72,92)	89 (77,95)	87 (74,94)	93 (81,97)	94 (71,99)	94 (75,99)
Shropshire	86 (78,91)	87 (80,92)	88 (80,93)	87 (79,92)	77 (57,87)	71 (43,85)	77 (55,88)
Somerset	90 (84,94)	85 (76,90)	88 (79,93)	88 (79,93)	84 (65,92)	85 (65,94)	86 (66,94)
Mantel–Haenszel estimate, combining 5 Districts	88 (83,91)	85 (80,89)	87 (81,91)	86 (82,90)	84 (76,89)	88 (81,93)	85 (77,91)

* 95% confidence limits. † – insufficient numbers of cases for meaningful results.

Table 3. *Estimated efficacy (%) of pertussis vaccine, for the five Districts, by control group and method of analysis*

(Children aged less than 1 year are omitted from the crude analyses, and those aged less than 2 years of age are omitted from the DHSS vaccine uptake figures calculation.)

Source of controls	DHSS vaccine uptake figures	Child Register			Notification Register		
Method of analysis	Crude	Crude	M-H-F	PECAN	Crude	M-H-F	PECAN
Hampstead	50 (−14,78)*	61 (2,85)	58 (−12,84)	60 (−3,85)	60 (−29,87)	78 (−17,96)	—†
Paddington/ N. Kensington	86 (−9,98)	97 (70,100)	—	—	97 (65,100)	—	—
Tower Hamlets	73 (33,89)	83 (58,93)	84 (41,96)	86 (60,95)	86 (54,96)	92 (36,99)	—
Shropshire	75 (56,86)	77 (60,87)	77 (57,88)	78 (60,88)	61 (19,81)	70 (27,88)	65 (22,84)
Somerset	81 (67,89)	71 (49,84)	75 (48,88)	78 (57,89)	75 (33,91)	78 (11,94)	71 (42,100)
Mantel–Haenszel estimate, combining five Districts	75 (65,82)	76 (66,84)	77 (65,85)	79 (70,86)	73 (55,84)	80 (64,89)	77 (61,86)

* 95% confidence limits. †, insufficient numbers of cases for meaningful results.

Table 4. *Efficacy of pertussis vaccine by dose, broken down by source of controls and by method of analysis*

(As there were insufficient numbers with one or two doses within each District for meaningful analysis, the observations were pooled.)

Source of controls	Dose	Crude method	PECAN method
Child Register	1	50* (−2,75)†	60* (25,79)†
	2	76 (46,90)	80 (61,90)
	⩾ 3	76 (67,83)	79 (70,86)
Notification Register	1	51 (−22,81)	63 (4,86)
	2	53 (−43,85)	58 (−6,83)
	⩾ 3	72 (56,82)	77 (55,84)

* Percentages.
† 95% confidence limits.

about 90% were found.) The proportions identifiable in the Child Registers were considerably higher in the rural than in the urban areas.

Table 2 shows estimates of measles vaccine efficacy for each Health Authority, calculated by seven different procedures (three control groups and three analytical methods). The results are in general consistent with one another, but the following trends are evident:

1. The crude estimates derived from uptake statistics controls are similar for all areas visited. The estimate for all areas combined is 88%.

2. In the urban areas the estimates were consistently higher using the Notification Register controls than using the Child Register controls. This is not true for the rural areas, and the opposite trend was found in Shropshire.

3. The estimates are in general high, approximating the 85–90% value obtained in the MRC trial of measles vaccine in England (MRC, 1968). The only exceptions are the low estimates obtained with Child Register controls in two urban areas (Hampstead and Paddington/North Kensington) and with Notification Register controls in Shropshire.

The pertussis vaccine efficacy estimates are shown in Table 3. They show greater variation between Districts than do those for measles, but within Districts the estimates are consistent. It should be noted that the DHSS statistics estimates imply a comparison of a complete (3 dose course) against no vaccine or an incomplete (0–2 dose course), but that the other estimates compare complete courses against no recorded vaccine at all. The estimated vaccine efficacies appear particularly low for Hampstead and high for Paddington/North Kensington.

Table 4 shows estimates of vaccine efficacy for one, two and three doses of pertussis vaccine. Despite the small number of cases with incomplete courses recorded, there is evidence that even a single dose imparts some protection and that a completed course provides appreciably more.

Measles and pertussis vaccine efficacies were also calculated separately for males and females, for different age groups (by year of age), and by duration since vaccination (by year) but revealed no evidence of trends or differences.

DISCUSSION

This investigation demonstrates that it is feasible, indeed extremely simple, to estimate measles and pertussis vaccine efficacy on the basis of the disease notification and child health records which are currently maintained in Local Government and Health Authority offices in England and Wales. We have outlined several methods for doing this; the relative ease of each is largely dependent upon the location and nature of the local records.

All the methods require linkage of disease notification and Child Health Registers. In some areas (e.g. Shropshire and Somerset), the room containing notification information (and hence 'belonging' to Local Government) is adjacent to the room containing the Child Health Register (which 'belongs' to the District Health Authority). In other areas (e.g. Hampstead, Paddington/North Kensington and Tower Hamlets) these offices are in separate buildings some distance apart. Furthermore, the boundaries of Local Government areas and District Health Authorities are often different, which means that more than one Child Health Register may have to be consulted to identify cases notified to one MOEH. Thus the physical linking of the information, and the permission and ethical clearance to do so, is an obvious factor affecting such work. An equally important determinant of simplicity is the nature of the Child Register; in particular the ease with which a specified individual can be located in the file.

Most manual registers are in date of birth order. It is tedious to identify individual cases (e.g. of measles or pertussis) in such Registers, as the notification slip gives only a year of age (and this may be an estimate). On the other hand, once a case has been identified in such a Register, the selection of age-matched controls is simple. The NCHCS can provide microfiche Registers in either name or date of birth order, and vaccination information may be included on either. Identification of cases and selection of controls is simple if both listings are available. Only the name order Register was available in Shropshire, however, and in this case we resorted to systematic random sampling to select controls. The interactive computerized Child Health Register designed and used in Somerset was found to be much superior to the others for finding a child, because it allows immediate retrieval of an individual's vaccination history on the basis of name. On the other hand a name index may be less useful in urban than in rural districts, particularly in areas with large immigrant populations because there may be many children in such communities with similar names, and individuals may appear under different 'surnames' on the notification slip and in the Child Register. In Somerset controls were found from a printout and could not be chosen interactively.

The vaccine efficacy estimates derived by the several methods were, in general, quite consistent (Tables 2 and 3). Furthermore, most appear sufficiently similar to published estimates of measles (MRC, 1968) and pertussis (Fine & Clarkson, in press) vaccine efficacies as to be credible. Though we have no detailed local independent information against which to validate our estimates, we can be reasonably confident from other studies that the measles vaccines used in England and Wales have 85–95% efficacy (MacGregor *et al.* 1981; Marks, Halpin & Orenstein, 1978) and thus use this as an expected range against which to judge our results. This suggests that the Hampstead and Paddington/North Kensington

estimates based on Child Register controls, and the Shropshire estimate based on Notification Register controls, are too low. We may be able to identify the major bias in each of these situations.

The low measles vaccine efficacies derived from Child Register controls in urban areas are probably attributable to two biases. First, some of the cases had been notified several years prior to our study, but the vaccination information was drawn from the current Child Health Registers. This means that the cases represent a more stable population than do the Child Register controls, as some of the latter could have moved into the District only shortly before we examined the records, whereas a case had to have remained on the Register for several years in order to have been included in the study. This problem of transient populations is particularly severe in urban areas. It would not be surprising if transient populations were less likely to be vaccinated than long term residents or that records of such populations are sometimes lost when they move. Either of these possibilities would lead to underestimates of the proportion vaccinated among the controls and hence to low estimates of vaccine efficacy. (But note that an ongoing routine monitoring system would not use such 'old' notifications, and thus would suffer less from this problem.) Second, the Child Register controls are not matched for 'notifiability'. All the cases are by definition associated with notifying family practitioners, whereas this is not true for all the Child Register controls. It may be that family practitioners who take care to notify diseases are in general more interested in childhood illnesses and their prevention than are those who do not. Once again this bias would favour raising the average proportion vaccinated among cases and reducing it among controls, and hence would lead to reduced estimates of vaccine efficacy. Indeed, it was because of this potential bias that we examined the Notification Register control group.

The low measles vaccine efficacy derived for Shropshire on the basis of Notification Register controls is less easily explained, but may be related to the fact that most (89%) of these controls were cases of scarlet fever. The low estimate of measles vaccine efficacy could be explained if individuals notified for scarlet fever were for some reason particularly unlikely to have received measles vaccine, perhaps because some of the scarlet fever cases were misdiagnosed measles. This may be a general phenomenon, in so far as a restriction of Notification Register controls to scarlet fever cases alone led to reductions (not statistically significant) in the measles vaccine efficacy estimate in the two other areas which had sufficient such controls for analysis.

The accuracy of our estimates of pertussis vaccine efficacy is more difficult to assess. Though we find broad variation between areas, this is in itself not inconsistent with the published literature (Fine & Clarkson, in press). It will be noted that our low estimates for Hampstead and high estimates for Paddington/North Kensington are based upon small numbers of cases (Table 1) and have very broad confidence intervals. Overall, our estimates are slightly lower than those of the recent study by the Public Health Laboratory Service. We discuss possible reasons for such differences elsewhere (Fine & Clarkson, in press; Fine, Clarkson & Miller, in preparation).

There was good agreement between the three methods used to calculate the vaccine efficacy. There is no evidence that the much more sophisticated PECAN

approach is so superior to the Mantel–Haenszel–Fleiss method as to justify its use here. Indeed, unless extra confounding factors (e.g. socioeconomic or nutritional status) are to be included in the analysis, this is to be expected. The Mantel–Haenszel–Fleiss method is itself sufficiently complicated to restrict its usefulness in a health department, unless a specific program were made available along with simple appropriate documentation. On the other hand, the results obtained using the simple 'crude' procedure, which could be carried out at the local level with nothing more than the simplest pocket calculator, appears sufficiently sound for the method to be recommended.

For readers with methodological interests, we would call attention to two particular features of the analyses presented here. First, it will be noted that none of our control groups has excluded past cases of the disease they were controlling for. Though this absence of exclusion is unusual in case-control studies, it has been pointed out that such an exclusion is in fact improper, and leads to overestimates of vaccine efficacy if a vaccine imparts solid and lasting protection against the disease in question (Smith, Rodrigues & Fine, 1984). This condition almost certainly holds for measles, and hence we believe the inclusion of past cases to be correct for estimates of measles vaccine efficacy. Whether it holds for pertussis is less clear. If the protection imparted by pertussis vaccine is less solid and lasting than that by measles vaccine then our inclusion criterion should have led to underestimates of its true efficacy (Smith, Rodrigues & Fine, 1984). A second methodological issue concerns our estimates based upon a theoretical control group derived from Area or District vaccine uptake statistics. Our method of estimating an age-matched control population from such statistics, and using these controls in a case-control manner, is algebraically identical to carrying out a cohort analysis using the vaccination status of each birth cohort at age two in order to define the denominators. In this context it should be pointed out that this method is not proper for the analysis of cases less than 2 years old given the definition of the vaccine uptake used in England and Wales (see Materials and Methods).

Of course, all of these procedures suffer from the fact that a routine vaccination programme is not a randomized controlled trial, and thus the estimates of vaccine efficacy may be influenced by a variety of confounding factors affecting vaccine uptake and disease notification. Most importantly, it should be recognized that these estimates relate to the efficacy of the recorded vaccination in protecting against notified disease. Neither of these reporting systems is perfect. A recent study suggests that 70–80% of vaccinations given are included in Health Authority records (Williams & Dajda, 1980). A false-positive record of vaccination should be uncommon, but it is important to recognize that any such errors, unless they tend to occur more frequently in either the cases or controls, will reduce the estimated vaccine efficacy (Schlesselman, 1982). The problem with case notification is rather different. Given that cases or ex-cases are not excluded from the control groups (see above), the incompleteness of notification is not a problem. On the other hand, erroneous notifications will lead to underestimates of vaccine efficacy. Given the problems of diagnosing the two diseases, this is more likely to affect estimates of the efficacy of pertussis than of measles vaccines. Though by no means denying these problems, we doubt that they introduce so

major a bias as to counterbalance the several advantages of establishing simple ongoing monitoring of vaccine efficacy at the local level.

Recommendation

The results of this exercise are sufficiently promising for us to encourage routine monitoring of vaccine efficacy in local health departments. Simplicity will be a major determinant of the method to be applied. Thus we would recommend the simple 'crude' calculation, whichever controls are used. The Notification Register controls, though theoretically sound in that they alone control for 'notifiability', have three problems: they reduce numbers available for analysis in that they are the most difficult to match with the cases; their matching raises computational complexities; and they may introduce biases because of ill-defined factors associated with their own epidemiology (e.g. the low estimates of measles vaccine efficacy based upon scarlet fever controls). We are thus left with the Child Register versus vaccine uptake statistic controls. The vaccine uptake statistics should provide a more precise estimate of vaccine uptake than a small number of age-matched controls, given that the statistics are based on the total cohort population. On the other hand, the vaccine uptake statistic has severe problems. It is not available at all for some cohorts and is not available until the third year after a cohort is born. It excludes any vaccinations carried out after the year during which the cohort reaches its second birthday, and hence provides an underestimate of vaccine uptake for the population. (We have found that approximately 6% of measles vaccinations and 8% of pertussis course completions occur after the second birthday (unpublished data).) And the statistic makes no allowance for movement into and out of an area. This problem is of particular relevance to urban areas with teaching hospitals (because of which the vaccine statistic denominator, being based on births alone, is too large) and to some suburban areas such as Buckinghamshire, which have ridiculously high vaccine uptake statistics (over 100% for some cohorts) because of a large influx of young children who enter the numerator but not the denominator of the statistic. Ideally the vaccine uptake for all cohorts could be found from the computerized Child Register itself, as has been demonstrated in Bradford for a single cohort (Baker, Bandaranayake & Schweiger, 1984). These uptakes would have none of the drawbacks of the DHSS league Table statistics, and they are available for all cohorts at all ages. The population is exactly that from which the cases are drawn and allowance is made for movement into and out of the District. If it were possible to interrogate the computer for such rates on a routine basis we would recommend their use. However at present this seems to be outside the routine scope of the systems in most Districts.

Until vaccine uptake figures can be obtained routinely from computer systems (say every month or quarter), we would recommend the Child Health Register as the most appropriate source of controls for routine monitoring. Given that this Register has to be consulted anyway in order to obtain the vaccination status of the index cases, the work involved in selecting controls is (usually) relatively straightforward. Matching by narrow age interval and sex is simple. Some Registers allow matching on duration of residence in the District (possible on the NCHCS or the Somerset system). The selection of multiple controls for each case

Table 5. *Illustration of calculation of vaccine efficacy in a Health Authority*

(Based on 53 cases of measles and 2 age- matched and sex-matched controls for each case selected from the Child Health Register. A running tally is maintained on a 2 × 2 table allowing periodic calculation of vaccine efficacy. A 95% confidence interval is calculated by the standard method (Schlesselman, 1982).)

Vaccination status as of date of onset of the case	Notified cases	Controls from Child Health Register (two per case) matched for age (born within 1 month of case), sex and duration of residence in district
Yes	𝍸 𝍸 / (= 11)	𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 (= 65)
No	𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 // (= 42)	𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 𝍸 / (= 41)
Total	53	106

$$VE = 1 - \frac{41 \times 11}{42 \times 65} = 83{\cdot}4\,\%$$

$$\text{var}(\ln(1 - VE)) = 1/11 + 1/42 + 1/65 + 1/41$$

95% confidence interval for $VE = 1 - \exp\{\ln(1 - VE) \pm 1{\cdot}96\sqrt{[\text{var}\,(\ln(1 - VE))]}\}$
$= (64{\cdot}3\,\%,\ 92{\cdot}4\,\%)$

reduces the confidence interval on the final estimate. Whatever the criteria of matching, it should be relatively simple for clerical staff to select a recommended number of controls for each notified case, older than the recommended age for completing a vaccination course, which is identified in the Child Health Register. These can be tallied into a two-by-two table as shown in Table 5. Calculation of the vaccine efficacy, as illustrated in the Table, is straightforward. Such calculations may be carried out each time a new case and associated controls are entered, or at regular time intervals, or each time some agreed number of cases accumulate. The confidence interval on the estimate is dependent on the numbers of cases, the number of controls per case, the vaccine uptake and the vaccine efficacy, as shown in Fig. 1. Consideration of Table 5 and Figure 1 should facilitate decisions as to the number of controls to be selected per case and the frequency with which vaccine efficacy statistics are calculated. Of course the latter decision will be influenced by the incidence of notified disease in an area. If incidence drops dramatically below current levels, then routine monitoring may become impracticable for want of cases. In that respect, we believe that the increased vaccination consciousness associated with the routine monitoring would hasten that goal of vaccination programmes themselves, the elimination of target disease.

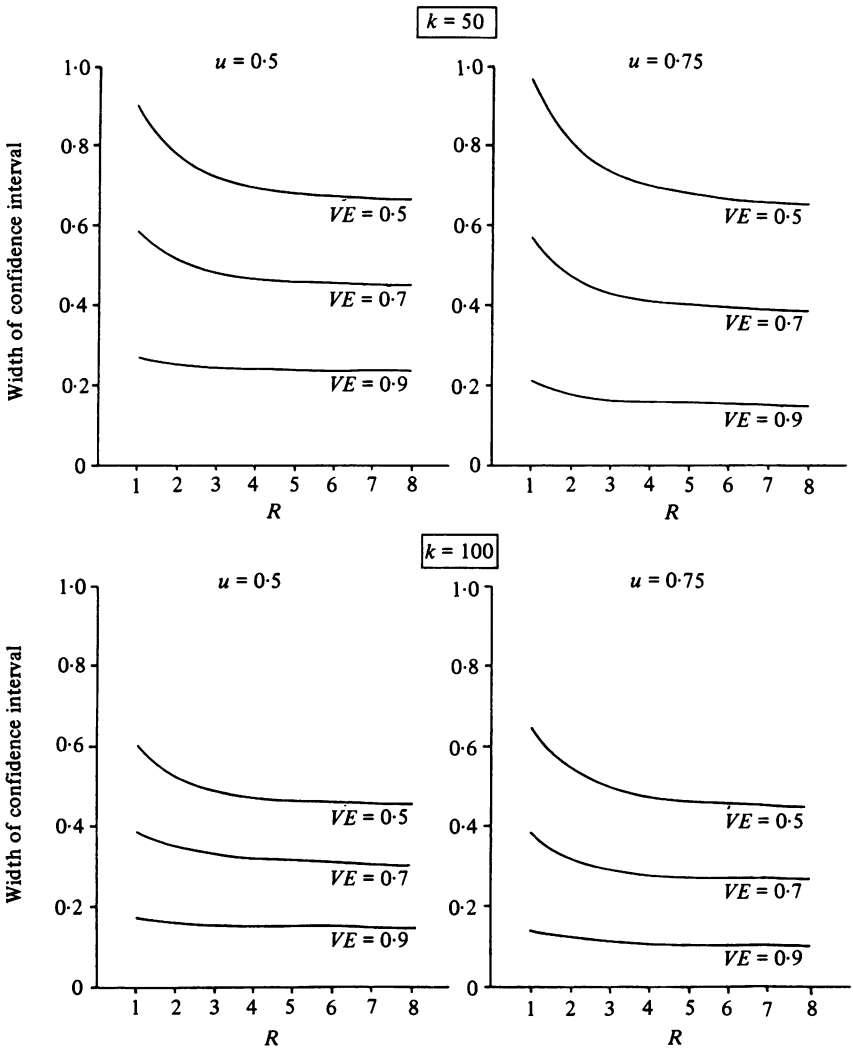

Fig. 1. Expected width of the confidence interval for estimating vaccine efficacy for different numbers of controls matched to each case ($R = 1$ to 8), two vaccine uptake rates ($u = 0{\cdot}5$ and $0{\cdot}75$), two numbers of cases ($k = 50$ and 100) and three levels of true vaccine efficacy ($VE = 0{\cdot}5$, $0{\cdot}7$ and $0{\cdot}9$).

The authors are grateful to the Department of Health and Social Security for its support of this work, to the MOEHs, DMOs, SCMs and the staff in Hampstead, Paddington/North Kensington, Tower Hamlets, Shropshire and Somerset for their hospitality and assistance in carrying out this study, and to Professor Eva Alberman and Dr Noel Gill for helpful comments on a draft of this paper.

REFERENCES

BAKER, M. R., BANDARANAYAKE, R. & SCHWEIGER, M. S. (1984). Differences in rate of uptake of immunisation among ethnic groups. *British Medical Journal* **288**, 1075–1078.

BRESLOW, N. E. & DAY, N. E. (1980). *Statistical Methods in Cancer Research*, vol. I. *The Analysis of Case-control Studies*. Lyon: International Agency for Research on Cancer.

CLARKSON, J. A. & FINE, P. E. M. (1985). The efficiency of measles and pertussis notification in England and Wales. *International Journal of Epidemiology* **14**, 153–168.

CLARKSON, J. A. & FINE, P. E. M. (1987). Delays in notification of infectious disease. *Health Trends* **19**, 9–11.

DEPARTMENT OF HEALTH AND SOCIAL SECURITY. Community Health Services Statistics – vaccination and immunisation acceptance rates. For birth cohorts 1968–1980 (excluding 1972–3). Unpublished documents.

DHSS/NHS Steering group on Health Services Information. Community Health Services Information: A report of working group D, January 1983.

FINE, P. E. M. & CLARKSON, J. A. Reflections on the efficacy of pertussis vaccines *Reviews of Infectious Diseases*. In press.

FLEISS, J. L. (1984). The Mantel–Haenszel estimator in case-control studies with varying numbers of controls matched to each case. *American Journal of Epidemiology* **120**, 1–3.

MACGREGOR, J. D., MACDONALD, J., INGRAM, E. A., MCDONNELL, M. & MARSHALL, B. (1981). Epidemic measles in Shetland during 1977 and 1978. *British Medical Journal* **282**, 434–436.

MANTEL, N. & HAENSZEL, W. (1959). Statistical aspects of the analysis of data from retrospective studies of disease. *Journal of the National Cancer Institute* **22**, 719–748.

MARKS, J. S., HALPIN, T. & ORENSTEIN, W. A. (1978). Measles vaccine efficacy in children previously vaccinated at 12 months of age. *Pediatrics* **62**, 955–960.

MEDICAL RESEARCH COUNCIL MEASLES VACCINES COMMITTEE (1968). Vaccination against measles: clinical trial of live measles vaccine given alone and live vaccine preceded by killed vaccine. *British Medical Journal* **2**, 449–452.

ORENSTEIN, W. A., BERNIER, D. H., DONDERO, T. J., HINMAN, A. R., MARKS, J. S., BART, K. J. & SIROTKIN, B. (1985). Field evaluation of vaccine efficacy. *Bulletin of the World Health Organisation* **63**, 1055–1068.

SCHLESSELMAN, J. J. (1982). *Case-control Studies: Design, conduct, analysis*. Oxford: Oxford University Press.

SMITH, P. G., RODRIGUES, L. C. & FINE, P. E. M. (1984). Assessment of the protective efficacy of vaccines against the common diseases using case-control and cohort studies. *International Journal of Epidemiology* **13**, 87–93.

WILLIAMS, W. O. & DAJDA, R. (1980). Validation of sources of pertussis immunisation data. *Journal of Epidemiology and Community Health* **34**, 309–311.